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ORIGINAL ARTICLE

Incidence and predictors of venous thromboembolism in medically ill hospitalized elderly cancer patients: a prospective observational study

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Abstract

Purpose The aim of this study was to estimate the incidence and predictors of venous thromboembolism (VTE) in medically ill hospitalized elderly cancer patients in a single Korean tertiary hospital.

Methods Patients were examined for deep vein thrombosis (DVT) by duplex and color Doppler ultrasonography (DUS) of both legs between days 5 and 14 of their hospital stays. The primary endpoint was the incidence of VTE by day 14, which was determined via a composite of DVT detected by routine DUS and symptomatic VTE.

Results A total of 140 patients with 31 hematologic and 109 nonhematologic malignancies were analyzed. The median age was 73 years, and 45.7% of the patients were female. The median length of hospital stay was 12 days. The modified Padua prediction score (PPS) ≥ 4 was 92.9%. The incidence of VTE by day 14 was 7.1%, including six proximal and four distal DVT cases. Being female, having a length of hospital stay of ≥ 13 days, and having a modified Padua prediction score of ≥ 6 were risk factors of VTE in univariate analysis. The incidence of VTE was 2.3%, 7.3%, and 41.7% in patients with 0–1, 2, and 3 of these risk factors, respectively.

Conclusion The incidence of VTE in medically ill hospitalized elderly cancer patients was lower in Korean patients than in Western patients. However, the risk of VTE in those with more than two risk factors (female, long length of hospitalization, and high PPS) increased considerably, and pharmacologic thromboprophylaxis is warranted in these cases.

Keywords Cancer · Venous thromboembolism · Elderly · Hospitalized · Risk factors

Introduction

Cancer is a well-established risk factor for venous thromboembolism (VTE). Approximately 20% of VTE cases are cancer-associated [1, 2], and the overall risk of VTE is 5- to 7-fold higher in cancer patients [3, 4]. However, current recommendations come from subgroup analyses of major clinical trials in which only 5.1–15% of the patients had cancer, and there has been no specific randomized study for hospitalized cancer patients, indicating a need for such a study. Aging is another potent risk factor for VTE [5], and thus, elderly cancer patients are especially susceptible to thrombosis development. Most recent clinical practice guidelines in oncology, therefore, recommend that hospitalized cancer patients without contraindications should be considered for VTE prophylaxis with anticoagulant treatment [6–8]. The American College of Chest Physicians (ACCP) also recommends anticoagulant prophylaxis for hospitalized medical patients with a high risk of VTE, a categorization that includes the majority of cancer patients [9]. Despite these recommendations, prophylaxis of VTE in hospitalized medical patients remains underutilized with a rate of 16–39.5% [10, 11]. Surprisingly, adherence to the guidelines in cancer patients is even lower than in those without cancer [12]. Zwicker et al., however, showed that, in academic medical centers with a high rate of pharmacologic thromboprophylaxis (TP) prescription, nearly two thirds of low-risk patients, who are not to use TP based on ACCP guidelines, received pharmacologic TP [13]. Both underutilization and non-targeted utility of TP are common failures preventing optimal prophylaxis.

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Physicians, particularly in Asian countries, do not comply with existing global guidelines for VTE prevention, due to the lower incidence of VTE in Asian populations [14–16]. Although the use of pharmacological TP in surgical patients has increased gradually [17], the majority of hospitalized medical patients in Korea do not routinely receive pharmacologic TP, except in the intensive care unit [18]. Our institution had likewise not performed routine pharmacologic TP for hospitalized cancer patients prior to this study. Non-targeted primary TP for hospitalized cancer patients would be inappropriate, but it would also be inappropriate to disregard TP. Considering the sparseness of VTE incidence data for this population and the need for TP policy in Korean medically ill hospitalized elderly cancer patients, we planned a prospective observational study to investigate the incidence and risk factors of VTE in these patients and to develop compliant TP strategies targeted toward the patients at highest risk.

