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# Клинические проявления и диагностика тромбоэмболии легочной артерии в рутинной клинической практике (данные Регионального сосудистого центра Рязанской области)

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## АННОТАЦИЯ

**Обоснование.** Данные об особенностях клинической картины и характере течения тромбоэмболии легочной артерии (ТЭЛА), проблемах ее диагностики в рутинной клинической практике (КП) ограничены, получены достаточно давно, чаще всего описываются в рамках венозных тромбоэмболий в целом и практически не включают отечественную популяцию пациентов с ТЭЛА. Данная работа выполнена в рамках регистра «СИРЕНА» (Российский РЕгистр пациеНтов с тромбоэмболией лёгочной Артерии).

**Цель.** Изучение особенностей клинико-демографического профиля и диагностики ТЭЛА в современной КП в сопоставлении с результатами других регистров ТЭЛА.

**Материалы и методы.** Тип исследования — регистр; на основании анализа медицинских карт получены сведения о демографическом профиле, клинической картине и результатах обследования пациентов с ТЭЛА (n = 107, возраст — 63 (52–74) лет, мужчин — 39,3%), проходивших стационарное лечение в одном из Региональных сосудистых центров г. Рязани. Период включения составил 13 месяцев (2018–2019 гг.).

**Результаты.** Из сопутствующей патологии наиболее часто встречались артериальная гипертензия (70,1%), ожирение (46,7%) и сахарный диабет (17,8%). У 26,2% пациентов выявлены факторы высокого риска, у 72,9% пациентов встречаются факторы умеренного и низкого риска в различных сочетаниях, у 5,6% не выявлено ни одного фактора риска развития ТЭЛА. Клинические проявления: одышка (93,5%), боль в грудной клетке (43,0%), резкая слабость (59,8%), тахикардия (29,0%), гипоксемия (27,1%), нестабильная гемодинамика (18,7%). Наиболее частый электрокардиографический признак — инверсия зубца Т в правых грудных отведениях (52,3%). Дисфункция правого желудочка выявлена в 38,1% случаев, повышение уровня тропонина — в 33,6%. По шкале PESI доля пациентов высокого и очень высокого риска в совокупности составила 46,7%. По результатам интегральной оценки тяжести ТЭЛА 34,6% пациентов перешли в классы более низкого риска, 14,0% — в классы более высокого риска; произошло расширение доли умеренного риска (с 23,4 до 62,6%) и сокращение совокупной доли пациентов высокого и очень высокого риска (с 46,7 до 32,0%).

**Заключение.** В современной клинической картине ТЭЛА характерна более высокая распространенность сопутствующей патологии и уменьшение доли традиционных провоцирующих факторов. Сохраняются трудности в диагностике ТЭЛА, связанные с наличием сопутствующей патологии, отсутствием традиционных факторов риска, неспецифичностью клинических проявлений и результатов дополнительных исследований.

**Ключевые слова:** тромбоэмболия легочной артерии; ТЭЛА; эпидемиология; клиника; диагностика; регистр; СИРЕНА

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# Clinical Manifestations and Diagnosis of Pulmonary Embolism in Routine Clinical Practice: Data from the Ryazan Regional Vascular Center

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## ABSTRACT

**BACKGROUND:** Data on the peculiarities of the clinical presentation and characteristics of pulmonary embolism (PE) and problems of its diagnosis in routine clinical practice (CP) are limited. Data obtained long ago are mostly described in terms of venous thromboembolism in general and practically do not include Russian patients with PE. The study was performed within the RusSlan REgistry of pulmoNary embolism (SIRENA) register.

**AIM:** To study the peculiarities of the clinical and demographic profile and diagnosis of PE in modern CP in comparison with the results of other PE registers.

**MATERIALS AND METHODS:** In this registry-based study, medical records were analyzed to obtain information on the demographic profile, clinical presentation, and examination results of patients with PE (n = 107; age, 63 (52–74) years; men, 39.3%) who received inpatient treatment in one of the Ryazan Regional Vascular centers. The study period was 13 months (2018–2019).

**RESULTS:** The most common concomitant pathologies were arterial hypertension (70.1%), obesity (46.7%), and diabetes mellitus (17.8%). High- and moderate-risk factors were identified in 26.2% and 72.9% of the patients, respectively. Low-risk factors identified in 5.6% of the patients in different combinations did not have a single risk factor for PE development. Clinical manifestations included shortness of breath (93.5%), chest pain (43.0%), severe weakness (59.8%), tachycardia (29.0%), hypoxemia (27.1%), and unstable hemodynamics (18.7%). The most frequent electrocardiographic sign was a T-wave inversion in the right chest leads (52.3%). Right ventricle dysfunction was detected in 38.1% of the cases and elevation of troponin levels in 33.6%. According to the Pulmonary Embolism Severity Index scale, high- and very-high-risk cases accounted for 46.7% of the cases. According to the results of the integrated assessment of PE severity, 34.6% and 14.0% of the patients moved to the lower- and higher-risk classes, respectively. The proportion of moderate-risk cases increased from 23.4% to 62.6%, and the high- and very-high-risk cases reduced from 46.7% to 32.0%.

