

# Cancer-Associated Thrombosis in Genitourinary Malignancies: A Real-World Analysis From the TESEO Registry

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**Background:** Cancer-associated thrombosis (CAT) is a frequent and clinically relevant complication in patients with genitourinary (GU) malignancies, but real-world data focused on this population are limited. We describe the clinical characteristics, management, and outcomes of venous thromboembolism (VTE) in patients with GU cancers.

**Methods:** We performed a retrospective analysis of patients with GU malignancies included in the registry of Thrombosis and neoplasia of SEOM (TESEO). Adult patients with histologically confirmed GU cancer and radiologically proven VTE were included.

**Results:** Data on a total of 337 patients were analyzed; most of the patients (75.4%) had advanced disease. Pulmonary embolism was the most frequent presentation (56.2%), and 51.2% of events were incidentally diagnosed. Median time from cancer diagnosis to VTE was 9 months, with shorter intervals observed in germ cell tumors. Low-molecular-weight heparin was the most commonly used anticoagulant (88.2%). Bleeding complications occurred in 11.3% of patients, mainly during the first month of treatment, with GU bleeding being the most frequent. Recurrent VTE was observed in 4.1% of patients. Median overall survival was 59 months and did not differ according to thrombotic characteristics. However, among patients with bladder cancer, bleeding events were associated with worse overall survival (adjusted hazard ratio 2.82; 95% confidence interval, 1.13–7.04;  $p = 0.019$  by log-rank test).

**Conclusions:** In this real-world cohort, CAT in GU malignancies predominantly occurred in advanced disease and was frequently diagnosed incidentally. Overall survival was mainly influenced by tumor-related factors, although bleeding events negatively affected outcomes in patients with bladder cancer, underscoring the need for individualized anticoagulation strategies.

**Keywords:** cancer-associated thrombosis; venous thromboembolism; genitourinary cancer; bleeding; real-world evidence

## Introduction

Cancer-associated thrombosis (CAT), which accounts for approximately 9% of deaths among patients with cancer [1]—a percentage that possibly is underestimated [2]—remains one of the most frequent complications in oncology and adversely affects morbidity and mortality rates [3]. Strongly associated with cytotoxic regimens, immune

checkpoint inhibitors and targeted therapy have not decreased CAT incidence [4], suggesting a more profound relationship between cancer and thrombosis than that explained by cancer therapies [5]. CAT risk varies according to tumor type, treatment, comorbid conditions, and patient-related factors [6], with molecular characteristics also influencing thrombotic risk in some malignancies [7]. Genitourinary (GU) cancers are among the solid tumors associ-

ated with increased thrombotic risk [8].

Management of venous thromboembolism (VTE) in GU malignancies remains challenging due to the need to balance thrombosis and bleeding risks, particularly in tumors involving the urinary tract or in patients undergoing invasive procedures [9]. Uncertainty persists regarding anticoagulation in patients at high risk of urological bleeding. Despite its relevance in care of patients with cancer, CAT remains underrepresented in clinical trial populations. Therefore, the aim of this study was to analyze CAT in GU malignancies using data from the registry of Thrombosis and nEoplasia of SEOM (TESEO) registry.

## Methods

GU malignancies registered in the TESEO database between January 2000 and February 2025 were included and retrospectively assessed in the analysis. TESEO is a prospective registry under the auspices and management of the Spanish Society of Medical Oncology, composed of 50 centers in Spain and Portugal, which collects data from patients with cancer who present with CAT. Eligible patients were adults (aged  $\geq 18$  years) with histologically confirmed GU cancer and radiologically confirmed symptomatic or incidental CAT. The TESEO registry was approved by the Ethics Committee of Hospital Universitario Gregorio Marañón (Madrid, Spain). Written informed consent was obtained from all patients prior to their inclusion in the database. TESEO approval for database use was obtained.

Collected variables included demographic data, date of cancer diagnosis, histological subtype, stage of disease, and cancer treatment. Detailed information regarding thrombotic events, diagnostic methods, treatment, and subsequent complications was also recorded. Bleeding events were categorized as major, clinically relevant nonmajor bleeding (CRNMB), or minor bleeding, according to International Society on Thrombosis and Haemostasis criteria [10]. Deaths were classified as CAT related when they were directly attributable to thromboembolic mechanisms in the absence of tumor progression or other concurrent causes.

The completeness of the data set was evaluated prior to analysis. Missing data were infrequent for baseline demographic and major clinical variables; however, a higher proportion of missingness was observed for selected variables such as molecular tumor characteristics. Analyses were performed using a complete-case approach without data imputation. Categorical variable values are presented as frequencies and percentages, and continuous variable values as median and interquartile range (IQR). Normality distribution was assessed using the Shapiro–Wilk test. Overall survival (OS) was defined as the time from cancer diagnosis to death from any cause, and was estimated using the Kaplan–Meier analysis and log-rank test. Proportional hazards assumption was assessed using Schoenfeld residu-

als. Cox regression was conducted to calculate hazard ratios (HRs), and adjustment for potential confounders was conducted (namely, age  $\geq 60$  years; Eastern Cooperative Oncology Group [ECOG] score  $\geq 2$ ; tumor, node, metastasis [TNM] stage; active disease; and active treatment at CAT event). All statistical analyses were performed using IBM SPSS Statistics version 29 (Armonk, NY, USA) and STATA version 14.2 (StataCorp, Texas, USA).

