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Features of in-hospital clinical course of pulmonary embolism in patients of different age groups

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Aim. To study the clinical course and management of patients with pulmonary embolism (PE) of various age groups hospitalized in a cardiology hospital.

Material and methods. This prospective single-center study in the period from 2016 to 2018 included 154 patients with PE verified by computed tomography. Statistical processing was conducted using the MedCalcVersion 16.2.1 software package (Softwa, Belgium).

Results. In all groups, female patients dominated, but the highest number of women (70,7%) belonged to the group of senile patients, while in the group <60 years, only half of patients with PE were women. Comorbid cardiovascular disease and deep vein thrombosis was diagnosed in eldest patients significantly more often than in those <60 years of age. The highest prevalence of cancer and recurrent PE were identified in the group of elderly patients. Thrombolytic therapy was performed most often in patients 60-75 years old, since these patients had a high risk of 30-day mortality according to Pulmonary Embolism Severity Index, but did not have severe comorbidities, as patients older than 75 years. An increase of right atrium size was found in the group of elderly and senile patients in comparison with patients <60 years. The highest pulmonary artery systolic and diastolic pressure was observed in the patients older than 75 years.

Conclusion. In the Kemerovo Oblast, PE most often develops in patients aged 60-75 years and is characterized by a more severe clinical course compared with patients younger than 60 years. Patients over the 60 years of age have severe cardiovascular comorbidity status, atrial fibrillation/flutter and recurrent PE. Surgical treatment for senile patients is limited due to the high risk of postoperative complications, which specifies high mortality. Patients <60 years of age are a third of all patients hospitalized with PE. They have a low risk of mortality, but have an unfavorable course of the hospital period.

Key words: pulmonary embolism, age, deep vein thrombosis, risk factors, cardiovascular comorbidity.

Relationships and Activities: none.

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Introduction

Modern medicine has achieved success in the diagnosis and treatment of pulmonary embolism (PE), despite this, hospital mortality remains high both in Russia and abroad [1]. It is the study of risk factors and management strategy during in-hospital period that the overwhelming majority of modern studies on PE are devoted to [2]. A number of modern papers focuses on young patients, as the most common group of patients with venous thromboembolism [3]. However, most studies show the highest hospitalization rates for PE among elderly patients >60 years of age. Thus, in a general hospital in Astrakhan, PE was diagnosed at the age of <30 years in 8%, 30-40 years — in 11%, 40-50 years — in 21%, 50-60 years — 23%, >60 years — 38% of patients [4]. The results of the prospective Framingham study also revealed a relationship of PE with old age, obesity, and cancer [5]. In the RIETE (Registro Informatizado Enfermedad TromboEmbolica) registry, the risk of unfavorable outcome was also associated with elderly and senile age [6]. The unfavorable course of PE in elderly patients with severe comorbidities has been confirmed in other works [7-9]. Recently, however, cases of hospitalization among young people diagnosed with PE are increasingly common. It is of interest to study the age characteristics of patients with PE and risk factors associated with a certain age group.

Thus, the aim was to determine the risk factors for development and unfavorable course of PE in different age categories of patients hospitalized in a cardiology hospital.

Material and methods

This prospective, single-center registry conducted from 2016 to 2018 included 154 patients who were hospitalized in Kuzbass Cardiology Center due to PE established by multislice computed tomography pulmonary angiography.

We collected medical history and complaints, assessed the objective status, and determined the 30-day mortality by calculating Pulmonary Embolism Severity Index (PESI). Subsequently, 16-lead electrocardiography was conducted. Laboratory parameters (complete blood count, biochemical blood test, D-dimer level, coagulation test) were determined. Echocardiography was performed to determine the right ventricular (RV) size and pulmonary artery pressure (PAP). Duplex ultrasound of lower limb veins was performed. This study was performed in accordance with the Helsinki declaration and Good Clinical Practice standards. The medical ethics committee approved this study. All patients signed informed consent. The baseline clinical characteristics of patients are presented in Table 1.

