ORIGINAL ARTICLE

CANCER RATE IN PULMONARY EMBOLISM DIAGNOSED CASES: A SINGLE-CENTER, RETROSPECTIVE STUDY

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Abstract

Introduction: The aim of this study was to evaluate the incidence of pulmonary embolism in relation to age, cancer, and other comorbidities; to assess clinical, laboratory, and radiological findings; and to examine the associated mortality rate.

Materials and Method: Patients diagnosed with pulmonary embolism were included in this single-center retrospective study. The patients were divided into two age groups: < 60 and > 60 years. The incidence of pulmonary embolism; presence of deep vein thrombosis, cancer, surgical history; other comorbidities; mortality rate; prevalence of embolism; and C-reactive protein and D-dimer levels were evaluated according to age group and sex.

Results: Of the 1,281 patients who underwent pulmonary computed tomography angiography for suspected pulmonary embolism, 235 were diagnosed with pulmonary embolism. Of these, 114 were female and 121 were male. The mean age was 62.3 ± 16.8 years. In the ≥60 age group, the proportion of females was significantly higher than that of males ($p < 0.05$). Cancer prevalence and C-reactive protein and D-dimer levels were also significantly higher in this group ($p < 0.05$). No statistically significant differences were observed between the age groups for the other evaluated parameters.

Conclusion: The incidence of pulmonary embolism is higher in the elderly population, and the presence of additional conditions, particularly cancer, further increases the risk of pulmonary embolism. Careful monitoring of elderly patients for comorbidities, risk factors, and complications—such as pulmonary embolism—is crucial. Early diagnosis and timely treatment play vital roles in reducing mortality and significantly improving quality of life.

Keywords: Pulmonary Embolism; Aged; Mortality; Neoplasms.

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INTRODUCTION

According to the World Health Organization (WHO), the number of people aged 60 years and older is expected to reach 1.2 billion. The elderly population is also increasing in our country (1), leading to a growing proportion of elderly patients in clinical settings. Early diagnosis and treatment of potential pathologies are crucial to reduce mortality, improve quality of life, and minimize healthcare costs in this patient group.

Pulmonary embolism (PE) is a life-threatening global health problem caused by the obstruction of the pulmonary arteries by thromboembolic materials (2). It most commonly results from thrombi in the deep veins of the lower extremities, which obstruct blood flow to the pulmonary arteries (3). Its incidence increases in the presence of malignancy, sepsis, trauma, prior surgery, and immobilization (4). Studies have shown that the frequencies of deep vein thrombosis (DVT) and PE increase with age. As both conditions significantly increase 1-year mortality, early diagnosis and prompt treatment are vital (5).

Pulmonary multidetector computed tomography angiography (MDCTA) plays a critical role in the diagnosis and follow-up of PE. Advances in CT technology now allow for the detection of even small segmental emboli, which are seen as contrast-filling defects within the vessel lumen. Additionally, MDCTA can help rule out other cardiac and pulmonary pathologies that present with similar clinical features. However, excessive use of this imaging modality exposes patients to unnecessary ionizing radiation; therefore, MDCTA should be reserved for cases in which clinical findings and laboratory tests such as D-dimer levels support a preliminary diagnosis (6).

The aim of this study was to determine the incidence of PE according to age group and to identify factors affecting mortality in patients aged > 60 years who underwent pulmonary MDCTA with a prediagnosis of PE at our institution.

MATERIALS AND METHOD

The study was approved by the Istanbul Okan University Non-Interventional Clinical Research Ethics Committee (decision number 36, meeting number 169; October 18, 2023).As this study was retrospective in nature, informed consent was not required. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

We retrospectively screened patients who underwent pulmonary MDCTA for suspected PE at our hospital between January 2018 and March 2022. Demographic data were obtained from the electronic medical records of the hospital.

