Original article

Venous thromboembolism among Thai patients with lymphoma

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Abstract:

Background: *Data remains limited regarding venous thromboembolism (VTE) among Thai patients with lymphoma.* ***Aims:*** *The study aimed to determine the prevalence, predictive factors, and clinical outcomes of VTE among Thai patients with lymphoma.* ***Methods:*** *The study employed a nested case-control design from a cohort of 1,769 lymphoma patients treated at Ramathibodi Hospital.* ***Results:*** *The prevalence of VTE was 5.1% (91 patients). Locations of VTE were deep vein thrombosis of the lower extremities (53.9%), pulmonary embolism (23.1%), splanchnic vein thrombosis (5.5%), jugular vein thrombosis (3.3%), cerebral venous thrombosis (1.1%), and VTE in > 2 sites (13.1%). Among 41 patients (45.1%), VTE occurred during treatment or up to 3 months after completing therapy whereas among 35 patients (38.4%) VTE was diagnosed before therapy. A control group of 455 patients was randomly selected from the database of lymphoma patients without VTE. Of patients with VTE vs. controls, 51.6 vs. 49.0%, respectively, were female (p = 0.64). The mean age was 57 vs. 61 years (p = 0.09), respectively. Types of lymphoma in the corresponding groups were B-cell non-Hodgkin lymphoma (NHL; 93. vs. 78.9%), T-cell NHL (5.5 vs. 11.7%), and Hodgkin disease (1.1 vs. 6.4%), respectively (p = 0.02). Using multivariate analysis, B-cell NHL type (odds ratio [OR] 4.4), bulky mass >10 cm (OR 2.2) and prechemotherapy platelet count > 350 x 10^9/L (OR 2.1) were independently predictive factors of VTE. The mortality rate in the study and control groups was 25.3 and 15.8%, respectively (p = 0.03).* ***Conclusion:*** *Prevalence of VTE among Thai patients with lymphoma is not low. B-cell NHL type, bulky mass, and elevated prechemotherapy platelet count were predictive factors of VTE. Patients with VTE exhibited higher mortality.*

Keywords : ● *Venous thromboembolism* ● *Thai* ● *Patients* ● *Lymphoma*

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นิพนธ์ต้นฉบับ

ภาวะหลอดเลือดดำอุดตันในผู้ป่วยโรคมะเร็งต่อมน้ำเหลืองในประเทศไทย

สิทธาคม ผู้สันติ[1] พิจิกา จันทราธรรมชาติ[2] กชวรรณ บุญญวัฒน์[2] ธีรยา พัววิไล[2] พิมพ์ใจ นิภารักษ์[2] สุภร จันท์จารุณี[2] และ พันธุ์เทพ อังชัยสุขศิริ[2]

