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Прогноз пациентов, перенесших тромбоэмболию легочной артерии, и факторы, его определяющие (результаты 12 месяцев наблюдения)

Ю. В. Тереховская^{1✉}, Н. Э. кызы Ахмедова², Д. И. Леоненко², Н. Н. Никулина²¹ Областной клинический кардиологический диспансер, Рязань, Российская Федерация;² Рязанский государственный медицинский университет имени академика И. П. Павлова, Рязань, Российская Федерация

АННОТАЦИЯ

Введение. Тромбоэмболия легочной артерии (ТЭЛА) — сердечно-сосудистое заболевание с высокой летальностью: у каждого десятого умершего по данным аутопсии причиной смерти является ТЭЛА. Несмотря на относительно длительную историю изучения ТЭЛА литературные данные по этой проблеме носят разрозненный, неполный характер и зачастую не представляют российскую популяцию.

Цель. Оценить выживаемость пациентов в течение 12 месяцев после перенесенной ТЭЛА и установить предикторы летального исхода.

Материалы и методы. Работа выполнена в рамках российского регистра СИРЕНА. Включено 107 пациентов (медиана возраста и интерквартильный размах — 63 (52–74) года), проходивших стационарное лечение в Областном клиническом кардиологическом диспансере г. Рязани (госпитализация с 01.05.2018 по 31.05.2019; период включения — 13 месяцев). Сбор информации во время госпитализации — по данным медицинской документации и объективного исследования, после выписки — посредством телефонного опроса. Период наблюдения — 12 месяцев от момента госпитализации; отклик — 84,5%.

Результаты. Выживаемость пациентов с ТЭЛА в течение 12 месяцев составила 77,1%; рецидив венозной тромбоэмболии развился у 6,5% пациентов, кровотечения — у 22,4% пациентов. Единственным статистически значимым предиктором развития летального исхода после выписки из стационара является наличие онкологического заболевания, в т.ч. в анамнезе (относительный риск (ОР) 4,4; 95% доверительный интервал (ДИ) 1,4–14,5; $p = 0,014$). Ведущими предикторами летального исхода от момента госпитализации до 12 месяцев являются: высокий риск согласно интегральной оценке тяжести и риска ранней смерти (ОР 9,9; 95% ДИ 1,2–79,5; $p = 0,031$), возраст ≥ 65 лет (ОР 5,1; 95% ДИ 1,7–15,2; $p = 0,003$), госпитализация с отличным от ТЭЛА первичным диагнозом (ОР 4,5; 95% ДИ 1,9–10,8; $p = 0,001$), снижение фильтрационной функции почек (ОР 4,3; 95% ДИ 1,7–11,1; $p = 0,003$). Кроме того, статистически значимо увеличивали риск летального исхода в этот период наличие в анамнезе атеросклеротических заболеваний, инсульта, сердечной недостаточности, онкологии, гемодинамическая нестабильность в остром периоде, потребность в петлевых диуретиках во время госпитализации и наличие синдрома SIQ3.

Заключение. Уровень летальности пациентов с ТЭЛА в одном из региональных сосудистых центров г. Рязани в 2018–2019 гг. в целом согласуется с данными предшествующих международных исследований. Ведущими предикторами летального исхода в течение 12 месяцев от момента госпитализации являются тяжелое состояние пациента на момент госпитализации, возраст ≥ 65 лет, несвоевременная диагностика ТЭЛА и снижение фильтрационной функции почек.

Ключевые слова: тромбоэмболия легочной артерии; ТЭЛА; отдаленный прогноз; прогностические предикторы; СИРЕНА

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Prognosis for Patients after Pulmonary Embolism and its Determining Factors (Results of 12-Month Follow-Up)

Yuliya V. Terekhovskaya¹✉, Nazly E. kyzy Akhmedova², Dar'ya I. Leonenko²,
Natal'ya N. Nikulina²

¹ Ryazan Regional Clinical Cardiology Dispensary, Ryazan, Russian Federation;

² Ryazan State Medical University, Ryazan, Russian Federation

ABSTRACT

INTRODUCTION: Pulmonary embolism (PE) is a cardiovascular disease with high mortality: according to autopsy data, PE is the cause of death in every tenth deceased person. Despite a relatively long history of studying PE, the literature data on this problem are scattered, incomplete and often do not represent the Russian population.