Of the 154 patients with established PE, 61,6% were women (men age, 66 years). More than half of the patients had hypertension (HTN), heart failure (HF), deep vein thrombosis (DVT). Such comorbidities as coronary artery disease (CAD) were observed in 22,1% of cases, type 2 diabetes (T2D) — in 13,6%, cancer — in 10,3%. A prior PE was observed in 18,2% of patients, while only 4% of patients previously took regular anticoagulant therapy. In 7,1% of patients, the use of hormonal therapy was a risk factor for PE, in 5,8% — trauma and immobilization; in the overwhelming number of cases PE was idiopathic.

The most common symptom of PE was shortness of breath (75,9%) and chest pain (31,2%), while loss of consciousness and hemoptysis was observed in 16,8% and 9,1%, respectively. Examination of patients revealed an increase in D-dimer level to an average of 3230 ng/ml. It is noteworthy that echocardiography revealed a pulmonary hypertension and increase in RV size. The mean PESI score was 89 (intermediate risk). The management tactics for patients with PE was different. The vast majority of patients (80,5%) received conventional anticoagulant therapy, while 16,8% of patients underwent thrombolytic therapy (TLT). Pulmonary thrombectomy was performed in 4 (2,5%) patients. Among all patients with an established PE, hospital mortality was 4,6% (n=7).

Statistical processing was carried out using the MedCalcVersion 16.2.1 software package (Softwa, Belgium). Qualitative traits are presented as frequencies and percentages. Quantitative indicators are presented as median with a quartile range (25^{th} and 75^{th} percentiles). Comparison in three groups was performed using the Kruskal-Wallis test with Bonferroni correction; in two groups — using the Mann-Whitney test for quantitative data. Qualitative data were compared using 3x2 and 2x2 contingency tables with Pearson's test and Fisher's exact test when the number of observations in the group was <5. The differences were considered significant at $p<0,05$.

Table 1

Clinical characteristics of patients with PE

Parameter	Patients with PE, n=154
Age, years	66 (56; 77)
HTN, n (%)	88 (57,1)
Female sex, n (%)	95 (61,6)
T2D, n (%)	21 (13,6)
CAD, n (%)	34 (22,1)
HF	81 (52,6)
DVT, n (%)	80 (51,9)
Cancer, n (%)	16 (10,3)
Prior pulmonary embolism, n (%)	28 (18,2)
Post-traumatic pulmonary embolism, n (%)	9 (5,8)
Prior anticoagulation therapy, n (%)	6 (3,9)
Prior hormonal therapy, n (%)	11 (7,1)
PESI score	89,0 (72,5; 112,5)
Chest pain, n (%)	48 (31,2)
Loss of consciousness, n (%)	26 (16,8)
Shortness of breath, n (%)	117 (75,9)
Hemoptysis, n (%)	14 (9,1)
SpO_2 (%)	93 (89; 96)
D-dimer, ng/ml	3230,0 (3230,0; 4946,2)
RV size, cm	2,6 (2,0; 2,8)
Pulmonary arterial pressure, mm Hg	49,0 (38,0; 59,7)

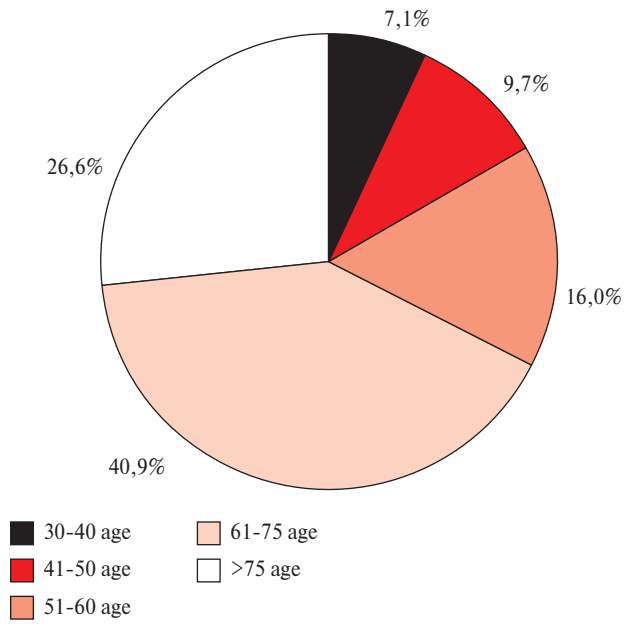

Figure 1. Age categories of patients with PE.

