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Pulmonary embolism - assessment of risk factors and emboli locations

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ABSTRACT:

INTRODUCTION: Pulmonary embolism (PE) is a widespread disorder, which appears as a result of closure or restriction of main pulmonary artery or its branches and is often associated with deep vein thrombosis (DVT). The severity and clinical picture is frequently erratic and what is worrying it is a major cause of hospitalization and mortality in Europe.

OBJECTIVE: The main purpose of our study was to demonstrate meaning of emboli location in prognosis, favour risk factors which could be overlooked by clinicians and help to avoid further misdiagnosis.

ABBREVIATED DESCRIPTION OF THE STATE OF KNOWLEDGE: We highlighted the importance of defining a genetic profile, personal and family history of VTE, especially in patients with atypical pulmonary symptoms. Moreover, the awareness of possible occurring PE among children, during serious infections or in patients with malignancy is still insufficient. Furthermore, according our analysis clinical symptoms in patients with pulmonary embolism are undoubtedly influenced by the location. The more massive the thrombus appears, the more serious consequences can be expected for the patient. Along with the size of the thrombus, the risk of its complications increases because of haemodynamic changes.

SUMMARY: Diagnosing of pulmonary embolism in hemodynamically stable patients is still challenging for clinicians. There were many attempts to find significant and unmistakable relationship between emboli location in pulmonary vasculature and prognosis. That knowledge could be helpful for clinicians in setting accurate diagnosis, implementing appropriate treatment and avoid possible life-threatening consequences. Risk stratification is crucial to the management and prognosis of patients with acute PE.

Key words: Risk factors, venous thromboembolism, acute pulmonary embolism, clot location

1. INTRODUCTION.

Pulmonary embolism.

Pulmonary embolism (PE) is a common disease, which appears as a result of restriction/closure of pulmonary artery or its branches by thrombus. PE is a often complication of deep vein thrombosis (DVT) and pulmonary emboli can be detected in up to 50% of adult patients with that disorder[1]. The severity and clinical picture is frequently floating, ranging from asymptomatic to even cardiopulmonary arrest[2]. This disease is difficult to diagnose, what makes the topic more interesting to observe.

Moreover, it is a major cause of hospitalization, morbidity and mortality in Europe. According epidemiological reports venous thromboembolism were associated with approximately 300 000 deaths in Europe[3].

Worthy to mention is fact that 59% of these cases were diagnosed post-mortem. Predisposing factors are for example immobilization, surgeries, medical history of venous thromboembolism (VTE), pregnancy or supplemental estrogen. In the elderly population, VTE occurs usually in the context of obesity, medical procedures and underlying malignancy.

On the other hand in children and teenagers is mainly associated with gene mutations in the presence of underlying conditions[4].

Implementing effective treatment in pulmonary embolism is often complicated. There is always a risk of major bleeding like intracranial haemorrhage, in patients who received thrombolytic therapy. Main techniques used to diagnose pulmonary embolism are pulmonary arteriography, scintigraphy of the lungs and CTA.

Anatomy of pulmonary arteries.

Pulmonary trunk is the structure that begins in the right ventricle, which is also the prolongation of the arterial cone and is covered with visceral layer on almost its entire length, which is about 50mm. Together with the aorta is covered by the common mucous sheath and it is the most superficially located vascular trunk. Pulmonary trunk splits into the two ending branches, i.e. right pulmonary artery and left pulmonary artery and its average diameter is about 28-32mm, however, the cross-sections range from 30mm to 60mm. The left surface of the pulmonary trunk borders on the left vestibule, the right one with the right auricle, the segment of the coronary artery and the ascending part of the aorta.

2. PURPOSE.

The analysis of available literature and presentation of various clinical trials associated with pulmonary embolism. The main purpose of our study was to favour some groups, factors which could be overlooked by clinicians and help to avoid misdiagnosis. We mainly focused on inherited thrombotic disorders, patients with malignancy ,paediatric patients and we tried to distinguish some infection which substantially increase risk of PE.