## Results

### *Patient Characteristics*

A total of 337 patients were included. Of these, 144 had bladder cancer, 79 had renal cancer, 83 had prostate cancer, and 31 had germ cell tumors ( $n = 15$  with seminoma; and  $n = 16$  with non-seminoma). The median age was 68 years (IQR, 59–75). Apart from prostate and testicular cancers, 82% of the cohort were male; the ECOG score was 0–1 in 70% of cases.

With respect to cardiovascular risk factors, 51.8% of participants were former smokers and 14.5% were current smokers. More than half of the cohort had arterial hypertension, 36.7% had dyslipidemia, 14.5% had chronic kidney disease, and 14.8% had cardiovascular disease. The median body mass index was 26.77 kg/m<sup>2</sup>. Participants' cancer characteristics and tumor-related treatments are presented in Table 1. Additional baseline characteristics are detailed in **Supplementary Table 1**.

At the time of CAT diagnosis, 5% of patients were receiving thromboprophylaxis (70.6% were receiving low-molecular-weight heparin [LMWH]), and 9.2% had a previous history of thrombosis. Additionally, 15.7% of patients had a central venous catheter placed.

### *Characteristics of CAT*

The most frequent site of VTE was pulmonary circulation (56.2%), followed by deep vein thrombosis of the limbs (32%) and abdominopelvic involvement (12.7%). Catheter-related thrombosis accounted for 8% of cases, with a higher incidence observed in patients with non-seminomatous germ cell tumors (43.8%).

Diagnosis was incidental in 51.2% of patients. Asymptomatic presentation, which represents a subset of incidental events, was observed in 27.5% of the overall cohort. Median time from cancer diagnosis to the development of VTE was 9 (IQR, 2–40) months, with marked differences among tumor types: a shorter interval in testicular cancer (1–2 months) and a longer interval in prostate cancer (median 40 months).

Although 80.5% of patients were diagnosed in the outpatient setting, 19.2% of patients required hospital admission. Among hospitalized patients with available data on length of stay, 16.1% had a hospital stay longer than 15 days, and this was more frequent among patients with seminomatous germ cell tumors. Duration data were not avail-

**Table 1. General characteristics of the population.**

| Characteristic            | Total (N = 337) | Type of cancer <sup>1</sup> |                   |                      |                                  |                                   |
|---------------------------|-----------------|-----------------------------|-------------------|----------------------|----------------------------------|-----------------------------------|
|                           |                 | Bladder<br>(n = 144)        | Renal<br>(n = 79) | Prostate<br>(n = 83) | Testicular: seminoma<br>(n = 15) | Testicular: non-seminoma (n = 16) |
| Age, median (IQR), years  | 68 (59–75)      | 69 (63–75)                  | 64 (57–72.75)     | 74 (66.5–79.5)       | 40 (32–48)                       | 36.5 (28–40.5)                    |
| Male sex                  | 277 (82)        | 110 (76.4)                  | 54 (68.4)         | 82 (100)             | 15 (100)                         | 16 (100)                          |
| ECOG score                |                 |                             |                   |                      |                                  |                                   |
| 0                         | 75 (22.2)       | 28 (19.4)                   | 14 (17.7)         | 17 (20.5)            | 7 (46.7)                         | 9 (56.3)                          |
| 1                         | 163 (48.2)      | 74 (54.4)                   | 37 (46.8)         | 39 (47)              | 6 (40)                           | 7 (43.8)                          |
| 2–4                       | 99 (29.3)       | 42 (29.2)                   | 28 (35.5)         | 27 (32.5)            | 2 (13.3)                         | 0 (0)                             |
| TNM stage                 |                 |                             |                   |                      |                                  |                                   |
| I                         | 10 (3)          | 1 (0.7)                     | 1 (1.3)           | 4 (4.8)              | 1 (6.7)                          | 3 (18.8)                          |
| II                        | 29 (8.6)        | 21 (14.6)                   | 1 (1.3)           | 1 (1.2)              | 3 (20)                           | 3 (18.8)                          |
| III                       | 43 (12.7)       | 23 (16)                     | 6 (7.6)           | 3 (3.6)              | 6 (40)                           | 5 (31.3)                          |
| IV                        | 255 (75.4)      | 99 (68.8)                   | 71 (89.69)        | 75 (90.4)            | 5 (33.3)                         | 5 (31.3)                          |
| Active tumor              | 298 (88.2)      | 123 (85.4)                  | 71 (89.9)         | 78 (94)              | 13 (86.7)                        | 13 (81.3)                         |
| Cancer-specific treatment | 222 (65.9)      | 103 (71.5)                  | 44 (55.7)         | 55 (66.2)            | 9 (60)                           | 11 (68.8)                         |
| Thromboprophylaxis        | 17 (5)          | 6 (4.2)                     | 3 (3.8)           | 6 (7.2)              | 1 (6.7)                          | 1 (6.3)                           |
| CVC                       | 53 (15.7)       | 31 (21.5)                   | 2 (2.5)           | 6 (7.2)              | 3 (20)                           | 11 (68.8)                         |

CVC, central venous catheter; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; TNM, tumor, node, metastasis (staging).

<sup>1</sup>Data are reported as no. (%) unless otherwise indicated.

able for seven patients, either due to missing information or ongoing hospitalization at the time of data collection. Intensive care unit admission was reported separately as an indicator of severity. A complete description of CAT characteristics according to tumor type is presented in Table 2. Details regarding patient location at diagnosis and advanced therapeutic interventions are provided in **Supplementary Table 2**.

