Journal of
Cardiology & Cardiovascular
Surgery

Original Article

DOI: 10.51271/JCCVS-0058

Facilitating factors of venous risk among patients diagnosed with pulmonary thromboembolism followed in different clinical settings

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Cite this article: Tümüklü ÜT, Kerestecioğlu C, Felek D. Facilitating factors of venous risk among patients diagnosed with pulmonary thromboembolism followed in different clinical settings. *J Cardiol Cardiovasc Surg.* 2025;3(3):50-55.

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Received: 08/08/2025 ◆ **Accepted**: 25/09/2025 ◆ **Published**: 27/09/2025

ABSTRACT

Aims: This study aims to analyze the risk factors contributing to the development of pulmonary thromboembolism (PTE) from a multidisciplinary perspective, focusing on clinical, demographic, and laboratory variables that may influence venous thrombosis pathogenesis. By elucidating the interrelationships among these factors, the study seeks to support preventive strategies and provide a scientific basis for diagnostic and management processes.

Methods: This study was conducted through a systematic evaluation of the diagnostic data—including clinical, laboratory, and imaging findings—of individuals aged 18 to 80 years who were followed for PTE between 2023 and 2025 at the Chest Diseases, Cardiovascular Surgery, and Internal Medicine Departments of Yozgat Bozok University Research and Training Hospital. Patients with uncertain diagnoses, individuals under 18 years of age, and those who received only prophylactic treatment were excluded. Imaging data (thoracic CT angiography (CTA), scintigraphy, abdominal CT, and venous Doppler ultrasound) were analyzed based on prior reports without performing any additional procedures. Clinical variables such as smoking status, comorbid conditions, surgical history, immobility, and hormonal factors in female patients, along with laboratory parameters including complete blood count, biochemistry, blood gas analysis, and D-dimer levels, were reviewed retrospectively.

Results: A total of 41 patients (25 female, 16 male) diagnosed with PTE were evaluated. The mean age of participants was 61.59±17.92 years. The average age was 62.56±17.93 years in women and 60.06±18.40 years in men. Among 11 patients with available data on body mass index (BMI), the mean BMI was 29.97±3.05. Of these, 5 were overweight, 5 had class 1 obesity, and 1 had class 2 obesity. The most common comorbidities included hypertension (n=24), diabetes mellitus (n=10), coronary artery disease (n=7), and hyperlipidemia (n=4). Among the 4 smokers, the average consumption was calculated as 21 pack-years. Surgical history was present in 17.1% of cases, and a history of immobilization was identified in 14.6%. Malignancy was observed in 2.4%, history of pregnancy in 4.9%, and oral contraceptive use in 2.4% of the patients. Genetic mutations related to hereditary thrombophilia were found in 19.5% of patients. Laboratory analyses revealed a mean hemoglobin (Hb) level of 13.25±2.12 g/dl, significantly lower than the reference range ($p=0.0225$). Blood urea nitrogen (BUN) was elevated, with a mean level of 27.16±10.43 mg/dl ($p=0.0004$). Arterial blood gas analysis showed a mean sO_2 of 74.92±12.35%, pO_2 of 52.21±10.87 mmHg, and pCO_2 of 30.26±6.14 mmHg, all significantly below normal reference values ($p<0.0001$). The mean D-dimer level was 3.31±2.36 µg/ml ($p<0.001$). According to CTA, bilateral embolism was observed in 15 patients, segmental/lobar embolism in 14, and multiple emboli in 12. Deep vein thrombosis (DVT) was detected in 4 patients via Doppler ultrasound, while 21 patients showed no evidence of DVT.

Conclusion: This study underscores the multifactorial etiopathogenesis of PTE and emphasizes the importance of a personalized and holistic evaluation approach in diagnosis and treatment. Risk factors such as age, obesity, comorbidities, surgical history, immobility, and genetic predisposition were shown to be significant contributors to PTE development. Low Hb levels and marked hypoxemia-hypocapnia reflected the systemic impact of the condition, while elevated D-dimer levels and CTA findings played a crucial role in early diagnosis. The findings highlight that integrating clinical, laboratory, and radiological data within a multidisciplinary framework can enhance risk stratification and improve patient outcomes.

