

The impact of age and sex on clinical symptoms in low and intermediate-low risk pulmonary embolism

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ABSTRACT

Aims: The diagnostic process of pulmonary thromboembolism (PTE) can be complex due to its wide spectrum of clinical presentations. The type and frequency of symptoms vary not only with the embolism risk category but also in relation to individual demographic factors such as age and sex. This study aims to evaluate the influence of demographic variables on clinical presentation by investigating the distribution of symptoms according to age and sex in patients with acute PTE classified as low or intermediate-low risk.

Methods: This retrospective, cross-sectional study was conducted at the Emergency Department of Dışkapı Yıldırım Beyazıt Training and Research Hospital between February 1, 2020, and February 1, 2021. A total of 329 patients aged 18 years and older who were classified as low or intermediate-low risk according to the 2019 European Society of Cardiology guidelines were included in the study. The patients' demographic characteristics and clinical symptoms were retrospectively analyzed. Symptom distributions were compared across different age and sex groups.

Results: The most frequently reported symptoms among patients were dyspnea (79.3%) and chest pain (53.7%). Leg pain and/or swelling were significantly more common in younger male patients (26%, $p=0.001$), while presyncope was more frequently observed in older female patients (27.3%, $p=0.001$). Hemoptysis was found to be significantly less common in older female patients compared to other groups (8.2%, $p=0.012$).

Conclusion: The symptom profile in PTE varies significantly based on patients' demographic characteristics. Our study suggests that recognizing these differences during the diagnostic process may help facilitate clinical management by preventing diagnostic delays, particularly in patient groups presenting with atypical symptoms.

Keywords: Gender, pulmonary embolism, symptoms, age

INTRODUCTION

Pulmonary thromboembolism (PTE) is a serious cardiopulmonary emergency characterized by a wide range of clinical manifestations, often posing diagnostic challenges.¹ The presentation and severity of symptoms vary depending not only on the size and location of the embolus but also on individual patient characteristics such as age, sex, and cardiopulmonary reserve. This heterogeneity necessitates the evaluation of symptoms in the context of demographic factors to enable early diagnosis and the development of appropriate treatment strategies.² PTE may present along a broad clinical spectrum, ranging from an asymptomatic course to hemodynamic instability or sudden death. In the literature, the most commonly reported clinical symptoms are dyspnea and pleuritic chest pain, while syncope is recognized as a key indicator of right ventricular dysfunction.³ Additionally, although rare, hoarseness due to Ortner's syndrome-caused by compression of the recurrent laryngeal nerve by a dilated

pulmonary artery has also been reported.⁴ The influence of age on the clinical manifestations of PTE is well established, with older patients tending to present with more atypical symptoms. Moreover, due to hormonal and anatomical differences, sex is considered to play a significant role in symptomatology.⁵ While estrogen and related neurohormonal mechanisms are known to influence the pathophysiology of thromboembolic events, the specific impact of these factors on the clinical presentation of PTE remains insufficiently explored.

PTE often presents with common symptoms such as dyspnea and chest pain, which may mimic other conditions seen in the emergency department, thereby complicating the diagnostic process.⁶ It is well recognized that the clinical course and symptomatology of PTE can vary depending on the embolism risk level. Therefore, the evaluation of demographic factors such as age and sex is of critical importance in PTE patients.

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Considering these demographic variables plays a key role in facilitating early diagnosis and planning effective treatment strategies. In this study, patients classified as high risk with hemodynamic instability were excluded, allowing for the analysis to focus solely on those in the intermediate-low and low risk groups. This approach aimed to enable a more consistent assessment of clinical findings within a homogeneous patient population and to more clearly elucidate the relationship between symptoms and demographic variables.

METHODS

Ethics

The study was approved by the Clinical Researches Ethics Committee of Ankara Etlik City Hospital (Date: 06.03.2024, Decision No: AEŞH-BADEK-2024-058). Throughout the study, the ethical principles outlined in the Declaration of Helsinki were strictly followed, and patient rights were fully respected.