AIM: To evaluate 12-month survival rate of patients after a past episode of PE and to establish predictors of fatal outcome.

MATERIALS AND METHODS: The work was carried out within the Russian SIRENA register. The study included 107 patients (age median and interquartile range 63 (52–74) years), who underwent inpatient treatment in Regional Clinical Cardiology Dispensary of Ryazan (hospitalization from 01.05.2018 to 31.05.2019; inclusion period 13 months). In the period of hospitalization, the information was taken from the data of medical records and objective examinations, and after the discharge — through telephone control. Follow-up period from the moment of hospitalization was 12 months; response — 84.5%.

RESULTS: The 12-month survival rate of patients with PE was 77.1%; recurrence of venous thromboembolism developed in 6.5% of patients, bleeding — in 22.4% of patients. The only statistically significant predictor of the development of a fatal outcome after discharge from hospital was the presence of cancer, including that in history (relative risk (RR) 4.4; 95% confidence interval (CI) 1.4–14.5; $p = 0.014$). The leading predictors of death from the moment of hospitalization within 12 months were high risk based on the integral assessment of severity and of early death risk (RR 9.9; 95% CI 1.2–79.5; $p = 0.031$), age ≥ 65 years (RR 5.1; 95% CI 1.7–15.2; $p = 0.003$), hospitalization with other than PE primary diagnosis (RR 4.5; 95% CI 1.9–10.8; $p = 0.001$), impaired filtration function of kidneys (RR 4.3; 95% CI 1.7–11.1; $p = 0.003$). Besides, a statistically significant increase in the risk of death during this period was associated with history of atherosclerotic diseases, stroke, heart failure, oncology, hemodynamic instability in the acute period, the need for loop diuretics during hospitalization and the presence of S1Q3 syndrome.

CONCLUSION: The mortality rate of patients with PE in one of the regional vascular centers of Ryazan in 2018–2019 generally agrees with the data of the previous international studies. The leading predictors of fatal outcome within 12 months from the moment of hospitalization include a severe condition of a patient at the time of hospitalization, age ≥ 65 years, untimely diagnosis of PE and reduction of filtration function of kidneys.

Keywords: *pulmonary embolism; PE; long-term prognosis; prognostic predictors; SIRENA*

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LIST OF ABBREVIATIONS

ACVE — acute cardiovascular event
 AF — atrial fibrillation
 CKD — chronic kidney disease
 CHF — chronic heart failure
 CI — confidence interval
 CT — computed tomography
 DVT — deep vein thrombosis
 ECG — electrocardiogram
 EchoCG — echocardiography
 GFR — glomerular filtration rate
 IESEDR — integral evaluation of severity and early death risk
 MNP — malignant neoplasms

PA — pulmonary artery
 PE — pulmonary embolism
 RCCD — Regional Clinical Cardiologic Dispensary
 PESI — Pulmonary Embolism Severity Index
 RF — respiratory failure
 RR — relative risk
 SIRENA — RusSlan REgister of patieNts with pulmonary Artery embolism
 TLT — thrombolytic therapy
 TV — tricuspid valve
 VTE — venous thromboembolism
 DUS — duplex ultrasound

INTRODUCTION

Pulmonary embolism (PE) is one of most common cardiovascular diseases in the world associated with a high mortality rate [1, 2]. This problem has been studied for several decades [3]. Even according to the results of Framingham study, PE was a cause of hospital death in 15.6% of cases [4]. According of the data of I. I. Zatevakhin, et al. (2002), in our country PE is found to be a cause of death on every 10th autopsy, with this, in half of the cases it was not identified in life [5].

The previously conducted cohort studies of PE had a number of limitations: (1) PE in them was analyzed within the syndrome of venous thromboembolism (VTE), and not as an independent condition; (2) these studies were conducted rather long ago without taking into account relatively frequently updated Clinical recommendations on the problem; (3) they practically did not include representatives of the Russian population [3].

In the earlier Russian publications, PE, as a rule, was considered in the aspect of some highly special situations (a complication of surgical interventions, obstetric pathology, malignant neoplasms (MNP), etc.) [3, 5, 6].

