

Prevalence and treatment of venous thromboembolism in patients with solid tumors

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Abstract. Cancer-associated venous thromboembolism (VTE) has exhibited a rising incidence rate. Research focusing on cancer-associated VTE and current anticoagulation therapy strategies is limited. The present study aimed to investigate the prevalence, characteristics and anticoagulation therapy strategies of cancer-associated VTE. The study was performed on patients with major solid tumors who were admitted to The First Affiliated Hospital of Guangxi Medical University (Nanning, China) between January 2020 and December 2020. The medical records of the patients' demographic characteristics, disease and treatment were extracted from the medical record data system and reviewed. The prevalence of cancer-associated VTE was calculated, followed by statistical analysis. Patients who received anticoagulation therapy for cancer-associated VTE were followed up for 1 year. The characteristics and efficacy of anticoagulation therapy strategies were compared and analyzed. A total of 4,926 patients with major solid tumors (mean age, 55.86±11.97 years) were included in the analysis, of which 117 (2.4%; 117/4,926) were diagnosed with cancer-associated

VTE. Patients with pancreatic cancer exhibited the highest prevalence of VTE (10.2%; 5/49), followed by patients with ovarian cancer (5.8%; 9/156) and lung cancer (3.3; 73/2,237). Multivariate analysis identified hypertension comorbidity [odds ratio (OR), 1.661; 95% CI, 1.031-2.674; P=0.037] and cancer stage (OR, 1.266; 95% CI, 1.079-1.486; P=0.004) as independent risk factors for cancer-associated VTE. Deep vein thrombosis (DVT) of the lower extremity accounted for 62.0%; 62/100) of all DVTs. Moreover, pulmonary embolism (PE) with lower extremity DVT accounted for 53.5% (23/43) of all PE cases. The majority of cancer-associated VTE cases (63.2%; 74/117) developed 30 days before or after a cancer diagnosis. In addition, cancer-associated VTE was dominated by symptomatic VTE (59.8%; 70/117). Only 74.4% (87/117) of patients with VTE received anticoagulant treatment, with a median duration of 79 days. The most common anticoagulant treatment strategies were heparin during hospitalization and direct oral anticoagulants (rivaroxaban) after discharge. The anticoagulants associated with bleeding events were rivaroxaban (4.2%; 3/72) and enoxaparin (1.9%; 1/54). In total, 62.1% (36/58) of the patients received anticoagulant treatment for <90 days. In conclusion, the results indicated that the prevalence of cancer-associated VTE is common and exhibits numerous characteristics. Rivaroxaban has been widely used in cancer-associated VTE treatment. However, compliance with long-term anticoagulant treatment is not adequate at present, while the efficacy and safety of rivaroxaban must be evaluated to improve long-term medication monitoring and follow-up among patients with cancer-associated VTE.

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Introduction

Venous thromboembolism (VTE), which includes deep venous thrombosis (DVT) and pulmonary embolism (PE), exerts a considerable disease burden with long-term complications and morbidity (1). Patients with cancer are at high risk of developing VTE. Results of a previous study indicated that the 12-month cumulative incidence of VTE following cancer diagnosis was

3%, which is 9-fold higher than that in the general population (2). VTE risk in patients with cancer increases by 3-fold overall and 6-fold in those receiving chemotherapy or targeted therapy (2). Certain patients with cancer exhibit abnormalities in each component of Virchow's triad contributing to thrombosis, due to patient-, tumor- and treatment-associated risk factors (3,4). This can result in malignancy with activation of the coagulation system and prothrombotic states that are exacerbated by chemotherapy, hormone therapy or surgery (4-6). Cancer-associated VTE is associated with poor survival, need for hospitalization and potential delay or interruption of anti-cancer therapy (3). VTE has become the second most common cause of death in patients with cancer (7).

