Original paper

Does COVID-19 determine short- and long-term prognosis in patients with pulmonary embolism? Analysis of data from a pulmonology centre in Świętokrzyskie, Poland

Czy COVID-19 determinuje krótko- i długoterminowe rokowanie u pacjentów z zatorowością płucną? Analiza danych z ośrodka pulmonologicznego w województwie świętokrzyskim

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Key words: pulmonary embolism, long-term outcome, COVID-19, SARS-CoV2.

Słowa kluczowe: zatorowość płucna, rokowanie długoterminowe, COVID-19, SARS-CoV2.

Abstract

Introduction: SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection has been associated with thrombotic complications, the pathophysiological mechanism of which is complex.
Aim of the research: To analyse factors influencing the prognosis of patients with pulmonary embolism and COVID-19 (coronavirus disease 2019).
Material and methods: A retrospective study was conducted on a group of 70 patients with pulmonary embolism and concomitant respiratory system infection. The patients were divided into those with a negative test result for the presence of the SARS-CoV-2 (n = 25) and those with a positive result (n = 45). Clinical and imaging characteristics of both groups were presented. Univariate and multivariable logistic regression analyses were performed to identify predictors of 30-day and 1-year mortality.
Results: The study revealed that short-term survival did not differ between the COVID (+) and COVID-19 (–) groups (40 (88.9%) vs. 18 (72.0%), p = 0.1), while long-term survival was higher in the COVID-19 (+) group compared to the COVID-19 (–) group (38 (84.4%) vs. 10 (40.0%), p = 0.0001). Factors influencing short-term survival were lymphocyte levels and left-sided intraparenchymal changes on imaging, while long-term survival was influenced by platelet count, INR, respiratory failure, oxygen saturation, fibrous-striated changes on imaging, and subpleural location. Both short- and long-term survival were determined by higher levels of erythrocytes, haemoglobin, longer prothrombin time, and the intensity of oxygen therapy. The only independent predictor of long-term mortality was concomitant neoplastic disease (OR = 29.03 (1.32–640.2); p = 0.03).
Conclusions: COVID-19 does not independently affect long-term survival in patients with pulmonary embolism.

Streszczenie

Wprowadzenie: Zakażenie SARS-CoV-2 (*severe acute respiratory syndrome coronavirus 2*) wiąże się z powikłaniami zakrzepowymi, których mechanizm patofizjologiczny jest złożony.
Cel pracy: Analiza czynników wpływających na rokowanie pacjentów z zatorowością płucną i COVID-19 (*coronavirus disease 2019*).
Materiał i metody: Retrospektywne badanie przeprowadzono w grupie 70 pacjentów z zatorowością płucną i współistniejącą infekcją układu oddechowego. Pacjentów podzielono na tych z ujemnym wynikiem testu na obecność wirusa SARS-CoV-2 (n = 25) i tych z wynikiem dodatnim (n = 45). Przedstawiono charakterystykę kliniczną i obrazową obu grup. Przeprowadzono jednoczynnikowe i wieloczynnikowe analizy regresji logistycznej w celu zidentyfikowania predyktorów 30-dniowej i 1-rocznej śmiertelności.
Wyniki: W badaniu wykazano, że krótkoterminowe przeżycie nie różniło się między grupami COVID-19 (+) i COVID-19 (–) (40 (88,9%) *vs* 18 (72,0%), p = 0,1), podczas gdy długoterminowe przeżycie było wyższe w grupie COVID-19 (+) w porównaniu z grupą COVID-19 (–) (38 (84,4%) *vs* 10 (40,0%), p = 0,0001). Poziomy limfocytów i lewostronne zmiany śródmiąższowe

w obrazowaniu wpływały na przeżycie krótkoterminowe, podczas gdy liczba płytek krwi, INR, niewydolność oddechowa, wysycenie tlenem, zmiany włóknisto-pręcikowe w obrazowaniu i lokalizacja podopłucnowa – na przeżycie długoterminowe. Zarówno krótko-, jak i długoterminowe przeżycie zależało od wyższego poziomu erytrocytów, hemoglobiny, dłuższego czasu protrombinowego i intensywności tlenoterapii. Jedynym niezależnym czynnikiem predykcyjnym długoterminowej śmiertelności była współistniejąca choroba nowotworowa (OR = 29,03 (1,32–640,2); p = 0,03).
Wnioski: COVID-19 nie wpływa niezależnie na długoterminowe przeżycie u pacjentów z zatorowością płucną.