This retrospective, cross-sectional, and observational study was conducted at the Emergency Department of Dışkapı Yıldırım Beyazıt Training and Research Hospital between February 1, 2020, and February 1, 2021. The study population consisted of patients aged 18 years and older who presented to the emergency department during the specified period and were diagnosed with acute PTE. The diagnosis of acute PTE was established based on clinical findings, laboratory tests, and radiological evaluations, with computed tomography pulmonary angiography-the gold standard diagnostic modality-being utilized for confirmation. The diagnostic criteria were assessed in accordance with current international guidelines.

Risk Stratification of Pulmonary Embolism

The risk levels of the patients included in the study were classified according to the criteria outlined in the 2019 European Society of Cardiology (ESC) Guidelines on Pulmonary Embolism.⁷ This classification considered hemodynamic stability, clinical findings, laboratory results, and imaging parameters. The high-risk group comprised patients exhibiting signs of hemodynamic instability, such as hypotension, shock, or cardiac arrest. The intermediate-high risk group included hemodynamically stable patients with clinical and laboratory indicators suggesting elevated risk. In this study, only patients categorized as low or intermediate-low risk were included. This approach was adopted to ensure a more homogeneous patient population and to minimize the confounding clinical impact of hemodynamic instability.

Patient data were retrospectively collected through the hospital's electronic medical record system. The variables included in the analysis comprised demographic characteristics (age and sex) as well as comorbid conditions (such as hypertension, diabetes mellitus, and malignancy). Additionally, symptoms reported by patients at the time of emergency department presentation-such as dyspnea, chest pain, syncope, and hemoptysis-were systematically recorded. Vital signs measured upon admission (blood pressure, heart rate, respiratory rate, and oxygen saturation) and physical examination findings were also evaluated.

Furthermore, patients' clinical course, treatment processes, and hospitalization status were monitored throughout their follow-up.

Sample Size Determination

The sample size for this study was calculated using the G*power 3.1.9.7 statistical power analysis software. A power analysis was conducted for the Chi-square test, which was planned for group comparisons to detect significant differences. An effect size (w) of 0.3 (moderate), an alpha error probability of 0.05, and a statistical power of 80% (0.80) were assumed. Considering the study aimed to evaluate four age-sex subgroups (young males, elderly males, young females, elderly females), it was estimated that each subgroup should include at least 130 patients, indicating a minimum total sample size of 520 patients.

However, our final cohort comprised 329 patients who met the predefined inclusion and exclusion criteria. The main reason for not reaching the target sample size was a marked decrease in the number of emergency department admissions during the study period, which coincided with the coronavirus disease 2019 (COVID-19) pandemic. Despite this limitation, the available sample size was deemed sufficient to perform meaningful and reliable analyses, considering the retrospective nature of the data and the study objectives. This issue has been acknowledged as a limitation and was taken into account when interpreting the results.

Inclusion Criteria

- Age 18 years or older
- Diagnosis of acute PTE following presentation to the emergency department
- Classified as intermediate-low or low risk according to the 2019 ESC guidelines
- Availability of complete clinical and radiological data

Exclusion Criteria

- Patients diagnosed with intermediate-high or high-risk PTE
- Cases with chronic PTE identified at the time of diagnosis
- Asymptomatic patients or those diagnosed incidentally
- Individuals under the age of 18
- Pregnant patients
- Patients with incomplete or missing clinical data
- Patients with a current diagnosis of COVID-19 infection or a documented history of previous COVID-19 infection

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as counts and percentages for categorical variables, and as mean $\pm$ standard deviation or median (minimum-maximum) for continuous variables, depending on the normality of distribution. The Kolmogorov-Smirnov test was used to assess the normality of data distribution. For

comparisons between groups, the independent samples t-test was used for normally distributed continuous variables, while the Mann–Whitney U test was applied for non-normally distributed variables. Differences between categorical variables were evaluated using the Chi-square test. When a significant difference was observed in multiple group comparisons, the Bonferroni correction was applied to adjust for multiple testing. Correlation analysis was performed to assess the relationships between symptoms and mortality. A p-value of <0.05 was considered statistically significant; after Bonferroni correction, the threshold for significance was set at $p<0.0125$.