To the best of our knowledge, a study performed in 1999 was the first to report that the rate of VTE in patients with cancer was only 0.6% (8). However, the incidence of cancer-associated VTE ranged from 1.3-22.6% in subsequent studies (2,9-13). Cancer-associated VTE has exhibited a sharp rise in 1-year cumulative incidence between 1997 and 2017 (2), which varies widely in different studies depending on cancer types, the follow-up duration and the detection method of thrombotic events. These increased rates may be due to the aggressiveness of anticancer therapies, greater awareness of the issue, improved diagnostic imaging techniques or improved cancer survival rates. Although the prevalence of cancer-associated VTE has previously been described (2,10,14), research focusing on VTE in patients with cancer in China is lacking (11). Furthermore, clinical practice guidelines for VTE treatment among cancer patients are continually updated. The American Society of Clinical Oncology (ASCO) first published a guideline focused on the topics in 2007, with updates in 2013, 2015 and 2019 (15). The 2019 ASCO clinical practice guideline re-affirmed that most hospitalized patients with cancer required thromboprophylaxis throughout hospitalization and suggested that rivaroxaban and edoxaban were options for VTE treatment (15). Research detailing current anticoagulation therapy strategies and implementation among patients with cancer-associated VTE is important, however, further investigations are required (3). The present study was performed to investigate and analyze the prevalence, characteristics and anticoagulation therapy status of cancer-associated VTE in a clinical setting, to provide a reference for its prevention and treatment.

Materials and methods

Patients and study design. The present retrospective cohort study was conducted at The First Affiliated Hospital of Guangxi Medical University (Nanning, China). Written informed consent was waived due to no identifiable patient data and the retrospective nature of the study. The Ethical Review Committee of The First Affiliated Hospital of Guangxi Medical University (Nanning, China; approval no. KY-E-059) approved the present study. The present study focused on hospitalized patients with major solid tumors that were admitted to the hospital from January 2020 to December 2020. Inclusion criteria were as follows: Inpatients aged ≥ 18 years with a diagnosis of primary lung, ovarian, breast, gastric, colorectal, cervical or pancreatic cancer. Patients with double primary cancer were excluded. Patients were identified according to

the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) guidelines (16). Patients who received anticoagulation therapy for cancer-associated VTE were followed up for 1 year. The study flow chart is displayed in Fig. 1.

Medical records primarily included baseline demographic information such as sex, age, ethnicity, educational background and marital status. Disease-associated information (diagnosis, diagnosis time, tumor staging, comorbidities and symptoms, among others) and treatment-associated information (treatment regimens, treatment initiation time, termination time and hemorrhagic complications) were also available. Data were abstracted from the medical database by medical records data specialists and reviewed by the first authors of the current study. The follow-up information was mainly collected through the review of medical records and/or contacting the patients via telephone communication. DVT included any thromboses in a deep leg/calf vein, pelvic vein, vena cava or upper extremity. DVT was diagnosed based on ultrasonographic results. PE was diagnosed via computerized tomographic pulmonary angiography. Both new and existing VTE in combination, as well as recurrent VTEs, were included in the analysis. In case of suspicious VTE symptoms, such as limb swelling, pain, chest pain, shortness of breath, dyspnea and others, the patient underwent diagnostic tests for VTE. Additionally, the screening decision of VTE was also based on the disease status and the clinical experience of physicians. Patients with multiple hospitalizations were regarded as one case and underwent comprehensive analysis during the observational year. Cancer stage was established through clinical evaluation, imaging and the Union for International Cancer Control TNM cancer classification (17). Patients who had completed all planned cancer treatments for 6 months and experienced recurrence were defined as new cancer cases and were handled as stage IV cases in the present study.

Statistical analysis. Data were annotated with an anonymous medical code and reviewed by the first authors of the present study. All data were subsequently analyzed using SPSS 17.0 software (SPSS, Inc.). The demographic and clinical characteristics of the patients were summarized and statistically analyzed. Continuous variables are presented as the mean \pm standard deviation, and categorical variables are presented as counts and percentages. The prevalence of cancer-associated VTE was calculated using the number of positive cases vs. the total number of patients. Categorical variables were compared using either χ^2 or Fisher's exact tests. $P < 0.05$ was considered to indicate a statistically significant difference. All variables with $P < 0.05$ following univariate analyses were examined for a second time using a logistic regression model.