Methods

Study population

All elderly patients (≥ 65 years old) admitted to the Division of Hematology and Medical Oncology of Seoul National University Bundang Hospital (SNUBH) between July 2012 and July 2014 were screened for their eligibility to participate in this study. We enrolled patients who had histologically confirmed malignancies and had to be hospitalized for ≥5 days. Patients admitted for scheduled chemotherapy were excluded if there were no other medical reasons for hospitalization. Other exclusion criteria were as follows: symptomatic VTE at admission, a known congenital thrombophilia or hypercoagulable state, a life expectancy of < 3 months, current anticoagulation treatment, and comorbidities requiring anticoagulant therapy during the prescreening and study period. None of the patients in the study were started on pharmacologic TP.

Study design

All patients were electronically prescreened for eligibility upon admission. Participants were examined for deep vein thrombosis (DVT) by duplex and color Doppler ultrasonography (DUS) of both legs between days 5 and 14 of their hospital stay. We conducted a systematic DUS of both lower legs from the calf to the common femoral vein. We confirmed the clinical suspicion of DVT or PE using relevant diagnostic modalities. Investigators recommended surveillance of PE in patients confirmed as having proximal DVT on DUS, but final treatment decisions were made by the attending physician. For VTE treatment, decisions to start anticoagulation treatment, to select appropriate anticoagulants, and to terminate anticoagulant treatment were the responsibility of both the investigators and attending physicians. Enrolled patients were closely supervised during hospitalization and followed for up to 35 days after admission. Patients were interviewed by telephone or in person through outpatient clinics to discover newly developed symptoms or signs of VTE, bleeding, or death between study days 28 and 35.

Statistics

The primary endpoint was the incidence of VTE by day 14, which was determined via a composite of DVT detected by routine DUS and symptomatic VTE. The secondary endpoints were the risk factors of VTE in the study population and the incidence of additional symptomatic VTE by day 35. In the absence of an autopsy, the cause of sudden and unexplained early death by day 35 was classified as a possible pulmonary embolism (PE). Patient characteristics were summarized using proportion and ranges for binary factors and using means, medians, and ranges for continuous factors. We calculated a Padua prediction score (PPS) for each patient, and we modified the PPS according to the proposed classification of body mass index (BMI) in Asians, through which the cutoff for obesity was adjusted from 30 to 25 kg/m^2 [19, 20]. Univariable analysis for association of risk factors with VTE was performed using a chi-square test. In addition to the 11 risk factors of PPS, gender, tumor type (hematologic vs. nonhematologic), and length of hospital stay (LOS) were included in the univariate analysis. Modified PPSs (a score of ≥ 6 indicates a high score) and LOS (≥ 13 days indicates a long hospital stay) were dichotomized according to the median value. Risk factors that were identified in the univariable analysis ($p < 0.1$) were used in a multivariable stepwise logistic regression model. An IMPROVE bleeding risk score [21] was calculated for each patient, with a score of ≥ 7 indicating a high risk for bleeding. We also analyzed the categorization of risk of bleeding with anticoagulant therapy based on ACCP suggestions [22]. We performed a Kaplan-Meier survival analysis using data from the Korean Ministry of the Interior and Safety. Survival was defined as the interval from the date of current admission to death from any cause. If the assumed VTE incidence by day 14 were to be 5% with a CI of 95% and a margin of error of 0.025%, then 292 samples would be needed to make a statistically powerful study. For patient safety, however, we decided to conduct the interim analysis and stop enrollment after the tenth occurrence of VTE. Two-sided p values of < 0.05 were considered to be statistically significant. Statistical analyses were performed using IBM SPSS ver. 21 for Windows (IBM Co., Armonk, NY). This study was approved by the Institutional Review Board at SNUBH (IRB number: B-1201-144-007). Written informed consent was obtained from the patients prior to study entry, and this study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