**CONCLUSION:** The modern clinical picture of PE is characterized by a higher prevalence of concomitant pathology and reduction of the rates of traditional risk factors. There remain difficulties in PE diagnosis, which are associated with the concomitant pathology, absence of traditional risk factors, and non-specificity of the clinical manifestations and results of additional examinations.

**Keywords:** *pulmonary embolism; PE; epidemiology; clinical manifestations; diagnostics; register; SIRENA*

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## LIST OF ABBREVIATIONS

VTE — venous thromboembolism  
ESC — European Society of Cardiology  
MN — malignant neoplasm  
CR — clinical recommendations  
CT — computed tomography  
RRCCD — Ryazan Regional Clinical Cardiology Dispensary  
DVT — deep vein thrombosis  
PE — pulmonary embolism

HRF — high risk factor  
LRF — low-risk factor  
MRF — moderate risk factor  
ECG — electrocardiogram  
EchoCG — echocardiogram  
PESI — Pulmonary Embolism Severity Index  
TAPSE — Tricuspid Annular Plane Systolic Excursion

## BACKGROUND

The high medical and social significance of venous thromboembolism (VTE) including pulmonary embolism (PE) has several reasons. First, along with myocardial infarction and stroke, PE determines the level of cardiovascular mortality in developed countries [1–3]. With this, even if PE is not the main pathogenetic factor, it can play a significant role in the occurrence of lethal outcomes [2, 4]. Second, PE can aggravate the course of pre-existing diseases including those that provoked it, such as malignant neoplasms (MN), cardiopulmonary and renal pathologies, and infections. Thus, in patients with oncological diseases, PE and deep vein thrombosis (DVT) may be independent markers of severity and activity of the main disease [5]. Besides, a prolonged intake of anticoagulants as part of prophylaxis of repeated PE increases the risk of hemorrhagic complications, especially in comorbid conditions [1, 6–8]. Third, the timely diagnosis of PE presents serious difficulties, as a proportion of patients die before medical care is provided [1, 9], and clinical manifestations of PE are diverse and nonspecific [1].

Herein, data on the peculiarities of clinical presentation and course of PE and problems of its diagnosis in routine clinical practice (CP) are limited and have been obtained long ago; they are mostly given for VTE, in general, and practically do not include the domestic population with PE [10–18]. This drove the implementation of the RusSlan Register of patients with pulmonary artery embolism; RusSlan Register of pulmonary embolism (SIRENA domestic PE register) that included medical organizations of different levels of medical care [19,20].

This study was performed within the SIRENA register and aimed to evaluate the clinical presentation, risk factors, comorbidity, and peculiarities of PE diagnostics in the Ryazan Regional Vascular Center in comparison with the total cohort of the SIRENA register and data of foreign registers.

## MATERIALS AND METHODS

The study was performed according to the protocol of the SIRENA register [19, 20] in the Ryazan Regional Clinical Cardiology Dispensary (RRCCD). It was approved by the local ethics committee of RRCCD (Protocol No. 9 of September 19, 2018). No additional interventions in patients' management were made, as it was a registry study; therefore, patients signed informed consent according to the standard procedures of RRCCD.

In the registry, patients with PE who underwent treatment in the RRCCD from May 1, 2018, to May 31, 2019 (inclusion period, 13 months) were included.

**Inclusion criteria:** aged  $\geq 18$  years, verified diagnosis of PE (based on the results of computed tomography (CT) with contrast enhancement of the pulmonary artery or autopsy), and hospitalized in RRCCD in the specified period.

**Exclusion criteria:** none.

All analyzed data (demographic, anamnestic, and clinical data) were obtained from the medical records of hospitalized patients.

The analysis included 107 patients (39.9% of men). The median and interquartile range (Me (Q1–Q3)) of age were as follows: all patients, 63 (52–74) years; men, 60 (53–71) years; and women, 66 (52–79) years. Of these, 56 patients who were successively hospitalized were included in the general database of the SIRENA register, and another 51 patients were included in the analysis according to the same inclusion and exclusion criteria after enrollment in the SIRENA register. These two cohorts were comparable with respect to age with a median of 65 (51–75.5) and 63 (53–73),  $p > 0.05$ ; men, 22 of 56 (39.3%) and 20 of 51 (39.2%) ( $p > 0.05$ ). There were 10 fatal cases (9.4% of the total cohort); autopsy was performed in these 10 cases.

Statistical analysis of data was performed using Statistica 13.0 (StatSoft Inc., USA). Descriptive statistics were used. The frequency of occurrence of a characteristic or event was represented as absolute values (n) and fractions (%). The correspondence of quantitative parameters to the normal distribution was

determined using the Shapiro–Wilk test. Continuous values with non-normal distribution were presented as median (Me) and interquartile range (Q1–Q3), except for the data shown in Table 2, which are presented as mean (mean) and standard deviation ( $\sigma$ ) for the possibility of the comparison with the general data of the SIRENA register [19]. The significance of the differences between these values in the groups was evaluated using the nonparametric Mann–Whitney test. Discrete quantities were compared using the  $\chi^2$  test with Yates continuity correction. If the number of cases in one of the compared groups was  $<5$ , the two-sided Fisher test was used. The differences were considered significant at  $p < 0.05$ .

