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ORIGINAL ARTICLE

Reduced- versus full-dose anticoagulants for the extended treatment of cancer-associated venous thromboembolism in Thai patients

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Abstract

Background: Reduced-dose anticoagulant therapy for extended treatment of cancer-associated venous thromboembolism (VTE) has been used to avoid bleeding. However, it may increase the risk of recurrent VTE.

Objectives: To study the rate of recurrent VTE and bleeding complications in Thai patients with cancer-associated VTE who were treated with full-dos/e or reduced-dose anticoagulants.

Methods: A retrospective cohort study was conducted in a single-center academic hospital. Electronic medical records were reviewed from 2016-2023. Patients with cancer-associated VTE who received anticoagulants for at least 3 months were evaluated. Reduced-dose anticoagulant was defined as a dose that was lower than the recommended standard dosage. The primary outcome was recurrent VTE. The secondary outcomes were major bleeding and clinically relevant nonmajor bleeding.

Results: A total of 229 patients were included. The median age was 65 years (IQR, 54-72). In the reduced-dose group, age and history of previous bleeding were higher than in the full-dose group. There were 169 (74%) patients and 60 (26%) patients who received full- and reduced-dose anticoagulants. The median time to reduce the dose was 3.6 months (IQR, 0.7-5.5). Of a total of 7 (3.1%) recurrent VTEs, 4 (2.4%) occurred in the full-dose and 3 (5.0%) in the reduced-dose groups (P = .4), respectively. The median time to recurrent VTE was 7.2 months (IQR, 3.5-12.4). There were 8 (3.5%) bleeding events, 7 (4.1%) and 1 (1.7%) in the full and reduced-dose anticoagulant groups (P = .35), respectively. The median follow-up time was 1.5 years (IQR, 1-3.1).

Conclusion: Older age and a history of previous bleeding were associated with the use of reduced-dose anticoagulants. Patients with cancer-associated VTE receiving reduced-dose anticoagulants had a numerically higher risk of recurrent VTE and lower bleeding outcomes compared with those receiving full-dose anticoagulants.

KEYWORDS
anticoagulants, Asian, cancers, treatment, venous thrombosis

Essentials

- Real-world data on reduced-dose anticoagulants in VTE cancer are limited.
- We studied recurrent VTE and bleeding outcomes in cancer-associated VTE.
- Older age and previous bleeding were associated with dose reduction.
- Numerically, higher VTE recurrence and lower bleeding were observed in the reduced-dose group.

1 | INTRODUCTION

Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common complication among patients with cancer. Patients with cancer have a higher risk of developing VTE than noncancer patients. In addition, 20% to 30% of patients with VTE are associated with cancer [1]. Patients with cancer-associated VTE have a higher rate of mortality [2].

Cancer is a persistent high-risk factor for recurrent VTE. The standard treatment of cancer associated with thrombosis is anticoagulants, including direct oral anticoagulants (DOACs) (rivaroxaban, apixaban, and edoxaban) and low molecular weight heparin (LMWH). It is recommended that patients with active cancer or those who are still receiving cancer-related therapy should remain on therapeutic dose anticoagulant until the cancer is in remission or unless they perceive a high risk of bleeding. However, being on a therapeutic dose anticoagulant for a long period poses an ongoing risk of bleeding [3].

Studies on unprovoked VTE have shown that reduced-dose anticoagulants after completion of 6 to 12 months of a therapeutic dose of DOACs were not associated with any difference in the risk of recurrent thrombosis or major bleeding when compared with the full-therapeutic doses [4,5]. In patients with cancer-associated VTE, a prospective study of reduced-dose apixaban in extended treatment (after completion of 6 months of full-dose treatment) found that the rate of recurrent VTE and major bleeding remains low [6]. A randomized, double-blind trial comparing apixaban 2.5 mg with 5 mg twice daily after 6 months of treatment demonstrated that major bleeding and recurrent thrombosis did not significantly differ between the groups. It seems that a lower dose of anticoagulant did not reduce the risk of bleeding in patients with cancer. However, these 2 trials studied apixaban but not LMWH, which is still a major anticoagulant used in Thailand.