Patient characteristics

Between July 2012 and July 2014, 175 patients were screened with DUS. Thirty-five patients were excluded due to the inadequate timing of DUS [within hospital day 5 ($n = 7$), after hospital day 14 ($n = 19$)], ongoing anticoagulation treatment ($n = 5$), and having a < 3-month life expectancy ($n = 4$). A total of 140 patients were analyzed, and their characteristics are summarized in Table 1. The median age was 73 years (range 65–95), and 45.7% of the patients were female. Except for one patient, 139 were active cancer patients with local or distant metastases who had had chemotherapy or radiotherapy treatment in the previous 6 months. The main reasons for hospitalization were infection problems; cancer-related complications, including pleural effusion, ascites, stent obstruction, compression fracture, and cord compression; uncontrolled pain; poor oral intake; and general weakness. The details of the Padua risk factors of the 140 patients are described in Table 1. At the time of current admission, the median values of PPS and modified PPS were 4 (range 3–10) and 5 (range 3–10), and 130 (92.9%) of the patients were high risk with a modified PPS of ≥ 4. The median and mean LOS was 12 days and 16 days (range 5–109), respectively.

Incidence of VTE

A total of 140 patients took systematic DUS examinations at a median of day 8 (range 5–14). The incidence of VTE by day 14 was 7.1% ($n = 10$), including six proximal (4.3%) and four distal (2.8%) DVT cases (Table 2). The sites of the six proximal DVT cases were as follows: femoral vein ($n = 1$), superficial femoral vein ($n = 1$), and popliteal vein ($n = 4$). Four distal DVT cases were identified in calf veins. Only one had symptomatic proximal DVT that presented with leg swelling of the involved site, which was confirmed by DUS at day 8. There was no symptomatic PE or sudden premature death from suspected PE by day 14. During the follow-up period between day 14 and day 35, the 133 patients who responded reported no additional thrombosis events. Among the seven patients untracked by day 35, 2 patients who were lost to follow-up were confirmed to be alive by day 35. Five patients who died by day 35 had died due to infection with rapidly progressed cancer ($n = 3$) and unknown causes ($n = 2$). The two cases with unexplained early death (one of which is case 10 in Table 6) may be explained by PE.

Risk factors for VTE

Table 3 displays the incidence of VTE by day 14 according to clinical risk factors. In univariate analysis, the incidence of VTE was significantly higher in female patients (12.5% vs. 2.6%, $p = 0.04$) and in those with a prolonged hospitalization of ≥ 13 days (11.9% vs. 2.7%, $p = 0.04$). VTE occurred more frequently in patients with a modified PPS of ≥ 6 (12.2% vs 4.4%, $p = 0.09$). The incidence of VTE was higher in patients with reduced mobility, but the difference was not statistically significant (11.9% vs 5.1%, $p = 0.15$). In our multivariable logistic regression analysis, which included three factors with $p < 0.1$ in univariable analysis, being female [overall risk (OR) 5.86, 95% confidence interval (CI) 1.14–29.94, $p = 0.03$] and having a hospital stay of ≥ 13 days (OR 5.71, 95% CI 1.11–29.23, $p = 0.03$) were independent strong risk factors for VTE (Table 4). Among those with 0–1, 2, or 3 of the risk factors (female, hospital stay ≥ 13 days, and modified PPS ≥ 6), the incidences of VTE by day 14 were 2.3%, 7.3%, and 41.7%, and the incidences of VTE by 35 days were 3.4%, 9.8%, and 41.7%, respectively (Table 5).

Treatment of VTE and outcomes

Baseline clinical characteristics, details of VTE, and outcomes of 10 patients with VTE are summarized in Table 6. Five patients, including four with proximal DVT and one with distal DVT, received anticoagulation treatment (ACT), though only two completed planned ACT. Case 3 did not do ACT due to contraindication of severe thrombocytopenia related to bone marrow involvement of lymphoma. Three patients stopped ACT early due to bleeding complications (cases 1 and 4) and deconditioning related to infection and uncontrolled underlying malignancy (case 5). Case 5 was treated with dalteparin but died on day 31 due to deconditioning from aspiration pneumonia, which was not related to thrombosis or bleeding. Six of 10 patients expired within 3 months due to disease progression ($n = 4$), aspiration pneumonia ($n = 1$), and unknown causes ($n = 1$, case 10, possible PE).