The above factors justified the relevance of implementation of SIRENA (RusSlan REgister of patieNts with pulmonary Artery embolism) register [7]. The analysis presented in the given work, was initiated within SIRENA register, further on, the cohort and methods of study were expanded [8, 9].

The **aim** of this study to evaluate 12-month survival rate of patients after pulmonary embolism and to identify predictors of death.

MATERIALS AND METHODS

The clinical data of patients (n = 107) hospitalized from 2018, May 01 to 2019, May 31 in the Regional Clinical Cardiologic Dispensary of Ryazan (RCCD functioning as a regional vascular center) with the verified diagnosis of

PE, were analyzed. Here, PE could have been established at the time of hospitalization, during hospitalization (including cases of PE developed during hospitalization) and/or on autopsy. No additional medical interventions were performed in the study, therefore, patients signed an Informed Consent of the standard form of RCCD. Fifty six patients were included in the cohort of the Russian SIRENA register. The inclusion of additional patients (n = 51) and the expansion of the list of analyzed parameters, were approved by the Local Ethics Committee at the RCCD of Ryazan (Protocol No. 9 of 2018, September 19).

Inclusion criteria:

- age \geq 18 years;
- inpatient treatment in the RCCD in the period from 2018, May 01 to 2019, May 31 (including signing the standard Informed consent form);
- verified diagnosis of PE based on the results of computed tomography (CT) with contrast of the pulmonary artery (PA) or results of autopsy.

Exclusion criteria: not provided.

The proportion of men in the analyzed cohort (n = 107) was 39.3%, the median of patients' age and the interquartile range were 63 (52–74) years. During the inpatient stage, 10 fatal cases were recorded (9.4%), in all of them autopsy was performed. Clinical information was collected based on medical records (outpatient records, abstracts, medical history) and direct questioning/physical examination of patients. After discharge, information was collected through a structured telephone survey (interviewing) of patients in 3, 6, 9 and 12 months after hospitalization. The response at the time of the final telephone contact (12 months) was 84.5%.

For statistical processing and analysis of the results, Statistica 13.0 (Stat Soft Inc., USA) and SPSS Statistics 20 (IBM Corp., USA) application programs package was used. The data are presented as the absolute number of cases (n), the proportion/frequency of the attribute (%),

the mean (M) and the square deviation (SD; in case of a normal distribution of the attribute) or median (Me) and the interquartile range (Q1–Q3; in case of distribution of the trait other than normal), relative risk (RR), 95% confidence interval (CI), the statistical significance of the differences (p). The compliance of the parameters with the normal distribution law was evaluated using Shapiro–Wilk test, the statistical significance of differences in quantitative parameters was evaluated using Student's test (in cases of normal distribution of the attribute) and Mann–Whitney test (for other cases), of the qualitative attributes — using χ^2 criterion with Yates adjustment for continuity (for $n < 5$ — a two-sided Fischer test was used). Predictors of a poor prognosis were established using Cox regression analysis models. Survival rate was evaluated by Kaplan–Mayer method. The differences were considered statistically significant at $p < 0.05$.

RESULTS

The survival rate of patients with PE *during hospitalization* (duration of hospitalization (Me (Q1–Q3) — 15 (13–18) bed days) was 90.6% ($n = 97$). *From the moment of discharge from the hospital to the follow-up point '12 months'*, a fatal outcome was recorded in 11 cases (Table 1), of these, in 5 cases, the cause of death was MNP, in 2 — bleeding, in 2 more — sudden cardiac death (no signs of PE were detected on autopsy), in one case — ischemic stroke and in one — chronic heart failure (CHF). Thus, the survival of patients *after discharge* from hospital (Me (Q1–Q3) — 11.5 (11.4–11.5) months) was 86.4% ($n = 71$), and for the *overall period of 12 months* after hospitalization — 77.1% ($n = 86$).