Results

A total of 4,926 patients with solid tumors (mean age, 55.86 ± 11.97 years; range, 19-92 years) were eligible for analysis, of which 40.9% were male (2,016/4,926) and 59.1% were female (2,910/4,926). Lung cancer (45.4%; 2,237/4,926) was the most common cancer type, followed by breast (21.9%; 1,078/4,926), colorectal (12.7%; 628/4,926), gastric (9.8%; 482/4,926), cervical (6.0%; 296/4,926), ovarian (3.2%;

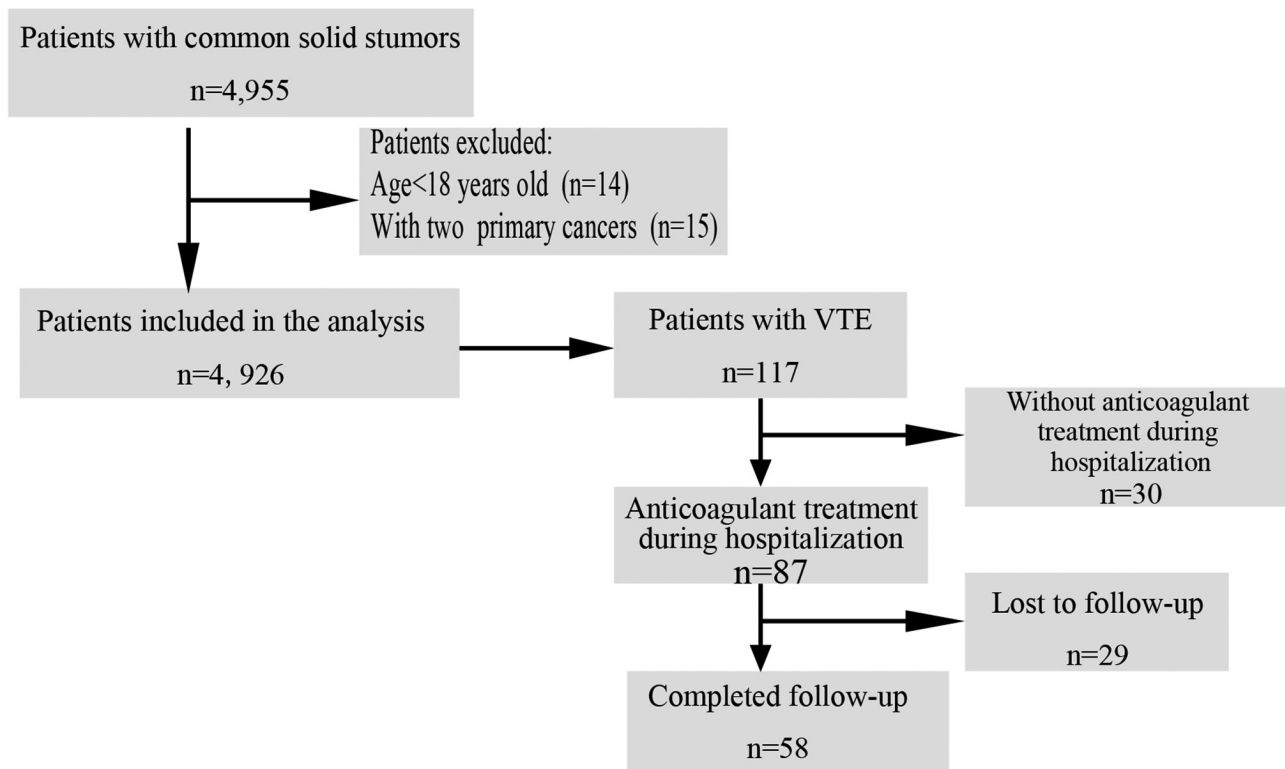


Figure 1. Study flow chart. A total of 4,926 patients were included and 117 patients with cancer were diagnosed with cancer-associated VTE. Out of the 117 patients, only 87 (74.4%) received anticoagulant treatment during hospitalization and 58 cases received and completed follow-up observation. VTE, venous thromboembolism.

156/4,926) and pancreatic cancer (1.0%; 49/4,926). There were statistically significant differences ($P < 0.05$) in VTE rates between different wards, cancer types and cancer stages, as well as between the presence and absence of hypertension. The characteristics of the study population are displayed in Table I. Multivariate analysis identified hypertension [odds ratio (OR), 1.661; 95% CI, 1.031-2.674; $P = 0.037$] and cancer stage (OR, 1.266; 95% CI, 1.079-1.486; $P = 0.004$) as independent risk factors for cancer-associated VTE.