RESULTS

A total of 520 patients were initially planned to be included in the study, and 456 patients were ultimately recruited. Of these, 7 patients were excluded due to chronic PTE, 18 patients were excluded as they were asymptomatic or incidentally detected, 48 patients were excluded due to being in the high or moderate-to-high risk group, 28 patients were excluded because of incomplete medical records, and 26 patients were excluded due to active or prior COVID-19 infection. As a result, 329 patients were included in the final analysis. The patient recruitment and selection process is summarized in the patient inclusion and exclusion flowchart (Figure).

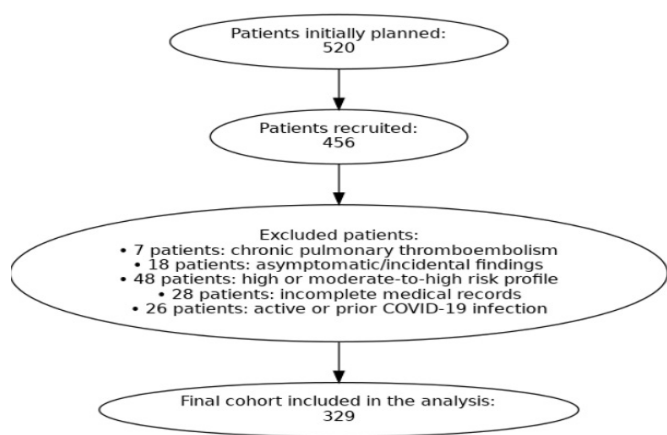


Figure. Patient inclusion and exclusion flowchart

The final study cohort consisted of 329 patients, of whom 190 (57.7%) were female and 139 (42.3%) were male. The mean age of the patients was 66 ± 16.5 years. Acquired risk factors were present in 52.2% of the cases ($n=172$), with immobilization being the most common, observed in 23.4% ($n=77$) of patients. Additionally, 51.1% ($n=169$) of patients had at least one comorbid condition. Among comorbidities, hypertension was the most frequently reported diagnosis (31.3%, $n=103$), followed by diabetes mellitus (14.3%, $n=47$).

Regarding presenting symptoms in the emergency department, 94.8% ($n=312$) of patients reported at least one symptom. The most common symptom was dyspnea, present in 262 patients (79.6%), followed by chest pain (63.5%, $n=209$) and cough (19.4%, $n=64$).

Detailed demographic and clinical characteristics of the study population are presented in Table 1.

Table 1. Demographic and clinical characteristics of the patients

	All patients n (%) 329 (100%)
Age, years (mean $\pm$ SD)	66 $\pm$ 16.5
Gender	
Female	190 (57.8%)
Male	139 (42.2%)
Acquired risk factor	172 (52.2%)
Immobilization	77 (23.4%)
Comorbidity	169 (51.1%)
Hypertension	103 (31.3%)
Diabetes mellitus	47 (14.3%)
Symptoms	312 (94.8%)
Shortness of breath	262 (79.6%)
Chest pain	209 (63.5%)
Cough	64 (19.4%)

SD: Standard deviation

In this study, the age groups were defined by using the median age within each sex category as a reference point, and patients were subsequently classified into “young” and “elderly” subgroups. Based on this method, the mean age for male patients was 50 ± 12.2 years in the young group and 78 ± 6.2 years in the elderly group. Among female patients, the mean age was 53 ± 11.5 years for the young subgroup and 79 ± 6.6 years for the elderly subgroup. Statistical analyses demonstrated that this age stratification was significantly associated with sex ($p<0.001$). Accordingly, the age classification considering sex-specific distributions was deemed an appropriate approach for evaluating clinical findings in the context of both age and sex. The distribution of ages by sex is presented in Table 2.

Table 2. Age distribution of patients by sex

	Young men n:77 (23.4%)	Old men n:62 (18.9%)	Young women n:80 (24.3%)	Old women n:110 (33.4%)	p value
Age (mean $\pm$ SD)	50 $\pm$ 12.2	78 $\pm$ 6.2	53 $\pm$ 11.5	79 $\pm$ 6.6	<0.001

SD: Standard deviation

The 329 patients included in the study were categorized into four groups based on sex and median age: younger males, older males, younger females, and older females. Symptom distributions were then analyzed across these subgroups. Although dyspnea and chest pain were the most commonly reported symptoms in all groups, the distribution of certain symptoms showed statistically significant differences according to age and sex.

