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Clinical outcomes of comorbid cancer patients with venous thromboembolism

A retrospective, single-center study in Korea

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Abstract

In this single-center, retrospective study, we aimed to report the clinical outcomes, among Asian comorbid cancer patients with venous thromboembolism (VTE), and compare them with those of VTE patients without cancer.

Between January 2013 and December 2017, a total of 322 consecutive patients—diagnosed with acute VTE involving the leg, pelvis, or lung—were screened for inclusion. Comorbid cancer patients with VTE (n = 135, 41.9%) were included in this study and analyzed in comparison with VTE patients without cancer (n = 187, 58.1%). The study outcomes were the composite incidence of symptomatic and radiologically confirmed recurrence of VTE, or any-cause mortality.

The study outcome incidence was 62.2% (n = 84) during a mean follow-up period of 10 months: VTE recurrence in 7 patients and any-cause mortality in 83. Upon multivariate analysis, higher body mass index, diabetes mellitus, cancer stage IV, and radiotherapy were independently associated with study outcome incidence. VTE involving the inferior vena cava (hazard ratio [HR], 12.1; 95% confidence interval [CI], 1.20–120.80; $P = .034$), lung cancer (HR, 16.5; 95% CI, 2.32–117.50; $P = .005$), and use of vitamin K antagonists (HR, 36.4; 95% CI, 3.00–442.70; $P = .005$) were independent predictors of VTE recurrence. Compared with VTE patients without cancer, the study outcome incidence was significantly higher among comorbid cancer patients with VTE (62.2% vs 7.5%, $P < .001$), although there was no significant difference in VTE recurrence between the 2 groups (5.2% in patients with cancer vs 3.7% in patients without cancer, $P = .531$).

We found that various cancer-related and patient-related factors were associated with outcomes among comorbid cancer patients with VTE. The composite incidence of VTE recurrence or any-cause mortality was significantly higher among cancer patients with VTE than among VTE patients without cancer.

Abbreviations: CI = confidence interval, DVT = deep venous thrombosis, HR = hazard ratio, OR = odds ratio, PE = pulmonary embolism, VTE = venous thromboembolism.

Keywords: cancer, complications, outcomes, pulmonary embolism, venous thrombosis

1. Introduction

Venous thromboembolism (VTE)—including deep venous thrombosis (DVT) of the leg or pelvis, along with its potentially severe complications, such as pulmonary embolism (PE)— is particularly common among middle-aged and elderly individuals. VTE is known to involve interactions between inherited predispositions to thrombosis and various other risk factors. VTE patients are susceptible to reduced survivability, substantial healthcare costs, and a high rate of recurrence.[1] Cancer is a major risk factor for VTE.[2–4] Despite the elucidation of independent risk factors and predictors for VTE recurrence and the development of primary and secondary prophylaxis, the incidence of VTE among cancer patients has generally remained unchanged. Moreover—given the growing elderly population and improved objective imaging technology, capacity, and increased utilization thereof—the rate of VTE diagnosis has increased.[1,5]

Several studies have shown that cancer patients may differ from the general population in terms of their VTE susceptibility and that the disparity is associated with ethnicity differences.[5–11] It is important to note that most epidemiological studies of VTE have largely been conducted on samples taken from predominantly European populations.[1] Reported incidence rates for VTE in Western countries have ranged from 45 to 117 per 100,000 person-years,[1,5–7] whereas the overall VTE incidence is reported to be lower in Asian countries.[8] In the West, studies indicate that cancer is associated with nearly 20% of all incident DVTs and PEs.[9,10] Patients with cancer-associated VTE are at a higher risk of bleeding complications during anticoagulant treatment, and they have a higher risk of recurrent VTE than

Editor: Kou Yi.

The authors have no funding and conflicts of interest to disclose.

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How to cite this article: Jeong J, Jeong MJ, Choi K, Kim MJ, Han Y, Kwon TW, Cho YP. Clinical outcomes of comorbid cancer patients with venous thromboembolism. Medicine 2019;98:37(e17181).

Received: 15 March 2019 / Received in final form: 23 July 2019 / Accepted: 21 August 2019

http://dx.doi.org/10.1097/MD.0000000000017181

patients with VTE and no cancer.[11–15] Although there is little empirical data regarding the outcomes of VTE among comorbid cancer patients—even less so for Asian populations—it is widely reported that VTE events are the second-leading cause of death among cancer patients as their cancer progresses.