Keywords: Pulmonary thromboembolism, venous thromboembolism, risk factors

INTRODUCTION

Pulmonary thromboembolism (PTE) represents one of the most serious and potentially fatal complications of venous thromboembolism (VTE). It is an acute-onset clinical condition that can pose an immediate threat to life. Often developing as a complication of deep vein thrombosis (DVT), PTE typically results from thrombi that form in the deep veins of the lower extremities and subsequently dislodge, obstructing the pulmonary arteries. This cascade disrupts pulmonary perfusion, imposes pressure overload on the right ventricle, induces hypoxemia, and—if left untreated—can lead to sudden death.[1,2]

According to the 2019 guidelines of the European Society of Cardiology, the annual incidence of PTE ranges from 39 to 115 per 100.000 individuals, varying significantly depending on demographic factors, healthcare infrastructure, and diagnostic/screening strategies across countries.[2] U.S.-based data report approximately 900.000 VTE events annually, of which an estimated 100.000 result in death.[10] PTE that develops during hospitalization is particularly significant, representing a leading cause of nosocomial morbidity and mortality.[3,4]

The pathophysiology of PTE is grounded in the interaction of three principal mechanisms known as Virchow's triad: venous stasis, endothelial injury, and hypercoagulability. One or more of these factors can substantially increase the risk of thrombosis in an individual.[12]

Major orthopedic procedures—such as hip and knee replacements—as well as abdominal and pelvic surgeries, elevate the risk of PTE five- to tenfold due to both direct vascular trauma and postoperative immobility.[3] Similarly, prolonged immobilization after trauma and restricted mobility due to neurological conditions increase thrombotic risk by promoting venous immobility.[3]

Cancer is a prominent predisposing factor for VTE, both through its intrinsic biological mechanisms and via treatment modalities such as chemotherapy. Cancer patients face a four- to sevenfold higher risk of developing VTE compared to the general population, with this risk influenced by tumor type and treatment regimen.[5]

Pregnancy and the postpartum period are physiologically prothrombotic due to hormonal shifts, increased coagulation potential, and mechanical limitations on venous return. The incidence of VTE is estimated to rise approximately fivefold during this time.[6]

Obesity contributes to thrombotic risk through both mechanical and inflammatory pathways. Increased intra-abdominal pressure impairs venous return, while chronic low-grade systemic inflammation and elevated procoagulant factors in obese individuals create a prothrombotic milieu.[7,9]

Hereditary thrombophilias—including Factor V Leiden mutation, Prothrombin G20210A mutation, protein C and S deficiencies, and antithrombin III deficiency—are associated with a markedly increased risk of VTE.[8,13,14] These genetic predispositions, when combined with environmental risk factors, can synergistically amplify the likelihood of thrombotic events.[15,16]

Cigarette smoking contributes to a prothrombotic state through endothelial dysfunction, systemic inflammation, and platelet activation. This effect is particularly concerning when combined with estrogen-containing oral contraceptives (OCP), where the thrombotic risk is further compounded in a synergistic manner.[9]

In light of this evidence, identifying and characterizing the risk factors that contribute to the development of PTE—and evaluating them through a multidisciplinary lens tailored to individual patients—are essential for both early diagnosis and the development of targeted preventive strategies. The aim of this study is to retrospectively analyze the facilitating factors that increase venous thrombotic risk in patients diagnosed with PTE across various clinical settings, thereby contributing to a region-specific risk profile based on national data.

METHODS

Ethics

The study protocol was reviewed and approved by the Non-interventional Clinical Researches Ethics Committee of Yozgat Bozok University (Date: 02.07.2025, Decision No: 2025-GOKAEK-2513_2025.07.02_530). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Due to the retrospective nature of the study, informed consent from the participants was not required. All data were anonymized in accordance with the Personal Data Protection Law No. 6698, and no interventions or additional medical procedures were performed on any patient within the scope of the study.