Although there is currently no strong evidence supporting the optimal time to dose- reduction of anticoagulant in cancer-associated VTE, in clinical practice, physicians have implemented dose-reduction strategies after completion of full-dose anticoagulant at various times after VTE diagnosis to minimize bleeding risk. Underdosing anticoagulants might pose an increased risk of recurrent thrombosis but could mitigate bleeding events. Therefore, we aimed to evaluate the rates of recurrent VTE and bleeding complications in Thai patients with cancer and VTE who were treated with full-dose anticoagulants compared with those who received reduced-dose anticoagulants in the real-world setting.

2 | METHODS

2.1 | Study design

A retrospective cohort study was conducted in a single academic hospital in Thailand. The study goal was to document the rates of recurrent VTE and bleeding complications in Thai cancer patients with VTE who were treated with a full dose of anticoagulants and those with reduced-dose anticoagulants in the extended treatment period. The study was approved by the Ethical Research Committee of the Faculty of Medicine Ramathibodi Hospital, Mahidol University (Approval No. MURA2023/303).

A list of patients who were diagnosed with VTE including PE and DVT from 2016-2023 was retrieved from the hospital database. Inpatients and outpatients were included. The inclusion criteria were as follows: (1) active cancer defined by cancer that had been diagnosed within the past 6 months or patients whose systemic anticancer treatment was being given; (2) diagnosed with VTE including PE or proximal lower extremity DVT. All VTEs were confirmed by diagnostic imaging either computed tomography of the chest or abdomen, computed tomography pulmonary angiography, or venous Doppler ultrasound; and (3) receiving anticoagulant therapy including LMWH (enoxaparin, bemiparin, and tinzaparin) or DOACs (rivaroxaban, apixaban, and edoxaban) for the treatment of VTE. Exclusion criteria were as follows: (1) anticoagulant therapy for <3 months. This criterion ensured that we included only those individuals who had received anticoagulants for an adequate duration. (2) Follow-up <6 months.

Patients were grouped into the full-dose group if receiving a therapeutic dose anticoagulant according to the product monograph, eg, enoxaparin 1 mg/kg twice a day in those with creatinine clearance > 30 mL/min. Details of the recommended dose are available in the Supplementary Material. Patients were categorized into the reduced-dose group if patients initially received a reduced-dose anticoagulant or received a full-dose anticoagulant initially and then reduced the dose that did not meet the recommended dosage at any time point during follow-up.

The primary outcome was recurrent VTE. Recurrent VTE was defined as the progression of thrombus confirmed by imaging. Patients could be asymptomatic at the time of recurrence. The secondary outcomes were major bleeding and clinically relevant nonmajor bleeding (CRNMB) defined by the International Society on Thrombosis and Haemostasis definitions [7,8]. Another secondary outcome was all-cause mortality. The patients were observed until the last follow-up visit or death.

Electronic medical records were reviewed. Data collection included baseline characteristics, type of VTE, type of cancer, stage of cancer, status of cancer, other thrombotic risks including previous history of VTE, inferior vena cava filter, immobilization > 72 hours, recent major surgery within 3 months, bleeding risk, type of anticoagulant, date of dose reduction, rationale for dose reduction, date of primary and secondary outcomes, location of bleeding, death, and last follow-up visit date.

2.2 | Statistical analysis

Baseline characteristics were summarized using descriptive statistics. Mean or median with their corresponding SD or IQR were calculated according to the distribution of continuous data. Categorical variables including the outcomes were reported in percentages. Survival analysis was performed using a Kaplan–Meier curve. The index date was the initiation date of anticoagulant treatment. Survival time was defined as a duration from the index date to the date of outcomes or the last follow-up visit whichever comes first. The primary and secondary outcomes between the full- and reduced-anticoagulant groups were analyzed using a Cox proportional hazard model. Univariate analyses were performed, and variables that were significant with a *P* value of <.1 were included in the multivariate analyses. The results were reported as hazard ratios (HRs) with 95% CI. A *P* value of <.05 was determined as a statistically significant difference. The sensitivity analysis was performed using a survival time from the date of reducing the dose (instead of index date) to the date of outcomes in the reduced-dose groups. Logistic regression was performed to evaluate factors associated with reduced dose of the anticoagulant. Statistical analysis was performed using STATA version 18.0 for Windows software.

3 | RESULTS

A total of 3326 individuals who met the eligibility criteria were identified. After initial screening, 1854 were excluded due to duplication of records. When the exclusion criteria were applied, 465 patients who had been prescribed anticoagulants for <3 months were excluded. In addition, we excluded 778 patients who had not been followed-up for a minimum of 6 months. A flow chart is shown in the Figure.