A total of 117 (2.4%; 117/4,926) patients with solid tumors were diagnosed with cancer-associated VTE. In the population analyzed in the present study, PE and DVT occurred with 0.9% (43/4,926) and 2.0% (100/4,926) prevalence, respectively. Among the different cancer types, patients with pancreatic cancer exhibited the highest prevalence of VTE (10.2%; 5/49), followed by patients with ovarian (5.8%; 9/156), lung (3.3%; 73/2,237), gastric (2.3%; 11/482), cervical (1.4%; 4/296), breast (0.9%, 10/1,078) and colorectal cancer (0.8%, 5/628). Moreover, the prevalence of cancer-associated VTE were significantly different between the cancer types ($P < 0.001$). The prevalence of PE and DVT also varied significantly between different cancer types (data not shown). Results of the present study demonstrated that PE was the main burden for patients with pancreatic cancer and lung cancer, while DVT was the main burden for patients with pancreatic cancer and ovarian cancer. Both PE and DVT occurred in various cancer stages with a significant difference in prevalence ($P < 0.001$; data not shown). Lower extremity DVT occurred in 1.3% (62/4,926) of all cancer cases, accounting for 62.0% of all DVT diagnoses and 53.0% of all VTE diagnoses in the present study. DVT

accompanied PE in 58.1% of all PE cases. Lower extremity DVTs accompanied by PE accounted for 53.5% of all PE cases. A total of 25.0% (26/104) of all DVTs were associated with a central venous catheter. Additionally, 25 patients exhibited dual diagnoses of both PE and DVT. Notably, this overlap created a disparity between the sums of all PE and DVT cases compared with the total number of VTEs. A summary of all VTEs experienced among patients with different cancer types is displayed in Table II.

Cancer-associated VTE was dominated by symptomatic VTE (59.8%; 70/117), with the most common symptoms including chest tightness, shortness of breath in patients with symptomatic PE and swelling in patients with symptomatic DVT. Most cases of cancer-associated VTE (63.2%; 74/117) developed 30 days before or after cancer diagnosis. Out of the 117 patients with cancer-associated VTE, 87 (74.4%) received anticoagulant treatment with or without adjuvant treatment, 52 received heparin treatment, 44 received rivaroxaban treatment and 6 received rivaroxaban combined with aescufen forte during hospitalization. After discharge, patients with VTE predominantly received direct oral anticoagulant (DOAC) treatment, such as rivaroxaban (57.3%; 67/117). The median duration of anticoagulant treatment was 79 days (range 3-420 days). The anticoagulants associated with bleeding events were rivaroxaban (4.2%; 3/72) and enoxaparin (1.9%; 1/54). A total of 62.1% (36/58) of patients received anticoagulant treatment for <90 days. The main reason for discontinuing anticoagulant treatment was the judgement of physicians (51.7%; 30/58), followed by the disappearance of the thrombus (24.1%; 14/58) and patient decisions

Table I. Baseline characteristics of the study population and associated prevalence of VTE (n=4,926).

