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# Epidemiology of Cancer Associated Venous Thromboembolism in An Argentinean Teaching Hospital

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## 1. Abstract

Cancer-associated thrombosis (CAT) is a major cause of morbidity and mortality in patients with malignancy. We report a retrospective case series of patients with cancer-associated venous thromboembolism (Ca-VTE) identified during routine clinical care at a tertiary teaching hospital in Argentina between July 01, 2022 and June 30, 2024. Adult patients with objectively confirmed venous thromboembolism (deep vein thrombosis and/or pulmonary embolism) and active solid or hematologic malignancies were identified through hospital databases and medical record review. Among 13,336 hospitalized patients, 179 had confirmed VTE, of whom 74 had cancer, yielding a Ca-VTE period prevalence of 41.34% (95% CI: 34.1%–48.5%). The most commonly associated malignancies were hematologic, gynecologic, and respiratory cancers. During the incidence period (12 months), 30 oncology patients of 6,707 patients developed hospital-acquired venous thromboembolism (HA-VTE), corresponding to an in-hospital cumulative incidence (CI) of 0.45% (95% CI: 0.29–0.61); thromboprophylaxis was administered in 53.06% of these cases. In-hospital mortality was significantly higher in patients with Ca-VTE than in the overall hospitalized population (risk ratio 3.15, 95% CI: 2.13 to 4.66; $p = 4.8 \times 10^{-8}$) but did not differ significantly from patients with VTE without cancer (risk difference 5.0%, 95% CI: −6.6–16.6; risk ratio 1.24, 95% CI: 0.77–2.01; $p = 0.38$). These findings highlight the substantial burden of CAT and support the need for continued surveillance and optimized thromboprophylaxis strategies in hospitalized patients with cancer.

## 2. Core Innovations and Key Points

What is known about the topic:

• Cancer-associated venous thromboembolism (Ca-VTE) is a frequent and clinically consequential complication, with risk varying by cancer type and disease burden.

• It contributes substantially to increased morbidity, healthcare costs, and diminished survival rates within the global oncology population.

What this study adds:

• This study confirms a high period prevalence of Ca-VTE (41.34%) among hospitalized patients with VTE in an Argentinean tertiary teaching hospital, associated with a significant 3.15-fold increase in all-cause in-hospital mortality.

• The findings expose a critical clinical gap: nearly half (46.94%) of the patients who developed hospital-acquired VTE had not received prior thromboprophylaxis, reinforcing the need for systematic risk assessment and optimized prophylactic strategies.

## 3. Introduction

Cancer-associated thrombosis (CAT), including venous thromboembolism (VTE) and arterial thrombosis, is highly consequential for patients with cancer and is linked with worsened survival. Additional manifestations of CAT include disseminat-

ed intravascular coagulation and thrombotic microangiopathy which are significantly less common and yet far more severe. VTE, including upper or lower-extremity deep vein, splanchnic, visceral and cerebral veins thrombosis (DVT) and pulmonary embolism (PE), is the most common thrombotic complication in patients with cancer.

In the setting of cancer-associated venous thromboembolism (Ca-VTE), available evidence suggests that the "oncologic" thrombus does not merely reflect stasis or nonspecific hypercoagulability, but rather a tumour-driven prothrombotic biology coupled to the host inflammatory response. In human histopathologic series (predominantly autopsy-based), intrathrombus tumour cells either as vascular wall invasion or small cellular clusters—have been documented in a meaningful proportion of DVT and PE specimens, and these cells frequently express tissue factor (TF) and/or podoplanin, supporting a direct tumour-mediated mechanism of coagulation activation and platelet aggregation.

In addition, thrombi in patients with cancer appear to exhibit a more "immunothrombotic" microenvironment, with greater involvement of TF-positive monocytes/macrophages and NETosis-consistent markers (e.g., citrullinated histone H3) that are most prominent in early phases of thrombus organization, suggesting that leukocyte–platelet–fibrin interactions contribute substantially to initiation and propagation of the thrombotic event. Multiple studies detected an increase in the incidence of CAT over time driven by an increase in PE ± DVT. We investigated the period prevalence (PP), the hospital acquired cumulative incidence (Ha-CI), and outcomes of Ca-VTE in patients with VTE admitted in an Argentinean teaching hospital.

## 4. Results

### 4.1. Baseline Characteristics of the Study Population

During the 24-month study period, a total of 13,336 patients were hospitalized at our institution [6-8]. Among these, 179 patients had objectively confirmed venous thromboembolism (VTE). Concurrently, a total of 74 patients with active solid or hematologic malignancies were identified as having cancer-associated venous thromboembolism (Ca-VTE). The mean age of the Ca-VTE cohort was 63.53 years, with a range of 20 to 93 years, and 30 (40.54%) were male.