This study aimed to investigate the clinical outcomes, among Asian comorbid cancer patients with VTE, and to analyze the predictors associated with these outcomes. We also aimed to compare outcomes between cancer patients with VTE and patients with VTE but without cancer.

2. Subjects and methods

2.1. Study design and population

This single-center, retrospective, observational study analyzed patient medical records extracted from a prospectively recruiting VTE registry. The present study protocol was reviewed and approved by the institutional review board of Asan Medical Center (IRB No. 2018–0672), which waived the need for informed consent because of the study's retrospective design.

Between January 2013 and December 2017, a total of 322 consecutive patients, aged 20 years and older, diagnosed at our hospital with a first acute VTE—involving the leg, pelvis, or lung—were screened for inclusion in this study. We restricted analyses to patients with an incident objectively diagnosed acute VTE and comorbid cancer irrespective of the time interval before or after the VTE diagnosis, if any evidence of cancer (i.e., diagnosis, treatment, progression, oncologist review) was found via medical record review. All medical records were reviewed from the date of first objectively diagnosed VTE or cancer until death or date of last medical record follow-up, whichever was earliest. Demographics, risk factors of interest, and other data—including clinical and anatomical characteristics, VTE and cancer management strategies, and clinical outcomes of all consecutive patients—were recorded prospectively in an Excel (Microsoft Corp., Redmond, WA) database and analyzed retrospectively.

2.2. Measurements and outcomes of interest

VTE included DVT of the leg or pelvis, or PE.[1] A DVT was defined when objectively diagnosed by symptoms and signs of acute DVT, and the diagnosis was confirmed by compression venous duplex ultrasonography, computed tomographic venography, or magnetic resonance imaging.[3] A PE was defined when objectively diagnosed by symptoms and signs of acute PE, and the diagnosis was confirmed by computed tomographic pulmonary angiography, or if a ventilation-perfusion lung scan was interpreted as highly suggestive of PE.[3] Demographics and risk factors were defined as previously published.[16,17] Body mass index, calculated as the weight in kilograms divided by height in meters squared, was based on the measurements of height and weight at the time of VTE diagnosis. Other patient-related factors were also recorded at the time of VTE diagnosis. All cancer-related information—such as types of cancer, stages, and treatments—was reported around the time of the VTE event of interest.

The study outcomes were defined as the composite incidence of symptomatic and radiologically confirmed recurrence of VTE, or any-cause mortality. To evaluate whether the prognosis of comorbid cancer patients with VTE was poorer than that of VTE patients without cancer, we compared the outcomes between comorbid cancer patients with VTE and those with VTE but without cancer selected from the same registry, with the same inclusion criteria, during the same study period. All VTE patients without cancer had acute-onset symptoms and signs of VTE at presentation and were objectively diagnosed with acute VTE using imaging studies. These patients were managed according to both their clinical statuses and initial imaging findings. Anticoagulation treatment was prescribed and administered using unfractionated heparin or low molecular weight heparin in the acute phase, followed by either oral vitamin K antagonists or novel anticoagulants. This treatment typically continued for 6 months. Patients were followed up in the outpatient clinic within 1, 3, and 6 months, and after that, according to each patient's clinical status. During each visit, any signs or symptoms suggesting aggravated DVT, PE, bleeding, or other complications were noted. In comorbid cancer patients with VTE, the type, dose, and duration of anticoagulant therapy were determined according to cancer types and stages, cancer treatment modalities, and patient-related factors, including nutritional status and liver and renal function, in addition to the location and extent of VTE.

2.3. Statistical analysis

Categorical variables are reported as frequencies or percentages, and continuous variables as means and standard deviations or medians and ranges. Categorical variables were compared using either the χ^2 test or Fisher exact test, where appropriate, whereas continuous variables were compared using either Student's t test or the Mann–Whitney U test, where appropriate. Univariate Cox proportional hazards regression models were fitted to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) of the predictors being investigated. Significant variables with a P value $< .1$ in the univariate analysis were subjected to multivariate analysis using the backward elimination method to identify any association between clinical variables and the study outcomes. Independent predictors were defined as those characteristics that were significantly associated with the study outcomes in multivariate analyses. P values $< .05$ were considered statistically significant. Statistical analyses were performed using SPSS Version 21.0 (IBM Corp., Armonk, NY).