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บทคัดย่อ

บทนำ *ปัจจุบันข้อมูลเกี่ยวกับภาวะหลอดเลือดดำอุดตันในผู้ป่วยโรคมะเร็งต่อมน้ำเหลืองยังมีน้อยและจำกัด* ***วัตถุประสงค์*** *เพื่อศึกษาความชุก ปัจจัยเสี่ยง และผลลัพธ์ทางคลินิกของผู้ป่วยโรคมะเร็งต่อมน้ำเหลืองที่มีภาวะหลอดเลือดดำอุดตันในประเทศไทย* ***วัสดุและวิธีการ*** *ทำการศึกษาแบบ nested case-control จากผู้ป่วยโรคมะเร็งต่อมน้ำเหลืองที่ได้รับการรักษาในโรงพยาบาลรามาธิบดี* ***ผลการศึกษา*** *จากผู้ป่วยโรคมะเร็งต่อมน้ำเหลืองที่ได้จากฐานข้อมูลของโรงพยาบาลรามาธิบดีทั้งหมด 1,769 คน พบผู้ป่วยที่มีภาวะหลอดเลือดดำอุดตัน 91 ราย (ร้อยละ 5.1) ประกอบด้วยภาวะหลอดเลือดดำอุดตันที่ขา (ร้อยละ 53.9) ภาวะลิ่มเลือดอุดตันในหลอดเลือดที่ปอด (ร้อยละ 21.3) ภาวะลิ่มเลือดอุดตันในหลอดเลือดดำในช่องท้อง (ร้อยละ 5.5) ภาวะลิ่มเลือดอุดตันในหลอดเลือดดำที่คอ (ร้อยละ 3.3) ภาวะลิ่มเลือดอุดตันในหลอดเลือดดำในสมอง (ร้อยละ 1.1) และภาวะหลอดเลือดดำอุดตันตั้งแต่ 2 ตำแหน่ง (ร้อยละ 13.1) ส่วนใหญ่พบภาวะหลอดเลือดดำอุดตันระหว่างให้การรักษามะเร็งต่อมน้ำเหลืองจนสิ้นสุดการรักษานาน 3 เดือน (ร้อยละ 45.1) รองลงมาพบตั้งแต่เริ่มหรือก่อนวินิจฉัยมะเร็งต่อมน้ำเหลือง (ร้อยละ 38.4) ผู้ป่วยกลุ่มควบคุมได้มาจากการสุ่มผู้ป่วยมะเร็งต่อมน้ำเหลืองที่ไม่มีภาวะหลอดเลือดดำอุดตันมีจำนวน 455 ราย เมื่อเปรียบเทียบผู้ป่วยที่มีและไม่มีภาวะหลอดเลือดดำอุดตัน พบว่าเป็นเพศหญิง ร้อยละ 51.6 และร้อยละ 49.0 (p = 0.64) อายุเฉลี่ยอยู่ที่ 57 และ 61 ปี (p = 0.09) ประเภทของมะเร็งต่อมน้ำเหลือง ประกอบด้วย มะเร็งต่อมน้ำเหลืองนอนฮอดจ์กินชนิดบีเซลล์ ร้อยละ 93.4 และ 78.9 มะเร็งต่อมน้ำเหลืองนอนฮอดจ์กินชนิดทีเซลล์ ร้อยละ 5.5 และ 11.7 และมะเร็งต่อมน้ำเหลืองฮอดจ์กิน ร้อยละ 1.1 และ 6.4 (p = 0.02) ตามลำดับ จากการวิเคราะห์พหุปัจจัยพบว่ามะเร็งต่อมน้ำเหลืองนอนฮอดจ์กินชนิดบีเซลล์ [odds ratio (OR) 4.4] ขนาดของก้อนมะเร็งน้ำเหลืองที่มากกว่าหรือเท่ากับ 10 เซนติเมตร (OR 2.7) และจำนวนเกล็ดเลือดก่อนให้ยาเคมีบำบัดที่มากกว่าหรือเท่ากับ 350 x 10^9/ลิตร (OR 2.1) เป็นปัจจัยอิสระที่มีผลต่อการเกิดภาวะหลอดเลือดดำอุดตัน อัตราการตายของผู้ป่วยที่มีและไม่มีภาวะหลอดเลือดดำอุดตันอยู่ที่ร้อยละ 25.3 และ 15.8 (p = 0.03)* ***สรุป*** *ความชุกของภาวะหลอดเลือดดำอุดตันในผู้ป่วยโรคมะเร็งต่อมน้ำเหลืองในประเทศไทยถือว่าไม่ต่ำ โดยมะเร็งต่อมน้ำเหลืองนอนฮอดจ์กินชนิดบีเซลล์ ขนาดของก้อนมะเร็งขนาดใหญ่ และจำนวนเกล็ดเลือดสูงก่อนให้ยาเคมีบำบัด เป็นปัจจัยที่มีผลต่อการเกิดภาวะหลอดเลือดดำอุดตัน ผู้ป่วยที่มีภาวะหลอดเลือดดำอุดตันมีอัตราการตายสูงกว่า*

คำสำคัญ : ● *ภาวะหลอดเลือดดำอุดตัน* ● *ไทย* ● *ผู้ป่วย* ● *มะเร็งต่อมน้ำเหลือง*

วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต. 2564;31:261-8.