### Clinical Course and Complications

Recurrent thrombosis events occurred in 5% of patients, and were more frequent in bladder cancer (4.9%). Pulmonary embolism (PE) was the main location (50%). The median time to the event was 6.5 months and, when PE presented, an increase in LMWH dose was prescribed for 50% of patients. A comprehensive description of clinical evolution, complications, and anticoagulation management is given in **Supplementary Table 3**.

Bleeding complications were observed in 11.3% of patients and were classified as minor (3%), CRNMB (5.6%), and major bleeding (2.7%). The median time to develop complications was 1 month (IQR, 0–2.25), and GU bleeding was the most frequent complication (23.7%). Hemostatic intervention was required for 1.5% of patients, and a further 2.1% required red blood cell or platelet transfusion. Table 3 details data on anticoagulation management. Overall, 36.1% of patients experienced progression of their underlying malignancy, which was synchronous with the thrombotic event in 8.9% of cases.

Discontinuation of anticoagulant therapy occurred in 21% of patients, mainly due to completion of planned treatment, bleeding complications, or transition to nonspecific

palliative care. During follow-up, 48.8% of patients died. The leading cause of death was cancer related in 78% of cases. The mortality rate was higher among patients with prostate (61.4%) or bladder (50%) cancer.

### Survival Analysis

Median overall survival (mOS) was 59 months (95% confidence interval [CI], 48.1–69.9), ranging from 38 months in bladder cancer to not reached in testicular tumors. When stratified survival analysis according CAT location was assessed, patients with PE had a mOS of 69 months (95% CI, 53–84) compared with 54 months in those who did not present with PE (95% CI, 41–101). No statistically significant difference was observed between groups (HR = 0.87; 95% CI, 0.63–1.20;  $p = 0.394$  by log-rank test) (Fig. 1). After adjustment for potential confounders, no significant differences in survival were observed by CAT location, with similar outcomes between patients with and without PE after multivariable adjustment (adjusted HR = 0.81; 95% CI, 0.58–1.12;  $p = 0.199$ ). Poor performance status (ECOG score  $\geq 2$ ) and advanced disease stage were independently associated with a higher outcome risk (for ECOG score  $\geq 2$ : HR = 1.49,  $p = 0.016$ ; for stage IV disease: HR = 4.26,  $p = 0.014$ ). No statistical differences were observed regarding tumor subtype.

Overall, thrombus extension in PE cases (unilateral vs. bilateral) did not influence OS (69 vs. 66 months for unilateral and bilateral PE, respectively) (adjusted HR = 0.97; 95% CI, 0.79–1.20;  $p = 0.423$  by log-rank test). After adjustment for potential confounders, multivariable Cox regression analysis demonstrated that the overall model was not statistically significant (likelihood ratio [LR]  $\chi^2 = 14.0$ ;

**Table 2. Characteristics of CAT.**

| Characteristic                                                      | Total, no. (%)<br>( <i>N</i> = 337) | Type of cancer, no. of patients, (%) |                           |                              |                                          |                                               |
|---------------------------------------------------------------------|-------------------------------------|--------------------------------------|---------------------------|------------------------------|------------------------------------------|-----------------------------------------------|
|                                                                     |                                     | Bladder<br>( <i>n</i> = 144)         | Renal<br>( <i>n</i> = 79) | Prostate<br>( <i>n</i> = 83) | Testicular:<br>seminoma ( <i>n</i> = 15) | Testicular: non-<br>seminoma ( <i>n</i> = 16) |
| Location                                                            |                                     |                                      |                           |                              |                                          |                                               |
| Pulmonary                                                           | 190 (56.2)                          | 75 (52.1)                            | 46 (58.2)                 | 56 (67.5)                    | 6 (40)                                   | 7 (43.8)                                      |
| DVT (upper and lower limbs)                                         | 108 (32)                            | 59 (41)                              | 16 (20.2)                 | 28 (33.7)                    | 2 (13.3)                                 | 3 (18.8)                                      |
| Abdomen                                                             | 43 (12.7)                           | 14 (9.7)                             | 17 (21.5)                 | 4 (4.8)                      | 5 (33.3)                                 | 3 (18.8)                                      |
| CVC related                                                         | 27 (8)                              | 14 (9.7)                             | 1 (1.3)                   | 3 (3.6)                      | 2 (13.3)                                 | 7 (43.8)                                      |
| Head and neck                                                       | 3 (0.9)                             | 0 (0)                                | 2 (2.5)                   | 1 (1.2)                      | 0 (0)                                    | 0 (0)                                         |
| Diagnosis                                                           |                                     |                                      |                           |                              |                                          |                                               |
| Incidental <sup>1</sup>                                             | 173 (51.2)                          | 73 (50.7)                            | 48 (60.8)                 | 40 (48.2)                    | 7 (46.7)                                 | 5 (31.3)                                      |
| Symptomatic                                                         | 164 (48.5)                          | 71 (49.3)                            | 31 (39.2)                 | 43 (51.8)                    | 8 (53.3)                                 | 11 (68.8)                                     |
| Asymptomatic <sup>2</sup>                                           | 93 (27.5)                           | 44 (30.6)                            | 24 (30.4)                 | 19 (22.9)                    | 4 (26.7)                                 | 2 (12.5)                                      |
| Time elapsed (months) from<br>cancer diagnosis to VTE, median (IQR) | 9 (2–40)                            | 8 (3–22.75)                          | 7 (1–28)                  | 40 (14–101)                  | 2 (0–5)                                  | 1.25 (0–22.5)                                 |
| Hospital management                                                 | 161 (47.8)                          | 61 (42.4)                            | 35 (44.3)                 | 49 (59)                      | 8 (53.3)                                 | 8 (50)                                        |
| Admission time, days <sup>3</sup>                                   |                                     |                                      |                           |                              |                                          |                                               |
| <7                                                                  | 80 (49.7)                           | 32 (52.5)                            | 18 (51.4)                 | 23 (46.9)                    | 2 (25)                                   | 5 (62.5)                                      |
| 7–15                                                                | 48 (29.8)                           | 21 (34.4)                            | 11 (31.4)                 | 12 (24.5)                    | 2 (25)                                   | 2 (25)                                        |
| >15                                                                 | 26 (16.1)                           | 6 (9.8)                              | 4 (11.4)                  | 12 (24.5)                    | 4 (50)                                   | 0 (0)                                         |
| ICU admission                                                       | 5 (3.1)                             | 1 (1.6)                              | 1 (2.9)                   | 2 (4.1)                      | 1 (12.5)                                 | 0 (0)                                         |
| Anticoagulant treatment                                             |                                     |                                      |                           |                              |                                          |                                               |
| LMWH                                                                | 298 (88.2)                          | 130 (90.3)                           | 72 (91.1)                 | 69 (83.1)                    | 11 (73.3)                                | 16 (100)                                      |
| DOAC and others                                                     | 7 (2.1)                             | 4 (2.8)                              | 0 (0)                     | 3 (3.6)                      | 0 (0)                                    | 0 (0)                                         |
| None                                                                | 2 (0.6)                             | 2 (1.4)                              | 0 (0)                     | 0 (0)                        | 0 (0)                                    | 0 (0)                                         |
| VCF                                                                 | 4 (1.2)                             | 4 (2.8)                              | 0 (0)                     | 0 (0)                        | 0 (0)                                    | 0 (0)                                         |