3. Results

3.1. Baseline and clinical characteristics

In total, 322 consecutive patients from our VTE registry were screened for inclusion in this study. Among these, 135 patients (41.9%) with a concomitant diagnosis of VTE and cancer were consecutively enrolled. The baseline and clinical characteristics of the included patients are presented in Table 1. Their mean age was 64.9 years (median, 66 years; range, 26–89 years), and 53.3% of the patients were women. Of these, 12 patients (8.9%) had a history of trauma, and 7 patients (5.2%) had a history of immobilization within 3 months before the diagnosis of VTE. The mean initial D-dimer concentration at the time of VTE diagnosis was 13.9 μg/mL (median, 10.3 μg/mL; range, 0.5–79.1 μg/mL).

DVT more frequently involved the right limb (56 patients, 41.5%), and bilateral DVT was noted in 42 patients (31.1%) (Table 2). The most common proximal veins involved were the iliac (35 patients, 25.9%) and femoral (29 patients, 21.5%) veins. Proximal DVT was diagnosed in 80.7% of the cases, and 19.3%

Table 1

Demographics and laboratory data of venous thromboembolism (VTE) patients with cancer (n = 135) and without cancer (n = 187).

Characteristics	VTE with cancer	VTE without cancer	*P* value
Mean age (yr)	64.9 ± 12.8	59.3 ± 17.4	.001
Female	72 (53.3)	93 (49.7)	.524
BMI (kg/m^2)	22.9 ± 3.5	24.6 ± 3.6	<.001
Smoking	28 (20.7)	36 (19.3)	.741
Diabetes mellitus	25 (18.5)	28 (15.0)	.397
Hypertension	56 (41.5)	73 (39.0)	.659
Dyslipidemia	15 (11.1)	13 (7.0)	.191
Coronary artery disease	2 (1.5)	10 (5.3)	.071
Cerebrovascular accident	3 (2.2)	11 (5.9)	.112
Chronic kidney disease	0	1 (0.5)	.999
Surgery*	40 (29.6)	18 (9.6)	<.001
Trauma/fracture*	12 (8.9)	27 (14.4)	.132
Immobilization*	7 (5.2)	9 (4.8)	.879
Laboratory data†			
WBC (× 10^3/μL)	7.9 ± 5.0	8.5 ± 2.7	.158
Hemoglobin (g/dL)	10.5 ± 2.0	12.9 ± 2.1	<.001
Hematocrit (%)	31.9 ± 5.8	38.6 ± 5.7	<.001
Platelet (× 10^3/μL)	221.0 ± 102.0	233.7 ± 79.1	.234
Neutrophil (%)	69.0 ± 14.5	66.8 ± 11.3	.131
CRP (mg/dL)	4.6 ± 5.3	2.1 ± 2.8.	<.001
D-dimer (μg/mL)	13.9 ± 12.6	9.8 ± 13.1	.007

Continuous data are presented as means ± standard deviation; categorical data are given as number (%).
BMI = body mass index, CRP = C-reactive protein, WBC = with blood cell.
* Within 3 months before the diagnosis of venous thromboembolism.
† Laboratory data at the time of venous thromboembolism diagnosis.

of the cases involved isolated calf DVT. Sixty-six patients (48.9%) had concomitant PE at the time of DVT diagnosis. All patients were given anticoagulation treatment immediately after VTE diagnosis, except 11 patients (8.1%) who had a bleeding complication (n = 4; 3 gastrointestinal bleeding and 1 hematuria), severe thrombocytopenia (n = 3), non-compliance (n = 2), and others (n = 2). A total of 11 (8.1%) were given follow-up treatment with vitamin K antagonists, while 69 (51.1%) were given novel anticoagulants, and 44 (32.6%) were given low molecular weight heparin. There were 3 patients (2.2%) with an objectively diagnosed acute VTE before the diagnosis of cancer, whereas most VTEs were diagnosed after the cancer (127 patients, 94.1%). Five VTEs (3.7%) were found incidentally on imaging studies obtained for reasons related to the cancer diagnosis. Various types of cancer were identified in our analysis: stomach (n = 19, 14.1%), lung (n = 15, 11.1%), biliary tract (n = 11, 8.1%), pancreas (n = 10, 7.4%), colon-rectum (n = 10, 7.4%), ovary (n = 10, 7.4%), and others. Regarding cancer stage and treatment modalities, 69.6% of cancers were stage III (n = 20, 14.8%) or IV (n = 74, 54.8%); 52.6% of patients received chemotherapy, 9.6% received radiotherapy, and 29.6% underwent surgery within the 3 months before the diagnosis of VTE (Table 3).