Study Design and Participants

This retrospective study was conducted by reviewing the clinical data of patients who were followed with a diagnosis of PTE between January 1, 2023, and January 1, 2025, in the Departments of Chest Diseases, Cardiovascular Surgery, and Internal Medicine at Yozgat Bozok University Research and Training Hospital. Patients aged between 18 and 80 years with a confirmed diagnosis of PTE were included. Cases with an uncertain diagnosis, individuals under 18 years of age, and those who had received only prophylactic treatment were excluded from the analysis. The study did not involve a comparative control group.

Imaging Evaluation

All radiological examinations performed during the diagnostic process were retrospectively assessed through archived records. These included thoracic computed tomographic angiography (CTA), scintigraphy, abdominal computed tomography (CT), and venous Doppler ultrasonography (USG), which are standard imaging modalities used in diagnosing pulmonary embolism. The imaging data were obtained exclusively from pre-existing patient reports in medical records; no new imaging procedures were conducted specifically for the study.

Clinical and Demographic Data

In addition to demographic variables such as age, sex, and body-mass index (BMI), information on clinical risk factors was collected, including smoking status, comorbid conditions (e.g., hypertension, diabetes mellitus, malignancy), history of surgery, immobilization, and—for female patients—pregnancy and OCP use. Laboratory parameters, including complete blood count, biochemical analysis, arterial blood gas parameters (pH, pO_2, pCO_2, sO_2), and D-dimer levels, were also retrieved from archival records. All data were gathered retrospectively through hospital files and the hospital information management system.

Statistical Analysis

The data analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean±standard deviation (SD), while categorical variables were expressed as frequencies and percentages (%). The Kolmogorov-Smirnov test was used to assess the normality of variable distribution. For comparisons between normally distributed groups, the Independent samples t-test was used; the Mann-Whitney U test was applied for non-normally distributed variables. Categorical data were analyzed using the Chi-square test. Correlation between chronic obstructive pulmonary disease (COPD), ascending aorta diameter, and cardiometabolic risk factors was evaluated using parametric (Pearson) or non-parametric (Spearman) correlation tests, as appropriate. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 41 patients diagnosed with PTE between 2023 and 2025 were included in the study. Of these, 25 were female and 16 were male. The mean age of the entire cohort was calculated as 61.59±17.92 years. When stratified by gender, the mean age of female patients was 62.56±17.93 years, while that of male patients was 60.06±18.40 years. These findings indicate that the study population encompassed a wide age range, and the mean ages of female and male patients were relatively comparable.

BMI data were available for only 11 patients. The mean BMI among these individuals was 29.97±3.05. According to the classification of obesity, 5 patients were overweight, 5 were categorized as having class 1 obesity, and 1 patient had class 2 obesity. No patients in the study group were underweight, of normal weight, or classified as having class 3 obesity.

A substantial proportion of the patient population had one or more chronic comorbidities. The most commonly observed comorbidity was hypertension, identified in 58.5% (n=24) of patients, followed by diabetes mellitus in 24.4% (n=10), coronary artery disease in 17.1% (n=7), and hyperlipidemia in 9.8% (n=4). In 21.9% of patients (n=9), no accompanying chronic disease was documented. Among the combinations of comorbidities, the coexistence of hypertension and diabetes mellitus was most prominent, occurring in 22% (n=9) of patients.

Analysis of smoking status revealed that 4 patients were active smokers—2 women and 2 men. The average smoking exposure among these individuals was 21 pack-years.

A history of surgical intervention was present in 17.1% (n=7) of patients, all of whom were female. Surgical procedures varied and included hysterectomy, thyroidectomy, tibial fracture repair, spinal surgery, hip arthroplasty, myomectomy, great saphenous vein (GSV) radiofrequency ablation, and coronary artery bypass grafting. Additionally, 14.6% (n=6) of patients had a history of prolonged immobility, predominantly among female patients (12.2%, n=5), with only one male case (2.4%). The remaining 85.4% (n=35) of the cohort had no reported history of immobilization.