All examinations were performed using a 64-slice CT scanner (Optima CT 660; General Electric Medical Systems, Milwaukee, Wisconsin, USA). A water-soluble, nonionic intravenous contrast agent (350–370 mg/mL iodine) was administered using an automatic dual-head injector system at a dose of 1 mL/kg (90–100 mL total) at an injection rate of 3–5 mL/s via an 18-gauge cannula placed in the antecubital vein. Image acquisition began 12 s after injection, with contrast timing planned using the bolus monitoring technique.

Two- and three-dimensional maximum intensity projection (MIP) images were generated from pulmonary phase MDCTA images. MDCTA images and reports were retrospectively reviewed by an experienced radiologist (D.D.). Cases of PE were identified and classified as unilateral, bilateral, or massive embolisms based on the MDCTA findings.

The incidence of embolism according to age and sex; history of deep vein thrombosis (DVT), cancer, prior surgery, other comorbidities; and the relationship between C-reactive protein (CRP) and D-dimer levels and age and thrombus burden were analyzed. Additionally, the factors contributing to mortality were reviewed.

RESULTS

PE was diagnosed in 235 of the 1,281 patients who underwent pulmonary MDCTA for suspected PE. Of these, 114 (48.5%) were female and 121 (51.5%) were male. Ninety-six patients (40.9%) were aged ≤ 59 years, and 139 patients (59.1%) were aged ≥ 60 years. The mean age was 62.3 ± 16.8 years.

A total of 105 patients (44.7%) had comorbid conditions, such as diabetes mellitus, hypertension, or chronic obstructive pulmonary disease. In terms of embolism distribution, 121 (51.5%) patients had unilateral PE (Figure 1), 81 (34.5%) had bilateral PE (Figure 2), and 33 (14.0%) had massive PE (Figure 3).

DVT was detected using Doppler ultrasonography in 95 (40.4%) patients. Malignancy was present in 38 patients (16.2%), and 53 patients (22.6%) had a history of surgery. A total of 27 patients (11.5%) died. The mean CRP level was 2.4 mg/dL, and the mean D-dimer level was 0.9 µg/mL (Table 1). No significant differences ($p > 0.05$) were observed between the ≤ 59 and ≥ 60 age groups in terms of comorbidity rate, embolism localization, DVT rate, or history of surgery (Table 2). The proportion of female patients was significantly higher in the ≥ 60 age group compared to the ≤ 59 age group ($p < 0.05$) (Table 2). Similarly, the cancer rate was significantly higher in the ≥ 60 age group ($p < 0.05$) (Table 2). CRP and D-dimer levels were significantly higher in patients

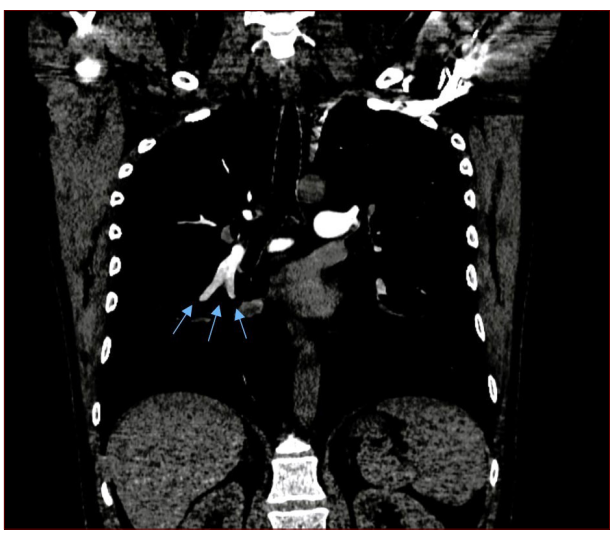

Figure 1. MDCTA coronal sections showing hypodense areas compatible with thrombus in the segmental branches of the right pulmonary artery to the lower lobe (small blue arrows).