Table 1. Adverse Events in Patients with Past PE within 12 Months from Moment of Hospitalization

Parameters	Period of Hospitalization	From Discharge to 12 Months	Total
Number of analyzed cases, n	107	82	107
Duration of observation period, Me (Q1–Q3), days	15 (13–18)	350 (348–352)	365
Fatal outcome, n_1 (% of n)	10 (9.4)	11 (13.4)	21 (19.6)
Repeated episode of venous thromboembolism, n_2 (% of n)	4 (3.7)	3 (3.7)	7 (6.5)
Bleeding, n_3 (% of n)	20 (18.7)	2 (2.4)	22 (20.6)

After discharge from hospital, a relapse of PE developed in 2 cases, and in one more case, a relapse of deep vein thrombosis of the lower extremities (i. e., the total frequency of repeated VTE in this period was 3.7%). Within 12 months of hospitalization, a relapse of PE was recorded in 5.6% of cases, and VTE in total — in 6.5%. It is not possible to evaluate the frequency of chronic postthromboembolic pulmonary hypertension, since only 34 of 82 (41.5%) surveyed patients underwent a control echocardiographic examination. At the time of the '12 months' telephone contact, 71 of 82 (86.6%) of the surveyed patients continued intake of anticoagulants; the average period of intake in cases of cancellation/discontinuation of intake was 5.2 months.

At the next stage, the survival rate of patients after PE was analyzed, depending on various factors. Of the fourteen analyzed factors, 11 factors showed themselves as predictors of a fatal outcome *at the hospital stage* (Table 2). The first factor by the RR level with a sufficient margin was not a clinical, but rather an organizational one — 'other than PE diagnosis at the time of hospitalization' (i. e. late diagnosis or under-diagnosis of PE), it increased the risk of death during hospitalization by 16.2

times ($p = 0.001$). The second factor was 'age of patient ≥ 65 years' (RR 10.1; 95% CI 1.3–79.5). Comorbidity also demonstrated high prognostic significance: the presence of atherosclerotic diseases (RR 9.9; 95% CI 2.1–46.5), acute cerebrovascular event (ACVE) and atrial fibrillation (AF) in history (RR 5.3; 95% CI 1.4–20.5 and RR 4.4; 95% CI 1.1–16.9, respectively), chronic kidney disease (CKD; RR 4.7; 95% CI 1.2–18.2), CHF (RR 3.9; 95% CI 1.1–13.9). Factors of the clinical condition of a patient with PE recorded as predictors of death include: hemodynamic instability (RR 7.6; 95% CI 2.1–27.2), respiratory failure (RF; RR 7.2; 95% CI 2.0–25.5) and high risk according to the integral evaluation of the severity and of early death risk (IESEDR; RR 3.2; 95% CI 1.6–6.6).

The number of predictors of death for the period *from discharge to the final follow-up point '12 months'* (duration, Me (Q1–Q3) — 11.5 (11.4–11.5) months) sharply decreased — only the presence of MNP in history was statistically significant (RR 4.4; 95% CI 1.1–14.5; Table 3). Besides, the factors 'age ≥ 65 years' and 'GFR < 60 ml/min $\times 1.73$ m²' were on the border of statistical significance. Thus, in this period, most significant for the development of a lethal outcome were general population predictors.

Table 2. Predictors of Death in Patients with Pulmonary Embolism in Inpatient Stage (n = 107)

Parameters	RR	95% CI	p
S ₁ Q ₃ syndrome	0.03	(0.0; 17.0)	0.28
Malignant neoplasm in history	2.0	(0.5; 7.8)	0.32
Need for diuretics in hospital	3.1	(0.9; 10.9)	0.07
High risk according to integral evaluation of severity and early death risk	3.2	(1.6; 6.6)	0.002
Chronic heart failure	3.9	(1.1; 13.9)	0.004
Atrial fibrillation (in history as well)	4.4	(1.1; 16.9)	0.033
Chronic kidney disease	4.7	(1.2; 18.2)	0.025
Acute cerebrovascular event in history	5.3	(1.4; 20.5)	0.016
Glomerular filtration rate < 60 ml/min x 1.73 m ²	5.6	(1.2; 26.3)	0.03
Respiratory failure with oxygen therapy	7.2	(2.0; 25.5)	0.002
Hemodynamic instability	7.6	(2.1; 27.2)	0.002
Atherosclerotic disease	9.9	(2.1; 46.5)	0.004
Age ≥ 65 years	10.1	(1.3; 79.5)	0.028
Hospitalization with other than pulmonary embolism diagnosis (not pulmonary embolism)	16.2	(2.8; 62.5)	0.001

Notes: CI — confidence interval, RR — relative risk

Hospitalization with the primary diagnosis other than PE, increasing the risk of *hospital death* by 16.2 times (p = 0.001, Table 2), had no effect on the prognosis *at a later stage* (p = 0.39, Table 3), even with a delay of the diagnosis of PE for 7 days or more (RR 1.6; 95% CI 0.4–6.1;

p = 0.53). It should be noted that the cause of the delay of diagnosis: associated with the patient (for example, late turning for help) or with the medical institution (incorrect interpretation of the clinical picture, etc.), was of no significance at the analyzed stage (p > 0.05).