Only one patient (2.4%) had a history of malignancy, specifically colon cancer. No other cases of active cancer were recorded. Among female patients, 4.9% (n=2) had a history of pregnancy, and 2.4% (n=1) had a recorded history of OCP use.

Hereditary thrombophilia was identified in 19.5% (n=8) of patients. The majority of these individuals were women, with only one male patient affected. The most common genetic abnormality was protein C resistance, found in 4.9% (n=2) of cases. Other inherited thrombophilic conditions—each observed in one patient (2.4%)—included Factor V Leiden mutation, heterozygous prothrombin gene mutation, various forms of MTHFR gene mutations, PAI-2 gene mutation with homozygous MTHFR mutation, and F13 homozygous mutation with MTHFR C and A variants.

Evaluation of basic laboratory parameters revealed that the mean hemoglobin (Hb) level was 13.25±1.83 g/dl. The mean platelet count (PLT) was 269.12±81.70x10^3/µL, AST level was 22.69±11.90 U/L, and ALT level was 30.15±35.68 U/L. Among renal function tests, the mean blood urea nitrogen (BUN) level was 27.16±18.18 mg/dl, while serum creatinine—available for a subset of patients—was calculated at 1.00±0.45 mg/dl.

When these laboratory findings were compared with standard reference ranges for the general adult population, several statistically significant differences were noted. The mean Hb level in patients with PTE was 13.25 g/dl, below the reference average of 14.0 g/dl, and this reduction was statistically significant (p=0.0225). Similarly, the BUN level was significantly elevated at 27.16 mg/dl compared to the reference average of 15.0 mg/dl (p=0.0004). Differences in platelet count, AST, ALT, and creatinine levels, however, were not statistically significant (p>0.05) (**Table 1**).

Table 1. Mean and standard deviation values of basic laboratory parameters in the patient group diagnosed with pulmonary thromboembolism (PTE)

Parameter (unit)	PTE mean	Reference mean	Difference	p-value
Hb (g/dl)	13.25	14.0	-0.75	0.0225
PLT (x10^3/µL)	269.12	250.0	19.12	0.1817
AST (U/L)	22.69	20.0	2.69	0.1958
ALT (U/L)	30.15	25.0	5.15	0.4058
BUN (mg/dl)	27.16	15.0	12.16	0.0004
sCr (mg/dl)	1.0	0.9	0.1	0.2287

Hb: Hemoglobin, PLT: Platelets, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, BUN: Blood urea nitrogen, sCr: Serum creatinine

When the arterial blood gas parameters of patients diagnosed with PTE were compared with general clinical reference averages, several noteworthy findings emerged. The mean pH

value was 7.40, which was identical to the standard reference value (7.40), and no statistically significant difference was observed (p>0.05). However, the mean oxygen saturation (sO_2) in the PTE group was calculated as 74.92±16.27%, which is markedly below the reference average of 95%. This difference was found to be statistically significant (p<0.0001). Similarly, the mean partial oxygen pressure (pO_2) in PTE patients was 52.21 mmHg, significantly lower than the reference value of 75 mmHg (p<0.0001). The mean partial carbon dioxide pressure (pCO_2) was measured at 30.26 mmHg, which was also significantly lower than the reference value of 40 mmHg (p<0.0001) (**Table 2**).

Table 2. Mean values, differences, and p-values obtained by comparing arterial blood gas parameters of patients diagnosed with pulmonary thromboembolism (PTE) with clinically accepted reference averages

Parameter (unit)	PTE mean	Reference mean	Difference	p-value
pH	7.42	7.40	0.02	0.2558
pO_2 (mmHg)	46.52	75.0	-28.48	0.0000
pCO_2 (mmHg)	36.14	40.0	-3.86	0.0456
sO_2 (%)	71.56	95.0	-23.44	0.0000

pH: Acid-base balance of arterial blood, pO_2: Partial Pressure of oxygen, pCO_2: Partial pressure of carbon dioxide, sO_2: Oxygen saturation

In the study, D-dimer levels were found to have a mean value of 3.31±2.36 µg/ml. This level is markedly elevated when compared to the generally accepted upper reference limit of 0.5 µg/ml.