### 4.2. Period Prevalence and Hospital-Acquired Cumulative Incidence

The cross-sectional analysis of the VTE registry yielded an overall Ca-VTE period prevalence of 41.34% (95% CI: 34.1%–48.5%) among the total hospitalized population experiencing thrombotic events. For the assessment of hospital-acquired cumulative incidence (HA-CI), a focused 12-month sub-cohort encompassing 6,707 total admitted patients was analyzed between July 01, 2022, and June 30, 2023. Within this timeframe, 30 oncology patients developed new, objectively diagnosed hospital-acquired venous thromboembolism (HA-VTE) whose signs, symptoms, and diagnostic confirmations manifested strictly 48 hours or later following index admission.

This corresponded to an institutional in-hospital cumulative incidence of 0.45% (95% CI: 0.29%–0.61%). Evaluation of clinical management revealed that standard mechanical or pharmacological thromboprophylaxis had been administered in only 53.06% of these HA-VTE cases prior to the thrombotic event, leaving a prophylaxis omission rate of 46.94%. The detailed distributions of clinical periods, target populations, and calculated rates are summarized in Table 1.

### 4.3. Distribution of Malignancies and Stratification by Age

The malignancies most frequently associated with VTE were hematologic neoplasms (22.97%, 17/74), gynaecologic cancers (22.97%, 17/74), and respiratory tract cancers (18.92%, 14/74); other tumour sites accounted for the remaining 35.13% of cases (26/74). The clinical presentations, including site-specific deep vein thrombosis (DVT) and pulmonary embolism (PE), varied across the oncological cohort. When stratifying the institutional cohort of hospital-acquired conditions by age demographics, patients aged 60 to 69 years demonstrated an in-hospital cumulative incidence (CI) of 37.5% (95% CI: 15.2%–64.6%), representing 6 out of the 16 validated subjects within that specific stratum. The comprehensive breakdown of age-specific event frequencies and cumulative distribution rates across all evaluated biological subgroups is formalized in Table 2.

Table 2. Hospital-Acquired Cumulative Incidence of Ca-VTE Stratified by Age.

**Table 1**: Period Prevalence and Hospital-Acquired Cumulative Incidence of Ca-VTE.

| Period of Study | No. of Patients | No. of Patients with VTE | No. of Patients with Ca-VTE | PP (%) | HA-CI (%) | 95% CI |
|---|---|---|---|---|---|---|
| 07/01/2022 to 06/30/2024 | 13,336 | 179 | 74 | 41.34 | — | 34.1 – 48.5 |
| 07/01/2022 to 06/30/2023 | 6,707 | 89* | 30* | — | 0.45 | 0.29 – 0.61 |

Note:

- Ca-VTE: cancer-associated venous thromboembolism.
- VTE: venous thromboembolism.
- PP: period prevalence.
- HA-CI: hospital-acquired cumulative incidence.
- 95% CI: 95 percent confidence interval.
- *Symptoms/signs not present on admission.

**Table 2**: Hospital-Acquired Cumulative Incidence of Ca-VTE Stratified by Age.

| Age (years) | No. of patients with in-hospital VTE (n = 89) | No. of patients with hospital-acquired Ca-VTE (n = 30) | Hospital-acquired CI (%) | 95% CI |
|---|---|---|---|---|
| 16–49 | 24 | 8 | 33.3 | 15.6 – 55.3 |
| 50–59 | 5 | 1 | 20 | 0.5 – 71.6 |
| 60–69 | 16 | 6 | 37.5 | 15.2 – 64.6 |
| 70–79 | 28 | 12 | 42.9 | 24.5 – 62.8 |
| 80–89 | 15 | 3 | 20 | 4.3 – 48.1 |
| 90–99 | 1 | 0 | 0 | 0.0 – 97.5 |

Note:

• Ca-VTE: cancer-associated venous thromboembolism.

• VTE: venous thromboembolism.

• CI: cumulative incidence.

• 95% CI: 95 percent confidence interval.

### 4.4. In-Hospital Mortality and Risk Estimates

All-cause in-hospital mortality was significantly higher in patients with Ca-VTE compared to the general hospitalized population, demonstrating a distinct and highly significant risk ratio (RR) of 3.15 (95% CI: 2.13 to 4.66; $p = 4.8 \times 10^{-8}$). Conversely, when comparing the Ca-VTE cohort directly to hospitalized patients who developed VTE without underlying malignant disease, the mortality rates did not differ to a statistically significant degree. The absolute risk difference (RD) between these two thromboembolic subgroups was 5.0% (95% CI: −6.6%–16.6%), corresponding to a comparative RR of 1.24 (95% CI: 0.77–2.01; p = 0.38), confirming equivalent short-term vital risks once an acute clot manifest.