Table 3. Predictors of Death in Patients with Pulmonary Embolism from Discharge to Final Follow-Up Point '12 Months' (n = 97)

Parameters	RR	95% CI	p
Respiratory failure with oxygen therapy ⁵	20.04	(0; 43.5)	0.36
Chronic kidney disease ⁸	0.1	(0; 21.5)	0.61
Presence of S1Q3 syndrome ¹⁴	0.2	(0; 1.5)	0.12
Atrial fibrillation (in history as well) ⁹	1.2	(0.2; 9.1)	0.89
Unstable hemodynamics ⁴	1.4	(0.3; 6.3)	0.69
Atherosclerotic diseases ³	1.8	(0.5; 6.1)	0.35
Hospitalization with a different diagnosis (not pulmonary embolism) ¹	1.9	(0.5; 7.0)	0.39
Need for diuretics in hospital ¹²	2.2	(0.6; 7.5)	0.21
Chronic heart failure ¹⁰	2.7	(0.8; 8.9)	0.1
High risk in integral evaluation of the severity and early death risk ¹¹	3.0	(0.3; 32.8)	0.37
Acute cerebrovascular event in history ⁷	3.1	(0.7; 14.1)	0.15
Glomerular filtration rate < 60 ml/min x 1.73 m ²⁻⁶	3.4	(1.0; 11.5)	0.054
Age ≥ 65 years ²	3.6	(1.0; 13.7)	0.057
Malignant neoplasm in history¹³	4.4	(1.4; 14.5)	0.014

Notes: ¹⁻¹⁴ — the upper indices indicate the rank position of the factor as a predictor of an immediate poor prognosis in Table 2; CI — confidence interval, RR — relative risk

In evaluation of the influence of the analyzed factors on the total 12-month mortality (i. e. *from the moment of admission to hospital to 12 months after hospitalization*)

of patients with PE, the predictors of a poor near-term prognosis were found to preserve their influence in general, but with change in their order (Table 4).

Table 4. Predictors of Death in Patients with Pulmonary Embolism from Moment of Hospitalization to Final Follow-Up Point '12 Months' (n = 107)

Parameters	RR	95% CI	p
Presence of S ¹ Q ³ syndrome ¹⁴	0.1	(0; 0.9)	0.038
Respiratory failure with oxygen therapy ⁵	1.9	(0.7; 4.9)	0.19
Atrial fibrillation (in history as well) ⁹	2.5	(0.8; 7.5)	0.1
Chronic kidney disease ⁸	2.6	(0.8; 8.7)	0.13
Need for diuretics in hospital¹²	2.6	(1.1; 6.1)	0.003
Malignant neoplasm in history¹³	2.9	(1.2; 6.9)	0.02
Chronic heart failure¹⁰	3.2	(1.4; 7.5)	0.008
Unstable hemodynamics⁴	3.3	(1.4; 7.9)	0.008
Acute cerebrovascular event in history⁷	3.6	(1.3; 9.9)	0.013
Atherosclerotic diseases³	3.7	(1.5; 8.8)	0.003
Glomerular filtration rate < 60 ml/min x 1.73 m²,⁶	4.3	(1.7; 11.1)	0.003
Hospitalization with a different diagnosis (not pulmonary embolism)¹	4.5	(1.9; 10.8)	0.001
Age ≥ 65 years²	5.1	(1.7; 15.2)	0.003
High risk on integral evaluation of severity and early death risk¹¹	9.9	(1.2; 79.5)	0.031

Notes: ¹⁻¹⁴ — the upper indices indicate the rank position of the factor as a predictor of a poor near-term prognosis in Table 2; CI — confidence interval, RR — relative risk

With this, the factor 'hospitalization with a different (non-PE) primary diagnosis' moves to the 3rd position (Table 4), but, nevertheless, remains a factor of a poor prognosis in extension of the follow-up period to 12 months from the moment of hospitalization. In this regard, it was reasonable to additionally analyze the factors associated with this predictor of a poor prognosis (Table 5; n = 104 — cohort of patients in whom index PE developed before hospitalization).