Introduction

The global public health emergency caused by coronavirus disease 2019 (COVID-19) was officially lifted in May 2023. However, the SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) persisted in the population with a high potential for mutation. During the pandemic, it was established that the virus increased the risk of cardiovascular complications and coagulation disorders during infection [1, 2]. Thromboembolic complications were found to be more common not only in the acute phase but also after the first 30 days of infection, leading to higher mortality and poor outcomes [3]. Indirectly, coagulation disorders occurring not only in the acute phase of infection may be indicated by better clinical outcomes in high-risk patients hospitalised for COVID-19 who received rivaroxaban prophylaxis for 35 days [4]. The pathophysiology of haemostasis disorders in COVID-19 infection is associated with the disruption of cellular response, including neutrophils and monocytes/macrophages, endothelial inflammation, cytokine release syndrome, and dysregulation of fibrinolysis [5]. Such a mechanism may contribute to vessel occlusion by thrombotic material, but also promote the occurrence of in situ pulmonary thrombosis [5]. Simultaneously, the association of inflammatory state with the risk of thromboembolic disease was reported even before the onset of the pandemic [6, 7]. Studies have also established that bacterial pneumonia is a risk factor for the development of pulmonary embolism during its course [8].

Aim of the research

The aim of our study was to determine the factors influencing the course and prognosis of patients with pulmonary embolism and concomitant COVID-19 infection in relation to a group of patients with pulmonary embolism and respiratory tract infection of aetiology other than COVID-19.

Material and methods

The study group consisted of patients treated in the pulmonary, internal medicine, and intensive care units of the Regional Specialist Hospital in Czerwona Góra, located in the Świętokrzyskie Voivodeship, Poland. According to data from the Central Statistical Office, in the Świętokrzyskie Voivodeship in the year 2021, 5815 individuals were treated for lung diseases in pulmonary departments, with a total of 208 pulmonary beds [9]. The majority, 151 beds, were allocated to the hospital in Czerwona Góra (72.59%), highlighting its predominant role in the diagnosis and treatment of respiratory diseases. The hospital is considered the largest pulmonary healthcare facility in the Świętokrzyskie Voivodeship, diagnosing 80% of patients with lung diseases (including cancer), and showing a significant concentration of services related to interstitial lung disease. According to the Ministry of Health data from 2014, 81% of patients with this diagnosis were hospitalised in this facility [10]. Figure 1 presents a map of pulmonary centres in the Świętokrzyskie Voivodeship.

The analysed group comprised patients diagnosed with pulmonary embolism and respiratory system infection from 1 January 2020 to 1 October 2022, identified using ICD-10 codes. The group consisted of 70 patients, further divided into those with a negative test result for the presence of the SARS-CoV-2 (n = 25) and those with a positive result (n = 45). Patients with positive results on antigenic and/or molecular RT-PCR tests were considered COVID-19 (+). Patients were considered COVID-19 (–) if they had a negative result on antigen and/or RT-PCR testing for SARS-CoV-2 infection and a negative test for the presence of influenza A/B virus antigens, and presented clinical features of respiratory tract infection upon admission such as cough, fever, malaise, or dyspnoea, along with possible signs of infectious background evident on radiographic examination. The study compared 2 groups of patients: those with pulmonary embolism without confirmed COVID-19 infection (–) and those with pul-

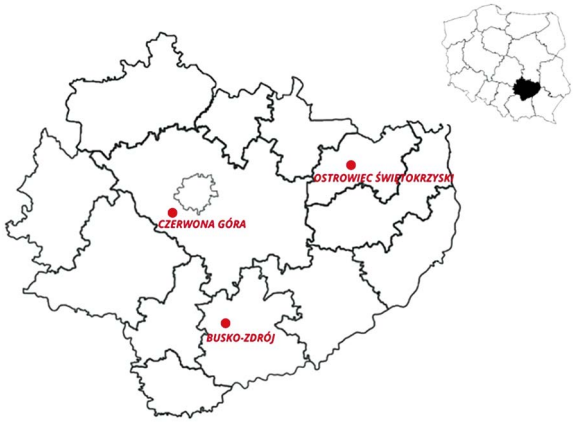

Figure 1. Map showing the location of pulmonology centres in the Świętokrzyskie region (Poland)