Characteristic	Total, n (%)	Without VTE, n (%)	VTE, n (%)	P-value	χ^2 -value
Sex					
Female	2,910 (59.1)	2,851 (98.0)	59 (2.0)	0.054	3.706
Male	2,016 (40.9)	1,958 (97.1)	58 (2.9)		
Age range, years					
18-30	88 (1.8)	87 (98.9)	1 (1.1)	0.360	4.352
31-40	433 (8.8)	423 (97.7)	10 (2.3)		
41-50	976 (19.8)	956 (98.0)	20 (2.0)		
51-60	1,626 (33.0)	1,593 (98.0)	33 (2.0)		
>60	1,803 (36.6)	1,750 (97.1)	53 (2.9)		
Ethnicity					
Han	3,067 (62.3)	2,993 (97.6)	74 (2.4)	0.735 ^a	1.274
Zhuang minority	1,694 (34.4)	1,657 (97.8)	37 (2.2)		
Yao minority	85 (1.7)	82 (96.5)	3 (3.5)		
Other minorities	80 (1.6)	77 (96.3)	3 (3.8)		
Wards					
Respiratory Medicine	1,106 (22.5)	1,048 (94.8)	58 (5.2)	<0.001	89.832
Gynecology	242 (4.9)	233 (96.3)	9 (3.7)		
Colorectal Surgery	350 (7.1)	349 (99.7)	1 (0.3)		
Digestive and Liver Diseases	924 (18.8)	917 (99.2)	7 (0.8)		
Oncology	1,207 (24.5)	1,179 (97.7)	28 (2.3)		
Radiation Oncology	241 (4.9)	241 (100.0)	0 (0.0)		
Thoracic Surgery	670 (13.6)	668 (99.7)	2 (0.3)		
Others	186 (3.8)	174 (93.5)	12 (6.5)		
Cancer types					
Lung	2,237 (45.4)	2,164 (96.7)	73 (3.3)	<0.001	46.162
Ovarian	156 (3.2)	147 (94.2)	9 (5.8)		
Breast	1,078 (21.9)	1,068 (99.1)	10 (0.9)		
Colorectal	628 (12.7)	623 (99.2)	5 (0.8)		
Gastric	482 (9.8)	471 (97.7)	11 (2.3)		
Cervical	296 (6.0)	292 (98.6)	4 (1.4)		
Pancreatic	49 (1.0)	44 (89.9)	5 (10.2)		
Diabetes comorbidity					
Yes	291 (5.9)	287 (98.6)	4 (1.4)	0.248	1.335
No	4,635 (94.1)	4,522 (97.6)	113 (2.4)		
Hypertension comorbidity					
Yes	4,188 (85.0)	712 (96.5)	26 (3.5)	0.026	4.933
No	738 (15.0)	4,097 (97.8)	91 (2.2)		
Cancer stage					
Stage I	901 (18.5)	891 (98.9)	10 (1.1)	<0.001	34.604
Stage II	723 (14.8)	718 (99.3)	5 (0.7)		
Stage III	836 (17.1)	819 (98.0)	17 (2.0)		
Stage IV	1,386 (28.4)	1,329 (95.9)	57 (4.1)		
Undefined	1,031 (21.1)	1,008 (97.8)	23 (2.2)		

^aFisher's test; other variables were compared using χ^2 tests. VTE, venous thromboembolism.

(22.4%; 13/58). In patients receiving anticoagulant treatment until thrombolysis was complete, the mean time needed to complete thrombolysis was 233.14±112.40 days. The clinical characteristics of patients with VTE are shown in Table III.

Discussion

Cancer and cancer-associated treatment methods are well-established VTE risk factors (3). The present study

Table II. Summary of VTE in different cancer types.

Cancer type	Total, n (%)	Total VTE, n (%)	PE with or without DVT, n (%)	PE with DVT, n (%)	PE with lower extremity-DVT, n (%)	DVT, n (%)	Lower extremity-DVT, n (%)
Lung	2,237 (45.4)	73 (3.3)	36 (1.6)	21 (0.9)	21 (0.9)	59 (2.6)	45 (2.0)
Ovarian	156 (3.2)	9 (5.8)	2 (1.3)	2 (1.3)	1 (0.6)	9 (5.8)	7 (4.5)
Breast	1,078 (21.9)	10 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	10 (0.9)	1 (0.1)
Colorectal	628 (12.7)	5 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	5 (0.8)	1 (0.2)
Gastric	482 (9.8)	11 (2.3)	1 (0.2)	0 (0.0)	0 (0.0)	10 (2.1)	4 (0.8)
Cervical	296 (6.0)	4 (1.4)	1 (0.3)	1 (0.3)	1 (0.3)	4 (1.4)	3 (1.0)
Pancreatic	49 (1.0)	5 (10.2)	3 (6.1)	1 (2.0)	0 (0.0)	3 (6.1)	1 (2.0)
Total	4,926	117 (2.4)	43 (0.9)	25 (0.5)	23 (0.5)	100 (2.0)	62 (1.3)

VTE, venous thromboembolism; DVT, deep venous thrombosis; PE, pulmonary embolism.

