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Prevalence of Thrombotic Complications in Critically Ill Cancer Patients with COVID-19 Admitted to the Intensive Care Unit

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A B S T R A C T

Introduction: Critically ill cancer patients with COVID-19 are at elevated risk for thrombotic complications due to the prothrombotic effects of both malignancy and SARS-CoV-2 infection. This study aimed to assess the prevalence and clinical impact of thrombosis in this high-risk population.

Materials and Methods: This observational study was conducted at Tabriz University of Medical Sciences, involving 100 adult cancer patients with confirmed COVID-19 admitted to the intensive care unit (ICU). Data on demographics, cancer type, thrombotic events, laboratory findings, and clinical outcomes were collected. Ethical approval was obtained under code IR.TBZMED.REC.1403.021.

Results: Thrombotic complications occurred in 41% of patients, with deep vein thrombosis (22%) and pulmonary embolism (18%) being most common. Patients with thrombosis had significantly higher ICU mortality (63.41% vs. 38.98%, $p = 0.011$), longer ICU stays, and elevated D-dimer levels (mean 4.86 vs. 2.94 µg/mL, $p < 0.001$).

Conclusion: Thrombosis is highly prevalent and associated with poor outcomes in critically ill cancer patients with COVID-19. These findings emphasize the need for enhanced risk stratification, early detection, and personalized thromboprophylaxis in this vulnerable group.

Introduction

The global COVID-19 pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1], has led to unprecedented challenges in critical care medicine. Among the populations most vulnerable to severe manifestations of COVID-19 are patients with underlying malignancies [1]. These individuals often present with a compromised immune system due to either the malignancy itself or its treatment, making them more susceptible to infections and associated complications.

As the pandemic evolved, it became increasingly evident that COVID-19 is associated not only with respiratory distress but also with a high incidence of thrombotic events, particularly in critically ill patients admitted to intensive care units (ICUs) [2-5]. Thrombotic complications, including venous thromboembolism (VTE), arterial thrombosis, and disseminated intravascular coagulation (DIC), have emerged as prominent contributors to morbidity and mortality in COVID-19 [6].

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The pathophysiological underpinnings of this prothrombotic state are multifactorial and include endothelial dysfunction, cytokine storm-induced hyperinflammation, platelet activation, and coagulopathy resembling sepsis-induced disseminated intravascular coagulation [7].

The virus's affinity for angiotensin-converting enzyme 2 (ACE2) receptors expressed on endothelial cells has been implicated in the endothelial injury and microvascular thrombosis observed in severe cases [8].

Cancer patients, particularly those with advanced disease or undergoing aggressive treatments such as chemotherapy, are already at increased risk for thrombosis. Malignancy itself induces a hypercoagulable state through various mechanisms, including tumor cell expression of procoagulant factors, cytokine-mediated activation of the coagulation cascade, and interactions between tumor cells and host vascular or immune cells [9]. Furthermore, factors such as immobility, central venous catheters, and supportive therapies exacerbate this risk. When COVID-19 infection is superimposed on cancer, the already elevated risk of thrombotic events is further magnified, leading to an alarming confluence of risk factors in critically ill oncologic patients [10].

Several studies have reported that the prevalence of thrombotic complications in hospitalized COVID-19 patients can range from 20% to over 40%, with even higher rates observed in those requiring ICU admission [11]. In cancer patients, this prevalence may be significantly amplified, although the data remain sparse and somewhat heterogeneous. Despite the routine implementation of thromboprophylaxis, breakthrough thrombotic events are frequently documented in this population, raising concerns regarding the adequacy of current prophylactic strategies and the need for individualized anticoagulation regimens [12].

Critically ill cancer patients with COVID-19 represent a unique and complex subgroup. Their immunocompromised status, potential for multisystem involvement, and the overlapping complications of cancer and COVID-19 make clinical management particularly challenging. ICU admission in these patients is often necessitated by respiratory failure, hemodynamic instability, or septic shock—conditions that independently contribute to an increased thrombotic risk [13]. Moreover, diagnostic challenges due to nonspecific symptoms, limitations in imaging modalities, and the risk of transport-related decompensation often hinder timely recognition and management of thrombotic events in this cohort [14].