CVC, central venous catheter; DOAC, direct oral anticoagulant; DVT, deep vein thrombosis; IQR, interquartile range; LMWH, low-molecular-weight heparin; VCF, vena cava filter; VTE, venous thromboembolism.

<sup>1</sup>Incidental VTE refers to events detected on imaging performed for reasons other than suspected thrombosis.

<sup>2</sup>Asymptomatic cases are a subset of incidental events; therefore, percentages are not mutually exclusive and may exceed 100%.

<sup>3</sup>Admission time percentages are calculated based on patients with available data (n = 154). Data were missing or unavailable for seven hospitalized patients. ICU admission is included within the group of hospitalized patients and overlaps with duration categories. Duration categories are mutually exclusive.

p = 0.123). No statistical differences were observed regarding tumor subtype.

Persistence of residual thrombus on follow-up did not translate into a statistically significant OS difference in the multivariable model (LR  $\chi^2$  = 20.04; p = 0.018): 52 months (95% CI, 36–not reached [NR]) in those who presented with residual clot versus 61 months (95% CI, 52–84) in those who did not (HR = 1.27; 95% CI, 0.62–2.57; p = 0.859 by log-rank test). No statistical differences were observed according to tumor subtype.

The presence of recurrent thrombosis conferred an mOS of 27 months (95% CI, 10–NR), in contrast to the 61 months (95% CI, 52–75) mOS for those in whom thrombosis did not recur. However, such a difference did not reach statistical significance when multivariable Cox regression model was performed (adjusted HR = 1.322 [95% CI, 0.56–2.30], p = 0.399 by log-rank; LR  $\chi^2$  = 29.09, p = 0.0006) (Fig. 2). No statistical differences were observed according to tumor subtype.

In the multivariable analysis stratified according to the presence of a bleeding episode (composite end point major or CRNMB events), patients without bleeding had an mOS of 66 months (95% CI, 53–82), whereas those who developed a bleeding episode had an mOS of 44 months (95% CI, 13–130). This difference did not reach statistical significance (adjusted HR = 1.40 [95% CI, 0.85–2.30], p = 0.06 by log-rank test; LR  $\chi^2$  = 28.72, p = 0.0004) (Fig. 3).

Due to the different clinical implications of bleeding according to primary cancer location, subgroup analyses by cancer type were conducted. When bladder cancer bleeding events were assessed, after adjustment for potential confounders (LR  $\chi^2$  = 24.5; p = 0.0019), a detriment in mOS was observed in those patients who presented with a bleeding event (43 months [95% CI, 29–70] vs. 13 months [95% CI, 8–NR]; adjusted HR = 2.82 [95% CI, 1.13–7.04], p = 0.019 by log-rank test) (Fig. 4). No difference was observed when bleeding was evaluated for prostate, renal, or germ-cell cancer.