## RESULTS

In 3 of 107 cases (3.8%), PE developed during hospitalization; therefore, the analysis of the diagnostic quality included 104 cases (94.4%). In 80 of 104 cases, the diagnosis on admission was PE, and in 19 cases, the diagnoses were other diseases, such as acute coronary syndrome ( $n = 9$ ), paroxysm of atrial fibrillation ( $n = 5$ ), and decompensation of heart failure ( $n = 5$ ). In another five patients, PE was diagnosed posthumously based on autopsy results.

The demographic and anamnestic data of the analyzed cohort of patients with PE in comparison with the general cohort of patients from the SIRENA register and with the results of the international studies

are presented in Table 1. The attention is drawn to a larger proportion of women in our cohort (60.7%), lower frequency of reversible risk factors (immobilization, 4.7%; previous surgical interventions, 12.2%; traumas, 0.9%); thus, a higher frequency of chronic comorbidity referred to low-risk factors (arterial hypertension, 70.1%; obesity, 46.7%; diabetes mellitus, 17.8%).

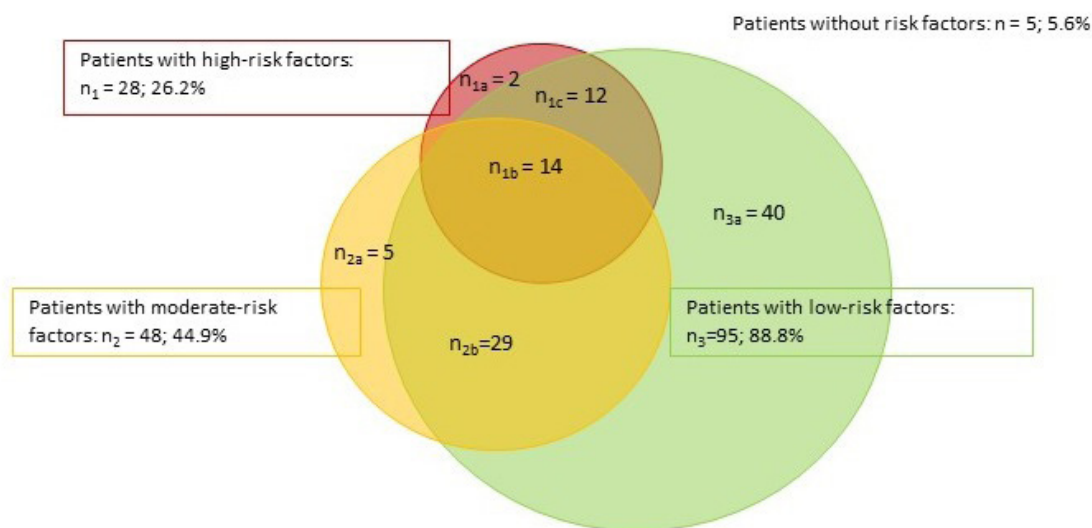
*High risk factors* (HRF), according to the classification of the European Society of Cardiology (ESC) [1], were recorded in each fourth patient, 26.2% ( $n = 28$ , Figure 1) and their combinations in 3.7% of cases ( $n = 4$ ). According to the frequency of occurrence, HRF were distributed as follows:

- Previous VTE ( $n = 24$ ; 22.4%), including one case of kava-filter implantation.
- Hospitalization for heart failure ( $n = 6$ ; 5.6%).
- Recent trauma or myocardial infarction (1 case each; 0.9%).

With this, only 6 of 28 patients with HRF were regularly taking anticoagulants, and another eight patients had been taking the drugs earlier but stopped intake in the period from several days to 6 months before the development of the index PE.

Patients with *moderate-risk* factors (MRF) accounted for 31.8% ( $n = 34$ ) of the analyzed cohort (14 of them also had HRF, that is, a higher risk level, Figure 1).

*Low-risk* factors were recorded in 95 (88.8%) patients and 40 patients without HRF and MRF (37.4%, Figure 1).



**Fig. 1.** Ratio of patients with high-, moderate-, and low-risk factors for venous thromboembolism and their combinations.

*Notes:* The area of the colored circles (red, yellow, and green) reflects the number of cases with a certain level of risk factor (high, moderate, and low, respectively) for venous thromboembolism. The overlapping zone shows the number of cases with a simultaneous existence of different levels of risk factors:  $n_{1a}$ , patients with isolated high risk factors;  $n_{1b}$ , patients with high-, moderate-, and low-risk factors;  $n_{1c}$ , patients with high- and low-risk factors;  $n_{2b}$ , patients with moderate- and low-risk factors; and  $n_{3a}$ , patients with isolated low-risk factors.