Results

Among the studied patients with PE, persons of elderly age groups prevailed (40,9%). Senile patients were hospitalized in 26,6%, while about a third of all patients were young and middle-aged (Figure 1).

All 154 patients were divided into 3 groups depending on age: 1 — patients <60 years old (n=50; 32,2%), 2 — elderly patients 60-75 years old (n=63; 40,9%) and 3 — senile patients >75 years old (n=41; 26,6%). Subsequently, these groups were compared with each other (Table 2).

In all groups, female patients predominated, however, the largest number of women (70,7%) belonged to the senile age group, while in the group <60 years old, only half of the PE patients were women (p=0,04). At the same time, in the group of senile patients, a significant prevalence of comorbid cardiovascular pathology (HTN, T2D, CAD, HF, non-

Table 2

Clinical factors in groups of PE patients of different ages

Parameter	<60 years of age, n=50	60-75 years of age, n=63	>75 years of age, n=41	p
	1	2	3	
Female sex, n (%)	25 (50,0)	40 (63,5)	29 (70,7)	0,040 1-2=0,211 1-3=0,043 2-3=0,581
HTN, n (%)	22 (44,0)	32 (50,7)	24 (58,5)	0,01 1-2=0,091 1-3=0,041 2-3=0,751
T2D, n (%)	3 (6,0)	10 (15,8)	8 (19,5)	0,038 1-2=0,105 1-3=0,074 2-3=0,967
CAD, n (%)	4 (8,0)	13 (20,6)	17 (41,5)	<0,0001 1-2=0,049 1-3=0,0001 2-3=0,034
HF, n (%)	14 (28,0)	22 (34,9)	19 (46,3)	0,017 1-2=0,236 1-3=0,036 2-3=0,396
AF/AFL, n (%)	4 (8,0)	12 (19,0)	12 (29,3)	0,004 1-2=0,110 1-3=0,012 2-3=0,484
Cancer, n (%)	2 (4,0)	10 (15,8)	4 (9,8)	0,119
DVT, n (%)	3 (6,0)	7 (11,2)	10 (24,9)	0,0007 1-2=0,508 1-3=0,016 2-3=0,128
Prior pulmonary embolism, n (%)	10 (20,0)	17 (26,9)	3 (7,3)	0,001 1-2=0,520 1-3=0,131 2-3=0,021
Post-traumatic pulmonary embolism, n (%)	2 (4,0)	7 (11,2)	5 (12,2)	0,207
Symptoms and clinical course				
PESI score	72,5 (65,0; 90,0)	105 (95,0; 127,0)	118 (99,5; 140,0)	<0,0001 1-2<0,0001 1-3<0,0001 2-3=0,073
SpO_2 (%)	99 (93,4; 100)	93 (89,5; 96,5)	90 (87,2; 93,7)	0,134
Shortness of breath, n (%)	33 (66,0)	37 (58,7)	25 (48,7)	0,359
Chest pain, n (%)	14 (28,0)	14 (22,2)	6 (14,6)	0,157
Heart rate, bpm	90 (81; 98)	96 (83; 110)	99 (80; 118)	0,748
RR, bpm	18 (16; 20)	18 (17; 22)	20 (16; 23)	0,491
D-dimer, ng/ml	2800 (1792; 4791)	3250 (2144; 5000)	4584 (3000; 5000)	0,184
Positive troponin test, n (%)	12 (24,0)	11 (17,5)	7 (17,0)	0,616
Treatment strategy				
In-hospital TLT, n (%)	13 (26,0)	27 (42,8)	14 (34,1)	0,542
Surgery, n (%)	5 (10,0)	1 (1,6)	0	-

Notes: AFL — atrial flutter, AF — atrial fibrillation, RR — respiratory rate.

sinus rhythm) was revealed, compared with the group of patients <60 years old. At the same time, the highest incidence of cancer and a recurrent PE were found in the group of elderly patients (60-75 years old). The PESI score increased significantly from the first to the third group, and was the highest in the group of senile patients.