**Table 3. Clinical evolution and complications.**

| Complication                                  | Total<br>(N = 337) | Type of cancer <sup>1</sup> |                   |                      |                                  |                                   |
|-----------------------------------------------|--------------------|-----------------------------|-------------------|----------------------|----------------------------------|-----------------------------------|
|                                               |                    | Bladder<br>(n = 144)        | Renal<br>(n = 79) | Prostate<br>(n = 83) | Testicular: seminoma<br>(n = 15) | Testicular: non-seminoma (n = 16) |
| Recurrent VTE                                 |                    |                             |                   |                      |                                  |                                   |
| Arterial                                      | 3 (0.9)            | 2 (1.4)                     | 0 (0)             | 0 (0)                | 0 (0)                            | 1 (6.3)                           |
| Venous                                        | 14 (4.1)           | 7 (4.9)                     | 3 (3.8)           | 3 (3.6)              | 1 (6.7)                          | 0 (0)                             |
| Time (months) to rethrombosis, median (IQR)   | 6.5 (2.75–12.5)    | 8 (5–14)                    | 10 (5–NA)         | 2 (2–NA)             | 8                                | 3                                 |
| Venous rethrombosis location                  |                    |                             |                   |                      |                                  |                                   |
| PE                                            | 7 (50)             | 4 (57.1)                    | 2 (66.7)          | 0 (0)                | 1 (100)                          | 0 (0)                             |
| Lower or upper extremity                      | 6 (42.9)           | 3 (42.9)                    | 1 (33.3)          | 2 (66.7)             | 0 (0)                            | 0 (0)                             |
| Other                                         | 1 (7.1)            | 0 (0)                       | 0 (0)             | 1 (33.3)             | 0 (0)                            | 0 (0)                             |
| Anticoagulation management after rethrombosis |                    |                             |                   |                      |                                  |                                   |
| 1%–25% increase in dose                       | 4 (28.6)           | 3 (42.9)                    | 0 (0)             | 1 (33.3)             | 0 (0)                            | 0 (0)                             |
| 26%–50% increase in dose                      | 3 (21.4)           | 2 (28.6)                    | 0 (0)             | 0 (0)                | 1 (100)                          | 0 (0)                             |
| Switch to DOAC                                | 1 (7.1)            | 1 (14.3)                    | 0 (0)             | 0 (0)                | 0 (0)                            | 0 (0)                             |
| Bleeding                                      |                    |                             |                   |                      |                                  |                                   |
| Minor                                         | 10 (3)             | 7 (4.9)                     | 1 (1.3)           | 2 (2.4)              | 0 (0)                            | 0 (0)                             |
| Major or clinically relevant                  | 28 (8.3)           | 7 (4.9)                     | 8 (10.1)          | 10 (12)              | 2 (13.4)                         | 1 (6.3)                           |
| Time (months) to bleeding, median (IQR)       | 1 (0–2.25)         | 0.5 (0–2)                   | 1 (0–2)           | 2 (0.25–4.75)        | 0.5 (0–NA)                       | 0 (0)                             |
| Bleeding source                               |                    |                             |                   |                      |                                  |                                   |
| Gastrointestinal                              | 2 (5.3)            | 0 (0)                       | 2 (22.2)          | 0 (0)                | 0 (0)                            | 0 (0)                             |
| Genitourinary                                 | 9 (23.7)           | 4 (28.6)                    | 3 (33.3)          | 3 (25)               | 0 (0)                            | 0 (0)                             |
| Brain                                         | 3 (7.9)            | 1 (7.1)                     | 0 (0)             | 2 (16.7)             | 0 (0)                            | 0 (0)                             |
| Other                                         | 2 (5.3)            | 1 (7.1)                     | 0 (0)             | 0 (0)                | 1 (50)                           | 0 (0)                             |
| Anticoagulation management after bleeding     |                    |                             |                   |                      |                                  |                                   |
| No anticoagulation                            | 18 (47.4)          | 9 (64.3)                    | 4 (44.4)          | 5 (41.7)             | 0 (0)                            | 0 (0)                             |
| 25% reduction                                 | 4 (10.5)           | 0 (0)                       | 3 (33.3)          | 1 (8.3)              | 0 (0)                            | 0 (0)                             |
| 50% reduction                                 | 1 (2.6)            | 0 (0)                       | 0 (0)             | 1 (8.3)              | 0 (0)                            | 0 (0)                             |
| Prophylactic doses                            | 10 (26.3)          | 5 (35.7)                    | 2 (22.2)          | 1 (8.3)              | 1 (50)                           | 1 (100)                           |
| Switch of anticoagulant                       | 5 (13.15)          | 0 (0)                       | 0 (0)             | 4 (33.3)             | 1 (50)                           | 0 (0)                             |
| Anticoagulation suspension                    | 71 (21)            | 32 (22.2)                   | 16 (20.3)         | 12 (14.5)            | 5 (33.3)                         | 6 (37.5)                          |
| Death                                         | 165 (48.8)         | 72 (50)                     | 38 (48.1)         | 51 (61.4)            | 1 (6.7)                          | 3 (18.8)                          |
| Cause                                         |                    |                             |                   |                      |                                  |                                   |
| CAT                                           | 2 (1.2)            | 0 (0)                       | 0 (0)             | 1 (1.9)              | 1 (6.7)                          | 0 (0)                             |
| Cancer                                        | 127 (78)           | 52 (72.2)                   | 29 (76.3)         | 45 (88.2)            | 0 (0)                            | 1 (33.3)                          |
| Mixed                                         | 15 (9.1)           | 7 (9.7)                     | 5 (13.2)          | 2 (3.9)              | 0 (0)                            | 1 (33.3)                          |
| Bleeding                                      | 2 (1.2)            | 1 (1.4)                     | 1 (2.6)           | 0 (0)                | 0 (0)                            | 0 (0)                             |
| Other                                         | 19 (11.5)          | 12 (16.7)                   | 3 (7.9)           | 3 (5.9)              | 0 (0)                            | 1 (33.3)                          |

CAT, cancer-associated thrombosis; DOAC, direct oral anticoagulant; IQR, interquartile range; NA, not available or not reached; PE, pulmonary embolism; VTE, venous thromboembolism.

<sup>1</sup>Data are reported as no. (%) unless otherwise indicated.