There is a pressing need to better characterize the burden of thrombotic complications in this vulnerable population to guide clinical decision-making and inform prophylactic and therapeutic strategies [15]. Understanding the prevalence and nature of thrombosis in critically ill cancer patients with COVID-19 could help stratify risk, optimize anticoagulation protocols, and ultimately improve patient outcomes. It may also provide insights into the pathophysiological intersections between cancer-associated thrombosis and COVID-19–related coagulopathy [16].

Furthermore, elucidating these patterns has implications beyond the current pandemic. With the increasing recognition of cancer-associated coagulopathy and the heightened risk introduced by infectious triggers such as SARS-CoV-2, a more nuanced approach to thrombosis prevention and management in critically ill cancer patients is warranted [17]. Such efforts will not only inform responses to future infectious threats but may also contribute to the broader field of cancer thrombosis research [18].

In light of these considerations, the present study aims to evaluate the prevalence and types of thrombotic complications in critically ill cancer patients with COVID-19 admitted to the ICU. By identifying the frequency, timing, and clinical correlates of these events, this study seeks to contribute to the growing body of knowledge on COVID-19–associated coagulopathy and offer evidence to refine clinical protocols in this high-risk population.

Methods

Study Design and Setting

This retrospective observational cohort study was conducted at Imam Reza Hospital, a tertiary care academic medical center affiliated with Tabriz. The study period covered admissions between March 1, 2020, and December 31, 2022, coinciding with the peak period of the COVID-19 pandemic. Ethical approval was obtained from the institutional review board (IRB Code: IR.TBZMED.REC.1403.021), and all procedures were carried out in accordance with the principles of the Declaration of Helsinki.

Patient Selection

We included all adult patients aged 18 years or older who had an active malignancy and were admitted to the intensive care unit (ICU) with a confirmed diagnosis of COVID-19 via reverse transcription polymerase chain reaction (RT-PCR) during the study period. Active cancer was defined as a diagnosis of solid or hematologic malignancy within the last 6 months, ongoing cancer treatment (chemotherapy, radiotherapy, or immunotherapy), or evidence of metastatic disease.

Patients were excluded if they met any of the following criteria:

1. Incomplete or missing key medical records,
2. Known hereditary thrombophilia (e.g., Factor V Leiden),
3. Receiving therapeutic anticoagulation prior to ICU admission for other indications

(e.g., atrial fibrillation, prior venous thromboembolism),

4. Repeat ICU admissions during the same hospital stay.

Data Collection

Demographic and clinical data were extracted from the hospital's electronic health records by trained researchers. Variables included age, sex, body mass index (BMI), type and stage of cancer, presence of metastasis, recent cancer therapy (within the last 30 days), and major comorbidities such as hypertension, diabetes, and chronic kidney disease.

COVID-19-related data included date of positive PCR, symptoms at presentation, oxygen and ventilatory support requirements, inflammatory and coagulation markers (D-dimer, fibrinogen, CRP, ferritin, platelet count), and imaging findings. The date and type of thrombotic complications, if any, were recorded.

Outcome Measures

The primary outcome was the prevalence of thrombotic complications, including venous thromboembolism (VTE), arterial thrombosis (e.g., stroke, myocardial infarction), and disseminated intravascular coagulation (DIC) during ICU admission. Diagnoses were confirmed by appropriate imaging studies and/or laboratory criteria:

- **DVT:** confirmed by duplex ultrasonography,
- **Pulmonary embolism:** confirmed by computed tomography pulmonary angiography (CTPA),
- **Arterial events:** confirmed through CT angiography, ECG, or echocardiography depending on the case,
- **DIC:** assessed using the International Society on Thrombosis and Haemostasis (ISTH) DIC scoring system.

Secondary outcomes included ICU length of stay, need for mechanical ventilation, and use of vasopressors, renal replacement therapy (RRT), in-hospital mortality, and thrombosis-related mortality.

Statistical Analysis

Data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized as frequencies and percentages, and continuous variables were presented as means ± standard deviations or medians with interquartile ranges (IQR), depending on data distribution.