focused on patients with lung, ovarian, breast, colorectal, gastric, cervical and pancreatic cancer to determine the prevalence, characteristics and anticoagulation therapy strategies for cancer-associated VTE in a clinical setting. The overall prevalence of cancer-associated VTE was 2.4% and this was significantly different among cancer types. The main cancer types affected by VTE were pancreatic, ovarian and lung cancer. The incidence rates observed in the present study were higher than those obtained in a previous study, which indicated that the incidence rate of VTE was 1.79% in patients with solid tumors and 4.49% in patients with ovarian cancer, 4.42% in patients with pancreatic cancer and 2.57% in patients with lung cancer. Results of this previous study also indicated that patients were at a relatively high risk of developing VTEs (11). The results of the present study are comparable to those obtained by Mulder *et al* (2), who revealed that the 12-month cumulative incidence of VTE following cancer diagnosis is 3% and that pancreatic cancer (4.4%) exhibits the highest 6-month cumulative incidence of VTE across cancer types. A previous study demonstrated an overall VTE rate of 4.1%, including DVTs (3.4%) and PEs (1.1%), in which pancreatic (8.1%), ovarian (5.6%), lung (5.1%) and stomach (4.9%) cancers were also predominant cancers burdened with VTE (18). An updated literature review on cancer-associated VTE indicated that patients with pancreatic, brain, lung and ovarian cancer were at the greatest risk of VTE development, with a lower risk observed in patients with breast cancer (5). Results of the present study demonstrated that cancer-associated VTE is common in the clinical setting. The prevalence of cancer-associated VTE varies widely in different studies depending on the study design, cancer types, follow-up time and detection method for thrombotic events. However, results of previous studies have demonstrated that patients with pancreatic, ovarian, lung and gastric cancer exhibit a higher risk of VTE than other cancers (2,5,9,18). This may be associated with the occurrence of cancer metastasis or advanced cancer stages. The characteristics of VTE in patients with cancer in China remain unclear; thus, further investigations of cancer-associated VTE are required.

Although previous studies have identified the association between medical comorbidities and a higher risk of VTE in

patients with cancer, statistically significant differences in VTE development were only observed among patients with cancer with and without renal failure, respiratory disease, obesity or infection comorbidities (5,19,20). The present study found that patients with cancer and hypertension exhibited a higher risk of VTE development (OR, 1.661) compared with patients without hypertension. Hypertension as a cardiovascular risk factor associated with thrombotic disease was previously examined in a study of myeloproliferative neoplasm (21). We hypothesized that the presence of hypertension may induce endothelial dysfunction. Thus, physicians should control and review vascular comorbidities in patients with cancer.

Cancer stage (OR, 1.266) was also an independent risk factor for cancer-associated VTE in the present study. Cancer stage and metastasis have previously been recognized as high-risk factors for VTE (2,5,10,11,19,20,22). A review on cancer-associated thrombosis has indicated that cancer stage, rather than cancer type, was the dominant risk factor for VTE (6). Stage IV cancer with metastatic spread and increased tumor burden contributes to increasing thromboembolic risk, which in turn accelerates tumor aggressiveness and poor prognosis by forming fibrin microclots that protect circulating tumor cells from shear stress and natural killer cell-mediated attacks (23,24). Thus, VTE, metastatic spread and cancer aggressiveness interact to promote cancer development, therefore the prevention and treatment of cancer-associated VTE are crucial for a favorable outcome.

Overall, DVT prevalence was higher than PE prevalence in patients with cancer-associated VTE in the present study (2.0% vs. 0.9%), which is consistent with the results of previous studies, showing that DVT was more common than PE (10,12,14). However, Cohen *et al* (13) showed that PE (53.7%) was more prevalent than DVT (46.3%) in patients with active cancer, a notable difference from the findings of the present study. We hypothesize that the prevalence of PE may be higher than the data (0.9%) we found. Since some patients may refuse diagnostic imaging detection, PE may be undiagnosed. In addition, only those patients with suspicious PE symptoms would undergo diagnostic imaging tests to confirm the presence or absence of PE, allowing certain PE cases to go undiagnosed. The prevalence of PE and DVT was also

Table III. Clinical characteristics of VTE cases.