Table 2

Clinical characteristics of venous thromboembolism (VTE) patients with cancer (n = 135) and without cancer (n = 187).

	VTE with cancer	VTE without cancer	*P* value
Involved limb			
Right	56 (41.5)	43 (23.0)	<.001
Left	33 (24.4)	122 (65.2)	<.001
Bilateral	42 (31.1)	22 (11.8)	<.001
DVT location			
Proximal DVT	109 (80.7)	150 (80.2)	.906
Inferior vena cava	20 (14.8)	24 (12.8)	.610
Iliac vein	35 (25.9)	62 (33.2)	.163
Femoral vein	29 (21.5)	46 (24.6)	.514
Popliteal vein	25 (18.5)	18 (9.6)	.021
Isolated calf DVT	26 (19.3)	37 (19.8)	.906
Concomitant PE	66 (48.9)	81 (43.3)	.322
Anticoagulation treatment	124 (91.9)	175 (93.6)	.552
LMWH	44 (32.6)	7 (3.8)	<.001
NOAC	69 (51.1)	141 (75.8)	<.001
VKA	11 (8.1)	27 (14.5)	.081
None	11 (8.1)	12 (6.4)	.552

DVT = deep vein thrombosis, LMWH = low molecular weight heparin, NOAC = novel anticoagulant, PE = pulmonary embolism, VKA = vitamin K antagonist.

Table 3

Cancer types, stages, and treatments among comorbid cancer patients with venous thromboembolism (n = 135).

	n (%)
Types	
Stomach	19 (14.1)
Lung	15 (11.1)
Biliary tract	11 (8.1)
Pancreas	10 (7.4)
Colon-rectum	10 (7.4)
Ovary	10 (7.4)
Liver	6 (4.4)
Bladder	6 (4.4)
Prostate	6 (4.4)
Breast	6 (4.4)
Others	36 (26.7)
Stages	
Stage I	18 (13.3)
Stage II	18 (13.3)
Stage III	20 (14.8)
Stage IV	74 (54.8)
Treatments*	
Chemotherapy	71 (52.6)
Radiotherapy	13 (9.6)
Surgery	40 (29.6)

* Within 3 months before the diagnosis of venous thromboembolism.

3.2. Predictor analysis associated with study outcomes

The study outcome incidence—meaning the composite incidence of VTE recurrence or any-cause mortality—was 62.2% (n = 84) during the mean follow-up period of 9.9 ± 12.8 months (median, 4.0 months; range, 0–66 months). Seven patients (5.2%) had a VTE recurrence, and 83 patients (61.5%) died.

After adjustment for potential confounding variables, multivariate analysis indicated that higher body mass index was a significant protective predictor associated with the study outcomes (HR, 0.84; 95% CI, 0.78–0.91; $P < .001$), whereas diabetes mellitus (HR, 1.78; 95% CI, 1.07–2.95; $P = .026$), cancer stage IV (HR, 1.81; 95% CI, 0.09–3.01; $P = .022$), and radiotherapy (HR, 2.13; 95% CI, 1.11–4.11; $P = .024$) were independently associated with composite VTE recurrence or any-cause mortality (Table 4). Pancreatic cancer was found to have a borderline non-significant association with the study outcomes (HR, 1.98; 95% CI, 0.97–4.02; $P = .060$). DVT involving the inferior vena cava (HR, 12.1; 95% CI, 1.20–120.80; $P = .034$), lung cancer (HR, 16.5; 95% CI, 2.32–117.50; $P = .005$), and use

Table 4

Factors associated with the composite incidence of venous thromboembolism recurrence or any-cause mortality.