It is disorder, which is frequently complicated to diagnose and further clinical decisions depend on different variables, e.g. clot location. There were many attempts to find significant and unmistakable relationship between clot location in pulmonary vasculature and prognosis. There is no approved meaning of clot location in massive and submassive pulmonary embolism and it is still questionable.

Pulmonary embolism is life-threatening condition, which cannot be neglected by clinicians and hence we want to present organized, accessible and accurate source of knowledge for all medical practitioners.

3. DETAILED DESCRIPTION OF STATE OF KNOWLEDGE.

3.1 DIAGNOSIS

CLINICAL PICTURE.

When the clinical picture indicates the suspicion of pulmonary embolism, patient should be subjected to further testing. Patients with pulmonary embolism often present dyspnoea, chest pain, haemoptysis and/or syncope. Chest pain is a frequent symptom of pulmonary embolism and is normally caused by pleural irritation. The main reason of that pain is distally located emboli. Shock or arterial hypotension are not so common, although crucial in indicating central PE. On the other hand it is very important to be aware of fact that many patients have no specific symptoms and in that cases PE is discovering accidentally during diagnostic procedures for another disease entities.

In central PE, character of pain in chest is anginal and it demands differential diagnosis with acute coronary syndrome (ACS) or aortic dissection. Dyspnoea can be severe and acute in central or mild and transient in peripheral PE.

Knowledge about predisposing factors to venous thromboembolism is significant in assessing the probability of PE, which increases with number of present predisposing factors.

Hypoxemia is a frequent finding in blood gas analysis in cases of acute PE, although up to 40% of patients have normal oxygen saturation. Hypocapnia is also regularly present.

Results of chest x-ray imaging are usually abnormal, but non-specific for PE. However, it may be helpful in excluding other causes of dyspnoea and chest pain.

In electrocardiography are possible to see changes such as inversion of T waves in leads V1-V4, complete or incomplete block of right bundle-branch, which indicate right ventricular (RV) strain. These electrocardiographic variations are generally found in more severe cases of PE, in milder cases the only anomaly possible to observe may be sinus tachycardia (40% of patients). With acute PE one of the most frequent atrial arrhythmias is atrial fibrillation.

ASSESSMENT OF CLINICAL PROBABILITY.

Despite the limited sensitivity and specificity individual symptoms and studies, their combination submitted for clinical assessment or using prediction rules allows to classify patients with suspected PE. The most frequent using prediction rule is The *Wells'* Criteria, which is simple and based on information not difficult to obtain. The Revised Geneva Scoring System is also simple and standardized. Both rules are using three (low, moderate, high clinical probability) and two-category schemes (likely or unlikely).

According to both these scales, the percentage of patients in which confirmed PE can be expected about 10% in high risk of pulmonary embolism, 30% in moderate risk of pulmonary embolism and 65% in high risk of pulmonary embolism[3][5].

D-DIMER TESTING.

Plasma level of D-dimers is elevated in presence of acute thrombosis, because coagulation and fibrinolysis are activating equally. Unfortunately, positive predictive value of increased level of D-dimers is low and D-dimer testing is not helpful in confirmation of PE, because fibrin is also producing in many other cases such as cancer, inflammation, bleeding, trauma, surgeries and necrosis. On the other hand ELISA assays have a high diagnostic sensitivity (even >95%) and can be used to exclude PE with a low or a moderate pre-test probability.

MULTIDECTOR COMPUTED TOMOGRAPHY ANGIOGRAPHY.

MDCT-angiography has become the study of choice in diagnosing and imaging patients with suspicion of PE. It enable to visualize pulmonary vasculature, even to segmental level.

According Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED II) study a sensitivity of 83% and specificity of 96% for MDCT were observed. A negative CT angiography (CTA) has high negative predictive value for PE among patients with a low or intermediate probability (96% and 89%). In group of patients with high clinical likelihood of PE positive CTA has a high positive predictive value (96%).

Many provided studies has proved that only on the basis CTA results it is possible to exclude PE. As an example, it can be used a study involving 756 patients with clinical suspicion of PE, who underwent lower limb ultrasonography and CT. The percentage of patients in whom

proximal deep vein thrombosis (DVT) was detected, despite negative MDCT was low- 0,9% (95% CI 0.3-2.7).