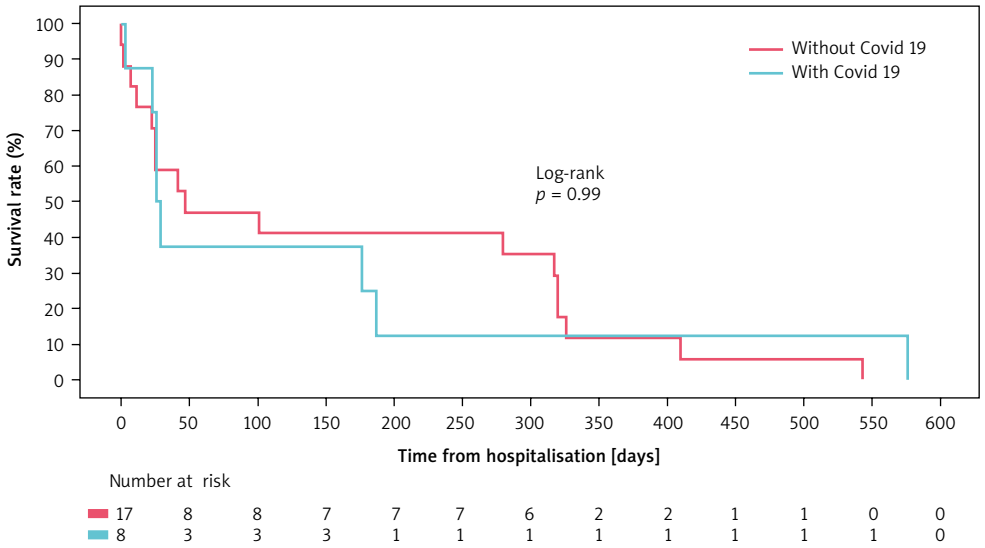

Figure 2. Long-term survival of patients with pulmonary embolism grouped by COVID-19 status

monary embolism with confirmed COVID-19 infection (+). Antithrombotic treatment was conducted according to generally accepted principles for managing pulmonary embolism in both patient groups. During hospitalisation, mainly low-molecular-weight heparins were administered at a dose adjusted for body weight. No patient received fibrinolytic therapy. The study focused on factors influencing the course of pulmonary embolism in these 2 groups, as well as their 30-day and 1-year survival post-hospitalisation.

Statistical analysis

Continuous data were described by means and standard deviations. Categorical data were summarised by frequencies and percentages. Group comparisons were performed using the χ^2 or Fisher exact test for categorical variables, and the *t*-test for continuous normally distributed variables. Normality of distributions was checked by the Shapiro-Wilk test. Univariable and multivariable analyses according to factors affecting the 30- or 365-day mortality were done with logistic regression models. For these univariable and multivariable analyses, odds ratios (OR) with 95% confidence intervals (95% CI) were calculated. Multivariable logistic regression analysis was performed with the stepwise forward selection method. The Kaplan-Meier method was applied for creating survival curves, and the log-rank test was used to compare survival depending on COVID-19 status. A 2-tailed p-value < 0.05 was considered statistically significant. All statistical analyses were performed using the R software package version 4.0.3.

Results

The study included 70 individuals with pulmonary embolism and respiratory system infection, among whom 45 were diagnosed with SARS-CoV-2 infection, with an average age of 63.9 (16.3) years upon hospital admission. In the COVID-19 (+) group, compared to the COVID-19 (–) group, high leukocytosis was more common, while hypercapnia and heart failure were less frequent. Additionally, the COVID-19 (+) group exhibited lower one-year mortality, but Kaplan-Meier survival curves showed no differences in survival between COVID-19 (+) and COVID-19 (–) patients diagnosed with pulmonary embolism (Figure 2). The baseline clinical characteristics of the study participants are presented in Table 1. Clot localisation in the main pulmonary arteries and air bronchograms were significantly more common in the COVID-19 (–) group. On the other hand, subpleural localisation of interstitial changes, involvement of lower lobes, bilateral parenchymal changes, and a predominance of fibrous-striated interstitial changes were significantly more common in the pulmonary embolism with COVID-19 (+) group (Table 2). Tables 3 and 4 present baseline characteristics for 30-day and 365-day survival. Short-term survivors had a lower incidence of respiratory failure, lower INR (international normalised ratio), lymphocyte, red blood cell and haemoglobin levels, and parenchymal lesions were less often localised to the left lung. Long-term survivors had less frequent respiratory failure and had higher oxygen saturation, lower oxygen flow during oxygen therapy, lower INR, higher levels of platelets, red blood cells, and haemoglobin, higher numbers of fibrous strips and subpleural peripheral lesions, and less frequent malignancy. Logistic regression analysis showed that higher lymphocyte levels contributed to reducing the risk of death in short-term observation, while in long-term observation, a higher platelet count and higher saturation values were associated with a lower risk of death. A higher level of erythro-

Table 1. Baseline characteristics of clinical parameters of patients with pulmonary embolism according to COVID-19 status