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age	1.01 (0.99–1.03)	.192	NA	NA
Female	0.90 (0.59–1.39)	.641	NA	NA
BMI	0.83 (0.78–0.89)	<.001	0.84 (0.78–0.91)	<.001
Smoking	0.88 (0.56–1.40)	.592	NA	NA
Diabetes mellitus	1.93 (1.19–3.13)	.008	1.78 (1.07–2.95)	.026
Hypertension	1.05 (0.68–1.61)	.842	NA	NA
Dyslipidemia	0.90 (0.45–1.81)	.768	NA	NA
CAD	2.49 (0.61–10.20)	.206	NA	NA
CVA	1.20 (0.30–4.91)	.797	NA	NA
Inferior vena cava	1.51 (0.64–2.04)	.645	NA	NA
Iliac vein	0.90 (0.54–1.49)	.687	NA	NA
Femoral vein	1.08 (0.65–1.80)	.757	NA	NA
Popliteal vein	1.30 (0.77–2.19)	.334	NA	NA
Calf vein	0.68 (0.37–1.26)	.224	NA	NA
Concomitant PE	1.03 (0.67–1.59)	.900	NA	NA
Stomach	1.09 (0.59–2.01)	.792	NA	NA
Lung	1.63 (0.84–3.17)	.151	NA	NA
Biliary tract	1.06 (0.50–2.21)	.887	NA	NA
Pancreas	2.65 (1.31–5.36)	.007	1.98 (0.97–4.02)	.060
Cancer stage IV	2.73 (1.66–4.48)	<.001	1.81 (0.09–3.01)	.022
Chemotherapy*	1.78 (1.13–2.81)	.013	1.22 (0.76–1.96)	.405
Radiotherapy*	2.36 (1.27–4.37)	.006	2.13 (1.11–4.11)	.024
Surgery*	0.77 (0.47–1.25)	.287	NA	NA

BMI = body mass index, CAD = coronary artery disease, CI = confidence interval, CVA = cerebrovascular accident, HR = hazard ratio, PE = pulmonary embolism.
* Within 3 months before the diagnosis of venous thromboembolism.

Table 5

Factors associated with venous thromboembolism recurrence.

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age	1.00 (0.94–1.06)	.892	NA	NA
Female	1.27 (0.28–5.75)	.758	NA	NA
BMI	1.00 (0.81–1.25)	.970	NA	NA
Smoking	0.71 (0.14–3.70)	.686	NA	NA
Diabetes mellitus	0.04 (0.00–NA)	.555	NA	NA
Hypertension	0.98 (0.21–4.47)	.977	NA	NA
Dyslipidemia	1.18 (0.14–9.92)	.874	NA	NA
CAD	1.00 (0.00–NA)	.999	NA	NA
CVA	0.05 (0.00–NA)	.777	NA	NA
Inferior vena cava	4.21 (0.93–19.10)	.063	12.1 (1.20–120.80)	.034
Iliac vein	0.53 (0.06–4.38)	.552	NA	NA
Femoral vein	2.37 (0.51–10.90)	.269	NA	NA
Popliteal vein	0.04 (0.00–291.80)	.470	NA	NA
Calf vein	0.03 (0.00–101.40)	.404	NA	NA
Concomitant PE	0.46 (0.09–2.40)	.355	NA	NA
LMWH	0.03 (0.00–132.60)	.421	NA	NA
NOAC	0.40 (0.09–1.78)	.228	NA	NA
VKA	5.70 (1.23–26.4)	.026	36.4 (3.00–442.70)	.005
No anticoagulant	4.73 (0.55–40.5)	.156	NA	NA
Stomach	2.62 (0.51–13.50)	.252	NA	NA
Lung	10.10 (2.04–50.20)	.005	16.5 (2.32–117.50)	.005
Biliary tract	0.04 (0.00–NA)	.588	NA	NA
Pancreas	0.05 (0.00–NA)	.751	NA	NA
Cancer stage III, IV	3.51 (0.42–29.40)	.248	NA	NA
Cancer stage IV	4.11 (0.70–24.00)	.117	NA	NA
Chemotherapy*	1.52 (0.32–7.20)	.597	NA	NA
Radiotherapy*	0.05 (0.00–NA)	.698	NA	NA
Surgery*	0.29 (0.04–2.49)	.262	NA	NA

