Original article

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Pulmonary embolism in patients with and without active cancer: outcomes and treatment patterns from a single-center registry

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Pulmonary embolism (PE) is a common and serious complication in cancer patients, often associated with distinct clinical features and outcomes. This study aimed to compare the characteristics and early prognosis of PE in patients with and without cancer.

We retrospectively analyzed 395 patients hospitalized for acute PE between 2018 and 2024. Patients were categorized by the presence of active cancer. Demographic data, laboratory and echocardiographic parameters, treatment patterns, and outcomes were compared. The primary end-point of the study was all-cause hospital death. The secondary end-points were the use of thrombolytic therapy in patients with and without active cancer and the occurence of major bleeding.

Cancer patients were older (67.7±12.7 vs. 66.3±15.8 years, p=0.014) and had higher D-dimer (6852 vs. 4368 ng/mL, p=0.022), BNP (693.5 vs. 489.4 pg/mL, p=0.032), WBC (14.7 vs. 12.1×10⁹/L, p=0.0001), and LDH (1280 vs. 722 U/L, p=0.0001). They were less likely to receive fibrinolysis (10.9% vs. 25.1%, p=0.019). Hospital mortality was higher in cancer patients (23.4% vs. 14.2%, p=0.056), although rates of major bleeding were similar.

Patients with cancer-associated PE exhibit distinct biomarker profiles and are treated less aggressively, with a trend toward higher short-term mortality. These findings highlight the need for tailored risk-benefit assessments in this high-risk population.

Key words: cancer associated pulmonary embolism, outcomes

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Plućna emoblija kod pacijenata sa aktivnim cancerom i bez aktivnog kancera: ishod i obrasci lečenja dobijeni iz registra jednog centra

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Plućna embolija (PE) predstavlja čestu i ozbiljnu komplikaciju kod pacijenata sa malignim bolestima. Kliničke karakteristike i ishodi ove populacije obolelih često se razlikuju u poređenju sa pacijentima bez maligne bolesti. Cilj rada bio je poređenje karakteristika i rana prognoza kod pacijenata sa PE udruženom sa aktivnim malignitetom u odnosu na pacijente bez maligne bolesti.

Retrospektivno je analizirano 395 pacijenata hospitalizovanih zbog akutne PE u periodu 2018–2024. U zavisnosti od maligne bolesti, pacijenti su podeljeni u dve grupe. Analizirani su demografski podaci, laboratorijski i ehokardiografski parametri, terapijski režim i ishodi. Primarni ishod bila je ukupna bolnička smrtnost, dok su sekundarni ishodi obuhvatali primenu trombolitičke terapije i pojavu velikih krvarenja.

Pacijenti sa malignitetom bili su stariji (67.7±12.7 vs. 66.3±15.8 years, p=0.014), imali su više vrednosti D-dimera (6852 vs. 4368 ng/mL, p=0.022), BNP (693.5 vs. 489.4 pg/mL, p=0.032), leukocita (14.7 vs. 12.1×10⁹/L, p=0.0001) i LDH (1280 vs. 722 U/L, p=0.0001) u poređenju sa pacijentima bez maligne bolesti. Kod njih je fibrinolitička terapija ređe primenjivana (10.9% vs 25.1%, p=0.019). Bolnička smrtnost je bila veća u grupi sa malignitetom (23.4% vs 14.2%, p=0.056), dok se učestalost velikih krvarenja nije značajno razlikovala.

Pacijenti sa PE udruženom sa malignim bolestima imaju veće vrednosti biomarkera, ređe dobijaju trombolitičku terapiju I imaju sa većom stopom nepovoljnih ishoda. Rezultati ukazuju na potrebu za individualizovanom procenom terapijskog pristupa u ovoj visokorizičnoj populaciji.

Ključne reči: plućna embolija udružena sa malignitetom, ishod

Introduction

Pulmonary embolism (PE) is a potentially life-threatening manifestation of venous thromboembolism (VTE), with cancer representing one of its most significant risk factors (1,2). The association between malignancy and thrombosis is multifactorial, involving tumor-related procoagulant release, endothelial dysfunction, inflammatory cytokines, and immobility (3). Notably, PE may be the first clinical sign of occult cancer, and it is often associated with poorer outcomes in cancer patients compared to non-cancer populations (4).

Cancer patients with acute PE represent a high-risk subgroup, often presenting with more advanced thrombosis, abnormal biomarker profiles, and higher risk for both recurrence and bleeding (5,6). These complexities influence treatment decisions, especially regarding the use of systemic thrombolysis, which remains controversial due to the increased hemorrhagic risk in malignancy (7). While direct oral anticoagulants (DOACs) have improved outpatient management in cancer-associated thrombosis (CAT), the acute phase of PE in this population still poses considerable clinical challenges.