In other study, all patients underwent chest MDCT. In patients left untreated, because of negative CT, three-month thromboembolic risk was very low (1,1%; 95% CI 0.6-1.9). Above mentioned results show primacy of CTA among other methods in diagnosing of PE.

In four-chamber projection in CTA there is possible to observe RV enlargement (comparison of end-diastolic diameter of both ventricles) that show dysfunction of right ventricle of the heart. Prognostic value of RV enlargement was confirmed in cohort study of 457 patients.

There was observed deterioration or death in hospital in 52 patients. (44 with RV dysfunction and 8 without RV dysfunction detected in CT- 14.5% vs. 5.2%; $p < 0.004$).

To sum up, available data indicate that negative MDCT is sufficient to exclude PE in patients with low clinical probability. The only aspect of CT diagnosing, which is still uncertain, are groups of patients with emboli located in distal parts of pulmonary vasculature (sub-segmental level). Positive predictive value is also low. In this situation there is a possibility to use compression ultrasonography (CUS), to ensure that the patient has no proximal DVT.

ECHOCARDIOGRAPHY.

Acute PE can lead to increased pressure in right ventricle and to progressive dysfunction, which can be observed in echocardiography. Echocardiographic findings include RV dilation, increased RV/LV diameter ratio, hypokinesia of free wall of the right ventricle or increased velocity of jet of tricuspid regurgitation. Negative result in echocardiography is associated with negative predictive value in 40-50% and for that reason it cannot exclude PE. The signs of RV dysfunction can also be found in other cardiac or respiratory diseases. Dilation of the right ventricle of the heart is observed in at least one-fourth of patients with PE and for that reason echocardiography is helpful in risk stratification of the PE.

According performed meta-analysis RV dysfunction is frequently associated with higher risk of short-term mortality in haemodynamically stable patients. Except for that echocardiography enable to identify right-left shunt through a patent foramen oval and presence of thrombus in the right heart, both clinical situations are associated with higher mortality in patients with acute PE.

MARKERS OF RV DYSFUNCTION.

Increased pressure in RV is associated with excessive stretching of myocardium, which leads to elevation of plasma levels of brain natriuretic peptide BNP or N-terminal (NT)- proBNP. According performed meta-analysis a large part of patients with acute PE had increased level of natriuretic hormones on admission (577 out of 1132, 51%).

MARKERS OF MYOCARDIAL INJURY.

Transmural RV infarction was observed in patients, who died with massive PE. Elevated concentration of troponins on admission in connection with PE was associated with worse prognosis. Meta-analysis covering in total 1985 patients demonstrated increased level of cardiac troponins (I and T) in 50% of patients with acute PE. Increased levels of these markers were associated with high mortality in both haemodynamically stable patients OR 5.90; 95% CI 2.68-12.95] and unselected patients [OR 9.44; 95% CI 4.14-21.49].

3.2 RISK FACTORS

PAEDIATRIC PATIENTS

According many previous clinical studies, pulmonary embolism in children and adolescents is not common disorder (0.07-0.14 per 10,000 according The Canadian and Dutch registries). Nevertheless, cases of VTE in group of younger patients are also present. For this reason, clinicians need to be aware of that possibility in paediatric patients with nonspecific symptoms. As distinct from adults we can also observe different mechanism of developing PE such as anomalies of the pulmonary artery and congenital heart disease[6][7].

Rajpurkar et al conducted systematic review of prevalence of PE in younger patients.

Authors identified many risk factors such as presence of central venous catheters (23%), obesity (13%), immobilisation (38%). They also emphasized importance and the prevalence of the hypercoagulable state (protein C deficiency 17%, factor V Leiden 14%). Mean age of thromboembolic pulmonary embolism (TE-PE) was 14,86 years, 51% of cases were males[7]. In comparison to TE-PE in situ pulmonary artery thrombosis were not associated regularly with present thrombophilia.