Comparisons between patients with and without thrombotic events were performed using Chi-square or Fisher's exact test for categorical variables and Student's t-test or Mann–Whitney U test for continuous variables. A multivariable logistic regression model was used to identify independent predictors of thrombosis, adjusting for age, cancer type, stage, D-dimer level, and other relevant covariates. A two-tailed p-value < 0.05 was considered statistically significant

Study Context

This observational study was conducted at Tabriz University of Medical Sciences, Iran, with the enrollment of 100 critically ill cancer patients diagnosed with COVID-19 and admitted to the intensive care unit (ICU). All study protocols were approved by the university's Ethics Committee under the code IR.TBZMED.REC.1403.021.

Results

The cohort had a mean age of 61.37 years with a predominance of male patients (58%). Solid tumors were more common than hematologic malignancies, reflecting the general oncologic ICU population. Common comorbidities included hypertension (52%) and diabetes mellitus (38%). The average body mass index (BMI) was 26.43 kg/m², placing most patients in the overweight category. The median ICU stay was 13.5 days, and a significant proportion (72%) required invasive mechanical ventilation, indicating the severity of COVID-19 in this subgroup (Table 1).

Table 1. Baseline Characteristics of the Study Population (N = 100)

Characteristic	Value
Mean Age (years)	61.37 ± 12.49
Male Sex (%)	58.00%
Solid Tumors (%)	65.00%
Hematologic Malignancies (%)	35.00%
Mean BMI (kg/m²)	26.43 ± 4.87
Hypertension (%)	52.00%
Diabetes Mellitus (%)	38.00%
Median ICU Stay (days)	13.50 (IQR: 9.00–18.75)
Invasive Mechanical Ventilation (%)	72.00%

Among the 100 ICU cancer patients with COVID-19, thrombotic complications were observed in 41.00% of cases. The most frequent event was deep vein thrombosis (22%), followed by pulmonary embolism (18%). Arterial thrombosis and catheter-related thrombosis occurred in 9% and 6% of

patients, respectively. Disseminated intravascular coagulation was identified in 7% of patients. These findings underscore a high burden of thrombotic complications in this vulnerable population, despite standard thromboprophylaxis protocols (Table 2).

Table 2. Prevalence and Types of Thrombotic Events

Type of Thrombotic Event	Number of Cases (n)	Prevalence (%)
Deep Vein Thrombosis (DVT)	22	22.00%
Pulmonary Embolism (PE)	18	18.00%
Arterial Thrombosis	9	9.00%
Catheter-Related Thrombosis	6	6.00%
Disseminated Intravascular Coagulation (DIC)	7	7.00%
Total Patients with ≥1 Event	**41**	**41.00%**

Patients who developed thrombotic events had significantly worse clinical outcomes compared to those without thrombosis. ICU mortality in the thrombosis group was markedly higher (63.41% vs. 38.98%, $p = 0.011$), and these patients required longer ICU stays and mechanical ventilation more frequently. Elevated D-dimer levels (mean 4.86 μg/mL vs. 2.94 μg/mL, $p < 0.001$) were strongly associated with thrombotic complications, highlighting their potential role as a prognostic marker in this setting.

Table 3. Clinical Outcomes Based on Thrombotic Status

Outcome	Thrombosis Group (n = 41)	No Thrombosis Group (n = 59)	*p*-value
ICU Mortality (%)	63.41%	38.98%	0.011
Median ICU Stay (days)	15.00 (IQR: 11.00–20.00)	12.00 (IQR: 8.00–16.00)	0.023
Mechanical Ventilation (%)	85.37%	62.71%	0.007
Mean D-dimer (μg/mL)	4.86 ± 2.12	2.94 ± 1.47	<0.001

Discussion

This study evaluated the prevalence and clinical impact of thrombotic complications in critically ill cancer patients with confirmed COVID-19 infection admitted to the intensive care unit (ICU) of Tabriz University of Medical Sciences. With a thrombotic event rate of 41%, our findings underscore the significant burden of coagulopathy in this vulnerable patient population. These results align with and expand upon prior evidence demonstrating an elevated risk of thrombosis among both cancer patients and critically ill individuals with COVID-19, suggesting a synergistic effect of malignancy and SARS-CoV-2 infection on thrombotic risk [8].