Previous studies have reported inconsistent findings regarding mortality, treatment intensity, and bleeding outcomes in cancer-associated PE (8). There is an ongoing need to characterize the clinical presentation and short-term prognosis in this specific population, especially in real-world hospital settings.

This study aimed to compare demographic, clinical, echocardiographic, and laboratory features of PE patients with and without cancer, and to explore differences in the use of fibrinolytic therapy, in-hospital mortality, and bleeding complications.

Methods

This was a retrospective observational study conducted at a single tertiary care center, including consecutive patients hospitalized with confirmed acute pulmonary embolism (PE) between January 2018 and December 2024. The diagnosis of PE was established by computed tomography pulmonary angiography (CTPA).

Relevant data were derived from medical history during hospitalization. All patients were asked about comorbidities and underwent measurements of oxygen saturation, systolic arterial pressure, heart rate, and basic laboratory blood assessments at presentation to the hospital. Echocardiography imaging, cardiac troponin (cTn), and brain natriuretic peptide (BNP) blood levels were obtained on the first day of hospitalization for a considerable number of patients (see footnote of Table 1). According to the presence of severe hypotension or right ventricle (RV) dysfunction, acute PE patients were stratified into high-risk, intermediate risk, or low-risk patient groups, according to the 2019 ESC PE guideline.

Patients were categorized into two groups based on the presence or absence of active cancer, defined as a diagnosis of malignancy within the previous six months, ongoing anticancer treatment, or recurrent/metastatic disease. All patients with active cancer had medical reports that confirmed pathophysiology diagnosis of cancer, localization, stage, TNM classification, and chemotherapy and/or radiotherapy protocol regimen applied. Patients who were classified as no-cancer group had no previous medical documentation of malignancy and no suspicion of having cancer according to initial clinical, laboratory, and imaging evaluation, and had spontaneous or provoked PE due to other major or minor transient or persistent risk factors according to PE-GL. Demographic data, clinical presentation, laboratory

parameters (including D-dimer, BNP, CRP, LDH), echocardiographic findings, and ECG patterns were extracted from electronic medical records.

The echocardiographic exam was performed as the initial imaging in patients with shock, and in the majority of cases, it was done after the CTPA. The focus of the echocardiography was on right ventricle diameters and function, as per current guidelines.

Endpoints

The primary endpoint was intra-hospital death. The secondary endpoints of the study were the use of fibrinolytic therapy, length of hospital stay, and major bleeding during hospitalization as defined by criteria of the International Society of Thrombosis and Hemostasis (ISTH).

Stathistical analysis

Continuous variables were expressed as mean ± standard deviation (SD) and compared using independent-samples t-tests. Categorical variables were presented as counts (percentages) and compared with chi-square or Fisher's exact tests, as appropriate. A p-value <0.05 was considered statistically significant. Analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

Ethics. Local Review Boards were give permission to collect data. Patients were informed that their clinical data were registered in the local single-center PE registry without revealing identity.

Results

Among 395 consecutive patients with PE from the Single Center PE Registry (part of the regional REPER registry), 331 (83.8%) had no history of cancer, and 64 (16.2%) fulfilled the criteria for classification based on a reliable history of malignancy (group II).

Sex distribution, frequency of dyspnea, syncope, chest pain, and most comorbidities were comparable between groups. Cancer patients were slightly older (67.7±12.7 vs. 66.3±15.8 years, p = 0.014) and had a lower BMI, although this difference did not reach statistical significance. However, hypertension was significantly more prevalent among non-cancer patients (61% vs. 46.9%, p = 0.025). Deep vein thrombosis at presentation was observed less frequently in patients with cancer (17.2% vs. 32%, p = 0.009), while previous bleeding events were markedly higher in this group (21.9% vs. 5.1%, p = 0.0001). Although the prevalence of right ventricular dysfunction and reduced left ventricular ejection fraction did not differ significantly, resolution of S waves on ECG was less common in cancer patients (3.1% vs. 15.4%, p = 0.0001). A shock index greater than one was slightly more frequent in the cancer group (21.9% vs. 21.1%, p = 0.034). No significant differences were noted in ESC risk stratification categories. These findings underscore the distinct clinical profile of PE patients with cancer, particularly regarding bleeding history and concurrent DVT, which may influence management strategies. (Table 1)

Laboratory values differed notably, with cancer patients exhibiting higher D-dimer (6851.9 vs. 4368.4 ng/mL, p=0.022), BNP (693.5 vs. 489.4 pg/mL, p=0.032), WBC counts (14.7 vs. 12.1×10⁹/L, p=0.0001), LDH (1280 vs. 722 U/L, p=0.0001), and platelet counts (243 vs. 228 ×10⁹/L, p=0.011). (Table 2)