Variable		Total	COVID-19 (+)	COVID-19 (–)	*P*-value
Age [years]		63.9 (16.3)	63.1 (15.6)	65.2 (17.6)	0.60
Gender male, *n* (%)		58 (82.9)	37 (82.2)	21 (84.0)	0.99
Respiratory failure*, *n* (%)		53 (75.7)	32 (71.1)	21 (84.0)	0.23
Oxygen therapy during gas analysis [l/min]		7.7 (15.0)	8.0 (15.5)	7.1 (14.4)	0.72
Oxygen saturation [< 95%]		52 (74.3%)	30 (66.7%)	52 (74.3%)	0.05
Partial pressure of O_2 [mm Hg]#	< 65	44 (62.9%)	24 (53.3%)	20 (80.0%)	0.06
	65–95	23 (32.9%)	19 (42.2%)	4 (16.0%)	
	> 95	3 (4.3%)	2 (4.4%)	1 (4.0%)	
Partial pressure of O_2 [mm Hg]#		62.2 (13.4)	64.3 (12.7)	58.2 (14.0)	0.06
Partial pressure of CO_2 [mm Hg]#	< 32	16 (22.9%)	10 (22.2%)	6 (24.0%)	0.03
	32–48	50 (71.4%)	35 (77.8%)	15 (60.0%)	
	> 48	4 (5.7%)	0 (0.0%)	4 (16.0%)	
Partial pressure of CO_2 [mm Hg]#		36.3 (8.6)	34.7 (5.2)	39.0 (12.3)	0.38
INR		1.3 (0.2)	1.3 (0.1)	1.4 (0.3)	0.1
Platelets [g/l]	< 150	11 (15.7%)	6 (13.3%)	5 (20.0%)	0.7
	150–400	48 (68.6%)	31 (68.9%)	17 (68.0%)	
	> 400	11 (15.7%)	8 (17.8%)	3 (12.0%)	
Platelets [g/l]		278.9(150.5)	287.1(133.4)	264.2(179.4)	0.25
White blood cells [g/l]	< 4	2 (2.9%)	2 (4.4%)	0 (0.0%)	0.04
	4–10	32 (45.7%)	16 (35.6%)	16 (64.0%)	
	> 10	36 (51.4%)	27 (60.0%)	9 (36.0%)	
White blood cells [g/l]		26.6 (120.3)	33.2 (149.3)	14.7 (22.4)	0.37
Lymphocytes [g/l]		1.5 (0.9)	1.3 (0.7)	1.8 (1.2)	0.13
Red blood cells [T/l])		4.5 (1.6)	4.7 (1.9)	4.2 (0.7)	0.22
Haemoglobin [g/dl]		13.2 (2.3)	13.6 (1.9)	13.2 (2.3)	0.07
Previous PCI or CABG, *n* (%)		5 (7.1)	1 (2.2)	4 (16.0)	0.05
Heart failure, *n* (%)		17 (24.3)	6 (13.3)	11 (44.0)	0.004
Diabetes, *n* (%)		11 (15.7)	7 (15.6)	4 (16.0)	0.99
Arterial hypertension, *n* (%)		32 (45.7)	20 (44.4)	12 (48.0)	0.77
Obesity, *n* (%)		13 (18.6)	9 (20.0)	4 (16.0)	0.76
Neoplastic disease, *n* (%)		11 (15.9)	6 (13.3)	5 (20.8)	0.5
Survival 30 days from admission, *n* (%)		58 (82.9)	40 (88.9)	18 (72.0)	0.1
Survival 12 months from admission, *n* (%)		48 (68.6)	38 (84.4)	10 (40.0)	0.0001

**Respiratory failure according to Campbell: type I – partial, hypoxaemic, type II – complete, hypoxaemic, and hypercapnic. #Gasometry test was performed using capillary blood. CABG – coronary artery bypass grafting, COVID-19 – coronavirus disease 2019, INR – international normalised ratio, PCI – percutaneous coronary intervention.*

cytes and haemoglobin significantly reduced the risk of death in patients with pulmonary embolism, in both 30-day and one-year observations post-hospitalisation. A higher INR decreased this risk in long-term observation. Respiratory failure, both type I and II according to Campbell, increased the risk of death in long-term observation, while more intensive oxygen therapy significantly increased the risk of death in both 30-day and 12-month observations from hospital admission. Regarding changes in imaging studies,

Table 2. Baseline characteristics of imaging findings in patients with pulmonary embolism according to COVID-19 status

Variable	Total	COVID-19 (+)	COVID-19 (–)	*P*-value
Thrombus in large pulmonary arteries*	25 (41.7%)	9 (23.7%)	16 (72.7%)	< 0.001
Thrombus in segmental and/or subsegmental arteries	56 (93.3%)	37 (97.4%)	19 (86.4%)	0.14
Thrombus in arteries of both lungs	21 (35.0%)	16 (42.1%)	5 (22.7%)	0.1
Thrombus in arteries of left lung	19 (31.7%)	11 (28.9%)	8 (36.4%)	0.55
Thrombus in arteries of right lung	19 (31.7%)	11 (28.9%)	8 (36.4%)	0.55
Parenchymal lesions located in both lungs	44 (81.5%)	30 (93.8%)	14 (63.6%)	0.01
Parenchymal lesions located in the left lung	5 (9.3%)	1 (3.1%)	4 (18.2%)	0.15
Parenchymal lesions located in the right lung	5 (9.3%)	1 (3.1%)	4 (18.2%)	0.15
Parenchymal lesions – fibrous stripes	25 (46.3%)	19 (59.4%)	6 (27.3%)	0.02
Ground-glass opacities	38 (70.4%)	23 (71.9%)	15 (68.2%)	0.77
Air bronchogram	10 (18.5%)	1 (3.1%)	9 (40.9%)	< 0.001
Parenchymal lesions located subpleural	29 (53.7%)	26 (81.2%)	3 (13.6%)	< 0.001
Parenchymal lesions located in lower lobes	43 (79.6%)	29 (90.6%)	14 (63.6%)	0.04