Among the 17 ACCP-suggested risk factors for bleeding with anticoagulant therapy, 129 patients had ≥ 2 risk factors including both an age of > 65 years and active cancer, and 11 patients aged 65 years had additional bleeding risk factors like diabetes ($n = 2$), renal failure ($n = 1$), thrombocytopenia ($n = 2$), antiplatelet therapy ($n = 1$), anemia ($n = 4$), and reduced functional capacity ($n = 4$). For 10 patients with VTE, their IMPROVE bleeding risk score was a median of 5 (range 3.5–10), and 3 (30%) patients had a score of ≥ 7.0, which, according to the IMPROVE bleeding risk score scale, indicated a 12% risk of bleeding complications. For 130 patients without VTE, the median score was 4.5 (range 3.5–12.0), and 11 (8.5%) had a score of ≥ 7.0. Two patients who stopped anticoagulant treatment due to gastric tumor bleeding (case 1) and hematochezia (case 4) had an IMPROVE bleeding score of 10 and 5.5, respectively. Underlying ischemic colitis was a probable additional risk factor for bleeding in case 4.

Survival of study populations

The median overall survival of 140 patients was 7.9 months (95% CI, 5.1–10.6) with a median follow-up period of

Table 1 Clinical characteristics of 140 patients

Characteristics		No.	%
Gender	Female	64	45.7
	male	76	54.3
Age, years	Median (range)	73 (65–95)	
BMI, kg/m^2	Mean (range, SD)	22.5 (14.1–31.9, 3.58)	
Hematologic malignancy	All	31	22.1
	Leukemia	4	2.9
	Lymphoma	16	11.4
	Multiple myeloma	11	7.9
Nonhematologic malignancy	All	109	77.9
	GI	35	25.0
	Lung	38	27.1
	Hepatobiliary	15	10.7
	Breast	3	2.1
	Genitourinary/gynecologic	5	3.6
	Esophageal	3	2.1
	Others*	10	7.2
Metastatic disease/nonhematologic malignancy		88/109	80.7
Length of hospital stay, median (range)		12 (5–109)	
Padua risk factors			
Active cancer		139	99.3
Previous VTE		2	1.4
Reduced mobility		42	30.0
Known thrombophilia		0	0
Trauma/surgery within last 30 days		3	2.1
Age more than 70 years)		97	69.3
Heart/respiratory failure		0	0
Acute myocardial infarction or ischemic stroke		0	0
Acute infection/rheumatologic disorder		50	35.7
Obesity (≥ BMI 25 kg/m2)		36	25.7
Obesity (≥ BMI 30 kg/m2)		6	4.3
Ongoing hormonal treatment		0	0
Padua prediction score (PPS), median (range)		4 (3–10)	
PPS ≥ 4		123	87.8
Modified PPS**, median (range)		5 (3–10)	
Modified PPS ≥ 4		130	92.9

*Two patients with tongue cancer, and each one case with adrenal cortical carcinoma, angiosarcoma, gastrointestinal stromal tumor, glioblastoma, melanoma, mesothelioma, thymic carcinoma, and thyroid cancer

**The cut-offs of BMI for obese was adjusted from 30 to 25 kg/m^2 according to proposed classification of BMI in Asians

7.3 months (range 0.2–33 months), and 97 deaths occurred by the cutoff date of March 2015. By day 35, five patients had died, including two possible fatal PEs. Although we had planned to enroll only patients with a life expectancy of more than 3 months, 32 patients (22.8%) survived < 3 months from the date of current admission. The causes of death for those patients were progressed disease ($n = 21$), infection ($n = 6$), pneumonitis ($n = 1$), and unknown ($n = 4$). Fifty-nine total patients (42.1%) expired within 6 months.

Discussion

The incidence rate of VTE in each cancer study should be interpreted cautiously, as direct comparison between studies is complicated by methodological heterogeneity. In the absence of well-designed prospective studies for this study's population, our results should be compared with previous randomized controlled studies (RCTs) that used similar study design and methods. The primary outcomes of three representative RCTs

Table 2 Incidence of venous thromboembolism by day 14

VTE events	VTE at day 14 ($n = 140$)		Details
	No	%	
Any	10		
Asymptomatic proximal DVT	5	3.6	CFV (1), POP (4)
Symptomatic proximal DVT	1	0.7	SFV (1)
Symptomatic distal DVT	0	–	
Asymptomatic distal DVT	4	2.8	Calf vein (4)
Symptomatic PE (%)	0	–	
Incidence of VTE by day 14	10	7.1	