The factor 'age ≥ 65 years' ranked second among the predictors of death within 12 months after PE (Table 4). The first factor, having gained sufficient statistical power over a 12-month period, is 'high risk on IESEDR' (Table 4). Its effect on survival of patients with PE within 12 months is shown in Figure 1. Besides, a poor 12-month prognosis has its own predictors — 'the need for loop diuretics' and 'the presence of S1Q3 syndrome on an electrocardiogram (ECG)' (Table 4).

DISCUSSION

The literature data on the near-term and long-term prognosis for patients with past PE demonstrate a fairly high variability of parameters, which is probably

due to different inclusion criteria and changes in the management tactics of this category of patients over the past 30 years. The results of this study (mortality of 9.4% at the stage of inpatient treatment and 19.6% in 12 months) are comparable with the data of both Worcester DTV study (1991; 12% and 19%, respectively [10]; p > 0.05), and the RIETE register (2008; 3-month mortality 8.65% [11]; p > 0.05), EMPEROR (2011; 30-day mortality 5.4% [12]; p > 0.05). In the total cohort (n = 609) of the Russian SIRENA register (2021), hospital mortality also amounted to 9.9% [13], p > 0.05. At the same time, according to the results of FOCUS study (2022; n = 1017), the mortality rate for 24 months was 5 times lower [14] than in our cohort for 12 months, p < 0.001.

On the one hand, this tendency can be explained by objective reasons: differences in inclusion criteria, greater severity of the clinical condition of the cohort analyzed by us [8, 9].

On the other hand, the search for predictors of an unfavorable prognosis demonstrated the leading significance of a *subjective* factor in our cohort — the untimely diagnosis of PE (or no diagnosis during life) 16.2 times increases the risk of hospital death (95% CI 2.8–62.5; p = 0.001). Moreover, this factor preserves its

Table 5. Comparative Characteristics of Patients with Pulmonary Embolism Depending on Diagnosis on Admission (n = 104)

Parameters	Diagnosis on Admission		p
	Pulmonary Embolism	Another	
n	80	24	–
Age, Me (Q1; Q3), years	61 (47; 73)	71 (57; 79)	1,0
Hospitalization in non-working hours, % of n	50.0	75.0	0.036
Evaluation of GENEVA score and/or Wells, % of n	7.5	0	0.33
GENEVA score ¹ , Me (Q1; Q3)	10 (7; 12)	8 (5; 12)	0.19
Well score¹, Me (Q1; Q3)	4 (2; 4)	3 (2; 4)	0.03
Increase in cardiac troponins, % of n	31.3	37.5	0.75
Sinus rhythm on electrocardiogram, % of n	91.3	62.5	0.002
Atrial fibrillation on electrocardiogram, % of n	7.5	37.5	< 0.001
S1Q3 syndrome on electrocardiogram, % of n	28.8	8.3	0.055
Dilatation of the right ventricle on echocardiography, % of n	73.8	62.5	0.43
Elevated pressure on tricuspid valve on echocardiography, % of n	81.3	87.5	0.76
Deep vein thrombosis of lower extremities in duplex ultrasound, % of n	78.8	79.2	1.0
Computed tomography-angiography of pulmonary artery, % of n	98.8	87.5	0.038
Volume of damage to pulmonary artery system, Me (Q1; Q3), %	72 (45; 88)	70 (50; 78)	0.92
'Symptom-hospitalization' period < 7 days, % of n	56.3	62.5	0.76
'Hospitalization-diagnosis' period (for cases of lifetime identification of Pulmonary Embolism, n = 100), Me (Q1; Q3), hours	0	18 (11; 43)	< 0.001
Pulmonary Embolism Severity Index score ¹ , M ± SD	96.3 ± 30.8	118.2 ± 44.9	0.095
Indications for thrombolytic therapy, n1 (% of n)	14 (17.5)	9 (45.8)	0.01
Thrombolytic therapy conducted for indications, n2 (% of n1)	10 (71.4)	5 (55.6)	0.66
Period from time of hospitalization to administration of thrombolytic agent, Me (Q1; Q3), hours	2 (1; 6)	17.5 (7; 31)	0.004