Despite similar right ventricular function and sPAP, cancer patients were less likely to receive fibrinolysis (10.9% vs. 25.1%, p = 0.019) and showed a trend toward higher in-hospital mortality (23.4% vs. 14.2%, p = 0.056). Major bleeding rates were comparable. (Table 2)

Cox proportional hazards models showed that cancer (HR = 0.575; 95% CI: 0.322–1.029; p = 0.062) was not independently associated with time to death. However, in models incorporating ESC risk stratification, both intermediate- and high-risk groups exhibited significantly worse survival (p < 0.001). In a combined model, active cancer remained non-significant (HR = 0.601; p = 0.090), whereas high-risk PE was associated with a markedly increased hazard (Figures 1-2).

ESC risk stratification emerged as a strong, independent predictor of early mortality, whereas active cancer did not achieve statistical significance, highlighting the predominant influence of PE severity over cancer status in mortality risk assessment.

Kaplan-Meier survival curves comparing patients with and without active cancer revealed a non-significant trend toward worse survival in the cancer group over the follow-up period (23.4% vs. 14.2%; log-rank p = 0.056) (Figure 4). Kaplan-Meier analysis also demonstrated that ESC risk stratification strongly predicted mortality, regardless of cancer status (log-rank p = 0.0001, adjusted for malignancy) (Figures 3-4).

Discussion

This retrospective analysis highlights key differences in the clinical profiles and outcomes of patients with and without PE who have cancer. While age was slightly higher among patients with malignancy, hemodynamic parameters and echocardiographic findings, including right ventricular (RV) function and pulmonary artery pressures, were comparable between groups. However, laboratory values differed substantially: cancer patients had significantly elevated D-dimer, BNP, LDH, and WBC counts, which may reflect heightened inflammatory and prothrombotic activity associated with malignancy (1, 3, 5).

Importantly, cancer patients were significantly less likely to receive fibrinolytic therapy (10.9% vs. 25.1%, p = 0.019), likely due to perceived or actual concerns about bleeding risk. While the incidence of major bleeding was not significantly different between groups, the observed trend toward higher hospital mortality in cancer patients (23.4% vs. 14.2%, p=0.056) is consistent with prior literature suggesting worse early outcomes in this population (4,6,9). The cause of death in patients with PE and cancer is multifactorial, and both PE and cancer contribute more or less to this outcome. This was the reason why we chose this outcome instead of PE-related death, which is more inaccurate and speculative. (4) Nonetheless, the higher prevalence of prior bleeding among cancer patients (21.9% vs. 5.1%) highlights a key dilemma: the same cohort that may benefit most from aggressive PE therapy often carries the greatest hemorrhagic risk (10).

Biomarkers such as BNP and D-dimer, which were elevated in cancer patients, are known predictors of right ventricular dysfunction and PE severity (10). Although imaging parameters did not differ significantly, these laboratory markers may serve as early indicators of clinical deterioration in malignancy-associated PE and support their use in initial risk stratification (11).

The Kaplan-Meier analysis revealed a trend toward reduced survival among cancer patients, although it did not reach statistical significance. This aligns with data from the RIETE registry and others, suggesting that cancer confers a multifaceted mortality risk not solely attributable to thrombotic burden (12).

Our findings are in agreement with the ESC guidelines recommending personalized treatment in cancer-associated PE, especially regarding thrombolytic therapy and anticoagulation levels [13]. Despite the observational design and limited sample size, the study underscores the clinical complexity of cancer-associated PE and suggests that under-treatment may contribute to worse outcomes.

Further prospective studies are needed to define optimal management strategies for this high-risk group and to balance bleeding risk against mortality benefit from more aggressive therapies. Prospective studies are also warranted to clarify optimal thresholds for thrombolysis in this vulnerable population and to explore the role of catheter-directed or reduced-dose regimens as potential strategies to mitigate bleeding (14,15).

Limitations

The retrospective nature of the study limits control over data collection, potentially impacting the accuracy and consistency of recorded clinical variables. Additionally, the relatively small sample size—particularly within the cancer-associated PE subgroup—restricts the ability to perform more robust statistical analyses of clinical outcomes, presentation, and bleeding risk. Additionally, there was a sample size imbalance between patients with and without cancer.

Conclusion

Cancer-associated PE patients exhibited unique laboratory patterns—higher D-dimer, BNP, LDH, and WBC levels—and were less frequently treated with fibrinolytic agents. Despite higher in-hospital mortality, major bleeding rates were similar, emphasizing the need for personalized risk assessment. These results highlight the complexity of treating PE in cancer patients and underscore the importance of developing tailored, Patient-Specific cancer care pathways for PE.

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