**Table 1.** Demographic and Anamnestic Data of Patients with Pulmonary Embolism in the SIRENA Register in Comparison with the Results of Earlier Studies

Parameters	SIRENA register		Other studies (literature data)								
	Ryazan	Total cohort [19]	Worcester DVT [10]	STAC [11]	Huerta C., et al. [12]	Worcester VTE [13]	RIETE [14]	EMPEROR [15]	SWIVTER [16]	PREFER [17]	Shah P., et al. [18]
Years of inclusion of patients	2018–2019		1985–1986	1993–1997	1994–2000	1999–2003	2001–2006	2005–2008	2009–2010	2013–2014	2013–2014
n	107	609	131	2444*	3006	549	15520*	1880	1247*	1399	260614
<b>Demographic Data</b>											
Mean age, years	62	63	66	68	63	65	–	56	61	62	–
Women, % of n	60.7	50.7	49.0	49.7 <sup>†</sup>	53.0	56.4	50.3 <sup>†</sup>	52.8	48.5 <sup>†</sup>	47.8 <sup>†</sup>	52.8
<b>High Risk Factors for Venous Thromboembolism, % of n</b>											
Previous venous thromboembolism	22.4	–	–	–	–	14.3 <sup>‡</sup>	15.9 <sup>‡</sup>	24.2	23.1	20.2	–
Previous deep vein thrombosis	19.6	19.4	–	–	–	–	–	11.9	–	–	–
Previous pulmonary embolism	7.5	9.2	–	–	–	–	–	12.3	–	–	–
Hospitalization for heart failure	5.6	6.2	–	–	10.1	8.2	–	7.5	–	–	13.5 <sup>†</sup>
Traumas	0.9	2.8	14.0 <sup>§</sup>	6.4 <sup>†</sup>	2.6	9.1 <sup>†</sup>	–	4.7	7.3 <sup>†</sup>	10.0 <sup>†</sup>	–
Myocardial infarction	0.9	3.0	9 <sup>†</sup>	–	8.7 <sup>†</sup>	–	–	6.8 <sup>†</sup>	–	–	–
<b>Moderate Risk Factors for Venous Thromboembolism, % of n</b>											
Malignant neoplasms	17.8	17.1	27.0	18.9	15.9	39.8 <sup>§</sup>	20.4	28.0 <sup>†</sup>	25.3	8.6 <sup>‡</sup>	14.1
Congestive heart failure	11.2	–	31.0 <sup>§</sup>	–	–	–	–	–	6.5	5.9 <sup>†</sup>	–
Stroke	8.4	9.9	8.0	–	–	–	–	2.8 <sup>§</sup>	5.9	2.7 <sup>§</sup>	9.5
Intake of oral contraceptives	8.3	–	–	–	–	–	–	4.4	–	–	–
Chemotherapy	3.7	–	–	–	–	8.0	–	–	12.5 <sup>†</sup>	–	–
Postpartum period	1.9	–	–	–	–	–	–	0.9	–	–	–
Hemotransfusion	0.9	3.0	–	–	–	–	–	–	–	–	–
<b>Low-Risk Factors for Venous Thromboembolism, % of n</b>											
Arterial hypertension	70.1	65.7	–	–	25.0 <sup>§</sup>	–	–	45.6 <sup>§</sup>	–	46.3 <sup>§</sup>	58.0 <sup>†</sup>
Elderly age	59.8	–	–	–	–	–	–	–	–	–	–
Obesity	46.7	–	38.0	–	19.2 <sup>§</sup>	42.4	27.2 <sup>§</sup>	26.9 <sup>§</sup>	14.0 <sup>§</sup>	–	21.8 <sup>§</sup>
Diabetes mellitus	17.8	15.2	–	–	6.0 <sup>§</sup>	–	–	–	9.1 <sup>‡</sup>	11.2 <sup>†</sup>	22.0
Varicose vein disease	17.8	31.4 <sup>‡</sup>	–	–	4.5 <sup>§</sup>	–	20.2	–	13.2	17.5	–
Previous surgical intervention	12.2	15.6	19.0	14.6	35.5 <sup>§</sup>	29.2 <sup>§</sup>	12.9	14.4	13.6	14.0	–
Immobilization	4.7	12.6 <sup>†</sup>	–	15.1 <sup>†</sup>	–	48.3 <sup>§</sup>	3.6	11.6 <sup>†</sup>	18.5 <sup>§</sup>	17.8 <sup>§</sup>	–
<b>Other Anamnestic Data, % of n</b>											
Chronic obstructive pulmonary disease	1.9	8.9 <sup>†</sup>	34.0 <sup>§</sup>	–	10.0 <sup>†</sup>	–	–	8.5 <sup>†</sup>	11.2 <sup>†</sup>	10.7 <sup>†</sup>	24.8 <sup>§</sup>
Chronic kidney disease	9.3	9.0	–	–	–	–	–	–	7.1	6.4	14.5 <sup>§</sup>