**Pulmonary trunk, right and left pulmonary arteries, lobar arteries.*

Table 3. Baseline characteristics according to 30-day survival

Variable		Survived (*n* = 58)	Dead (*n* = 12)	Total (*n* = 70)	*P*-value
Age [years]		62.8 (16.4)	68.8 (15.5)	63.9 (16.3)	0.35
Male gender, *n* (%)		50 (86.2)	8 (66.7)	58 (82.9)	0.2
COVID-19 (+), *n* (%)		40 (69.0)	5 (41.7)	45 (64.3)	0.1
COVID-19 (–), *n* (%)		18 (31.0)	7 (58.3)	25 (35.7)	
Respiratory failure*, *n* (%)		41 (70.7)	12 (100.0)	53 (75.7)	0.03
Oxygen saturation# (%)		89.8 (6.9)	88.5 (4.9)	89.6 (6.6)	0.17
Oxygen therapy during gas analysis [l/min]		5.6 (11.9)	17.7 (23.6)	7.7 (15.0)	0.05
Partial pressure of O_2 [mm Hg]#		62.1 (12.7)	62.5 (16.8)	62.2 (13.4)	0.55
Partial pressure of CO_2 [mm Hg]#		35.3 (5.8)	41.1 (16.2)	36.3 (8.6)	0.29
INR		1.3 (0.1)	1.5 (0.4)	1.3 (0.2)	0.04
Platelets, *n* (%)	< 150 g/l	8 (13.8)	3 (25.0)	11 (15.7)	0.63
	150–400 g/l	40 (69.0)	8 (66.7)	48 (68.6)	
	> 400 g/l	10 (17.2)	1 (8.3)	11 (15.7)	
Platelets [g/l]		280.9(133.8)	269.2(222.1)	278.9(150.5)	0.26
White blood cells [g/l]		30.0 (132.1)	10.2 (4.7)	26.6 (120.3)	0.51
Lymphocytes [g/l]		1.6 (0.9)	0.9 (0.5)	1.5 (0.9)	0.01
Red blood cells [T/l]		4.6 (1.7)	3.9 (0.5)	4.5 (1.6)	0.01
Haemoglobin [g/dl]		13.5 (2.3)	11.9 (1.6)	13.2 (2.3)	0.01
In- hospital mortality, *n* (%)		0 (0.0)	8 (66.7)	8 (11.4)	N/A
Neoplastic disease		9 (15.8)	2 (16.7)	11 (15.9)	1
Parenchymal lesions located in the both lungs		40 (85.1)	4 (57.1)	44 (81.5)	0.11
Parenchymal lesions located in the left lung		2 (4.3)	3 (42.9)	5 (9.3)	0.01
Parenchymal lesions located in the right lung		5 (10.6)	0 (0.0)	5 (9.3)	1

**Respiratory failure according to Campbell: type I – partial, hypoxaemic, type II – complete, hypoxaemic, and hypercapnic. #Gasometry test was performed using capillary blood. COVID-19 – coronavirus disease 2019, INR – international normalised ratio.*