Notes: ¹ — calculated retrospectively when performing the register

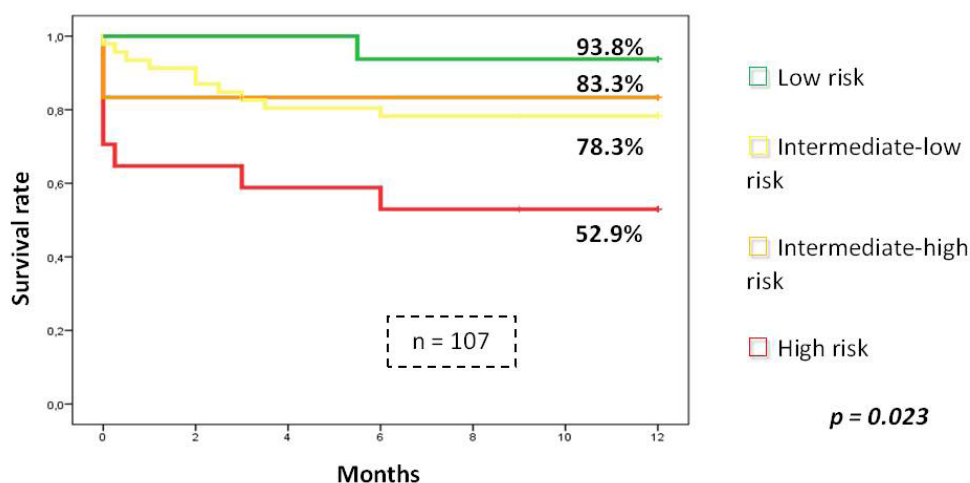


Fig. 1. Survival rate of patients with PE from the moment of hospitalization within 12 months depending on initially determined category of early death risk.

influence on the prognosis for a longer period — within 12 months (RR 4.5; 95% CI 1.9–10.8; $p = 0.001$).

It was found that patients with other than PE primary diagnosis were 1.5 times more likely to be admitted to the hospital in 'unlucky' hours (after the end of the working day / at night, on weekends). The frequency of determining PE on the clinical probability scales in the cohort as a whole was extremely low (9.4%), and the retrospectively calculated on the Wells scale probability for patients with an unspecified diagnosis at the time of hospitalization was lower (3 points vs. 4, $p = 0.03$). Also, patients hospitalized with a diagnosis other than PE were 5 times more likely (37.5% vs. 7.5%, $p < 0.001$) to have AF at the time of hospitalization (which was probably regarded as a *sufficient* cause for worsening of the patient's condition). With that, the coverage of patients of this group with contrast CT of PA was 11.3% lower ($p = 0.038$), and the time before the start of thrombolytic therapy (TLT) in its administration was 15.5 hours longer (17.5 hours vs. 2 hours, $p = 0.004$). It is important to note that patients hospitalized with a different (non-PE) diagnosis were 2.6 times more likely (45.8% vs. 17.5%, $p = 0.01$) to have indications for TLT (i. e., had a more severe condition).

The relevance of the problem of late diagnosis of PE in routine clinical practice is confirmed by the results of meta-analysis by R. van Maanen, et al. (2022), according to which the average delay in diagnosis is 6.3 days [15].

Another 'finding' worthy of discussion is the prognostic significance of the IESEDR. Initially, IESEDR was developed as a tool for evaluation of early mortality on the basis of the PESI scale (Pulmonary Embolism Severity Index), which determines the risk of 30-day mortality [16], but the authors considered it reasonable to analyze the validity of the prognostic significance of IESEDR for a longer period — 12 months.

As a result, from the point of view of prognostic value *during hospitalization*, this criterion yielded to a number of factors, including non-identification of PE at the time of hospitalization, age ≥ 65 years and comorbid pathology (diseases of atherosclerotic genesis, ACVE, CKD, AF, CHF); it did not expectedly demonstrate prognostic value *after discharge* (here, general population factors turned out to be more important). However, when these two periods were combined, it was the IESEDR factor that convincingly came out on top. In other words, the *integral severity of the patient's condition during the acute period of PE determines his prognosis not only during hospitalization, but also during the subsequent 12 months*.