According to the presence of symptoms at VTE onset, patients with incidental events had a longer mOS compared with those with clinically suspected VTE: 66 months (95% CI, 47–82) versus 59 months (95% CI, 47–84). This difference was not statistically significant in the multivariate Cox regression model (adjusted HR = 0.89; 95% CI, 0.65–1.23;  $p = 0.452$  by log-rank test) (Fig. 5). No statistical differences were observed according to tumor subtype.

## Discussion

Our analysis of TESEO data provides a real-world overview of CAT in patients with GU malignancies, and indicates CAT predominantly occurs in advanced disease. Given the design of the TESEO registry, which includes only patients with CAT, incidence and relative risk estimations could not be assessed. The predominance of bladder, renal, and prostate cancers is consistent with previous reports [11]. Germ cell tumors had the shortest median time to CAT diagnosis (1–2 months), although with substantial

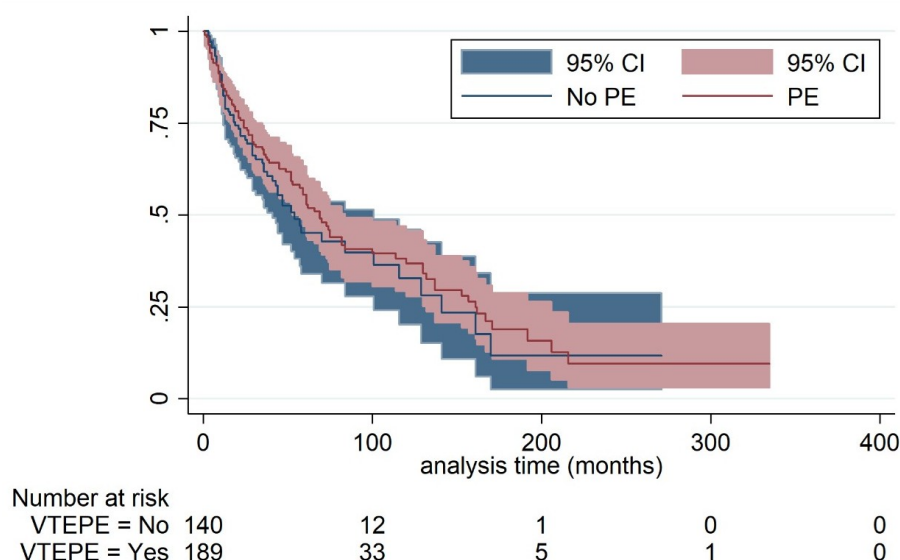


**Fig. 1. Overall survival according to pulmonary embolism (PE).** VTE, venous thromboembolism; CI, confidence interval.

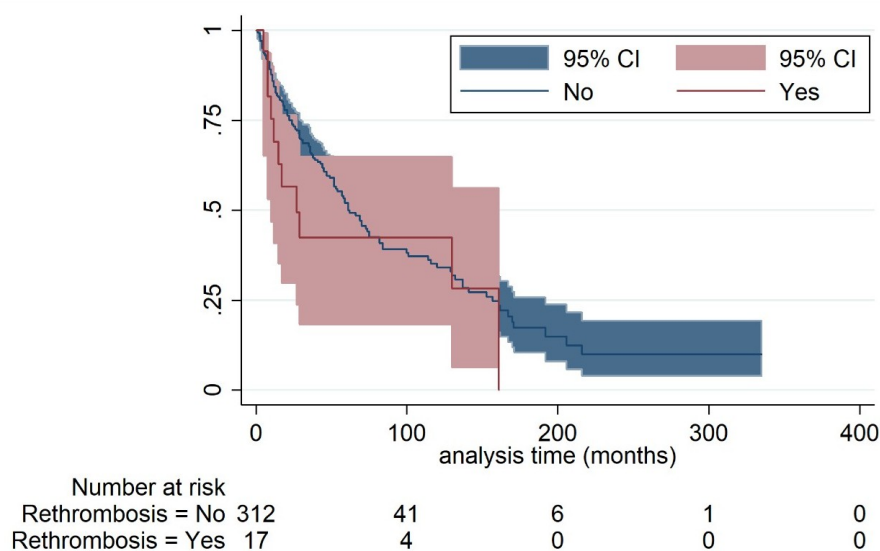


**Fig. 2. Overall survival according to rethrombosis.** CI, confidence interval.

variability, particularly in non-seminoma tumors, for which the upper limit of the IQR reached 22.5 months, reflecting a wide temporal distribution. This may reflect the impact of intensive chemotherapy and bulky retroperitoneal disease, both recognized risk factors for thrombosis [12,13]. In fact, the presence of large retroperitoneal lymphadenopathies in germ cell tumors is proposed as a more accurate risk factor for CAT than Khorana score [13]. Overall, biological context and timing of cancer disease may play a role in CAT risk; however, the lack of molecular data precluded further biological interpretation.