According to recent review study performed by Rajpurkar et al in 2018, the most significant risk factor of pulmonary embolism among children who were hospitalized were central venous catheters (CVCs). Authors also mentioned about other significant risk factors such as hormonal supplementation, cancer, immobility or infection. Neshat-Vahid et al demonstrated a relation between V Leiden factor and CVC-related VTE[6][8][9].

It has been proved that abnormalities of the anticoagulants such as presence of active protein C resistance (factor V Leiden), prothrombin gene mutation G20210A or proteins C,S and antithrombin deficiency are associated with VTE. Moreover, there is a disorder called antiphospholipid antibody syndrome characterizing presence of lupus anticoagulant (LA) and anticardiolipin antibodies (ACA), which is also associated with venous thromboembolism[4]. There are multiple genetic factors that may increase venous thromboembolism risk. Factor V Leiden (FVL) is known as most common prothrombotic polymorphism and may have developed through genetic drift or natural selection in Caucasians (high prevalence in this population ranging from 4 to 10%) [10][11]. There are two possible variants of FVL and what is worth to remember homozygotes characterize higher risk of thrombotic events. Martinelli et al found higher risk for thrombosis among patients with different thrombophilic defects in comparison to people with normal coagulation and according results they obtained factor V Leiden carriers developed less serious clinical manifestations of thrombosis [11]. **(Table 1.)** Occurrence of inherited thrombophilia depends on various circumstances, such as malignancy, central venous catheters, combined oral contraceptives or hormone replacement therapy [8].

A. Kosch and co-workers reported the case of 13 year old boy with the homozygous A20210A PT mutation, who was misdiagnosed and started therapy of pneumonia after onset of clinical symptoms of respiratory disease [1]. Except for earlier mentioned mutation of prothrombin, laboratory screening revealed protein S deficiency and elevation of level of

lipoprotein (a). That is another case, which illustrates that the rare event of PE can be overlooked in paediatric patients and known genetic profile of patients could be helpful in setting a diagnosis. Congenital thrombophilia is one of the most common reason among teenagers presenting with pulmonary embolism, what was also presented in the study performed by Biss and al. In that study they also demonstrated a low diagnostic value of D-dimer level in diagnosing pulmonary embolism in children.[6][12][13].

There was described clinical course and laboratory findings of a 17-year girl suspected of deep vein thrombosis six months after she had started taking oral contraceptives (OC). Laboratory findings: decreased level of free PS antigen, increased level of PAI-1, APC ratio <2 and D-dimers persistently high. DVT was approved by phleboscintigraphy of the left leg. The diagnosis of pulmonary embolism was likely delayed, because the only symptom was persisting tachycardia.

Genetic study revealed that patient was a heterozygous carrier of factor V Leiden, prothrombin 20210A and MTHFR C677T (hyperhomocysteinemia).The received data highlight the importance of taking a thorough personal and family history prior to the onset of taking OC. Advanced thrombophilia testing could be beneficial for teenage females who are making decisions about contraception and help to avoid possible consequences [4].

In 2015, Gruettner and co-workers re-evaluated the risk factors of PE in their entirety. In their study they examined 492 patients with suspicion of PE and included all possible risk factors such as obesity, OC, immobilization, malignant disease, thrombophilia and inherited predispositions.

Accordingly, their results presented significant risk of pulmonary embolism for parameters of a history of DVT, thrombophilia and contraceptive use. For comparison these factors are not included in the Wells or Geneva scores. Only thrombophilia, history of DVT or PE and OC achieved statistically significant results [13].

Table 1.

Different risks of thrombosis in four coagulation defects associated with inherited thrombophilia.