The prevalence of thrombotic events observed in our cohort exceeds that reported in general ICU populations with COVID-19, where rates of thrombosis typically range from 20% to 30% despite prophylactic anticoagulation [9-12]. This disparity is likely attributable to the unique prothrombotic milieu associated with malignancy [13], compounded by the inflammatory and endothelial disruptions seen in severe COVID-19 [9]. Malignant disease, particularly solid tumors and hematologic cancers, is well-recognized to promote a hypercoagulable state through multiple mechanisms, including tumor-derived tissue factor expression, platelet activation, and cytokine release [14-16]. In our study, solid tumors were slightly more prevalent than hematologic malignancies, yet both groups experienced high rates of thrombotic complications [17], reinforcing the broad relevance of this risk across cancer subtypes [11].

The most common thrombotic events in our study were deep vein thrombosis (22%) and pulmonary embolism (18%), findings consistent with existing literature that identifies venous thromboembolism (VTE) as the predominant form of thrombosis in COVID-19 [18-20]. However, we also observed non-negligible rates of arterial thrombosis (9%), catheter-related thrombosis (6%), and disseminated intravascular coagulation (7%). These findings emphasize the spectrum of coagulopathy in COVID-19 and the importance of maintaining a high index of suspicion for atypical thrombotic manifestations, especially in cancer patients receiving central venous access, chemotherapy, or parenteral nutrition [12-14].

Importantly, thrombotic complications were significantly associated with adverse clinical outcomes in our study. Patients who developed thrombosis had higher ICU mortality (63.41% vs. 38.98%), longer ICU stays, greater need for invasive mechanical ventilation [21], and significantly elevated D-dimer levels [15]. These observations suggest that thrombosis is not merely a marker of disease severity but may actively contribute to clinical deterioration in this patient population [22-24]. The elevated D-dimer levels in the thrombosis group further support the utility of this biomarker in risk stratification, as previously documented in both oncologic and COVID-19 contexts [25-27]. While D-dimer is nonspecific and influenced by malignancy, its extreme elevation may help identify patients at particularly high risk for thrombotic

events who might benefit from intensified anticoagulation [16].

Despite the use of standard thromboprophylaxis protocols, thrombotic events occurred in more than 40% of patients, raising questions about the adequacy of existing anticoagulation strategies in this subgroup [28-30]. There is ongoing debate in the literature regarding optimal dosing of anticoagulants in critically ill COVID-19 patients, with some trials suggesting benefit from intermediate or therapeutic dosing in selected patients [17]. However, cancer patients, especially those with hematologic malignancies or recent chemotherapy, often carry concurrent bleeding risks, complicating anticoagulation decisions [31-33]. Our findings highlight the urgent need for individualized thromboprophylaxis regimens that carefully balance thrombotic and hemorrhagic risks in cancer patients with COVID-19 [18].

Additionally, the high incidence of thrombosis observed despite prophylaxis may reflect diagnostic challenges inherent in critically ill patients. Routine screening for asymptomatic VTE is not standard practice, and diagnostic imaging is often limited in unstable patients [34-36]. As a result, thrombotic events may be underrecognized or diagnosed late, contributing to poor outcomes [19]. This underscores the need for heightened clinical vigilance, liberal use of bedside imaging (e.g., compression ultrasonography), and the development of standardized protocols for early detection of thrombosis in high-risk ICU patients [20].

Our study has several strengths, including a focused patient population, comprehensive data collection, and its setting in a tertiary care university hospital. However, limitations must also be acknowledged [37-39]. The sample size, though adequate for exploratory analysis, limits the generalizability of our findings [40-42]. Additionally, the observational nature of the study precludes determination of causality, and data on bleeding events were not collected, preventing evaluation of the net clinical benefit of intensified anticoagulation [43]. Lastly, while we stratified patients by thrombotic status, more granular analysis by cancer type, stage, and treatment history may further elucidate differential risks within the oncologic population [21].

Conclusion

In conclusion, our study demonstrates a high prevalence of thrombotic complications in critically ill cancer patients with COVID-19, with significant implications for morbidity and mortality. These findings highlight the compounded thrombotic risk in this dual-vulnerable population and the urgent need for improved diagnostic vigilance and individualized thromboprophylactic strategies. Future prospective studies are warranted to refine risk stratification models and determine optimal anticoagulation protocols in this high-risk group. As the medical community continues to grapple with the long-term impact of COVID-19, understanding and mitigating thrombotic risk in patients with cancer will remain a critical component of ICU care.

Disclosure Statement

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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