Diagnosis was incidental in 51.2% of patients, particularly in those with renal cancer (60.8% in our cohort),

consistent with previous reports indicating that a substantial proportion of cancer-associated VTE is incidentally detected [14], reflecting the widespread use of routine imaging in contemporary oncology practice. Previous studies have shown no prognostic significance of type of presentation at VTE diagnosis [15], but a potential increased risk of thrombosis recurrence may be implied when incidental CAT is diagnosed [16]. In line with previous evidence, the mode of presentation (incidental vs. symptomatic) was not independently associated with OS after multivariable adjustment. These findings support the clinical relevance of incidental CAT. LMWH was used by 88.2% of patients in our cohort, consistent with current clinical guidelines rec-

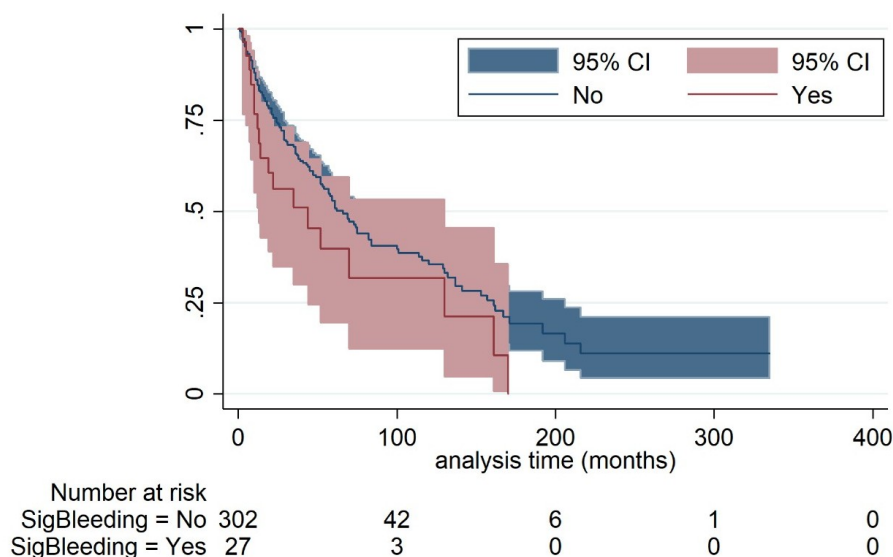


**Fig. 3. Overall survival according to bleeding.** SigBleeding: significant bleeding; CI, confidence interval.

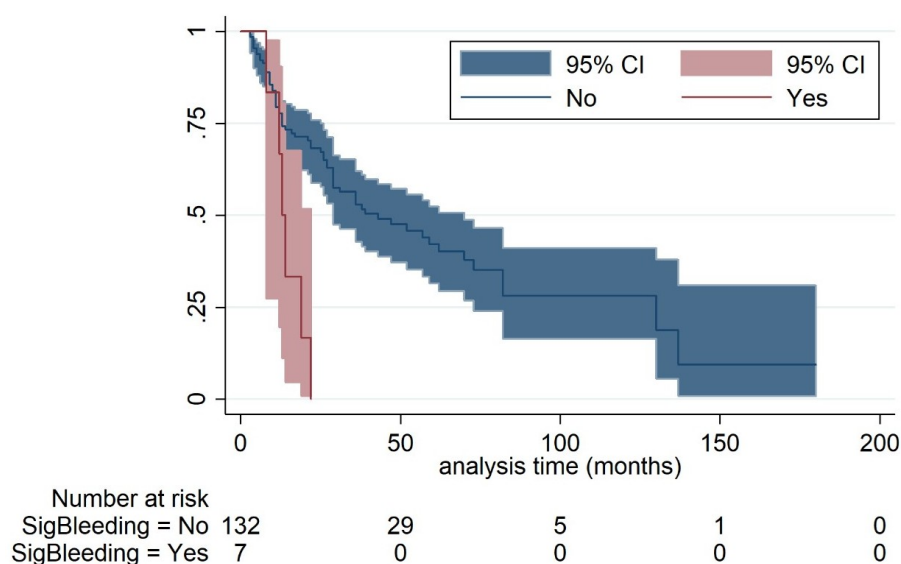


**Fig. 4. Overall survival according to bleeding in bladder cancer.** SigBleeding: significant bleeding; CI, confidence interval.

ommending LMWH or direct oral anticoagulants (DOACs) for CAT treatment [17,18]—a preference that could be attributed to the inclusion period comprising the time before DOACs approval and a national regulatory policy that prevented DOAC prescription in cases of CAT. Bleeding complications occurred in 11.3% of patients, with major bleeding events being relatively infrequent (2.7%), which is a lower rate compared with similar real-world cohorts [19]. As expected, most cases were located within the GU tract (23.7%). Median time to bleeding onset was 1 month in the TESEO cohort. Although the overall bleeding rate was comparable or slightly lower than that reported in other real-world cohorts, these findings underscore the need for careful early monitoring, particularly in patients with tumors

involving the urinary tract.

Several thrombotic characteristics were evaluated for their potential impact on survival. No statistically significant differences in OS were observed according to CAT location (i.e., PE vs. non-pulmonary events), thrombus extension, persistence of residual thrombus, or the occurrence of recurrent thrombosis after multivariable adjustment. These results suggest thrombotic features alone do not independently determine prognosis in this population and should not be overinterpreted, particularly given the limited number of events and lack of statistical significance.

In the overall cohort, bleeding events were not independently associated with OS after multivariable adjustment. In contrast, a significant association between bleed-