A total of 229 patients were included in the study. One hundred sixty-nine (73.8%) patients received a full-dose anticoagulant. Sixty (26.2%) patients were in the reduced-dose group. In the reduced-dose group, 9 (15%) patients received a reduced dose at treatment initiation due to very high bleeding risk, and 51 (85%) patients had the dose reduced later after a period of receiving a full dose. In patients who had the dose reduced later, 16 (26.7%), 24 (40%), and 47 (78.3%) had the dose reduced within 1, 3, and 6 months after initiation of anticoagulant treatment, respectively. One hundred fifty-two patients received LMWH (66.4%), and 77 (33.6%) patients received DOACs for anticoagulation.

The median age of all patients was 65 years (IQR, 53-72 years). The median age in the full- and the reduced-dose groups were 64 (IQR, 54-70 years) and 70 (IQR, 58-78 years), respectively. The median age in the reduced-dose group was significantly higher than that in the full-dose group (*P* = .01). The gender distribution and body weight at baseline were similar between the 2 groups. The most common types of cancer were lung cancer and gynecologic cancer (21.8%). In terms of thrombotic risk, the common factors observed were inferior vena cava filter (5.2%) and recent major surgery (3.2%). The most common bleeding risk factor was being elderly (age > 65 years; 45%). In the reduced-dose group, a history of previous bleeding was significantly higher than in the full-dose group (8.3% vs 1.2%; *P* = .005). Other baseline characteristics are presented in Table 1. The median time to reduce the anticoagulant dose was 3.56 months (IQR, 0.77-5.15 months). Overall, the median follow-up time was 1.6 years (IQR, 0.94-3.08). The median follow-up time was 1.39 years (IQR, 0.91-2.86 years) and 2.15 years (IQR, 1.17-3.86 years) in the full- and reduced-dose groups, respectively.

Reasons to reduce the dose of anticoagulant were not specified in the medical records for most of the patients (91.6%, 55 out of 60 patients). Only 4 (6.8%) patients had the reasons documented. Two patients (3.3%), 1 patient (1.7%), and 1 patient (1.7%) had their dosage reduced due to renal insufficiency, previous bleeding, and being elderly, respectively. Through logistic regression, age (odds ratio [OR], 1.03; 95% CI, 1.01-1.06; *P* = .012) and previous bleeding (OR, 7.0; 95% CI, 1.28-38.25; *P* = .025) were associated with the anticoagulant dose reduction.

3.1 | Recurrent VTE

During the follow-up periods, recurrent VTE occurred in 7 (3.1%) of all patients. Recurrent VTE occurred in 4 out of 169 patients (2.4%) and 3 out of 60 patients (5%) in the full-dose and reduced-dose groups, respectively. The incidence rate of recurrent VTE was 1.19% per patient-year (0.09% per patient-month) and 2.01% per patient-year (0.17% per patient-month) in the full- and reduced-dose groups, respectively. There was no significant difference in recurrent VTE between the 2 groups (HR, 2.01; 95% CI, 0.45-9.0; *P* = .36) (Table 2). The median time to recurrence was 7.3 months (IQR, 3.7-8.7 months) in the full-dose group. The median time to recurrence following reducing the dose was 2.9 months (IQR, 0.5-12.2 months) in the reduced-dose groups. Early recurrence (within 3 months) occurred in 2 of 3 (66.7%) and 1 of 5 (25%) patients in the reduced-dose and full-dose groups, respectively. After adjusting for the status of cancer, previous VTE was significantly associated with recurrence VTE (HR, 25.36; 95% CI, 2.97-216.1; *P* = .003).