Notes: «–», no data; \* in the study, n is given for venous thromboembolism, in general; † difference with our data at  $p < 0.05$ , ‡ difference with our data at  $p < 0.01$ , § difference with our data at  $p < 0.001$ ; risk factors given in clinical recommendations but not specified in the given table were not recorded in our study



In most cases (72.9% of the total cohort and 68.4% of patients without HRF), multiple MRF and LRF (general cohort, 2.8; cohort without HRF, 2.7%) were noted. In addition, 59.8% of patients were of older and senile age according to the classification of the World Health Organization. Among patients with malignant neoplasms (n = 19), metastasis was recorded in seven patients, of which four patients received chemotherapy. Among women, 13.8% (n = 9) were taking oral contraceptives, and two women developed PE in the postpartum period.

Overall, in 67.3% of cases (n = 72), patients with PE had no obvious provoking factors of temporary/reversible character, and in 5.6% (n = 5) of cases, not a single factor predisposing to VTE development was found.

The leading complaints of patients are characterized by the following triad (Table 2):

- Shortness of breath (93.5%) .
- Severe weakness (59.8%).
- Chest pain (43.0%).

**Table 2.** Clinical Manifestations of Pulmonary Embolism in the SIRENA Register in Comparison with Data of Earlier Studies

Parameters	SIRENA Register		Other Studies (Literature Data)			
	Ryazan	General Cohort [19]	Worcester DVT [10]	EMPEROR [15]	SWINTER [16]	PREFER [17]
Years of inclusion	2018–2019	2018–2019	1985	2005–2008	2009–2010	2013–2014
n	107	609	131	1880	644	1399
<b>Complaints</b>						
Shortness of breath, % of n	93.5	88.8	77.0 <sup>†</sup>	50.1 <sup>‡</sup>	82.5 <sup>†</sup>	75.6 <sup>‡</sup>
Severe weakness, % of n	59.8	–	–	–	–	–
Chest pain, % of n	43.0	29.8 <sup>†</sup>	55.0	39.4	–	45.5
Syncope/presyncope, % of n	29.0	30.0	10.0 <sup>†</sup>	5.5 <sup>‡</sup>	11.3 <sup>‡</sup>	8.2 <sup>‡</sup>
Cough, % of n	21.5	17.3	–	–	–	–
Hemoptysis, % of n	6.5	8.5	13.0	7.6	–	3.4
Abdominal pain, % of n	0	–	–	–	–	–
<b>Results of Objective Examination</b>						
Systolic arterial pressure < 90 mm Hg, % of n	8.4 (18.7)	4.9	10.0	–	6.1 <sup>†</sup>	–
Tachycardia, % of n	29.0	–	43.0*	–	25.5	16.7 <sup>†</sup>
Heart rate, beat/min, Mean±σ	97.4 ± 19.7	94.8 ± 19.5	–	–	–	–
Tachypnea, % of n	20.6	–	70.0 <sup>†</sup>	–	–	16.2 <sup>†</sup>
Respiratory rate-1, Mean±σ	29.1 ± 18.1	21.2 ± 4.6 <sup>†</sup>	–	–	–	–
SaO <sub>2</sub> , %, Mean±σ	90.7 ± 6.9	92.3 ± 5.9*	–	–	–	–
Moist rales in lungs, % of n	17.7	17.2	–	8.4 <sup>‡</sup>	–	–
Cyanosis, % of n	57.9	30.2 <sup>‡</sup>	18.0	–	–	2.2 <sup>‡</sup>
Asymmetry of legs, % of n	64.5	35.6 <sup>‡</sup>	–	–	–	–
Edema of legs, % f n	34.6	36.6	–	–	–	–

Notes: «–», no data; \* difference with our data at p < 0.05, † difference with our data at p < 0.01, ‡ difference with our data at p < 0.001; SaO<sub>2</sub> blood saturation

Only 35.5% of the patients presented with signs of respiratory failure (respiratory rate > 30 min<sup>-1</sup> and/or blood saturation < 90%). The duration from the development of clinical symptoms to the establishment of the diagnosis was 4 (1–10) days. Herein, only 62.6% of the patients sought medical help within a week of symptom onset.

Significant differences in the clinical manifestations of PE were recorded between patients with PE suspected as early as in the prehospital period and patients hospitalized with another diagnosis (Table 3). In the

cohort of patients with a diagnosis of PE confirmed later (n = 107), the Wells scale [1] showed a high probability for PE in 0.9% and the Geneva scale in 33.6% of cases.