A one-sample t-test revealed a p-value of 0.00000947, indicating statistical significance at the p<0.001 level. This finding demonstrates that the D-dimer levels of the patients included in the study were significantly higher than the reference value.

When the pulmonary CT angiography (CTA) reports of the patients were reviewed, the most frequently observed radiological finding was bilateral pulmonary artery involvement. A total of 15 patients showed widespread evidence of PTE in both lungs, suggesting a more diffuse disease distribution.

Additionally, in 14 patients, PTE was localized to the lobar or segmental level, indicating a more limited pattern of involvement. In the remaining 12 patients, multiple thrombus foci were noted at various anatomical levels, as described in their CTA reports.

Analysis of the Doppler USG findings for all 41 patients revealed that 51.2% (n=21) had reports stating "no evidence of DVT." Positive findings indicating the presence of DVT were reported in 9.8% (n=4) of patients. The remaining 39.0% (n=16) had no available Doppler USG data on record.

DISCUSSION

The findings obtained from the evaluation of 41 patients diagnosed with PTE in this study, when compared with existing literature, suggest that several risk factors play a significant role in the development of PTE. The mean age of the study group was 61.59±17.92 years, with a higher proportion of female patients. This aligns closely with the large-scale study conducted by Konstantinides and colleagues,[2] as presented in the 2019 ESC Guidelines, which reported that PTE is more commonly seen in older adults and women.[1,2,10] Similarly, Chen and colleagues[36] provided a detailed evaluation of the impact of age and sex differences on the incidence and mortality of pulmonary embolism.

Among patients with available BMI data, the average BMI was 29.97, with most individuals classified as overweight or obese. Obesity has previously been identified by Stein and colleagues[7] as an independent risk factor for VTE. In their study, obesity was shown to promote changes in the coagulation cascade and reduce venous return, thereby facilitating thrombus formation.[7,9] In addition, Pastori and colleagues[34] reported that obesity, when combined with coagulation abnormalities, further increases the risk of thrombosis.

In terms of comorbidities, hypertension was the most common, followed by diabetes mellitus, coronary artery disease, and hyperlipidemia. Notably, the coexistence of hypertension and diabetes may contribute to endothelial dysfunction and create a prothrombotic environment. This interaction has also been highlighted in the studies by Cushman[11] and Anderson,[12] which emphasize the role of such comorbidities in the pathogenesis of VTE.[4,11,12]

Although the proportion of patients who smoked was low, the reported intensity of smoking was considerable. This finding parallels that of Pomp et al.,[9] who established a correlation between cigarette smoking and hypercoagulability. Moreover, the thrombotic risk may be further heightened when smoking is combined with hormonal factors.[9,14]

It is noteworthy that all patients with a history of surgical intervention were female. This may reflect the higher frequency of gynecological surgeries in women, as well as postoperative immobility contributing to increased PTE risk. Geerts and colleagues[3] have also emphasized surgery as a major risk factor for VTE development in their studies on postoperative thrombosis.[3,24] Hayssen and colleagues[35] also demonstrated that surgical patients are predominantly classified within high-risk categories according to Caprini score–derived risk stratification.

The predominance of women among patients with a history of immobilization may be attributable to factors such as osteoporotic fractures and prolonged postoperative recovery, particularly in elderly women. Clinical models developed by Spyropoulos[4] and Anderson[12] have also confirmed immobilization as an independent risk factor for VTE.