VTE, venous thromboembolism; *DVT*, deep vein thrombosis; *PE*, pulmonary embolism; *CFV*, common femoral vein; *POP*, popliteal vein, *SFV*, superficial femoral vein

of hospitalized patients were VTE incidence by 14 days in the MEDENOX study, 15 days in the ARTEMIS study, and 21 days in the PREVENT study [23–25]. The incidence of VTE for the placebo group in each study was 14.9% for MEDENOX, 10.5% for ARTEMIS, and 4.96% for PREVENT. If we limit the results such that we only see those with proximal DVT and PE, the incidence was 5.6% in MEDENOX and 3.7% in ARTEMIS. Sub-analysis of MEDENOX showed that the incidence in patients with cancer increased to 19.5% in the placebo group [26].

In the present study, the incidence of VTE by day 14 in medically ill hospitalized elderly cancer patients was 7.1% (95% CI, 2.8–11.3%) including 6 proximal DVT (4.3%) and 4 distal DVT (2.8%) with no instances of PE or unexplained death by day 14. The incidence of VTE in our study was lower than the rates in the placebo groups of the RCTs, but the rate of proximal DVT was comparable. Given that proximal DVT accounts for about a third of total DVT events in other studies, the rate of proximal DVT in the current cohort was relatively high [23, 25, 27]. The lower incidence of VTE in the current study, compared with what is expected in patients with a similar number of risk factors worldwide, might be explained by a potential protective effect of Asian ethnicity. Asian ethnicities have consistently had the lowest risk for VTE [16], with a recent Korean population-based epidemiologic study reporting that the incidence of VTE in Korea was 23.4 per 100,000 people in 2009–2013, which is significantly lower than the 100 per 100,000 people incidence rate in Western countries [15]. The effect was shown not only in the general population but also in cancer patients [28, 29] but it is not necessarily consistent across studies [30–32].

We identified being female, having a long hospital stay, and having a high modified PPS of ≥ 6 as risk factors of VTE in elderly cancer patients. Kniffin et al. reported that patients who are > 65 years old and female have a higher risk of DVT and a lower risk of PE [33]. A higher risk of both DVT and PE in females was noted in a recent Korean epidemiologic study [15]. A few studies on cancer populations reported an increased risk of VTE in females [29, 34]. We confirmed that confounding variables including age, BMI, LOS, immobility, and PPS were all comparable between female and male patients, but further studies to verify this finding are warranted.

Hospitalization can result in immobilization, a well-known risk factor for patients [20]. However, the rate of reduced mobility, which is defined as bed rest with bathroom privileges for at least 3 days, was comparable between longer and shorter hospitalization (31.3 vs. 28.8%). In our study cohort, patients who were admitted for symptom and signs related to cancer progression showed a significantly higher rate of a longer LOS (≥ 13 days, 71.4 vs. 32.1%, $p = 0.000$) and the median LOS was longer (16 vs. 10 days, $p = 0.005$), compared to others. Predicting the LOS exactly at admission might be challenging and the possibility of misprediction inevitably exists without a well-validated predictive model of the LOS. In the near future, we need to develop a comprehensive model to predict the LOS in cancer patients at admission in order to make our risk prediction model practical. We found that the median overall survival was significantly shorter in patients with a hospital stay ≥ 13 days (4.5 vs. 11.7 months, $p = 0.004$). Therefore, we infer that additional factors related to cancer progression may affect the development of thrombosis. This may confound physician decision-making. For patients with long expected hospitalization, we should consider the prevention of VTE when considering if there is a true indication for hospitalization in order to increase overall life expectancy.