Characteristic	n	%
Type of VTE (n=117)		
Symptomatic	70	59.8
Asymptomatic	47	40.2
Time of VTE diagnosis (n=117)		
Before cancer diagnosis, days		
1-30	29	24.8
31-180	9	7.7
>180	0	0
After cancer diagnosis, days		
0-30	45	38.5
31-180	18	15.4
>180	16	13.7
VTE therapy during hospitalization (n=117)		
Without anticoagulant treatment	30	25.6
Anticoagulant treatment	87	74.4
Heparin	52	44.4
Warfarin	1	0.9
Direct oral anticoagulant (Rivaroxaban)	44	37.6
Rivaroxaban combined with aescufen forte	6	5.1
Thrombolysis	3	2.6
Inferior vena cava filter use	8	6.8
VTE therapy after discharge (n=117)		
Without anticoagulant treatment	40	34.2
Anticoagulant treatment	77	65.8
Heparin	12	10.3
Direct oral anticoagulant (Rivaroxaban)	67	57.3
Anticoagulant treatment (n=87)		
Lost to follow-up	29	33.3
Completed follow-up	58	66.7
1-14 days	13	22.4
15-30 days	8	13.8
31-90 days	15	25.9
91-180 days	11	19.0
181-365 days	10	17.2
>365 days	1	1.7
Reasons for discontinued anticoagulant treatment (n=58)		
Disappearance of the thrombus	14	24.1
Physician's other judgment	30	51.7
Patient's decision	13	22.4
Patient death	1	1.7

VTE, venous thromboembolism.

markedly different among different cancer types observed in the present study. PE predominantly occurred in patients with pancreatic and lung cancer, while DVT mainly occurred in patients with pancreatic and ovarian cancer. Pancreatic cancer is commonly detected at advanced stages and is accompanied by increased mucin expression and tumor cell-derived coagulation factor and cytokine secretion, which facilitate both PE

and DVT development (25). Khorana *et al* (26) indicated that PE was most frequent in patients with lung cancer, followed by gastric cancer. A previous study investigated patients with solid malignancies complicated with PE and demonstrated that patients with lung cancer exhibited a higher incidence of PE than patients with other solid tumors (27). However, the specific underlying mechanisms require further study.

In the present study, lower extremity DVTs accounted for 53.0% (62/117) of all VTEs and 53.5% (23/43) of PEs. This differs from a previous study demonstrating that 87.3% of DVTs without PE and upper extremity DVTs (47.2%) are more common than lower extremity DVTs in patients with cancer (11).

Central venous catheters were the major factor contributing to upper extremity DVTs. Central venous catheter-associated DVTs comprised 25.0% of total DVTs in the present study, which was notably lower than the percentage (74.9%) reported by Peng *et al* (11). These differences may be due to different central venous catheter applications and clinical practices. Additionally, the majority of PEs developed from lower extremity DVTs in the present study. PE (often developed from lower extremity DVTs) is the most dangerous form of VTE and can be fatal if left undiagnosed or untreated (28). Therefore, the prevention of VTE, particularly among patients with cancer and lower extremity DVTs, should not be overlooked. CT pulmonary angiography is widely available for PE testing, but is not adequate because some patients give up CTPA screening (1). Ultrasound surveillance and systematic anticoagulation therapy have also been evaluated for the improved management of lower extremity DVTs (29). Moreover, certain physical interventions, including leg or upper body exercises, intermittent pneumatic compression and compression stockings for lower extremity DVT prevention, have also been applied in the clinical setting (30-32). This highlights the importance of lower extremity DVT prevention. Further studies are required in patients with cancer.

In the present study, the majority of cancer-associated VTEs (63.2%) developed 30 days before or after cancer diagnosis. Comparable with the results of a previous study, the risk of VTE was the highest in the first 6 months following cancer diagnosis (11). Reasons for higher risk of cancer-associated thrombosis in the months surrounding cancer diagnosis are likely associated with higher tumor burden and intensive therapy (including surgery, radiation and systemic therapy). Moreover, cancer-associated VTE was dominated by symptomatic VTE (59.8%), which is consistent with the results of a previous study, highlighting that the majority of patients with lung cancer were symptomatic for VTE (33). The most common symptoms of VTE were chest tightness, shortness of breath and swelling. Thus, healthcare professionals should be familiar with the characteristics of VTE for earlier identification, evaluation, diagnosis and treatment.