Table 4. Baseline characteristics according to 365-day survival

Variable		Survived (*n* = 48)	Dead (*n* = 22)	Total (*n* = 70)	*P*-value
Age [years]		62.2 (16.9)	67.6 (14.5)	63.9 (16.3)	0.34
Gender, male, *n* (%)		40 (83.3)	18 (81.8)	58 (82.9)	1
COVID-19 (+), *n* (%)		38 (79.2)	7 (31.8)	45 (64.3)	< 0.001
COVID-19 (–), *n* (%)		10 (20.8)	15 (68.2)	25 (35.7)	
Respiratory failure*, *n* (%)		32 (66.7)	21 (95.5)	53 (75.7)	0.01
Oxygen saturation# (%)		91.2 (4.0)	86.0 (9.3)	89.6 (6.6)	0.02
Oxygen therapy during gas analysis [l/min]		4.5 (8.8)	15.5 (22.7)	7.7 (15.0)	0.03
Partial pressure of O_2 [mm Hg]#		63.1 (10.1)	60.0 (18.7)	62.2 (13.4)	0.07
Partial pressure of CO_2 [mm Hg]#		35.1 (5.6)	38.9 (12.8)	36.3 (8.6)	0.5
INR		1.2 (0.1)	1.4 (0.3)	1.3 (0.2)	0.002
Platelets (*n*, %)	< 150 g/l	3 (6.2)	8 (36.4)	11 (15.7)	0.01
	150–400 g/l	36 (75.0)	12 (54.5)	48 (68.6)	
	> 400 g/l	9 (18.8)	2 (9.1)	11 (15.7)	
Platelets [g/l]		297.9 (128.3)	237.4 (187.1)	278.9 (150.5)	0.02
White blood cells [g/l]		31.4 (144.6)	16.0 (23.9)	26.6 (120.3)	0.94
Lymphocytes [g/l]		1.5 (0.7)	1.4 (1.2)	1.5 (0.9)	0.08
Red blood cells [T/l]		4.7 (1.8)	4.0 (0.6)	4.5 (1.6)	0.01
Haemoglobin [g/dl]		13.8 (2.0)	12.0 (2.5)	13.2 (2.3)	0.002
In-hospital mortality		0 (0.0%)	8 (36.4%)	8 (11.4%)	N/A
Neoplastic disease		4 (8.3%)	7 (33.3%)	11 (15.9%)	0.03
Parenchymal lesions – fibrous stripes		21 (55.3%)	4 (25.0%)	25 (46.3%)	0.04
Parenchymal lesions located subpleural, peripheral parts		24 (63.2%)	5 (31.2%)	29 (53.7%)	0.03

**Respiratory failure according to Campbell: type I – partial, hypoxaemic, type II – complete, hypoxaemic, and hypercapnic. #Gasometry test was performed using capillary blood. COVID-19 – coronavirus disease 2019, INR – international normalised ratio.*

left-sided intraparenchymal changes were associated with an increased risk of death in short-term observation, while subpleural changes and fibrous-striated changes significantly reduced the risk of death in long-term observation. COVID-19 infection did not affect the mortality in patients with pulmonary embolism and concurrent respiratory system infection in the 30-day observation from the day of hospital admission. In long-term observation (12 months), COVID-19 infection significantly reduced the risk of death compared to the control group. Concomitant cancer was the only independent factor affecting mortality in long-term follow-up (Tables 5, 6).

Discussion

Our analysis revealed that among patients with pulmonary embolism and COVID-19 infection, there was no significantly higher mortality observed within 30 days of admission compared to the control group. However, during long-term observation, COVID-19 infection significantly reduced the risk of death compared to the control group. This intriguing observation may stem from distinct mechanisms contributing to coagulation disorders in the context of concomitant COVID-19 infection. The divergence might not only concern the acute phase of coagulopathy but also the convalescent period. Agudo *et al.* retrospectively analysed patients with thrombotic complications and COVID-19, observing them for at least 6 months from diagnosis to assess vascular reperfusion and the potential for discontinuation of anticoagulant therapy. Based on CT angiography, they found only 1 patient without complete reperfusion after 6 months of anticoagulant treatment, and no cases of recurrent thrombotic events were reported [11]. These observations may explain the results of our study, in which the lower mortality in the group of patients with pulmonary embolism and concomitant SARS-CoV-2 infection could be attributed to the resolution of inflammation and withdrawal of thrombotic-embolic changes. Another significant aspect could

Table 5. Factors affecting 30-day mortality in patients with pulmonary embolism

Variable	OR	95% CI	*P*-value
Age [years]	1.03	0.98–1.07	0.25
Gender, male	0.32	0.08–1.32	0.11
COVID-19	0.32	0.32	0.08
Respiratory failure*		N/A	
Oxygen saturation# [per 1%]	0.97	0.89–1.06	0.52
Partial pressure of O_2# [per 1 mm Hg]	1	0.96–1.05	0.92
Partial pressure of CO_2# [per 1 mm Hg]	1.07	0.99–1.16	0.09
Oxygen therapy during gas analysis [l/min]	1.04	1–1.08	0.03
INR per 1 unit	1.64	0.97–2.78	0.06
White blood cells	0.96	0.84–1.1	0.59
Lymphocytes	0.16	0.03–0.77	0.03
Red blood cells	0.31	0.11–0.83	0.02
Haemoglobin	0.76	0.58–0.99	0.04
Platelets [150–400 g/l vs. < 150 g/l]	0.53	0.12–2.46	0.42
Diabetes	3.64	0.87–15.33	0.08
Hypercholesterolaemia	0.48	0.1–2.44	0.38
Hypertension	1.23	0.35–4.27	0.74
Obesity	0.35	0.04–2.97	0.34
Neoplastic disease	1.07	0.2–5.71	0.74
Parenchymal lesions located in both lungs	0.23	0.04–1.28	0.09
Parenchymal lesions located in the left lung	16.87	2.15–132.51	0.01
Parenchymal lesions located in the right lung		N/A	
Parenchymal lesions – fibrous stripes		N/A	
Parenchymal lesions located subpleural, peripheral parts	0.61	0.12–3.01	0.54