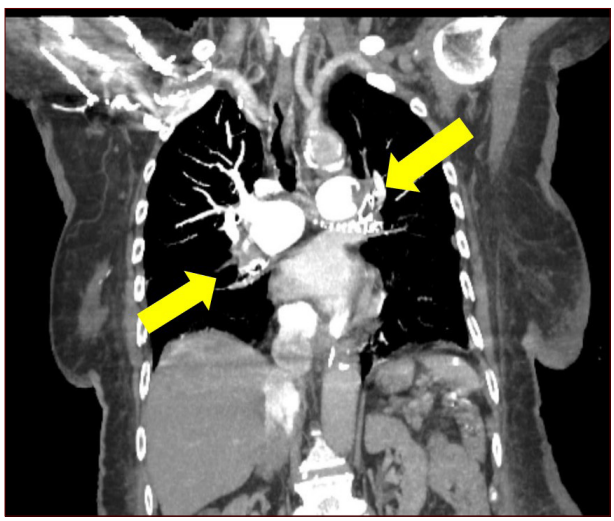

Figure 2. MDCTA coronal sections showing hypodense foci compatible with thrombus in bilateral pulmonary artery branches (thick yellow arrows)

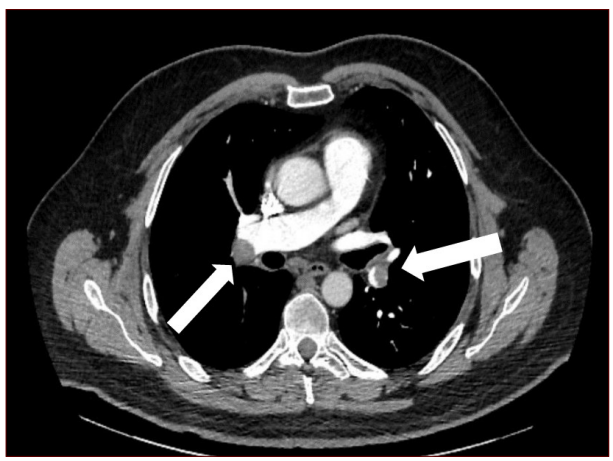

Figure 3. MDCTA axial sections showing hypodense filling defects in bilateral main pulmonary arteries consistent with massive pulmonary embolism (thick white arrows).

Table 1. Demographic, clinical and laboratory findings of patients

		Min-Max			Median	Mean ± SD/n (%)		
Age		20.0	–	95.0	65.0	62.3	±	16.8
Age	≤59					96		40.9%
	≥60					139		59.1%
Gender	Female					114		48.5%
	Male					121		51.5%
Comorbid Disease	(-)					130		55.3%
	(+)					105		44.7%
Localization	Unilateral					121		51.5%
	Bilateral					81		34.5%
	Massive					33		14.0%
Deep vein thrombosis	(-)					140		59.6%
	(+)					95		40.4%
Cancer	(-)					197		83.8%
	(+)					38		16.2%
Operation history	(-)					182		77.4%
	(+)					53		22.6%
CRP		0.1	–	32.2	2.4	6.0	±	7.4
D-Dimer		0.1	–	10.0	0.9	2.8	±	3.4
Mortality (Exitus)	(-)					208		88.5%
	(+)					27		11.5%

aged ≥ 60 years compared to those aged ≤ 59 years ($p < 0.05$). There was no significant difference in mortality rates between the age groups ($p > 0.05$) (Table 2).

Of the 235 patients with PE, 38 (16.17%) had an underlying malignancy. Lung cancer was the most common cancer type, detected in 17 patients (44.7%; 7.23% of all PE patients). 31.2% of this group was female and 68.8% was male. Pancreatic cancer was the second most common cancer, detected in 5 patients (13.2%); 80% of these patients were female and 20% were male. Renal cell carcinoma (RCC) and rectal cancer were detected in two patients (5.3%) each. Glioblastoma multiforme (GBM) was seen in four patients (10.5%). Other cancer types seen were small cell lung cancer, osteosarcoma, pleural sarcoma, astrocytoma, cardiac angiosarcoma), cholangiocarcinoma and cervical cancer.

Regarding cancer staging, 25.0% of lung cancers were Stage I, 12.5% Stage II, 12.5% Stage III, and 50% Stage IV. Of pancreatic cancer patients, 20% were Stage II, 20% Stage III, and 60% Stage IV. Half of rectal cancer patients were Stage III, while the other half were Stage IV. All GBM and RCC patients were Stage IV. Sarcomas and astrocytomas were cases with systematic metastases. These findings indicate that malignancy-associated PE cases mostly occur in advanced-stage cancers.