## 5. Discussion

Our single-centre institutional investigation provides a critical epidemiological characterization of cancer-associated venous thromboembolism (Ca-VTE) within a prominent Argentinean teaching hospital [6-8]. The observed period prevalence of 41.34% among hospitalized patients with VTE underscores the substantial and disproportionate burden that malignant disease exerts on thromboembolic development in the tertiary care setting. This finding aligns with expanding global literature confirming that the prothrombotic state inherent to active malignancy drastically multiplies the baseline risks of inpatient vascular complications [14-16].

The clinical biology of Ca-VTE provides important context for these outcomes. Emerging histopathological and microenvironmental data indicate that the “oncologic” thrombus is uniquely aggressive, frequently characterized by the expression of tissue factor (TF), podoplanin, and markers of intensive immunothrombosis such as NETosis-consistent factors. This underlying biological drive supports the rising trends in VTE incidence documented in broader international population studies over recent decades.

Our tracking of hospital-acquired venous thromboembolism (HA-VTE) revealed an in-hospital cumulative incidence of 0.45% among oncology patients. A vital finding of our study is the systemic omission of preventative care: 46.94% of the patients who developed hospital-acquired clots had not received any form of standard thromboprophylaxis prior to the event. This implementation gap reflects a prominent paradox in clinical oncology. Despite clear consensus guidelines advocating for proactive pharmacological protection in hospitalized cancer patients, clinicians frequently withhold anticoagulation due to a heightened fear of bleeding complications, thrombocytopenia, or overestimation of stability in patients with complex, fluctuating medical statuses [11-13,20].

Regarding survival, the presence of Ca-VTE increased the risk of in-hospital death more than threefold (RR 3.15) relative to the general inpatient population, illustrating the severe morbidity of acute thrombosis when superimposed on malignant disease. Interestingly, our data showed no statistically significant survival difference between VTE patients with cancer and VTE patients without cancer (p = 0.38). This suggests that once an acute, severe thromboembolic event occurs during immobilization or acute medical admission, the short-term prognosis is driven primarily by the immediate cardiopulmonary burden of the clot itself (e.g., right ventricular strain or respiratory failure) and general inpatient frailty, rather than the baseline oncological prognosis. The significant financial and clinical burden of managing these preventable hospital-acquired conditions reinforces the value of strict adherence to institutional safety metrics.

## 6. Study Limitations

This study has certain limitations that must be acknowledged. First, its retrospective cohort design relies on the accuracy of institutional administrative databases, ICD-10 diagnostic coding, and physical chart reviews, which can introduce misclassification or underreporting biases. Second, because our data

collection was strictly restricted to the index hospitalization and patients were not followed after discharge, we could not evaluate long-term cumulative incidence, recurrent events, or delayed out-of-hospital mortality. Finally, as a single-center study conducted at a specialized university teaching hospital with a high average length of stay (12.3 days) and an unselected tertiary case-mix [6-8], these specific prevalence and incidence rates may not be fully generalizable to smaller community or primary care facilities.

## 7. Conclusions

• Profound Clinical Burden: Cancer-associated venous thromboembolism (Ca-VTE) represents a massive epidemiological challenge at our institution, accounting for 41.34% of all documented inpatient thromboembolic events.

• Elevated Mortality Risk: Malignancy coupled with acute thrombosis drastically worsens patient prognosis, driving a 3.15-fold increase in the risk of all-cause in-hospital mortality compared to the general hospitalized population.

• The Prophylaxis Gap: Hospital-acquired thromboembolism (HA-VTE) presents a critical safety vulnerability, with an in-hospital cumulative incidence of 0.45%. Crucially, 46.94% of these patients did not receive guideline-recommended thromboprophylaxis prior to the event, highlighting a significant clinical implementation gap.

• Equivalency in Acute Phase Survival: Once an acute VTE occurs, short-term vital survival does not differ significantly between patients with or without cancer ($p = 0.38$). This suggests that short-term prognosis is driven primarily by the immediate physiological burden of the clot and inpatient frailty, rather than the baseline oncological status.

• Institutional Action Plan: There is an urgent need to mandate institutional risk-stratification models upon admission. Implementing systematic, automated electronic alerts or mandatory thromboprophylaxis checklists within electronic medical records could effectively close the documented prophylaxis gap, optimize resource allocation, and ultimately improve survival outcomes for hospitalized cancer patients.

## 8. Copyright Transfer

All individuals who participated in the preparation of this article hereby transfer the copyright for publication to Clinics of Oncology.

## 9. Authors' Contributions

All individuals who participated in the study design, data collection, and preparation of the manuscript take public responsibility for its content and approve the final version for submission.

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