The results of the analysis of instrumental examination methods are given in Table 4. In 10.3% of patients with electrocardiogram (ECG) data, no deviations were recorded, including sinus tachycardia. Echocardiography (EchoCG) was performed in 98.1% of the patients (n = 105) and revealed dysfunction of the right ventricle in 38.1% of the patients. Doppler ultrasonography of the lower limb veins was conducted

**Table 3.** Comparison of the Clinical Manifestations of Pulmonary Embolism in Patients Hospitalized with Suspicion of Pulmonary Embolism and Patients Hospitalized with Other Diagnosis

Parameters	Diagnosis at the Moment of Hospitalization		p
	Pulmonary Embolism	Other Diagnosis	
n	80	24	–
<b>Demographic Data</b>			
Age, years, Me (Q1–Q3)	61 (47–73)	71 (57–79)	1.0
Older and senile age, % of n	52.3	66.7	0.24
Women, % of n	57.5	70.8	0.35
<b>History</b>			
Previous deep vein thrombosis/pulmonary embolism, % of n	22.5	8.3	0.15
Previous malignant neoplasm, % of n	20.0	4.2	0.11
Previous immobilization/trauma /surgical intervention, % of n	16.3	20.8	0.56
Intake of oral contraceptives/recent deliveries, % of women	19.6	11.8	0.71
Varicose disease, % of n	20.0	12.5	0.55
Myocardial infarction, % of n	6.3	0	0.59
Hospitalization for heart failure, % of n	2.5	12.5	0.08
Congestive heart failure, % of n	8.8	16.7	0.27
Acute cerebrovascular accident, % of n	7.5	8.3	1.0
Arterial hypertension, % of n	60.0	87.5	<b>0.014</b>
Diabetes mellitus, % of n	13.8	20.8	0.52
Obesity, % of n	40.0	54.2	0.25
Chronic kidney disease, % of n	5.0	16.7	0.08
<b>Clinical Manifestations</b>			
Shortness of breath, % of n	93.8	95.8	1.0
Severe weakness, % of n	60.0	62.5	1.0
Chest pain, % of n	42.5	41.7	0.87
Syncope/presyncope, % of n	28.8	29.2	1.0
Hemoptysis, % of n	8.8	0	0.19
Abdominal pain, % of n	0	0	–
Systolic arterial pressure < 90 mm Hg, % of n	13.8	12.5	1.0
Tachycardia, % of n	27.5	37.5	0.45
Tachypnea, % of n	17.5	25.0	0.39
Moist rales in lungs, % of n	55.0	62.5	0.64
Cyanosis, % of n	13.8	29.2	0.12
Asymmetry of legs, % of n	66.3	58.3	0.48
Edema of legs, % of n	33.8	41.7	0.48
<b>Results of Additional Examination Methods</b>			
Sinus rhythm, % of n	91.3	62.5	<b>0.002</b>
Atrial fibrillation, % of n	7.5	37.5	<b>&lt; 0.001</b>
S1Q3 syndrome, % of n	28.8	8.3	0.055
Thrombus in the right heart chambers, % of n	2.5	16.7	<b>0.024</b>

**Notes:** From the analysis, three patients were excluded in whom pulmonary embolism developed during inpatient treatment for another disease

in 92.5%, of which in 15.1% of the patients, the PE source was not identified. CT with contrast enhancement of the pulmonary artery was conducted in 93.5% (n = 100) of the patients; in 3% (n = 3) of them, no defects were

found. Moreover, 2.8% of the patients (n = 3) underwent pulmonary angiography. The troponin level was determined in 75.7% of the patients (n = 81), and in 44.4% (n = 36) of them, the value exceeded the 99% percentile.

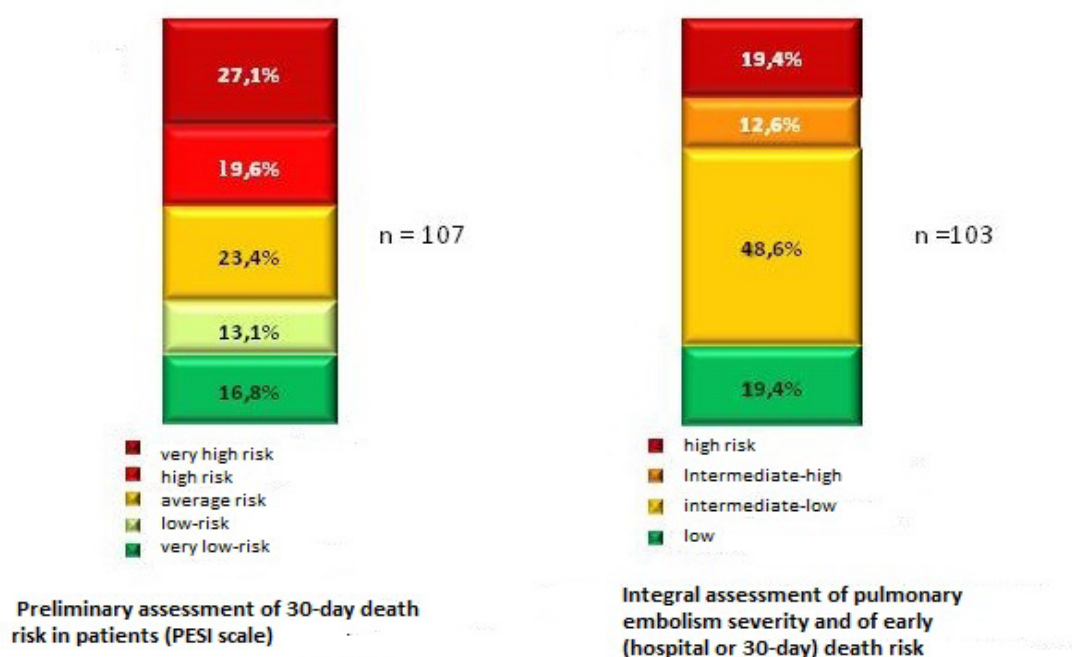
The Pulmonary Embolism Severity Index (PESI) [1] was evaluated based on the results of the analysis of clinical and demographic data (Fig. 2a). The total proportion of patients with high and very high risk was 46.7%.