Presentation with leg pain or swelling was significantly more frequent in younger male patients (26%, $p=0.001$). This symptom was observed in only 4.8% of older males, 13.8% of younger females, and 7.3% of older females. Presyncope was notably more common in the older female group, with 27.3% of patients presenting with this symptom. In comparison, the rates were 10.4% in younger males, 14.5% in older males, and 7.5% in younger females ($p=0.001$).

On the other hand, hemoptysis was significantly less frequent in older female patients (8.2%, $p=0.012$), while it was reported in 25% of younger females, 22.1% of younger males, and 19.4% of older males. Other symptoms such as dyspnea, chest pain, cough, and palpitations did not show statistically significant differences between groups ($p>0.05$).

A detailed breakdown of symptom distribution by patient subgroup is provided in [Table 3](#).

DISCUSSION

In this study, the distribution of symptoms according to age and sex was evaluated in cases of acute PTE classified as intermediate-low and low risk. The findings indicate that the clinical presentation of PTE is influenced not only by embolic burden and localization but also significantly by demographic factors. The most frequently reported symptoms were dyspnea (79.3%) and chest pain (53.7%), which are largely consistent with the prevalence rates reported in large cohort studies such as PIOPED-II.⁸ The frequency of chest pain similarly aligns with current observational data.

Moreover, hormonal and physiological differences associated with sex may particularly influence the clinical symptom profile in patients with intermediate-low and low-risk PTE. In women, estrogen is known to play a pivotal role in modulating vascular tone, the coagulation system, and endothelial function. In addition to its prothrombotic effects, postmenopausal hormonal changes have been shown to impact cardiopulmonary reserve capacity and autonomic nervous system responses. These physiological alterations may contribute to the higher prevalence of symptoms such as presyncope-linked to impaired hemodynamic adaptation-among older female patients.

The age at which PTE is diagnosed shows significant variation by sex. In general, PTE tends to occur at younger ages in male patients, a finding that is often attributed to certain risk factors more commonly observed in men.⁹ In contrast, PTE is typically diagnosed at older ages in women, which is thought to be influenced by hormonal changes and physiological alterations associated with the postmenopausal period.¹⁰ These demographic differences highlight the importance of age and sex as key determinants in the diagnosis of PTE and underscore the need for individualized approaches in risk assessment and clinical management.

In our study, a statistically significant difference in the mean age at diagnosis was also observed between male and female patients. Male patients were diagnosed with PTE at a younger age compared to females, who were diagnosed later in life. These findings are consistent with the current literature and emphasize the importance of considering sex- and age-specific risk factors and symptom profiles in clinical evaluation. Additionally, to classify patients by age and sex, “young” and “elderly” subgroups were created by using the median age within each sex group as a reference. This approach allowed for a more accurate analysis of clinical symptoms and risk factors by accounting for sex-specific age distributions. In our study, significant differences were observed between these age groups, supporting a clearer understanding of the impact of demographic variables on PTE presentation.

The analysis of symptoms based on age and sex revealed distinct clinical variations among different patient subgroups. Notably, the higher frequency of leg pain and swelling in younger male patients suggests an increased risk of deep vein thrombosis (DVT) within this group. The existing literature supports this observation, indicating that the lifetime risk of venous thromboembolism is higher in men compared to women.¹¹ In our study, ultrasonographic evaluations also showed a higher rate of DVT detection among younger male patients compared to other age and sex groups; however, this difference did not reach statistical significance. In a retrospective study conducted among Chinese patients with DVT, it was reported that age and sex influence the incidence of DVT, with a higher risk observed particularly in males and age-related triggers varying accordingly.¹² These findings support the notion that DVT may occur more frequently and present with more pronounced symptoms in male patients.