It should be noted that the patients did not differ in symptoms and clinical manifestations. Most often TLT was performed in the age group 60-75 years old,

Table 3

Echocardiographic parameters in groups of PE patients of different ages

Parameter	<60 years of age, n=50	60-75 years of age, n=63	>75 years of age, n=41	p
	1	2	3	
RV size, cm	2,5 (2,0; 2,8)	2,65 (2,2; 3,0)	2,65 (2,1; 2,9)	0,318
RVEF, %	48,5 (40,0; 51,5)	54,0 (35,0; 55,0)	49,0 (43,0; 50,0)	0,607
TAPSE	1,9 (1,7; 1,9)	1,8 (1,6; 1,9)	1,7 (1,3; 2,3)	0,709
LA diameter, cm	2,9 (2,6; 3,0)	2,5 (2,3; 3,2)	2,7 (2,5; 2,9)	0,936
RA Vmax, ml	56,0 (44,0; 66,0)	63,5 (38,0; 97,0)	65,0 (48,0; 103,0)	0,697
RA length, cm	4,9 (4,5; 5,1)	5,4 (5,1; 5,8)	5,6 (5,3; 6,1)	0,030 p_{1-2}=0,061 p_{1-3}=0,024 p_{2-3}=0,393
RA width, cm	4,4 (4,0; 4,6)	4,6 (3,9; 5,5)	4,2 (3,9; 5,0)	0,838
Pulmonary artery diastolic pressure, mm Hg	15 (9; 18,5)	19 (15; 23)	23 (18,7; 25)	0,048 p_{1-2}=0,063 p_{1-3}=0,04 p_{2-3}=0,343
Pulmonary artery diastolic pressure, mm Hg	41 (30; 44)	44 (40; 58)	57 (52; 62)	0,014 p_{1-2}=0,105 p_{1-3}=0,004 p_{2-3}=0,219

Notes: RVEF — right ventricular ejection fraction, RA Vmax — maximum RA volume, TAPSE — Tricuspid annular plane systolic excursion.

since these patients were characterized by a high PESI risk of 30-day mortality, but at the same time did not have severe comorbidities, as patients >75 years old. Pulmonary embolectomy underwent 10% of patients <60 years and one elderly patient; in all cases there was a favorable outcome. Figure 2 shows an in-hospital mortality. Noteworthy is the same mortality rate in the group of patients <60 years and >75 years old (~7%), while the lowest death rate was noted in elderly patients. Lethal outcome was associated with positive markers for myocardial damage (p=0,02), the embolism of pulmonary trunk (p=0,02), HTN (p=0,01), and respiratory failure (p=0,01) in the general sample of patients.

Table 3 shows echocardiographic data of patients with PE.

There was an increase in the right atrial (RA) size in the group of elderly and senile patients in comparison with patients <60 years old, while the maximum RA volume in the groups did not differ. The most unfavorable values of systolic and diastolic pulmonary pressure were observed in senile patients.

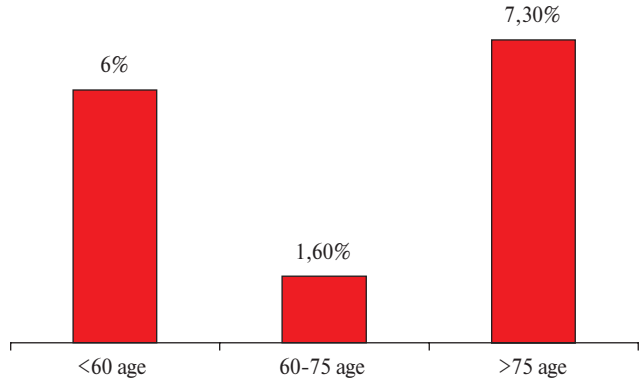

Figure 2. In-hospital mortality rate in PE patients of different ages.

Discussion

The distribution of PE by age groups in this study is comparable to the study carried out in a general hospital in Astrakhan, where PE was diagnosed at the age of <30 years in 8%, 30-40 years — in 11%, 40-50 years — in 21%, 50-60 years — in 23%, >60 years — in 38% of patients [4]. According to the study performed in B.A. Korolev clinical hospital, 138 elderly and senile patients with PE underwent surgical treatment [10]. A 2017 study found that 65% of patients with PE are ⩾60 years old with a mean age of 62 years, while the number of patients >80 years old is eight times more than patients <50 years old. In addition, this study showed that women predominate in the group of young patients, and after 50 years, the prevalence of PE in both sexes is the same [11], while in the present study, it was found that the older the patients, the more women were observed in the group.