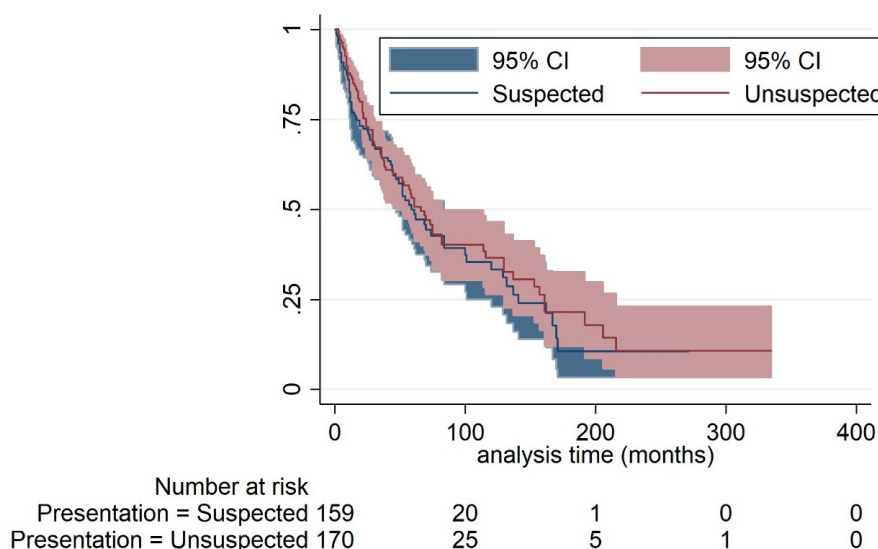


**Fig. 5. Overall survival according to type of presentation.** CI, confidence interval.

ing events and reduced survival was observed in patients with bladder cancer. This finding may reflect the complex interplay between local tumor burden, GU bleeding, and disease severity in this subgroup. However, relevant variables such as basal hematuria, urinary diversion, locally invasive disease, or recent urological procedures were not captured in the registry, limiting further interpretation.

Recurrent thrombosis was not independently associated with OS in our cohort after multivariable adjustment. These findings contrast with previous reports in which both end points (bleeding and rethrombosis) were identified as survival predictors in cancer cohorts [20]. Of the 1,812 patients with cancer included in the McBane *et al.* [20] cohort, a bleeding rate of 5.4% and a rethrombosis rate of 5.4% were reported. Of note, the population in their study included consisted of not exclusively GU tumors, pointing to a statistically significant survival difference on aggregated data. Indeed, when GU tumors were assessed, no sign of association between them and bleeding (major/CRNMB) or rethrombosis was observed [20]. In our cohort, no independent association was observed between most thrombotic characteristics and OS, whereas tumor-related factors were independently associated with outcomes.

The findings of this real-world analysis reinforce several relevant aspects of daily practice in patients with GU malignancies and CAT. First, the absence of an independent association between most thrombotic characteristics—including event location, thrombus extension, incidental presentation, or recurrence—and OS suggests anticoagulation decisions should primarily be guided by tumor-related factors and individual bleeding risk rather than by thrombotic phenotype alone. Second, the early occurrence of bleeding events, particularly within the first month of anticoagulation and predominantly involving the GU tract, highlights the importance of close clinical surveillance dur-

ing the initial treatment phase, particularly in bladder cancer. In this subgroup, careful selection of anticoagulant strategy, dose adjustments when appropriate, and early multidisciplinary collaboration among oncology, urology, and thrombosis specialists may be warranted. Third, the similar outcomes observed in incidental and symptomatic CAT support current recommendations for full therapeutic anticoagulation regardless of symptom presentation.

Overall, this study supports a personalized approach to CAT management in GU oncology, emphasizing individualized bleeding-risk assessment and tumor characteristics rather than uniform anticoagulation strategies. Subgroup analyses should be considered exploratory, given the limited number of events, and were not powered to detect statistically significant differences.

Several limitations should be acknowledged. The descriptive nature of this study limits causal inference, and the TESEO registry design precludes estimation of CAT incidence or relative risk. Additionally, the assessed GU population comprises several cancer types that often are not equivalent in biological behavior, treatment landscape, and prognosis, which could have blurred final assumptions regarding CAT. Detailed anticoagulation management data were not systematically collected, limiting assessment of treatment duration and discontinuation patterns. Additionally, the extended inclusion period (2000–2025) spans relevant changes in oncological care, diagnostic imaging, and supportive management, which may have influenced clinical outcomes. Although anticoagulation strategies remained relatively stable in this cohort, with limited use of DOACs, temporal effects cannot be completely excluded. Finally, missing molecular data and the low number of outcome events further limited exploratory and subgroup analyses.

## Conclusions

In summary, CAT in GU malignancies predominantly occurs in advanced disease and is frequently diagnosed incidentally. In this real-world cohort, OS was largely determined by tumor-related factors, and bleeding was associated with worse outcomes in bladder cancer, supporting individualized anticoagulation strategies in this subgroup. Future studies incorporating systematic tumor-specific and molecular data are warranted to refine risk stratification and optimize CAT management in GU oncology.

## Availability of Data and Materials

The datasets generated and/or analyzed during the current study are not publicly available due to institutional and ethical restrictions but are available from the corresponding author on reasonable request and with permission of the TESEO registry.

## Author Contributions

FJPM and BGM contributed equally to the conception and design of the study, data analysis, interpretation of the data, and drafting of the manuscript. FVM, ARL, PJF, ACB, IFP, JRP, LOM, DCL, PMP, MMM, MGH, MCC, and AMM contributed to data acquisition and interpretation, and critically revised the manuscript for important intellectual content. All authors contributed to the study design or data interpretation, participated in drafting or critically revising the manuscript, and approved the final version for publication. All authors agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## Ethics Approval and Consent to Participate

The TESEO registry was approved by the Ethics Committee of Hospital General Universitario Gregorio Marañón. This approval was subsequently extended to all participating centers. The registry is conducted in accordance with the principles of the Declaration of Helsinki and applicable national regulations. Written informed consent was obtained from all patients prior to their inclusion in the database.

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## Conflict of Interest

The authors have no conflicts of interest to declare.

## Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.56434/j.arch.esp.urol.20267906.106>.

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