**Respiratory failure according to Campbell: type I – partial, hypoxaemic, type II – complete, hypoxaemic, and hypercapnic; #Gasometry test was performed using capillary blood. ¥Due to the lack of a sufficient number of events, multivariable logistic regression was not performed for short-term survival. COVID-19 – coronavirus disease 2019, INR – international normalised ratio.*

be the selection of patients included in our analysis. Safiriyu *et al.* determined that in-hospital mortality risk was increased in patients with concurrent pulmonary embolism and COVID-19 (adjusted odds ratio [aOR]: 1.62; 95% CI: 1.17–2.24; $p = 0.004$) [12]. Additionally, a higher percentage of patients of African and Latino origin was observed in the study group. Similar conclusions were supported by Martin *et al.*, demonstrating the impact of racial and ethnic differences on deaths due to pulmonary embolism and accompanying SARS-CoV-2 infection [13]. There was an almost threefold higher rate among Native American/Alaskan Native individuals and non-Latino African Americans, and nearly twofold higher rate among Latinos. The convergence of these data, along with the fact that according to the 2021 National Census in our country, 97.7% of the total population identified as ethnically Polish [14], provides a basis for asserting that the studied group, ethnically homogeneous, may have influenced the final study outcome.

The association between cancer and thrombotic events has long been recognised, with cancer being an independent risk factor for mortality related to pulmonary embolism [15]. Our analysis demonstrated that oncological disease was an independent factor influencing increased mortality risk in patients with pulmonary embolism and respiratory system infection with COVID-19, both in positive and negative cases, during the 12-month observation period (OR = 29.03 (1.32–640.2); $p = 0.03$). Yousaf *et al.* did not confirm the impact of pulmonary embolism on mortality in COVID-19-positive patients, nor did they find an association between pulmonary embolism and coexisting diseases included in the study [16].

Table 6. Factors affecting 12-month mortality in patients with pulmonary embolism

Variable	Univariable			Multivariable		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Age [years]	1.02	0.99–1.06	0.2		N/A	
Gender, male	0.9	0.24–3.38	0.9		N/A	
COVID-19	0.12	0.04–0.38	< 0.001		N/A	
Respiratory failure*	10.5	1.29–85.22	0.03		N/A	
Oxygen saturation [per 1%]#	0.87	0.78–0.96	0.01		N/A	
Partial pressure of O_2 [per 1 mm Hg]#	0.98	0.94–1.02	0.36		N/A	
Partial pressure of CO_2 [per 1 mm Hg]#	1.06	0.98–1.14	0.13		N/A	
Oxygen therapy during gas analysis [l/min]	1.05	1.01–1.09	0.02		N/A	
INR per 1 unit	2.74	1.26–5.94	0.01		N/A	
White blood cells	1	0.99–1.01	0.65		N/A	
Lymphocytes	0.77	0.39–1.53	0.46		N/A	
Red blood cells	0.35	0.16–0.8	0.01		N/A	
Haemoglobin	0.68	0.52–0.89	0.01	0.62	0.37–1.04	0.07
Platelets [150–400 g/l vs. < 150 g/l]	0.13	0.03–0.55	0.01	0.034	0.001–1.36	0.07
Diabetes	3.22	0.86–12.05	0.08		N/A	
Hypercholesterolaemia	1.4	0.46–4.25	0.55		N/A	
Hypertension	2.2	0.79–6.16	0.13		N/A	
Obesity	0.6	0.15–2.44	0.48		N/A	
Neoplastic disease	5.5	1.4–21.6	0.02	29.03	1.32–640.2	0.03
Parenchymal lesions – fibrous stripes	0.27	0.07–0.99	0.048		N/A	
Parenchymal lesions located subpleural, peripheral parts	0.27	0.08–0.92	0.04		N/A	

**Respiratory failure according to Campbell: type I – partial, hypoxaemic, type II – complete, hypoxaemic, and hypercapnic; #Gasometry analysis from capillary blood. COVID-19 – coronavirus disease 2019, INR – international normalised ratio.*