Although 87.8% of participants had a high risk of thrombosis according to the PPS scale, the rate of VTE in those with modified PPSs of ≥ 4 and ≥ 6 was 7.7% and 12.2%, respectively, and almost all events were asymptomatic based on DVT-based detection methods and DUS surveillance. This discrepancy can be explained by two points. First, the risk of thrombosis in Korean hospitalized cancer patients is not as high as it is in Western patients when applying the same risk prediction model. Second, PPS scoring is not sufficient to identify in-patients with cancer who should be targeted for

Table 3 Univariable analysis for risk factors for venous thromboembolism by day 14

Risk factor		*N*	VTE, *n*	VTE, %	*p*
Active cancer	Yes	139	10	7.2	1.00
	No	1	0	0	
Previous VTE	Yes	2	0	0	1.00
	No	138	10	7.2	
Reduced mobility	Yes	42	5	11.9	0.15
	No	98	5	5.1	
Trauma/surgery within last 30 days	Yes	3	1	33.3	0.20
	No	137	9	6.6	
Age more than 70 years	Yes	97	7	7.2	0.95
	No	43	3	7.0	
Acute infection or rheumatologic disorder	Yes	50	3	6.0	0.49
	No	80	7	7.8	
Obesity*	Yes	36	2	5.6	1.00
	No	104	8	7.7	
Nonhematologic cancer	Yes	109	8	7.3	0.61
	No	31	2	6.5	
Gender	Female	64	8	12.5	0.04
	Male	76	2	2.6	
Modified Padua score* ≥ 6	Yes	49	6	12.2	0.09
	No	91	4	4.4	
Hospital stay ≥ 13 days	Yes	67	8	11.9	0.04
	No	73	2	2.7	

*The cut-offs of BMI for obese was adjusted from 30 to 25 kg/m^2 according to proposed classification of BMI in Asians

VTE, venous thromboembolism

pharmacologic TP, which is supported by similar findings by Zwicker et al. [13]. Additionally, we know that the diagnosis of cancer can, itself, increase the risk score by three points. Thus, most participants in cancer patient studies are automatically categorized as high risk. The PPS scoring system also lacks cancer-specific risk factors. Based on the presence of our three risk factors, the incidence of overall VTE and proximal DVT by day 14 was 2.3/1.1%, 7.3/4.9%, and 41.7/25.0% in patients presenting with 0–1 (low-risk), 2 (intermediate risk), and three factors (high risk), respectively. By day 35, when unconfirmed PE cases were included, the incidences of VTE were 3.4%, 9.8%, and 41.7% in each risk factor group. Thus, we cautiously suggest that TP may not be necessary for low-risk patients, accounting for about 60% of this study population.

Unexpectedly, 32 (22.8%) of the enrolled patients survived for <3 months from the date of current admission, despite our efforts to exclude such patients. Among these 32 patients, the cause of death of 21 was presumed to be due to cancer progression, which shows the fact that physicians are generally optimistic in their estimate of patient survival [35]. Those patients should not have been included in this study because early detection of asymptomatic thrombosis in them is likely to be clinically insignificant. Moreover, most of the current guidelines on VTE prophylaxis in cancer do not apply to palliative care patients [36]. For patients with advanced cancers, in addition to the challenge of judging the ratio of bleeding risk to benefit of TP, it is challenging to select the appropriate group with clinically meaningful TP when considering their life expectancy and the patient's quality of life. Because

Table 4 Multivariable analysis of risk factors of venous thromboembolism by day 14

Risk factor	Univariable			Multivariable		
	Odds ratio	95% CI	*p*	Odds ratio	95% CI	*p*
Female	5.28	1.08–25.86	0.04	5.86	1.14–29.94	0.03
Modified Padua score* ≥ 6	3.03	0.81–11.32	0.09	2.74	0.68–10.91	0.15
Hospital stay ≥ 13 days	4.81	0.98–23.5	0.04	5.71	1.11–29.23	0.03

*The cut-offs of BMI for obese was adjusted from 30 to 25 kg/m^2 according to proposed classification of BMI in Asians

Table 5 VTE by day 14 and day 35 according to risk group

Number of risk factors*	Patients, no. (%)	No. of dDVT/pDVT/ possible PE by day 35	Incidence of VTE by day 14, *N* (%)	Incidence of VTE by day 35, *N* (%)	Incidence of proximal DVT and possible PE by day 35, *N* (%)
0–1	87 (62.1)	1/1/1	2 (2.3)	3 (3.4)	2 (2.3)
2	41 (29.2)	1/2/1	3 (7.3)	4 (9.8)	3 (7.3)
3	12 (8.6)	2/3/0	5 (41.7)	5 (41.7)	3 (25.0)