On the basis of the presence or absence of signs of hemodynamic instability (18.7%), right ventricular dysfunction (37.4%), and elevated troponin level (33.6%), the integral assessment of PE severity was performed (Fig. 2b). Accordingly, 34.6% of the patients moved to low-risk classes and 14.0% to high risk classes, the proportion of moderate-risk classes increased from 23.4% to 62.6%, and the total proportion of patients with

high and very high risk reduced from 46.7% to 32.0%.

In intermediate-risk patients, troponin levels were determined only in 77.6% ( $n = 52$ ) of the cases, despite their high prognostic significance for this group [1]. Thus, in 35.8% ( $n = 52$ ) of the patients with troponin analysis, the results did not influence the patient management technique according to the clinical recommendations (CR) [1].

Moreover, in 43.0% of the patients, the glomerular filtration rate was  $<60$  mL/min/1.73 m<sup>2</sup>, 29.0% had decreased hemoglobin levels, and 4.7% had thrombocytopenia.



**Fig. 2.** Structure of the cohort of patients hospitalized with pulmonary embolism based on the calculation of the hospital or 30-day death risk.

Note: PESI, Pulmonary Embolism Severity Index [1].

## DISCUSSION

This study included patients who were hospitalized during the period under the implementation of the previous version of ESC CR on the diagnosis and treatment of PE [21]. However, the analysis did not include assessment of the quality of medical care provided to this category of patients; therefore, the authors considered it more acceptable and more practically significant to assess risk factors, clinical manifestations, results of diagnostic methods, and methods of their integral assessment in the context of the current version of the ESC CR [1].

Overall, the obtained demographic and anamnestic data are comparable with the results of previous studies that have been characterizing the portrait of patients with PE within almost 50 years [10–18]. The attention

is drawn by the growth in the number of patients with comorbid diseases, such as arterial hypertension, diabetes mellitus, and obesity (Table 1) [10–18]. However, currently, the number of unprovoked episodes of PE considerably increased, and only a small proportion of patients have traditional reversible risk factors in history.

According to our results, more common complaints in the current clinical presentation of patients hospitalized with PE include shortness of breath, syncopal conditions, cyanosis, and development of massive PE with the level of systolic arterial pressure  $<90$  mm Hg (Table 2) [10, 15–17]. Despite these peculiarities, clinical manifestations of PE, in general, remain nonspecific, and PE may run “under the mask” of other diseases and conditions. For example, in some of the patients, clinical presentation and alterations in the ECG may resemble those in acute



**Table 4.** Results of Instrumental Examinations of Patients with Pulmonary Embolism in the Analyzed Cohort in Comparison with the Total Cohort of the SIRENA Register

	Ryazan	Total Cohort 19	p
<i>Electrocardiography</i>			
n	107	609	–
Main rhythm			
sinus, % of n	84.1	94.6	<b>0.001</b>
atrial fibrillation/flutter, % of n	14.0	1.6	<b>&lt; 0.001</b>
pacemaker rhythm, % of n	0.9	1.0	0.9
nodular, % of n	0	0.7	0.4
other than nodular, % of n	0.9	2.2	0.4
S <sub>1</sub> Q <sub>3</sub> syndrome, % of n	23.4	25.0	0.7
Right bundle branch block, % of n	14.0	12.8	0.7
Left bundle branch block, % of n	9.4	5.1	0.08
ST displacement			
elevation, % of n	9.3	5.7	0.14
depression, % of n	8.4	7.7	0.8
Inverted T in V1–4 leads, % of n	52.3 <sup>‡</sup>	39.2	<b>0.01</b>
Sinus tachycardia, % of n	43.0	–	–
<i>Echocardiography</i>			
n <sub>1</sub> (% of n)	105 (98.1)	545 (89.5)	<b>0.004</b>
Left ventricular ejection fraction, %, Me (Q1–Q3)	64 (61–67)	58 (52–63)	–
Left ventricular ejection fraction < 40%, % of n <sub>1</sub>	2.9	7.5	0.09
Right atrial dimension, mm, Me (Q1–Q3)	43 (40–50)	47 (41–53)	–
Right ventricular dimension, mm, Me (Q1–Q3)	30 (26–34)	32 (28–37)	–
Right ventricular dilatation, % of n <sub>1</sub>	73.4	–	–
TAPSE, mm, Me (Q1–Q3)	1.7 (1.4–2.0)	1.6 (1.4–2.0)	–
Systolic pressure in the pulmonary artery, mm Hg, Me (Q1–Q3)	61 (55–75)	50 (39–65)	–
Pulmonary hypertension, % of n <sub>1</sub>	84.8	–	–
Thrombus in right heart chambers, % of n <sub>1</sub>	5.7	4.0	0.4
<i>Ultrasound Dopplerography of Lower Limb Veins</i>			
n <sub>2</sub> (% of n)	99 (92.5)	523 (85.9)	0.06
Deep vein thrombosis of lower limbs, % of n <sub>2</sub>	84.9	57.8	<b>&lt; 0.001</b>
<i>Computed Tomography with Enhanced Contrast of Pulmonary Artery</i>			
n <sub>3</sub> (% of n)	100 (93.5)	543 (89.2%)	0.18
lesion of ≥50% of the vascular bed, % of n <sub>3</sub>	71.0	–	–
lesion of 30%–49% of the vascular bed, % of n <sub>3</sub>	7.0	–	–
lesion of <30% of the vascular bed, % of n <sub>3</sub>	19.0	–	–
No defects identified, % of n <sub>3</sub>	3.0	6.3	0.2