Although our study included only intermediate-low and low-risk PTE cases, the significantly higher prevalence of presyncope in the older female group (27.3%) suggests that early hemodynamic alterations and right ventricular strain may manifest more prominently in this population. Age-related reductions in right ventricular functional reserve, decreased vascular compliance, and changes in autonomic regulatory mechanisms may contribute to the development of presyncope-like symptoms even in the absence of overt hemodynamic instability.¹³ Moreover, the literature highlights that presyncope may serve as an early indicator of potentially serious cardiovascular conditions, underscoring the need for

Table 3. Comparison of symptoms in acute pulmonary embolism according to age and sex					
	Young men n:77 (23.4%)	Old men n:62 (18.9%)	Young women n:80 (24.3%)	Old women n:110 (33.4%)	p value*
Dyspnea	56 (72.7%)	54 (87%)	65 (81.3%)	87 (79.1%)	0.208
Chest pain	51 (66.2%)	41 (66.1%)	55 (68.8%)	62 (56.4%)	0.295
Cough	19 (24.7%)	12 (19.4%)	11 (13.8%)	22 (20.8%)	0.388
Hemoptysis	17 (22.1%)	12 (19.4%)	20 (25%)	9 (8.2%)	0.012**
Palpitation	7 (9.1%)	6 (9.7%)	6 (7.5%)	16 (14.5%)	0.415
Leg pain/swelling	20 (26%)	3 (4.8%)	11 (13.8%)	8 (7.3%)	0.001**
Presyncope	8 (10.4%)	9 (14.5%)	6 (7.5%)	30 (27.3%)	0.001**

*Chi-square test was applied. **With Bonferonni correction, $p<0.0125$ was considered significant.

careful monitoring and management of such patients in the emergency department setting.¹⁴ In this context, for patients with PE presenting with presyncope, particularly elderly women, it is crucial to accurately assess the risk of possible complications and ensure appropriate clinical follow-up. This observation suggests that hemodynamic instability in elderly female patients may manifest with earlier clinical signs.

The lower frequency of hemoptysis observed in older female patients compared to other groups may suggest a reduced risk of pulmonary infarction in this population. Pulmonary infarction is typically associated with distal arterial occlusion and insufficient collateral circulation. According to the literature, aging may promote the development of collateral pulmonary vessels, which could reduce the incidence of infarction and, consequently, the occurrence of hemoptysis.¹⁵ Additionally, it has been reported that reduced alveolar tissue elasticity and changes in capillary membrane permeability in elderly individuals are among the factors that may limit the development of hemoptysis. Furthermore, in a study by Pribish et al.,¹⁶ it was noted that the incidence of hemoptysis was lower in females compared to males, and this difference was suggested to be attributable to physiological variations related to age and sex.

Limitations

This study has several limitations. First, it was conducted retrospectively at a single center, which may pose a risk of incomplete records and information bias, potentially affecting the accuracy of patient data. The evaluation of symptoms relied on patient self-reports and clinical documentation, which may have limited the ability to fully capture the diversity of subjective symptoms. Additionally, the relatively small study population and lack of representation from different ethnic groups may restrict the generalizability of the findings. Moreover, since the data collection period overlapped with the COVID-19 pandemic, there was a noticeable decline in patient admissions, and patients with an active or prior COVID-19 infection were excluded. These factors further limited the sample size and study scope and may affect the generalizability of the results.

CONCLUSION

This study demonstrated that symptom presentation in patients with intermediate-low and low-risk PTE can vary by age and sex. Notably, DVT-related symptoms were more frequently observed in younger males, while presyncope was more prominent among older female patients. Furthermore, the significantly lower rate of hemoptysis in older women suggests that age-related physiological changes may play a role in reducing the risk of pulmonary infarction in this population.

Recognizing these differences in symptom profiles may improve diagnostic accuracy, particularly in patients presenting with atypical symptoms, and facilitate more effective clinical management. Age- and sex-sensitive clinical assessment strategies may contribute substantially to the early diagnosis and treatment of PTE.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was approved by the Clinical Researches Ethics Committee of Ankara Etlik City Hospital (Date: 06.03.2024, Decision No: AEŞH-BADEK-2024-058).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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