THROMBOPHILIA	RISK RATIO	95% CONFIDENCE INTERVAL(CI)
Antithrombin deficiency	8.1	3.4 to 19.6
Protein C deficiency	7,3	2.9 to 18.4
Protein S deficiency	8.5	3.5 to 20.8
Factor V Leiden deficiency	2.2	1.1 to 4.7

PATIENTS WITH MALIGNANCY

Cancer is one of the most relevant risk factors for VTE, which occurs two to four times more often in patients with diagnosed malignancy. The highest prevalence of venous thromboembolism include lung, colon, and prostate cancer, whereas lung cancer is the most commonly related malignancy in patients with VTE [11][14]. According to data delivered by European Heart Journal Guidelines published in 2014, risk of venous thromboembolism episodes in patients with cancer is relevantly higher (even 46-fold comparing to healthy controls). The biggest amount of VTE events were among patients with lung, colon, prostate cancer. On the other hand the highest relative risk for venous thromboembolism is in multiple myeloma (MM), brain and pancreatic cancer [1]. The incidence of VTE events among patients with diagnosed malignancy is significant, especially in patients with metastatic-stage disease [15][16][17][18][19]. **(Table 2.)**

In 2017, Giordano et al emphasized significance of active cancer as a major risk factor for VTE and demonstrated that occurring of PE in patients with malignancy is more often in comparison to patients without cancer. The highest frequency of venous thromboembolism patients usually present during the first year after diagnosis and soon after implementing of anticoagulation treatment. Accordingly, the highest ratio of VTE episodes (4,1%) occurs in adenocarcinomas [2]. In the study conducted by Weeda et al were involved 603 patients with diagnosed acute PE and 124 of them had active cancer. 36 patients (29%) had lung, 19 (15,3%) genitourinary and 16 (12,9%) breast cancer. **(Table 3.)** Almost half of all patients presented metastatic disease (49,2%). After 30 days all-cause mortality reached 20,2% (25 out of 124). Existence of cancer-specific risk stratification tools such as POMPE-C, RIETE and Font criteria which can be useful for medical practitioners in management of patients with PE. These tools characterize high percentage of sensitivity [20].

In 2017, Seung-Ick Cha et al published results of their study, wherein they included 5005 patients with lung cancer and 267 (5,3%) was diagnosed with lung cancer and PE. Median age of patients at the diagnosis was 69 years (65,2% males). What is worthy to mention pulmonary embolism was identified before lung cancer diagnosis in 27 patients (10,1%) and in the remaining group PE occurred after the diagnosis (89,9%). Median period of time from diagnosis of lung cancer to PE was 4,5 months. The most common risk factor for pulmonary embolism in patients with lung cancer was chemotherapy with even a 3-fold increased risk [14].

Table 2.

In the table below are presented results of incidence of VTE among patients with diagnosed cancer.

Authors of the study	Results	Period of time
Chew HK, Wun T, Harvey D, Zhou H, White RH. Arch Intern Med. 2006;166(4):458.	235,149 cancer cases from a United States. Reported a diagnosis of VTE in 3775 (1.6 percent)	2 years
Yu YB Gau JP, Liu CY, Yang MH, Chiang SC, Hsu, HC et al. ThrombHaemost. 2012;108(2):225	Among 497,180 Taiwanese cancer patients 5,296 developed VTE (10-fold higher risk in comparison to the general Taiwanese population, 185 versus 15.9 cases per 100,000 person-years, respectively)	8 years
Alcalay A, Wun T, Khatri V, Chew HK, Harvey D, Zhou et al. J Clin Oncol. 2006; 24(7):1112	68,142 with colorectal cancer, the two year incidence of VTE was 2100 (3.1%)	2 years

Table 3.

The most common types of cancer among patients with confirmed active pulmonary embolism.

Type of cancer	Total (n=124)	% of patients
Lung	36	29%
Genitourinary	19	15,3%
Breast	16	12,9%
Prostate	12	9,7%
Colorectal	9	7,3%
Brain	9	7,3%
Hematologic	6	4,8%
Pancreas	4	3,2%
Other	13	10,5%

INFECTIONS

In 2018, Cohoon et al published case-control study which took place in Olmsted County in the period from 1988 to 2000. Over the 13-year period, 1308 (55,6% were women) residents of Olmsted County were identified with a first lifetime DVT (56%) or PE (44%). Infection was defined when was diagnosed and confirmed by a physician in the period of 92 days

before VTE events. Among the 1303 patients with venous thromboembolism 513 (39,4%) and 189 out of 1494 in control group had an infection in the previous 92 days.