Table 2. Demographic, clinical and laboratory findings of patients under and over 60 years of age

		Age ≤59 (n = 96)		Age ≥ 60 (n = 139)		p	
		Mean ± SD/n (%)	Median	Mean ± SD/n (%)	Median		
Gender	Female	37	38.5%	77	55.4%	0.011	X^2
	Male	59	61.5%	62	44.6%		
Comorbid Disease	(-)	52	54.2%	78	56.1%	0.768	X^2
	(+)	44	45.8%	61	43.9%		
Localization	Unilateral	51	53.1%	70	50.4%	0.638	X^2
	Bilateral	34	35.4%	47	33.8%		
	Massive	11	11.5%	22	15.8%		
Deep vein thrombosis	(-)	55	57.3%	85	61.2%	0.553	X^2
	(+)	41	42.7%	54	38.8%		
Cancer	(-)	88	91.7%	109	78.4%	0.007	X^2
	(+)	8	8.3%	30	21.6%		
Operation history	(-)	79	82.3%	103	74.1%	0.140	X^2
	(+)	17	17.7%	36	25.9%		
CRP		3.9 ± 6.0	1.1	7.4 ± 8.0	4.2	0.000	m
D-Dimer		2.2 ± 3.2	0.5	3.2 ± 3.5	1.6	0.003	m
Mortality (Exitus)	(-)	86	89.6%	122	87.8%	0.668	X^2
	(+)	10	10.4%	17	12.2%		

Mann-Whitney U test / X^2 Chi-square test

Different comorbidities were detected in patients diagnosed with pulmonary embolism. The most common were pneumonia (36 patients, 15.3%; mean age 65.5 years; 36.1% female, 63.9% male), chronic obstructive pulmonary disease (COPD) (35 patients, 14.9%; mean age 69.7 years; 25.7% female, 74.3% male), and COVID-19 infection (28 patients, 11.9%; mean age 56.9 years; 35.7% female, 64.3% male). Less common comorbidities included hypertension (6 patients, 2.6%), diabetes mellitus (5 patients, 2.1%), congestive heart failure (6 patients, 2.6%), coronary artery disease (3 patients, 1.3%), interstitial lung disease (3 patients, 1.3%), arrhythmia (4 patients, 1.7%), protein S deficiency and hyperhomocysteinemia (3 patients, 1.3%), sepsis (2 patients, 0.9%), cerebrovascular accident (2 patients, 0.9%), and Castleman disease (1 patient, 0.4%).

Statistical Method

Mean, standard deviation, median, minimum, maximum, frequency, and percentage values were used for descriptive statistics. The distribution of variables was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. The Mann-Whitney U test was used to compare quantitative independent variables that did not follow a normal distribution. The chi-square test was used to analyze qualitative independent variables. All statistical analyses were performed using SPSS software (version 27.0; IBM Corp., Armonk, NY, USA).

DISCUSSION

Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is a serious public health concern that can result in death. PE is the most common cause of mortality in hospitalized patients. Risk factors for VTE include hospitalization, immobilization, prior surgery, cancer, oral contraceptive use, pregnancy, and hormone replacement therapy.

DVT typically presents with clinical signs, such as pain, redness, edema, and increased warmth in the lower extremities. Doppler ultrasonography (US) generally reveals noncompressible thrombosed venous segments in the deep veins of the legs. In cases of PE, clinical findings may include dyspnea, syncope, hypotension, tachypnea, tachycardia, and hypoxia (7).

Pulmonary MDCTA should be performed to confirm the diagnosis, particularly when D-dimer levels are elevated. However, diagnosis may be delayed in elderly patients because of overlapping clinical features with other cardiopulmonary diseases, atypical presentations (such as altered mental status), and the lower diagnostic utility of D-dimer in this population (8).