The greatest prognostic stability was demonstrated by 'age ≥ 65 years' factor: in all the three subanalyses, it ranked second. A high prognostic value of age can be explained by the accumulation of the burden of concomitant pathology, which leads, on the one hand, to difficulties in differential diagnosis, and, on the other, to greater severity of the patient's condition and limitation

of diagnostic and therapeutic measures [8, 13, 17]. Our data on the influence of age ≥ 65 years on the prognosis are consistent with the results of other studies. Thus, according to SWINTER register (2012), mortality in elderly patients was 6.6% versus 3.2% among younger patients [18]. N. R. Friz, et al. (2020) recorded 12-month mortality rate among elderly patients 26.5% [19].

CONCLUSION

Thus, in routine clinical practice, the survival rate of patients with pulmonary embolism during the next 12 months remains low (77.1%), and most of the established predictors of death are unmodifiable.

The criterion 'age ≥ 65 years' demonstrated the highest stability for 12 months as a factor of unfavorable prognosis (it ranked second in each of the three subanalyses conducted), combining both the burden of comorbid pathology and reduction of the functional and compensatory reserves of the body.

The integral severity of the patient's condition during the acute period of pulmonary embolism, originally developed to determine only the nearest (30-day) prognosis, in our cohort demonstrated its prognostic value not only during hospitalization, but also during the subsequent 12 months.

One of the most significant factors for the unfavorable prognosis was a subjective factor associated with the quality of medical care: untimely diagnosis or under-diagnosis of pulmonary embolism 16.2 times increases the risk of death during hospitalization ($p = 0.001$), and 4.5 times during the subsequent 12-month period ($p = 0.001$). This fact dictates the need for further study of problems concerning the quality of diagnosis of pulmonary embolism, as well as the effective introduction of information about the peculiarities of its modern clinical picture into the educational process in order to increase the diagnostic alertness of doctors of any specialties.

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Вклад авторов: Тереховская Ю. В. — статистическая обработка данных, анализ результатов и литературных источников, написание текста; Ахмедова Н. Э. нзыы, Леоненко Д. И. — сбор конечных точек, заполнение индивидуальных регистрационных карт пациентов;

Никулина Н. Н. — концепция и дизайн исследования, редактирование и окончательное утверждение текста. Все авторы подтверждают соответствие своего авторства международным критериям ICMJE (все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией).

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ОБ АВТОРАХ

***Тереховская Юлия Викторовна;**

ORCID: <https://orcid.org/0000-0002-9537-1618>;

eLibrary SPIN: 4980-9875; e-mail: shera_11.11@mail.ru

Ахмедова Назлы Эльсевар кызы;

ORCID: <https://orcid.org/0000-0002-4050-7389>;

e-mail: ahmedova_an@mail.ru

Леоненко Дарья Игоревна;

ORCID: <https://orcid.org/0000-0002-3068-3127>;

e-mail: ossslacrimale@mail.ru

Никulina Наталья Николаевна, д.м.н., доцент;

ORCID: <https://orcid.org/0000-0001-8593-3173>;

eLibrary SPIN: 9486-1801; e-mail: natalia.nikulina@mail.ru

AUTHOR'S INFO

***Yuliya V. Terekhovskaya;**

ORCID: <https://orcid.org/0000-0002-9537-1618>;

eLibrary SPIN: 4980-9875; e-mail: shera_11.11@mail.ru

Nazly E. kyzy Akhmedova;

ORCID: <https://orcid.org/0000-0002-4050-7389>;

e-mail: ahmedova_an@mail.ru

Dar'ya I. Leonenko;

ORCID: <https://orcid.org/0000-0002-3068-3127>;

e-mail: ossslacrimale@mail.ru

Natal'ya N. Nikulina, MD, Dr. Sci. (Med.), Associate Professor;

ORCID: <https://orcid.org/0000-0001-8593-3173>;

eLibrary SPIN: 9486-1801; e-mail: natalia.nikulina@mail.ru

* Автор, ответственный за переписку / Corresponding author