Obviously, infections are related to thrombosis, because of damage of endothelium and initiation of the coagulation pathway. According the analysis, the highest importance of risk was added by intra-abdominal infection, then by oral infection, systemic bloodstream infection and lower respiratory infection (**Table 4.**). What is worthy to mention studies presented surprising fact of independence of oral infection as high risk factor of venous thromboembolism. To sum up analysis confirmed significant correlation between infection and VTE risk[21].

Table 4.

The most common infections associated with significantly increased odds of VTE.

Type of infection	P value	Odds ratio	95% Confidence interval
Intra-abdominal	0.0381	17.77	1.17-269.69
Oral	0.0037	11.61	2.22-60.82
Systemic bloodstream	0.0035	10.69	2.18-52.35
Lower respiratory (pneumonia)	<0.0001	3,64	2.00-6.63

3.3 EMBOLI LOCATION

Pulmonary embolism (PE) is caused by masses of emboli that obstruct the pulmonary arteries. The more massive the thrombus appears, the more serious consequences can be expected for the patient. The prognosis of patients with current pulmonary embolism depends on many factors, including its location. Thrombosis location is usually determined by computed tomography of pulmonary angiography. A thrombus located in the pulmonary trunk and right or left pulmonary artery is defined as central pulmonary embolism (CPE), and when the thrombus is located in the lobar arteries, segmental or sub-segmental arteries, it is defined as peripheral pulmonary embolism (PPE). A blood clot may settle, depending on its size, in an artery with a larger or smaller diameter. Many attempts have been made to find a significant and unambiguous relationship between the location of the thrombus in the pulmonary vessels and the prognosis. Unfortunately, many researchers have obtained dissonant results and, for this reason, have drawn completely different conclusions from their work. On the basis of current information collected, it appears that the location of the clot in massive and sub-mass pulmonary embolism is not of approved significance and is still doubtful and subject to many clinical trials.

However, the clinical studies carried out make it possible to broaden the range of factors taken into account when assessing the effects of pulmonary embolism.

Location dependence was demonstrated in a study of 350 patients hospitalized in the Department of Internal Medicine from 2004 to 2013. 255 of these patients had central pulmonary embolism (PE) and 275 had segmental or sub-segmental PE. 23% of patients with central pulmonary embolism (CPE) and 20% of patients with peripheral pulmonary embolism (EPP) had an earlier heart disease. 10% of CPE and 14% of PPE had chronic respiratory disease. Studies indicate that central pulmonary embolism is associated with higher mortality.

Patients with segmental or sub-segmental thrombosis had a longer survival at the age of 10, 26 and 96 months [22]. According to the authors' conclusions, a centrally located thrombus is associated with greater right ventricular stress, which leads to disturbances in gas exchange and haemodynamic state. Plasma levels of NT-ProBNP and troponin I are also higher. CPE is characterized by elevated levels of D-dimer in blood, which goes hand in hand with quantitative defects in fibrinolysis [23].

Another study shows that D-dimer measurement could be prognostic but only in patients under 50. In older patients the test is not so sensitive [24]. Next study proves that D-dimer level has no predictive value in spontaneous PE [25].

A higher D-dimer value may be related to another fact that, thanks to studies at the Pontevedra Hospital in Spain, central pulmonary embolism occurs in the elderly, while peripheral pulmonary embolism occurs in slightly younger patients. The average age of patients with sub-segmental pulmonary embolism is about 55 years, while the average age of patients with central pulmonary embolism is about 71 years. It is worth mentioning that patients with central pulmonary embolism are more likely to develop cancer, which is the most important coexisting disease. In terms of symptoms, dyspnoea is the most common symptom in patients with central peripheral embolism, while in peripheral pulmonary embolism the most common symptom is pain. This study also indicates a higher D-dimer value in patients with central pulmonary embolism. In addition, they usually perform worse results in blood gas analysis. In addition, patients with central and segmented lower limb oedema with embolism pulmonary embolism are more likely to experience lower limb oedema (25% of patients) compared to sub-segmental cases (9%)[23].