BMI = body mass index, CAD = coronary artery disease, CI = confidence interval, CRP = C-reactive protein, CVA = cerebrovascular accident, HR = hazard ratio, LMWH = low molecular weight heparin, NOAC = novel anticoagulant, PE = pulmonary embolism, WBC = with blood cell, VKA = vitamin K antagonist.
* Within 3 months before the diagnosis of venous thromboembolism.

of vitamin K antagonists (HR, 36.4; 95% CI, 3.00–442.70; $P = .005$) were independently associated with VTE recurrence (Table 5). Cancer stage was not a predictor of an increased incidence of VTE recurrence.

3.3. Comparison of study outcomes between comorbid cancer patients with VTE and those with VTE but without cancer

According to the same inclusion criteria, 187 VTE patients (58.1%) without cancer were identified during the same study period. All patients were given anticoagulation treatment immediately after VTE diagnosis, except 12 patients (6.4%) who had bleeding (n = 4; 3 patients with recent cerebral hemorrhages and 1 patient with gastrointestinal bleeding) and other (n = 8) complications. Of the patients without cancer, 7 (3.7%) experienced VTE recurrences and 7 (3.7%) died. The study outcome incidence was significantly higher among comorbid cancer patients with VTE than among VTE patients without cancer (62.2% vs 7.5%, $P < .001$), although there was no significant difference in VTE recurrence between the two groups (5.2% among cancer patients vs 3.7%, $P = .531$). The interval from the initial diagnosis of VTE to VTE recurrence was significantly shorter among comorbid cancer patients with VTE than among VTE patients without cancer (7.7 ± 9.4 months vs 26.9 ± 15.7 months, $P = .008$).

4. Discussion

The major finding of this study was that the incidence of VTE recurrence was significantly lower among Asian comorbid cancer patients with VTE than the reported incidence of patients from Western populations. Among all first VTE events, the proportion of cancer-associated VTE was higher in our patient population than that reported by Western studies.[5,9–11] In our analysis, various cancer-related and patient-related factors were significantly associated with the composite incidence of VTE recurrence or any-cause mortality, while the increased incidence of VTE recurrence was significantly associated with extensive DVT (involving the inferior vena cava), use of vitamin K antagonist, and cancer site (lung). The composite incidence of study outcomes was substantially higher among comorbid cancer patients with VTE than among VTE patients without cancer. However, there was no significant difference in the incidence of VTE recurrence between patients with and without cancer.

VTE is prevalent among older patients, and incidence rates are proportional to age for both men and women.[1,5] Furthermore, this disease entity recurs frequently, with a reported recurrence rate ranging from 4 to 13 per 100,000 person-years, despite improvements in effective primary and secondary prophylaxis.[1,5,7,18–20] The changing patient demographics and increasing proportion of elderly patients may further increase both VTE and active cancer.[12,19,21–23] The risk of developing VTE is exponentially increased among cancer patients compared with the general population or patients without cancer,[24–26] and this pattern of VTE developing in cancer patients has increased over

the years.[27] Owing to improvements in cancer treatment strategies, cancer patients survive longer than they did in the past, but this has led to increased VTE risk among cancer survivors. It is estimated that 20% to 30% of all first VTE events are associated with cancer, and with the increasing number of cancer survivors, the rise of potential VTE diagnoses is also expected to increase.[5] Active cancer is also an important independent predictor of VTE recurrence.[12,19,21–23] It is important to note that cancer is a heterogeneous disease. To accurately decipher the risk of VTE and its recurrence among cancer patients, pre-existing cancer conditions, such as type, stage, and treatment modalities must be taken into consideration when treating patients. Patient-related factors, such as age, immobility, prior history of VTE, and comorbidities, are also factors that play important roles in the development and recurrence of VTE.[5,27]

Racial or ethnic differences in environmental and genetic factors, comorbidities, and cancer-related characteristics may influence the incidence of VTE, patterns of VTE recurrence, and outcomes among comorbid cancer patients with VTE. In a retrospective cohort study observing > 1 million cancer patients admitted to US academic medical centers, variables, such as ethnicity and presence of comorbidities (i.e., arterial thromboembolism, pulmonary disease, renal disease, infection, and anemia), were found to significantly influence VTE development.[27] Patients of Black African descent seemed to be at increased risk (OR [odds ratio], 1.2; 95% CI, 1.1–1.2), whereas patients of Asian descent had a decreased risk of VTE compared with Caucasians (OR, 0.7; 95% CI, 0.7–0.8).