Results of the present study displayed that 74.4% (87/117) and 65.8% (77/117) of patients with cancer-associated VTE received anticoagulant treatment during hospitalization and after discharge, respectively. A DOAC, such as rivaroxaban, was widely used during hospitalization, particularly following discharge. Rivaroxaban use was consistent with the updated clinical practice guidelines (15,34), which indicated that DOACs, such as rivaroxaban, have been added as options for VTE treatment among patients with cancer. The present finding is also similar to that of a previous study, indicating that 57.6% of patients with cancer-associated VTE received oral anticoagulants (33). However, a recent study showed that only 25.0% of patients with cancer-associated VTE received anticoagulation therapy, and low-molecular-weight

heparin (LMWH) remained the most widely used anticoagulant drug among patients with advanced cancer (14). The difference may be attributed to the patients with advanced cancer having an increased risk of bleeding because of rivaroxaban use (14). Moreover, the results of the present study demonstrated that the anticoagulants associated with bleeding events were rivaroxaban (4.2%) and enoxaparin (1.9%). We hypothesize that rivaroxaban exerts a higher rate of bleeding. A meta-analysis including three randomized controlled trials and 1,739 patients with cancer-associated VTE indicated that DOACs exerted a greater reduction in VTE recurrence and an increased incidence of major bleeding compared with dalteparin (35). Results of another previous study demonstrated that rivaroxaban exerted significantly higher clinically relevant non-major bleeding than dalteparin (13% vs. 4%) (36). In conclusion, DOACs have been recommended as adequate and preferable options to LMWH for cancer-associated VTE therapy (15). Additional clinical trials addressing anticoagulation therapy strategies and their efficacy and safety are still needed.

Furthermore, guidelines recommend long-term anticoagulation therapy lasting at least 6 months for improved efficacy (15). The median duration of anticoagulant treatment was only 79 days in the present study. A total of 62.1% of patients received anticoagulant treatment for <90 days. Anticoagulation therapy strategies in daily clinical practice do not follow current guideline recommendations. The main reason for discontinuing anticoagulant treatment was the judgement of physicians (51.7%), followed by the disappearance of the thrombus (24.1%) and patient decisions (22.4%). We hypothesize that inadequate knowledge may contribute to discontinuing anticoagulant treatment. Moreover, high costs due to the long-term use of anticoagulants and the inconvenience due to subcutaneous injection of LMWH for patients may be barriers to continuing anticoagulant treatment. Therefore, long-term anticoagulation therapy remains challenging due to balancing the benefits and risks of bleeding as well as the inconvenience of LMWH.

The present study exhibits several limitations that should be acknowledged. The results of the present study relied on data obtained from a single medical center, which may be insufficient to estimate the prevalence of cancer-associated VTE for a more generalized population. Because of the retrospective nature of the present study, there may be cases that missed screening and went underdiagnosed, leading to the underestimation of the prevalence of VTE. In addition, the prevalence of cancer-associated VTE was not analyzed in relation to different chemotherapy regimens. Moreover, although the effects and bleeding complications of anticoagulation therapy were assessed in the present study, VTE recurrence was not measured due to the 1-year follow-up limit. Further research is required using prospective multicenter cohorts to detect new possible trends and assess the variety of treatment regimens with a longer follow-up, to further explore more operational management strategies for cancer-associated VTE and also assess the prognosis between patients with VTE and those without VTE.

At present, cancer-associated VTE is a common occurrence. Notably, the prevalence of cancer-associated VTE, PE (with or without DVT) and DVT is significantly different

among different cancer types. Patients with cancer and hypertension comorbidity, as well as patients with stage IV cancer, are at higher risk for the development of cancer-associated VTE. Moreover, the majority of cancer-associated VTE cases develop 30 days before or after cancer diagnosis. DOACs, such as rivaroxaban, have been widely used for anticoagulation therapy. However, more studies investigating the efficacy and safety of anticoagulant drugs are still needed. At present, compliance with long-term anticoagulant treatment is not adequate. The present study results highlighted that further VTE screening among patients with cancer is required, along with standardized anticoagulation therapy, long-term medication monitoring and patient follow-up.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

YY and YH designed the present study, applied for the ethics committee approval, provided general supervision, and revised and finalized the manuscript. HZ, FL and YL participated in the study design, reviewed the data analysis, drafted and revised the manuscript. BF contributed to the study design, drafted and revised the manuscript, and was involved in language editing and picture processing. TL and TD participated in the study design, collection of data, data analysis and writing of the manuscript. HZ and YH assessed the raw data and confirm the authenticity of all the data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The Ethical Review Committee of the First Affiliated Hospital of Guangxi Medical University approved the present study (Nanning, China; approval no. KY-E-059). Written informed consent was waived due to no identifiable patient data and the retrospective nature of the study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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