In 2016, a group of physicians decided to conduct a study on the influence of pulmonary thrombosis site on the treatment and results of pulmonary embolism treatment.

The study involved 269 patients (63.9% with central pulmonary embolism and 36.1% with peripheral pulmonary embolism). Data from the 90-day observation were available for 240 patients. Pulmonary embolism hypotension was more likely to be observed in patients with peripheral PMS and therefore more likely to be classified as massive compared to patients with central obstruction.

In both types of patients (central and peripheral) mortality was similar after 1, 3 and 7 days. With central pulmonary embolism there is a better chance of right ventricular failure. Thrombolysis directed to the catheter is more likely (18.3% vs. 3.3%, $p < 0.001$). In the case of peripheral pulmonary embolism, anticoagulation is more likely to be received only in therapy (69.1% vs. 55.8%, $P=0.03$). Higher mortality from all causes within 30 days (18.5% vs. 13.5%, $p=0.02$). Higher total mortality within 90 days [23].

In studies conducted by this group of doctors, no differences in the presence of symptoms such as hypoxaemia or tachycardia were found. Clot localization was not associated with the result and mortality associated with pulmonary embolism at the 90th day of life. On the other hand, only advanced age had an influence on the complex result.

Summarizing the results of this study show that the location of the clot is associated with different therapeutic solutions, but is not associated with PE-related results within 90 days. There is higher mortality in patients with pulmonary embolism, but many of them have low value and limited usefulness since there has been no detailed information on treatment.

Recent literature suggests that the main predictor of poor outcomes of pulmonary embolism treatment is hypotension and right ventricular stress.

Patients with central pulmonary embolism are considered to have more severe clinical signs of embolism than those diagnosed Segmental or sub-segmental embolism (PPE). The authors of the clinical studies examined whether there is a correlation between severity of pulmonary embolism and location of embolism In pulmonary vessels. The authors analyzed the results of lung computed tomography among 269 patients in the orthopaedic department, who have undergone endoplasty of the hip or knee joint. The analyzed cases of pulmonary embolism have been ranked based on pulmonary embolism severity index (PESI), which is divided into five parts classes (the fifth is the heaviest). All pulmonary CT scans are classified by heading Embolism (central, segmental, sub-segmental, unilateral, bilateral) [26].