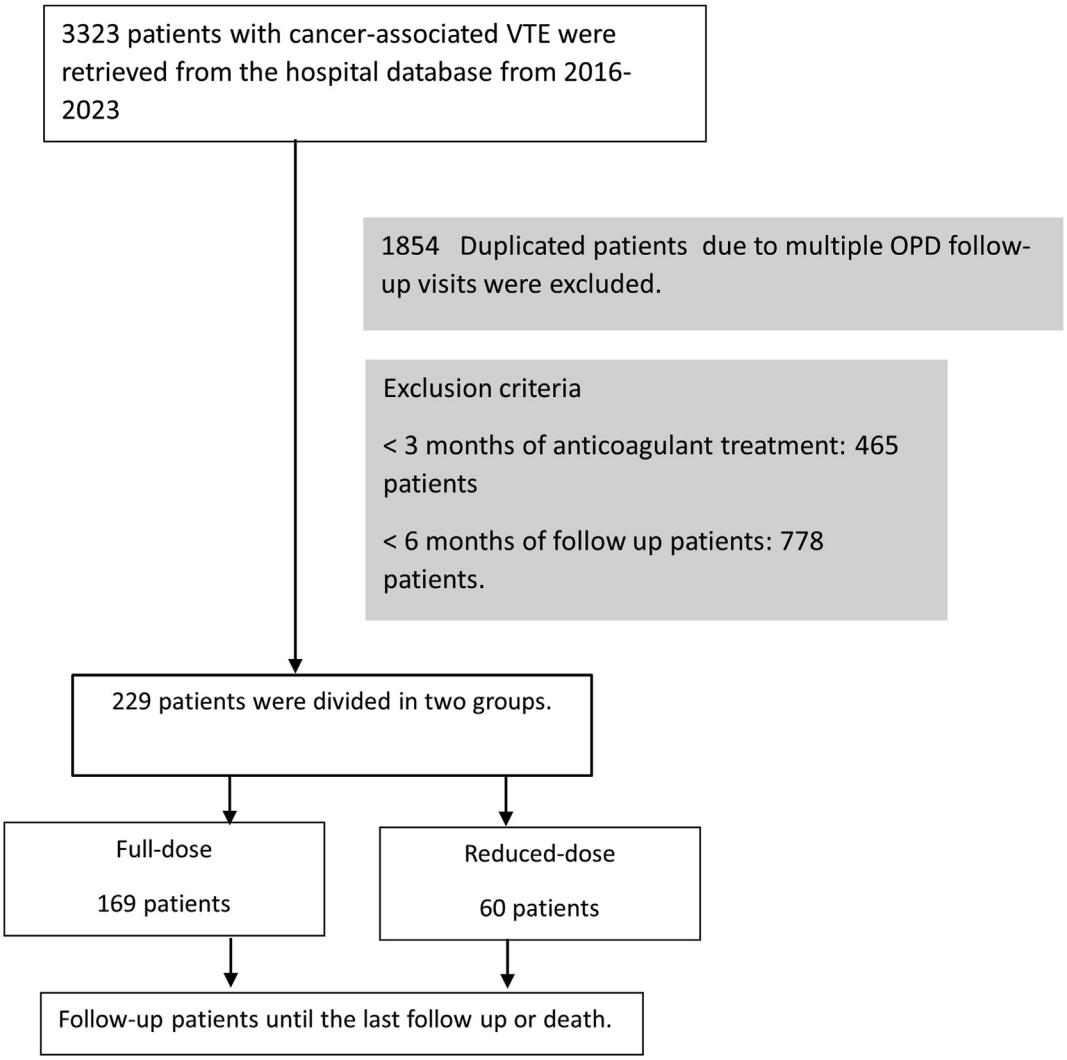

FIGURE Flow chart.

3.2 | Bleeding outcomes

During the follow-up periods, major bleeding and CRNMB occurred in 4 (1.7%) and 4 (1.7%) of all patients. The most common site of bleeding was upper gastrointestinal bleeding (50%) (Table 3). In the full-dose group, bleeding events occurred in 7 of 169 patients (4.1%). Major bleeding and CRNMB occurred in 3 patients (1.8%) and 4 (2.4%) patients, respectively. The incidence rate of bleeding was 2.1% per patient-year (0.17% per patient-month). In the reduced-dose group, major bleeding occurred in 1 (1.7%) patient. The incidence rate of bleeding was 0.7% per patient-year (0.06% per patient-month). There was no significant difference in bleeding outcomes between the 2 groups (HR, 0.37; 95% CI, 0.05-3.0; P = .35) (Table 2). The median time to bleeding was 8.5 months (IQR, 3.2-10.3 months) in the full-dose group and 10.8 months in the reduced-dose group. Patients treated with LMWH (7/150; 4.67%) were likely to bleed more than patients treated with DOACs (1/79; 1.27%; P = .18).

After adjusting for age, comorbidities, the HASBLED score, and previous bleeding history, body weight was associated with increased bleeding outcomes (adjusted HR, 1.06; 95% CI, 1.0-1.1; P = .046).