Although malignancy was identified in only one patient, this finding is consistent with the observations of Khorana et al.,[5] who demonstrated the thrombogenic impact of malignancies, particularly in the context of chemotherapy. Colorectal cancers, in particular, are frequently reported in the literature as having prothrombotic properties.[5,33]

The data related to pregnancy and OCP use support the understanding that both endogenous and exogenous estrogen can increase thrombotic risk through their effects on the coagulation system. Researchers such as Heit,[6] James,[26] and

Kalaitzopoulos[27] have explained this phenomenon in the context of increased venous stasis, changes in intravascular pressure, and hormonal fluctuations during pregnancy.[6,8,26,27]

Hereditary thrombophilic disorders were identified in a subset of patients. Conditions such as Factor V Leiden mutation, prothrombin gene mutation, and MTHFR polymorphisms are consistent with the findings of studies on inherited thrombophilia by Middeldorp,[13] Zöller,[16] and Franco.[15] These genetic factors are especially relevant in differential diagnosis, particularly in younger patients presenting with PTE.[13-16,28]

The laboratory findings of decreased Hb levels and elevated BUN suggest the systemic effects of PTE and the potential metabolic consequences of accompanying comorbidities. Similar observations were reported by Wada and colleagues[17] in their studies on post-traumatic hemostatic disorders, indicating that such hematological alterations may carry clinical significance.[17,20]

Arterial blood gas analyses in this study demonstrated the presence of hypoxemia (decreased sO_2 and pO_2) and hypocapnia (reduced pCO_2) in patients diagnosed with PTE. These findings are consistent with the pathophysiological mechanisms described by Carson[29] and Jaff,[31] who noted that acute PTE often leads to ventilation-perfusion mismatch, impairing oxygenation and triggering hyperventilation that results in excessive carbon dioxide elimination.[1,29,31] Moreover, Hasegawa and colleagues[37] reported that pulmonary embolism complicating sepsis and septic shock was associated with severe hypoxemia and increased mortality.

D-dimer levels in our study were substantially above the commonly accepted upper reference limit. In line with findings from the ADJUST-PE trial by Righini et al.[18] and Wells' study[19] on the role of D-dimer in DVT diagnosis, this biomarker is noted to have high sensitivity but limited specificity. In our cohort, D-dimer levels were significantly elevated, supporting its value as a diagnostic marker.[18,19,32]

CTA findings in this study illustrated the broad clinical spectrum of PTE, ranging from diffuse bilateral involvement to isolated segmental lesions. These findings are consistent with the work of Stein et al.,[23] who examined the diagnostic utility of multidetector CT in acute PTE. Imaging results obtained via CT have been shown to directly influence clinical decision-making.[22,30,33]

The relatively low number of patients with confirmed DVT on Doppler USG suggests that PTE can occasionally develop without obvious thrombotic events in the lower extremities. Nonetheless, as emphasized in the clinical guidelines by Ortel[21] and Barbar,[24] the presence of DVT increases clinical suspicion and serves as a valuable clue in establishing a diagnosis of PTE.[19,21,31]

Collectively, these findings reaffirm the critical importance of personalized evaluation strategies, interdisciplinary collaboration, and detailed risk factor assessment in improving clinical outcomes in the diagnosis and management of PTE.

Limitations

Nevertheless, the limited number of patients can be considered an inherent limitation of the study; conducting similar analyses in larger cohorts would enhance the generalizability of the findings and further increase the value of the results.

CONCLUSION

This study highlights the multifactorial nature of PTE, reflecting a complex clinical picture shaped by the interplay of individual and environmental risk factors. Advanced age, comorbidities, obesity, immobilization, history of surgery, hormonal factors, and genetic predisposition were identified as key contributors to thrombosis development.

Laboratory and imaging findings—particularly elevated D-dimer levels, hypoxemia, and widespread emboli on CT—emerged as strong diagnostic biomarkers. These results underscore the critical importance of early diagnosis and timely initiation of anticoagulant therapy in reducing mortality.

As a result, a multidisciplinary and personalized approach is essential in the management of PTE. Clinical decisions should not rely solely on laboratory results, but rather incorporate the patient's comprehensive medical history, comorbid conditions, and individual risk profile. This holistic strategy is a fundamental principle that directly influences both treatment success and patient quality of life.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study protocol was reviewed and approved by the Non-interventional Clinical Researches Ethics Committee of Yozgat Bozok University (Date: 02.07.2025, Decision No: 2025-GOKAEK-2513_2025.07.02_530).

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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