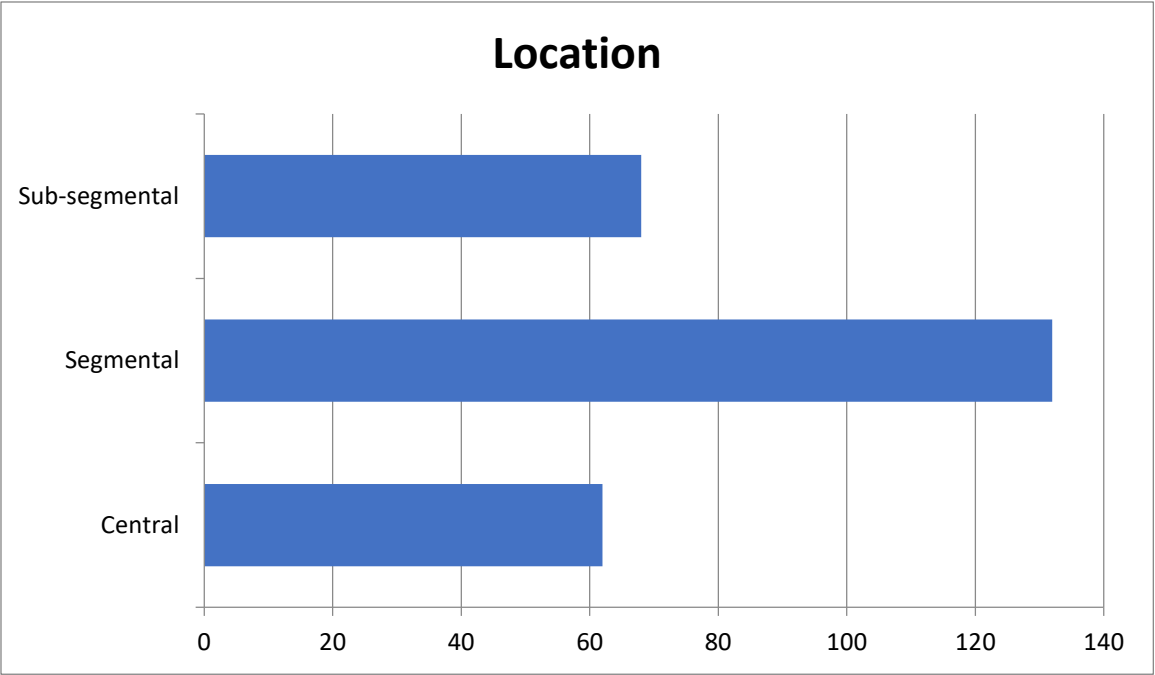


Table 5. Table shows the results in patients with pulmonary embolism. The most common localization is subsegmental. Emboli are usually located unilaterally.

Location	Number of patients
Centrally located pulmonary embolism	62 patients
Segmental pulmonary embolism	132 patients
Sub-segmental pulmonary embolism	68 patients
Unilateral pulmonary embolism	180 patients
Bilateral pulmonary embolism	89 patients

Patients with unilateral and bilateral lung localization embolism had a similar pulmonary embolism severity index (PESI). The severity and mortality rates of patients with pulmonary embolism are as follows similar in all cases analysed. Patients with a central location pulmonary embolism is considered to have more severe clinical signs embolisms other than those diagnosed as segmental or sub-segmental embolism [26].

Surely, the subject of pulmonary embolism is extremely extensive and it is hard to draw conclusions from the countless amount of work. Each work we studied brought something new to our conclusions, which we can then draw. Clinical symptoms in patients with pulmonary embolism are, of course, influenced by the location. Depending on the location, we can see different morphological results, however, among the studied factors that may affect clinical symptoms are multifaceted.

Considering the severity of clinical signs among patients with pulmonary embolism, it is important to consider both the patient's age and gender, circulatory capacity, but above all the location of the embolism as well as the general health condition. It seemed that the PESI test would be the ideal solution to determine the severity of clinical symptoms of pulmonary embolism, but mortality after PE was similar in patients with central, segmental, or subsegmental PE [26].

However, on the other hand, the authors of the text Central Versus Peripheral Pulmonary Embolism: Analysis of the Impact on the Physiological Parameters and Long-term Survival claim that apart from a greater impact on hemodynamics, gas exchange, and right ventricular dysfunction, central pulmonary embolism associates a shorter survival and an increased long-term mortality.

Additionally, the authors believe that patients with segmental or sub-segmental thrombosis had a longer survival at the age of 10, 26 and 96 months, which means that the conclusions we draw cannot be unambiguous, given that the authors of Impact of Pulmonary Arterial Clot Location on Pulmonary Embolism Treatment and Outcomes (90 Days) believe that In both types of patients (central and peripheral) mortality was similar after 1, 3 and 7 days [18][22].

SUMMARY AND CONCLUSIONS.

Diagnosing of pulmonary embolism in hemodynamically stable patients is still a challenge for clinicians and many previous studies have shown that PE has been often overlooked what caused higher mortality rate in patients with atypical symptoms [13]. For this reason, in our study we want to emphasize the significance of above mentioned risk factors. First of all, we highlighted the importance of defining a genetic profile, personal and family history of VTE, especially in patients with atypical pulmonary symptoms. Moreover, the awareness of possible occurring PE among children or during serious infections or in patients with malignancy is still insufficient [2]. That knowledge could be helpful for clinicians in setting accurate diagnosis, implementing appropriate treatment and avoid possible life-threatening consequences.

Pulmonary embolism location depends on the size of the blood clot. Along with the size of the thrombus, the risk of its complications increases because of haemodynamic changes. Nowadays, computed tomography pulmonary angiography enables to detect peripheral pulmonary embolism. However, the mortality due to PE has not changed significantly. Risk stratification is therefore crucial to the management and prognosis of acute PE [2][19].

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