3.3 | All-cause mortality

During the follow-up periods, 78 (34.1%) of all patients died. The incidence rate was 15.7%/patient-year. There were no VTE-related deaths. Death occurred in 60 of 169 patients (35.3%) and 18 of 60 patients (30.5%) in the full- and reduced-dose groups, respectively. The incidence rate of death was 17.4%/patient-year and 11.9%/patient-year in the full- and reduced-doses groups, respectively. There was no significant difference in all-cause mortality in the 2 groups (HRs, 0.69 [95% CI, 0.41-1.17]; P = .17) (Table 2).

3.4 | Sensitivity analysis

The survival time in the reduced-dose group was calculated from the date of dose reduction instead of the index date. The median follow-ups for the full- and reduced-dose groups were 1.39 years (IQR, 0.91-2.86 years) and 1.5 years (IQR, 0.82-3.32 years), respectively. The results of the sensitivity analyses regarding recurrent VTE, bleeding

TABLE 1 Baseline characteristics of 229 patients who received anticoagulants.

Variables	All (%) (*n* = 229)	Full-dose anticoagulants, % (*n* = 169)	Reduced-dose anticoagulants, % (*n* = 60)	*P* value
Age, y (median, IQR)	65 (54-72)	64 (54-70)	70 (58-78)	.01
Male	88 (38.4)	66 (38.8)	22 (37.3)	.84
Body weight, kg (mean, SD)	59.7 (13.6)	59.9 (13.7)	59.2 (13.2)	.79
Comorbidities	87 (37.9)	64 (37.6)	23 (39.0)	.86
Cancer type				.39
Lung cancer	50 (21.8)	41 (24.2)	9 (15.00)	
ynecologic cancer	50 (21.8)	36 (21.3)	14 (23.3)	
Gastrointestinal cancer	31 (13.5)	25 (14.8)	6 (10.0)	
Hematologic malignancy	25 (10.9)	14 (8.3)	11 (18.3)	
Genitourinary cancer	18 (7.8)	15 (8.9)	6 (10.0)	
Sarcoma	16 (6.9)	11 (6.6)	5 (8.3)	
Head and neck cancer	13 (5.6)	8 (4.8)	5 (8.3)	
Cholangiocarcinoma	7 (30)	5 (3.1)	2 (3.3)	
Pancreatic cancer	1 (0.4)	1 (0.7)	—	
Cancer stage				.99
Early stage	35 (15.2)	26 (15.3)	9 (15.0)	
Advanced stage	194 (84.7)	144 (84.7)	50 (83.3)	
Status of cancer				.42
Stable disease	32 (14.0)	23 (13.5)	9 (15.0)	
Progressive disease	165 (72.0)	126 (74.1)	39 (65.0)	
Complete remission	32 (14.0)	21 (12.4)	11 (18.3)	
VTE type				.49
DVT	114 (63.7)	85 (50.1)	29 (48.3)	
PE	91 (40.1)	65 (38.3)	26 (43.3)	
Both PE and DVT	24 (10.4)	20 (11.9)	4 (6.7)	
Symptomatic VTE	156 (68.1)	116 (68.3)	40 (66.7)	
Thrombotic risk				
Previous VTE	2 (0.8)	1 (0.6)	1 (1.6)	.43
Inferior vena cava filter	12 (5.2)	9 (5.3)	3 (5.0)	.95
Immobilization	5 (2.1)	4 (2.4)	1 (1.6)	.77
Major surgery	7 (3.1)	4 (2.4)	3 (5.0)	.17
Bleeding risk				
Elderly >65 years	103 (45.0)	74 (43.7)	29 (48.3)	.45
Previous bleed	7 (3.0)	2 (1.2)	5 (8.3)	.01
Renal impairment	13 (5.7)	9 (5.3)	4 (6.7)	.67
Antiplatelets/NSAIDs	12 (5.2)	11 (6.5)	1 (1.6)	.16

(Continues)

TABLE 1 (Continued)

Variables	All (%) (*n* = 229)	Full-dose anticoagulants, % (*n* = 169)	Reduced-dose anticoagulants, % (*n* = 60)	*P* value
Type of anticoagulant				.79
LMWH	152 (66.4)	112 (65.9)	40 (67.8)	
DOACs	77 (33.6)	58 (34.1)	19 (32.2)	
Dabigatran	3 (3.9)	2 (3.5)	1 (5.3)	
Rivaroxaban	45 (58.4)	33 (56.9)	12 (63.2)	
Apixaban	20 (26.0)	14 (24.1)	6 (31.6)	
Edoxaban	9 (11.7)	9 (15.5)	–	

DVT, deep vein thrombosis; DOAC, direct oral anticoagulant; LMWH, low molecular weight heparin; NSAID, non-steroidal anti-inflammatory drug; PE, pulmonary embolism.

outcomes, and death supported the results of the primary analyses (Table 4).