*Risk factors among the following: female, modified Padua score ≥ 6, hospital stay ≥ 13 days

VTE, venous thromboembolism; *dDVT*, digital deep vein thrombosis; *pDVT*, proximal deep vein thrombosis; *PE*, pulmonary embolism

symptomatic VTE increases symptom burden and reduces quality of life, a tailored approach is needed to start and discontinue primary TP for patients with advanced cancer in the palliative care setting.

The present study was unfortunately limited because the size of the sample was not sufficiently large for a statistically powerful study. We decided to enact the study with a minimum number of patients within a short period of time because the purpose of the study was to note our real-life experience when observing and treating patients for which global guidelines for pharmacologic TP in hospitalized cancer patients did not apply. Doing this quickly minimized the risk of patient need for preventative treatment for thrombosis, and it enabled us to quickly form and apply our own more effective guidelines. The interim analysis confirmed that the actual incidence was higher than the assumed incidence of 5%, so we had to stop further study. Additionally, many patients with a life expectancy shorter than 3 months were included, which limits the use of our results as decisive evidence in establishing general guidelines for VTE prophylaxis in hospitalized cancer patients. However, to our knowledge, this is the first prospective study specifically designed to evaluate the incidence of VTE in elderly cancer patients hospitalized in Korea.

This prospective observation study confirmed that the overall incidence rate of VTE was lower in the observed subset of the Korean population than in that of the Western population. However, the rate of VTE in those with more than two risk factors, including being female, having a high PPS, and having a long hospitalization, increased considerably and warranted pharmacologic TP. Based on the results of the present study, we believe that ethnic differences must be a fundamental factor to be considered in risk stratification and development of nationwide TP strategy. We should consider patient bleeding risk and, in the case of cancer patients, life expectancies for those who are indicated for VTE prophylaxis when deciding on treatment plans.

Table 6 Ten patients with deep vein thrombosis

	Sex	Age	Type of cancer	Hospital stay (day)	mPPS	IMPROVE bleeding score	Site of DVT	ACT, yes/no (duration)	IVC filter, yes/no	Bleeding, yes/no	Death/ alive	OS (months)	Cause of death
Case 1	F	87	Stomach	54	4	10	POP	Y (3 days)	Y	Y	Death	2.2	PD
Case 2	F	72	Lung	7	6	3.5	POP	Y (3 months)	N	N	Alive	15.7	–
Case 3	F	74	Lymphoma	36	7	7.5	POP	N	Y	–	Death	13.4	PD
Case 4	F	69	Breast	60	7	5.5	CFV	Y (4 days)	Y	Y	Death	2.7	PD
Case 5	F	73	Gall bladder	30	8	3.5	SFV	Y (21 days)	N	N	Death	1.0	Infection
Case 6	M	83	Esophagus	7	4	9.0	POP	N	N	–	Death	5.8	Infection
Case 7	F	66	Colon	23	6	3.5	Calf	N	N	–	Death	2.9	PD
Case 8	F	67	Lymphoma	77	4	3.5	Calf	Y (6 months)	N	N	Alive	23.6	–
Case 9	F	70	Kidney	14	9	4.5	Calf	N	N	–	Death	2.9	PD
Case 10	M	84	Lung	13	4	5.5	Calf	N	N	–	Death	1.8	Unknown

mPPS, modified Padua prediction score; *DVT*, deep vein thrombosis; *ACT*, anticoagulation treatment; *IVC*, inferior vena cava; *OS*, overall survival; *POP*, popliteal vein; *PD*, progressive disease; *CFV*, common femoral vein; *SFV*, superficial femoral vein

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Compliance with ethical standards

This study was approved by the Institutional Review Board at SNUBH (IRB number: B-1201-144-007). Written informed consent was obtained from the patients prior to study entry, and this study was conducted in accordance with the principles of the Declaration of Helsinki.

Conflict of interest The authors declare that they have no conflict of interest.

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