D-dimer is produced through the degradation of cross-linked fibrin by plasmin and serves as a marker of intravascular clot formation. Therefore, it plays a key role in the diagnosis of VTE. However, D-dimer levels may also increase during infections and various inflammatory conditions (9). The normal blood level is generally considered to be ≤ 0.5 µg/mL.

CRP is an acute-phase reactant that reflects inflammation and tissue damage. The normal blood concentration range is 0–5 mg/L. Tumor necrosis factor (TNF) is produced by the liver in response to cytokine stimulation, primarily by interleukin-6 (IL-6) and interleukin-1 (IL-1), and has a half-life of 4–6 h. CRP levels can also increase due to physical activity, smoking, alcohol use, diabetes mellitus, hypertension, and hormone therapy. Studies have shown that CRP levels are elevated during the acute phase of PE (10). It is thought that CRP levels increase as a result of exacerbation of hemorrhagic necrosis and the associated inflammatory response. Moreover, other studies have indicated that patients with PE and elevated CRP levels have higher mortality rates, suggesting that CRP could serve as an early predictor of mortality (11). In our study, both the average D-dimer and CRP levels were significantly higher in the ≥ 60 age group compared to the younger group.

The incidence of PE is known to increase in patients with cancer owing to various pathophysiological mechanisms. In this population, PE is the second most common cause of death after cancer itself (12). Therefore, prophylactic anticoagulant therapy is recommended after an acute PE episode in patients with cancer to reduce the risk of recurrence and mortality (13). In our study, the cancer rate was significantly higher in older age groups.

Based on the extent of embolism, PE can be classified as massive, submassive, or low-risk (segmental). Massive PE is characterized by systemic hypotension (systolic blood pressure < 90 mm Hg or a reduction of ≥ 40 mm Hg from baseline for at least 15 minutes not due to arrhythmia) or shock. Additional signs may include altered consciousness, oliguria, and evidence of tissue hypoperfusion and hypoxia (e.g., cold, clammy extremities). The diagnosis of massive PE relies on clinical findings supported by transesophageal echocardiography, pulmonary CTA, and laboratory data (14).

In a study of patients with a mean age of 65 years, mortality rates were 71.4% for massive PE, 44.5% for submassive PE, and 28.1% for low-risk PE ($p < 0.001$) (15). Pulmonary CTA revealed massive PE in 14% of patients, bilateral/submassive PE in 34.5%, and unilateral/low-risk PE in 51.5% of patients. No

significant differences in the extent of embolism or mortality rates were observed between age groups.

Studies have shown that the incidence of PE is higher in older populations, and the mortality rate of PE is significantly greater in patients aged 65 years and older compared to younger individuals (16,17). Consistent with the literature, PE was observed more frequently in elderly patients in our study. However, no significant difference in mortality rates was detected between the age groups. This highlights the importance of rapid diagnosis and timely treatment in reducing mortality.

In conclusion, the incidence of PE continues to increase in the elderly population. Particularly in elderly patients with comorbidities, such as cancer, PE can lead to longer hospital stays, higher healthcare costs, and increased mortality. Therefore, elderly patients should be closely monitored, and clinicians should maintain a high index of suspicion for PE when symptoms such as dyspnea or chest pain occur.

Limitations of the Study: The single-center, retrospective design limits the generalizability of our results. Multicenter, prospective studies would be beneficial to generalize the results to larger and more diverse populations. Furthermore, we believe that prospective studies with long-term follow-up and the ability to assess PE risk and mortality by specific cancer types will further clarify the issue of PE in elderly cancer patients.

Conflict of Interest: The authors declare that they have no conflicts of interest related to this study.

Availability of Data and Materials: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Compliance with Ethical Standards: This study was conducted in accirdance with the principles of the Declaration of Helsinki and current ethical regulations. The study was approved by theIstanbulOkan University Non-Interventional Clinical Research Ethics Committee (decision number 36, meeting number 169; October 18, 2023).

Informed Consent: Since this was a retrospective study, informed consent was not required.

Consent for publication: The authors agree to the publication of this study in the journal.

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