4 | DISCUSSION

In this study, we demonstrated that in real-world practice, a reduced dose of anticoagulant following a period of full-dose anticoagulant has been used in one-fourth of patients with cancer-associated VTE. Twenty percent of our patients had their anticoagulant dose reduced within 6 months of initiating anticoagulant treatment. Older age and a history of previous bleeding were associated with the reduced dose of anticoagulant. The reduced-dose group had almost a two-fold increase in risk of recurrent thrombosis and lower risk of bleeding outcomes, although the differences were not statistically significant. This aligns with the hypothesis that dose reduction strategies, while potentially minimizing bleeding risk, may increase the risk of recurrent VTE.

The median time to reduce the dose of anticoagulant in our study was 3.6 months (IQR, 0.77-5.15 months). Twenty percent of patients had the dose reduced within 6 months of initiating treatment. This is sooner than what is typically performed in randomized trials in cancer-associated VTE that administer a full dose of anticoagulant for at least 6 to 12 months before reducing the dose. Although a 25% reduction in the dose of dalteparin after 1 month of treatment has been studied [9], no reduction in the dose of anticoagulant was studied with tinzaparin [10], or enoxaparin in cancer-associated thrombosis.

We found that early recurrence (within 3 months of treatment) was more likely to occur in patients who had the dose reduced (66.7%) than in the full-dose group (25%). In 2 patients in the reduced-dose group, the time to dose reduction was 15 and 7 days, and the time to recurrence following the dose reduction was 0.49 and 2.88 months, respectively. One patient in the reduced-dose group had the dose reduced within 1 month of treatment, but recurrence of VTE occurred 12 months after reducing the dose. This observation supports previous literature on non–cancer-associated thrombosis, which suggests that anticoagulants should be administered for at least 3 months as the primary treatment for VTE to prevent recurrence [11]. Our find-

TABLE 2 Venous thrombosis, bleeding, and mortality outcome of patients receiving anticoagulants.

Outcomes, %	All patients, % (*n* = 229)	Full-dose[a] anticoagulants, % (*n* = 169)	Reduced-dose anticoagulants, % (*n* = 60)	Hazard ratio (95% CI)	*P* value
Recurrent VTE	7 (3.1)	4 (2.4)	3 (5.0)	2.01 (0.45-9.00)	.36
PE	5 (2.2)	2 (1.2)	3 (5.0)		
DVT	2 (0.8)	2 (1.2)	–		
Bleeding	8 (3.5)	7 (4.1)	1 (1.7)	0.37 (0.05-3.0)	.35
Major bleed	4 (1.7)	3 (1.8)	1 (1.7)		
CRNMB	4 (1.7)	4 (2.4)	–		
All-cause mortality	79 (34.5)	61 (36)	18 (30.5)	0.69 (0.41-1.17)	.17

VTE, venous thromboembolism; CRNMB, clinically relevant major bleeding; DVT, deep vein thrombosis; PE, pulmonary embolism.
[a]Full dose as reference group.

TABLE 3 Types of bleeding outcome of patients receiving anticoagulants compared between 2 groups.

Type of bleeding outcomes, %	All patients, % (*n* = 8)	Full-dose anticoagulants, % (*n* = 7)	Reduced-dose anticoagulants, % (*n* = 1)
Upper gastrointestinal bleed	4 (50)	3 (42.9)	1 (1.7)
Lower gastrointestinal bleed	1 (12.5)	1 (14.3)	0
Urogenital bleed	1 (12.5)	1 (14.3)	0
Retroperitoneal bleed	1 (12.5)	1 (14.3)	0
Nasopharyngeal bleed	1 (12.5)	1 (14.3)	0

ings could imply that dose reduction should not be commenced unless at least 3 months of a full-therapeutic dose has been administered to cancer patients.