Introduction

Venous thromboembolism (VTE) is a major cause of morbidity and mortality among patients with cancer. About 10-15% of patients with overt cancer will have symptomatic VTE during the course of their illness. On the other hand, about 16-40% of patients with a first episode of VTE were found to have a malignancy, and up to 30% received a diagnosis of new cancer within 1 year.[1,2]

Cancer is strongly associated with the occurrence of VTE because cancer cells can induce a hypercoagulable state by expressing tissue factors and secreting cytokines. Mechanical obstruction by the tumor mass also predisposes a patient to VTE. Cancer treatment may also increase the risk of VTE. The risk of VTE in hematologic malignancies has been considered to be lower than that in solid tumors. However, several recent studies have shown that VTE rate among patients with lymphoma was comparable with that observed among patients with solid tumors. The reported estimates of VTE incidence in lymphoma range from 3-7%, 3-6%, and 5-11% in Hodgkin, low grade non-Hodgkin, and high grade non-Hodgkin lymphomas, respectively.[3]

Data remains limited regarding VTE among Thai patients with lymphoma. Therefore, this study aimed at estimating the prevalence and predictive factors of VTE occurrence, as well as clinical outcomes of patients with lymphoma and VTE.

Materials and Methods

This study employed a nested case-control design (1:5) from a cohort of lymphoma patients from the Ramathibodi Hospital database (Figure 1). We selected unmatched controls from a group of patients not presenting VTE events using random sampling method. All patients with VTE were analyzed. All patients receiving a diagnosis of lymphoma according to the World Health Organization classification in Ramathibodi Hospital between October 2005 and September 2015 were included.[4] Clinical and pathological information associated with lymphoma including demographics, comorbid diseases, time of diagnosis, stage at diagnosis, and pathologic subtype were reviewed from medical records. Venous thromboembolism was defined as any case of objectively confirmed venous thrombosis including deep vein thrombosis of the extremities, pulmonary embolism, splanchnic vein