Notes: «–», no data; TAPSE, tricuspid annular plane systolic excursion

coronary syndrome, which leads to misdiagnosis in the prehospital stage, as confirmed by the data of Ermolaev et al. (2012) [22]. With this, there exists a pathogenetic “crossing” between PE and acute coronary syndrome. The appearance of anginal pain, ischemic alterations in the ECG, and elevation of the level of highly sensitive troponin cannot be explained only by damage to the right ventricle in its hemodynamic overload. Mazur et al. (2020) revealed the involvement of the left ventricle in the pathogenesis of anginal pain in PE due to the compression of the left main coronary artery by the

pulmonary trunk in their close anatomic vicinity [23].

Besides, our data confirmed that PE may run without clinical manifestations and alterations in ECG and EchoCG results traditionally described for it, which should be taken into account by practitioners.

Interestingly, not a single medical record of patients included in this register indicated abdominal manifestations of PE, whereas literature data indicate the probable presence of pain in the upper abdomen as the only clinical manifestation of PE [24–26]. This discrepancy between the results can be explained both

by the real absence of abdominal pain in the clinical picture and insufficient analysis of this sign by doctors.

The analysis of clinical manifestations of PE within register studies reflects the clinical presentation of patients who sought medical help and survived it. It cannot be excluded that in cases of fatal outcomes from PE before the medical care had been provided, the severity of the condition and clinical manifestations of PE were different.

In addition, the wide introduction of CT into CP resulted in the increased detection of asymptomatic and low-symptom thromboembolism of small branches of the pulmonary artery [27], which, of course, can change the modern clinical "portrait" of a patient with PE. In our study, no cases of asymptomatic course were registered, as the presence of clinical manifestations caused patients to seek medical help or allowed to suspect PE during inpatient treatment.

The impossibility of the assessment all patients with PE is an obvious limitation of all register studies of PE including the present study. However, at present, objective reasons limit a more global investigation of this matter, particularly the mentioned nonspecificity of clinical manifestations of PE and low frequency of autopsies in case of death occurred outside medical institutions [27, 28].

Finally, patients were included in the register before the coronavirus disease-2019 (COVID-19) pandemic. It is unreasonable to extrapolate register data to the population of patients with COVID-19, since the works of recent months convincingly show that with the underlying COVID-19, PE has serious differences; in particular, elevated D-dimer level is recorded in patients with COVID-19 even without VTE; thus, to exclude PE, this test should be used with higher threshold values [29]. Literature data also indicate a higher prevalence of thrombosis of the peripheral parts of the pulmonary arterial network, and a frequent absence of the source of thromboembolism, which allows suggesting a different pathogenesis associated not only with VTE but also with immunothrombosis in situ, which requires additional investigation [30, 31]. In such patients, a lower incidence of the right ventricle dysfunction is also specified [30].

## CONCLUSION

The clinical and demographic profile of patients with pulmonary embolism in the analyzed cohort generally corresponds to the results of previous studies. The most significant differences are a higher frequency of comorbid pathology, which can potentially complicate the diagnosis, course, and treatment of PE, and the existence of patients without any traditional provoking risk factors for VTE, which can also impede the timely diagnosis and treatment for PE.

Despite the obtained data on a sufficiently high proportion of cases of massive PE manifested by clinically evident arterial hypotension, our results confirm the nonspecificity of the clinical manifestations and results of additional examinations, which may lead to an erroneous preliminary diagnosis.

Thus, the nonspecificity of the clinical presentation of PE and the probability of its occurrence given the background of diverse pathology dictates the need for the high diagnostic alertness of doctors of different specialties and shows the importance of differential diagnosis.

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