Similarly, our analysis, aside from oncological disease, did not show an impact of comorbidities, including heart failure, on the course of pulmonary embolism in patients with concomitant respiratory tract infection. However, it should be noted that heart failure constitutes an independent risk factor for increased mortality. The severity of this condition can be demonstrated by a study describing the 6-year survival probability of older adults after their first hospitalisation due to heart failure, which showed that up to one-third of individuals died within the first year of hospitalisation [17]. In the case of COVID-19 infection, anaemia at admission was independently associated with increased all-cause mortality risk in hospitalised patients with COVID-19 [18]. Our study indicates that a lower level of red blood cells and haemoglobin was a statistically significant factor influencing mortality among patients with respiratory system infection and pulmonary embolism due to COVID-19, both in observations < 30 days and in long-term observation. Another factor influencing mortality in long-term observation was a lower INR, possibly resulting from a shift in haemostasis towards increased coagulability. Notable deviations in blood morphology were also found in lymphocytes and platelets – their reduced levels contributed to increased mortality. Similar findings were reported globally; Alsubhi *et al.* demonstrated a statistically significant decrease in both of these fractions in patients with acute pulmonary embolism who subsequently died [19]. Moreover, studies describing the use of morphological parameters as biomarkers for early detection of acute pulmonary embolism in COVID-19 patients are available in the literature [20].

Acute hypoxemic respiratory failure is the most common complication of COVID-19 [20]. Xia *et al.* investigated the impact of high-flow nasal oxygen therapy in patients with COVID-19 and hypoxaemic respiratory failure. The study showed that respiratory failure requiring high-flow oxygen therapy was as-

sociated with an unfavourable prognosis [21]. In our analysis, more intensive oxygen therapy significantly increased the risk of death in both short- and long-term observation, and respiratory failure at admission was a prognostically unfavourable factor increasing the risk of death in long-term observation.

An interesting result of our study is the difference in the occurrence of blood clots in COVID-19 (+) and (–) patients. Clots in the main pulmonary arteries (pulmonary trunk, right and left pulmonary arteries, lobar arteries) were significantly more common in patients with an ongoing respiratory system infection of COVID-19 (–), which may be related to the previously mentioned distinct mechanisms of coagulopathy during SARS-CoV-2 infection and the strong inflammatory response it induces. The CT imaging of the chest in the course of COVID-19-induced pneumonia is nonspecific. The most commonly observed changes include ground-glass opacities, reticular densities, vessel thickening, with a more peripheral distribution [22]. In our observation, among patients with pulmonary embolism and COVID-19 infection, fibrous-band-like changes predominated in chest CT scans, and air bronchograms were more frequently observed in the COVID-19 (–) group, which is probably associated with an ongoing respiratory system infection. The analysis also showed that fibrous-band-like changes reduced the risk of death in long-term observation. In patients with pneumonia in the course of COVID-19, it has been demonstrated that a stronger fibroproliferative response at admission was associated with increased mortality, but it did not correlate with long-term consequences of lung fibrosis in survivors [23]. It is challenging to explain why changes located subpleurally contributed to reduced long-term mortality, while left-sided localisation increased short-term mortality – further research involving larger groups of patients is required.

A separate issue in the discussion of the COVID-19 epidemic is the topic of applied preventive vaccinations. In some cases, the use of vaccination has been fraught with complications [24, 25].

Overall, our study highlights the complex relationships between pulmonary embolism and COVID-19, where differences in coagulation mechanisms influencing disease progression may be significant both in the acute phase and during the convalescent period. However, it is important to note that these results should be interpreted with caution due to the limitations of the study, including the size of the study group. Further research with larger patient cohorts is warranted to validate and extend these findings.

Study limitation: A limitation of this study is the relatively small size of the included patient group. The low number of events did not allow for the development of a multifactorial model regarding deaths within 30 days. Insufficient clinical data resulted in a lack of clinical risk stratification (e.g. PESI). Most patients in the COVID-19 (+) group were individuals who had obtained a positive result from an antigen and/or molecular RT-PCR test. This group included a few patients who were tested solely with the RT-PCR method, which may not necessarily indicate an active SARS-CoV-2 infection. This consideration is relevant, especially in the context of the control group, consisting of patients with pulmonary embolism with concomitant lung infection and/or respiratory failure. The study does not provide information about outpatient antithrombotic treatment and its duration.

Conclusions

The course of pulmonary embolism in patients with concomitant COVID-19 infection differed from the control group, which consisted of patients with pulmonary embolism and respiratory tract infection other than SARS-CoV-2 infection. Differences pertained to laboratory tests, imaging studies, as well as the localisation of thromboembolic changes in pulmonary vessels.

COVID-19 did not independently affect the long-term survival of patients with pulmonary embolism. The only independent predictor of long-term mortality was concomitant neoplastic disease

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Ethical approval

The study was approved by the Ethics Committee of the Świętokrzyskie Chamber of Physicians, No. 6/2023-VIII, dated 26 January 2023.

Conflict of interest

The authors declare no conflict of interest.

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