The Korean study showed a predominance of women with an average age of 64,8 years [12]. Another study found that patients aged >76 years had a higher percentage of submassive PE (91,1%; p=0,0006), RV dysfunction (91,1%; p=0,0001), increased systolic pulmonary pressure (42,64±16,70 mm Hg, p=0,00004) and an increased level of cardiac troponin I (0,22±0,40 ng/ml, p=0,004) compared with patients <76 years

old. Similar data were obtained in the present study: patients >75 years old have signs of an unfavorable disease course, as well as a high prevalence of comorbid cardiovascular disease, which worsens the prognosis in this category of patients [13].

The current results are consistent with the study by O. Ya. Vasiltseva (2013), where the mean age of patients with PE was 59 years, while at the age of 60-69 years, PE was detected in 37% of patients; there was a predominance of women with a prior PE [14]. The present study also showed that PE is more common in elderly patients (60-75 years old) compared to other age groups and more common in women in groups over 60 years old, which may be associated with a significant predominance of the female population in the Siberian region [15].

Recent studies disprove age as an independent risk factor for PE, explaining the increase in morbidity by an increase in the number of comorbidities [16]. Indeed, the study also found a higher prevalence of multimorbidity in patients of an older age group. The SWIVTER (2012) registry of patients with venous thromboembolism showed that 52% of patients were >65 years old, while they were more likely to have a massive PE; hospital mortality was 6,6% vs 3,2% (p=0,033) [17]. According to the study by O. Ya. Vasiltseva (2017), in the group of patients >70 years old, massive PE and blood clots in the large pulmonary artery branches increased the death risk (odds ratio (OR), 9,73; 95% confidence interval (CI), 5,65-16,76 (p<0,001); OR, 7,58; 95% CI, 4,37-13,15 (p<0,001)). The recurrent embolism and thrombophlebitis also increased the risk of death due to PE (OR, 2,60; 95% CI, 1,59-4,27 (p<0,001); OR, 3,62; 95% CI, 1,26-10,47 (p<0,001).

Diagnosis of PE in older age groups is extremely difficult due to non-pronounced clinical symptoms, concomitant cardiovascular disease, high prevalence of recurrent thrombosis associated with high mortality. According to the PIOPED study, among patients >65 years of age who died in hospital from PE, the diagnosis was made in only 21% [18]. As a cause of death in outpatients, PE is diagnosed at autopsy in 90% [19]. The unfavorable course of PE in elderly patients with severe comorbidities has been repeatedly confirmed in other papers [7-9]. In the present study, it was also determined that patients >75 years old had a high mortality rate, which is explained by severe comorbidities. However, the high mortality rate in a group of patients <60 years old requires detailed study. The unconditional benefit of TLT is shown in a sample of patients aged 60-75 years; this category of patients underwent TLT in a high percentage of cases and had the lowest in-hospital mortality.

The issue of a high incidence of PE and an increased risk of its unfavorable course in women was raised earlier by the authors [20]. In the study by N. G. Vardugina (2017), among women with PE, a high frequency of obesity (63,6%) and HTN (52,6%) was revealed, while the DVT was detected in 68%. Among women, bilateral PE was also more common (63%) with a predominant lesion of large pulmonary vessels [21].

Conclusion

In the Kemerovo and Kemerovo Oblast, PE most often develops in patients aged 60-75 years and is characterized by a more severe clinical course compared with patients younger than 60 years. Patients over the 60 years of age have severe cardiovascular comorbidity status, atrial fibrillation/flutter and recurrent PE. Surgical treatment for senile patients is limited due to the high risk of postoperative complications, which specifies high mortality. Patients <60 years of age are a third of all patients hospitalized with PE. They have a low risk of mortality, but have an unfavorable course of the hospital period along with patients >75 years old.

Relationships and Activities: none.

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