Significant findings suggest that there is a 2- to 3-fold increased risk of VTE recurrence among cancer patients compared with patients without cancer.[12,19,20,28] In a prospective cohort study observing 842 patients with VTE, Prandoni et al[12] found the 12-month cumulative incidence of VTE recurrence to be 20.7% among cancer patients on conventional anticoagulant treatment, whereas the incidence was 6.8% among patients without cancer on anticoagulant treatment. According to previous research,[22,23,29] high-risk predictors of VTE recurrence among cancer patients are female sex, cancer site (pancreatic, brain, lung, and ovarian cancers, as well as myeloproliferative or myelodysplastic disorders), stage IV cancer, cancer stage progression, previous VTE, and leg paresis. Low-risk predictors include cancer site (breast) and stage (stage I rather than stage II, III, or IV). However, because of the heterogeneity of cancer biology, types, and stages, further studies are needed to better understand the role of cancer-related and patient-related factors influencing VTE recurrence.

Despite the rise in the survival rate of cancer patients due to the recent advances in various treatment modalities, the prognosis of cancer patients with VTE is still poor. VTE events are reported to be the second-leading cause of death among cancer patients, after cancer progression.[14] Current discourse in the literature hypothesizes that improvements in prognosis and quality of life among cancer patients can be achieved through anticoagulant treatments aimed at preventing VTE events. However, cancer patients with VTE have an increased risk of bleeding complications during anticoagulant treatment and a higher risk of recurrent VTE than patients with VTE but without cancer.[2,12–15,21,30] According to a recent Cochrane Review of nine randomized clinical trials,[31] thromboprophylaxis significantly reduces the incidence of symptomatic VTE (relative risk, 0.62; 95% CI, 0.41–0.93), whereas this treatment also increases the risk of bleeding complications. In a Norwegian study involving 740 patients with a first VTE event, the 1-year case fatality rates were five times higher among cancer patients with VTE (63.4%; 95% CI, 54.5–71.8) than among VTE patients without cancer (12.6%; 95% CI, 10.1–15.5).[32] Additionally, in the RIETE registry, with a large prospective cohort of >35,000 VTE patients, the 3-month mortality was much higher among cancer patients with VTE compared with VTE patients without cancer (26% vs 4%, respectively).[13] Moreover, cancer patients who develop VTE have a lower survival rate than cancer patients without VTE.[33–36] This may be explained by the more aggressive types of cancers more frequently associated with a thrombogenic potential.[5]

This study has potential limitations. First, the retrospective design and the small study sample extracted from a single-center registry raise the possibility of selection and information biases on the part of the physicians or patients. Indication bias and patient self-selection may also have influenced our findings, and some clinical information was not clearly available in the medical records. The decisions to choose a treatment modality for cancer and an anticoagulant for VTE were mainly made by the physicians based on the expected level of the efficacy of the management strategies. Furthermore, our study cohort was entirely Asian; thus, our findings may not be generalizable to other ethnic groups. However, this may be both the strength and a limitation of our study. Considering that there may be ethnic differences between Asian and Western countries, and there is a paucity of consistent data on the outcomes of VTE among comorbid cancer patients in Asian populations, our findings may inform clinicians about outcomes in Asian patient populations. Finally, given the small sample size and the heterogeneity of cancer types and stages, this study was likely underpowered to provide sufficient evidence to support the overall relevance of our results.

In conclusion, our findings indicate that various cancer-related and patient-related factors were significantly associated with outcomes among comorbid cancer patients with VTE. The composite incidence of VTE recurrence or any-cause mortality was significantly higher among cancer patients with VTE than among VTE patients without cancer, whereas there was no significant difference in the incidence of VTE recurrence between patients with and without cancer. Future prospective trials with larger cohorts will lead to a better understanding of outcomes among these patients.

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