There was no significant difference in bleeding outcomes between the full-dose and reduced-dose groups. However, the number of major bleeds was proportionately higher in the full-dose than in the reduced-dose groups (4.1% vs 1.7%). Most bleeding outcomes occurred at a later stage of treatment and in those who received LMWH. This observation highlights the risk of bleeding with therapeutic anticoagulation in cancer patients. On the other hand, in the EVE trial, a randomized study of 5 mg twice daily and 2.5 mg twice a day apixaban following 6 to 12 months of full dose for extended treatment in cancer patients, no difference in bleeding outcome (major plus clinically relevant nonmajor bleeding) was observed during 12 months study period between those receiving a full dose of apixaban or a reduced dose of apixaban (12.2% vs 8.9%, respectively) [12]. The number of bleeding outcomes appears higher in the EVE trial compared with our study. This could be attributed to a higher proportion of gastrointestinal cancer in the EVE trial, which is associated with an increased risk of bleeding with DOACs [13].

Patients with renal insufficiency, elderly, and a history of previous bleeding were likely to be managed with lower doses of anticoagulation. These factors reflect common practical considerations of high-risk bleeding patients. Physicians tend to be more concerned about the risk of bleeding than the risk of thrombosis in this subgroup. It is also perceived that the risk of thrombosis might be lower in Asians than in Caucasians. However, cancer-associated thrombosis seems to be an important risk factor of VTE in Asian countries [14]. Future prospective trials to demonstrate the optimal duration of anticoagulant treatment in cancer patients should be further conducted.

This study has several strengths. It is a real-world study where anticoagulant treatment reflects the usual practice patterns of prescribing physicians. All patients included had objectively confirmed VTE. Additionally, we performed a manual chart review of electronic records to verify outcomes. There were minimal missing data. The median follow-up period was 2.2 years, allowing for a thorough evaluation of the long-term effects of treatment. However, some limitations should be discussed. The limited sample size reduced the statistical power to detect differences between groups. Furthermore, the reasons for physicians selecting full- or reduced-dose anticoagulants were not specified for most patients, and those at higher risk of bleeding were more likely to opt for the reduced-dose group. We did not collect data on thrombocytopenia, which could contribute to the risk of bleeding. Although the between-group comparison might be largely affected by underlying indications, we did not perform propensity score matching due to the limited number of patients. Future research should focus on a larger sample size and include propensity score matching to better understand the impact of dose reduction in anticoagulant therapy for cancer-associated VTE in real-world practice. Additionally, further studies should investigate the optimal timing for dose reduction to maximize patient safety and treatment efficacy.

TABLE 4 Result of primary analyses and sensitivity analyses.

	Primary analysis			Sensitivity analysis		
Outcomes	Full-dose anticoagulant	Reduced-dose anticoagulant	HR (95% CI)	Full-dose anticoagulant	Reduced-dose anticoagulant	HR (95% CI)
Median time to follow-up, y (IQR)	1.39 (0.91-2.86)	2.15 (1.17-3.86)	—	1.39 (0.91-2.86)	1.50 (0.82-3.32)	—
Recurrent VTE (% per patient-year)	1.19%	2.01%	2.01 (0.45-9.0), P = .36	1.19%	2.37%	2.22 (0.50-9.91), P = .30
Bleeding (% per patient-year)	2.1%	0.7%	0.37 (0.05-3.0), P = .35	2.1%	0.78%	0.48 (0.06-4.02), P = .50
Death (% per patient-year)	17.4%	11.92%	0.69 (0.41-1.17), P = .17	17.4%	14.04%	0.81 (0.48-1.37), P = .43

5 | CONCLUSION

Older age and a history of previous bleeding were associated with the use of reduced-dose anticoagulants. Patients with cancer-associated VTE receiving reduced-dose anticoagulants had numerically higher risk of recurrent VTE and lower bleeding outcomes than those receiving full-dose anticoagulants. This finding suggests that reduced-dose anticoagulants may lower the risk of bleeding, but they may have an increased risk of recurrent VTE, necessitating a careful balance in clinical share decision-making.

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RELATIONSHIP DISCLOSURE

There are no competing interests to disclose.

AUTHOR CONTRIBUTIONS

K.V. collected data, performed the study, and wrote the first draft of the manuscript. P.C., P.N., and T.P. designed the study. P.A. provided critical revision to the manuscript. K.B. designed the study, analyzed the data, and wrote the final version of the manuscript.

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SUPPLEMENTARY MATERIAL

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