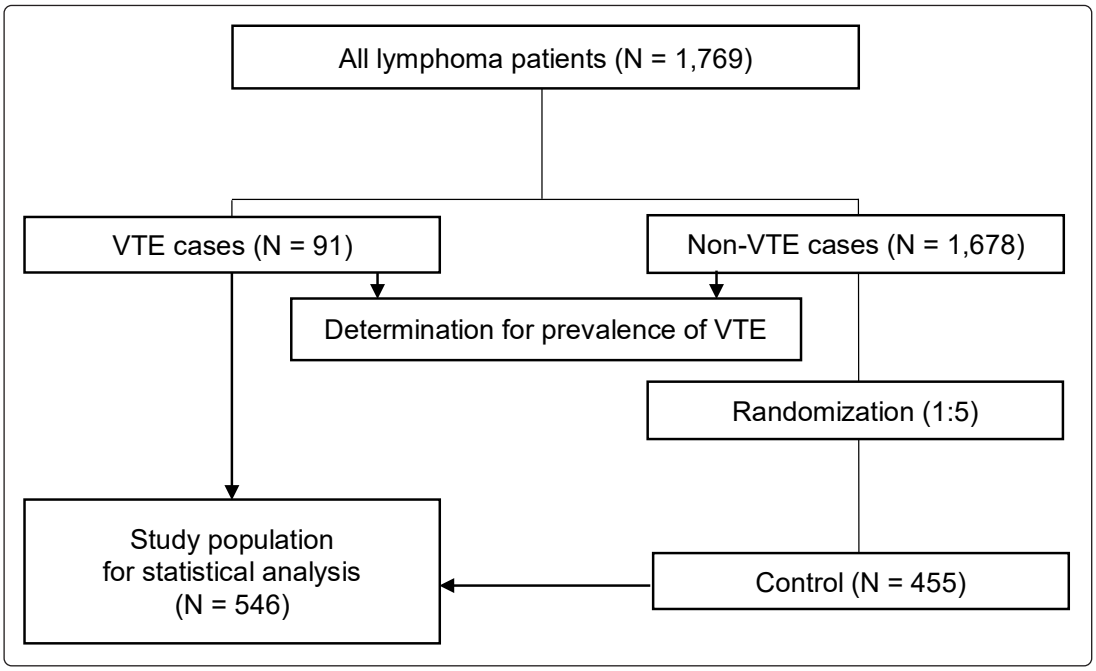


Figure 1 Flow chart of patients with lymphoma in this study, abbreviation: VTE, Venous thromboembolism

thrombosis, cerebral vein thrombosis, and other locations. The objectives of this analysis were to determine the prevalence of VTE among Thai patients with lymphoma, risk factors predictive of VTE, outcomes of VTE, and overall survival among these patients. All causes of mortality during and after treatment were also obtained. This study was approved by the institutional review committee.

Statistical analysis

Sample size was calculated according to the expected one-year VTE prevalence rate. We assumed the prevalence of VTE in our cohort would be 5% considering the prevalence reported in a related meta-analysis.[3] With the expected prevalence of 5%, a minimum of 313 patients were required for analysis. The prevalence of VTE was calculated by the number of patients developing VTE per 100 patients with lymphoma. Demographic characteristics were described using descriptive statistics. Chi-square and Fisher exact tests were used to compare categorical variables of the VTE group with those of the control group. Comparison of continuous variables between the 2 groups was analyzed using bivariate regression and Pearson's correlation coefficient. The logistic regression model was used to analyze independent predictive factors. Overall survival time and survival rate were estimated using Kaplan-Meier analysis, and survival curves were compared using the log-rank test. A two-sided *p*-value < 0.05 was considered statistically significant.

Results

A total of 1,769 patients with lymphoma were retrieved from the hospital database. A control group of 455 patients without VTE were randomly selected from the cohort of lymphoma patients. Of patients with VTE *vs.* controls, 51.6 *vs.* 49.0%, respectively, were female ($p = 0.64$). The mean age was 57 *vs.* 61 years ($p = 0.09$), respectively. Types of lymphoma in corresponding groups were B-cell non-Hodgkin lymphoma (NHL; 93.4 *vs.* 78.9%), T-cell NHL (5.5 *vs.* 11.7%) and Hodgkin disease (HD) (1.1 *vs.* 6.4%), respectively ($p = 0.02$). Median time from lymphoma diagnosis to VTE occurrence was 38 days (IQR 2-183). Baseline characteristics of patients with and without VTE are shown in Table 1. History of previous VTE was not observed in both groups.

Prevalence of VTE in this study was 5.1% (91 patients). Locations of VTE among these patients were deep vein thrombosis of lower extremities (53.9%), pulmonary embolism (23.1%), splanchnic vein thrombosis (5.5%), jugular vein thrombosis (3.3%), cerebral venous thrombosis (1.1%), and VTE in > 2 sites (13.1%). Among 41 patients (45.1%) VTE occurred during treatment or up to 3 months after completing therapy whereas among 35 patients (38.4%), VTE was diagnosed before therapy. VTE associated with mass compression was found among 13 patients (14.2%). VTE treatment and complications are shown in Table 2.

In a univariate analysis, B-cell NHL type [odds ratio (OR) 3.2; 95% confidence interval (CI): 1.4-7.7; $p = 0.01$], B symptoms (OR 2.3; 95%CI: 1.4-3.6; $p < 0.01$), bulky mass > 10 cm (OR 2.7; 95%CI: 1.6-4.7; $p = 0.02$), extranodal involvement > 1 site (OR 2.0; 95%CI: 1.2-3.3; $p < 0.01$) and serum lactate dehydrogenase higher than the upper normal limit (OR 1.9; 95%CI: 1.0-3.5; $p = 0.04$) were significantly associated with VTE, whereas international prognostic index (IPI) score > 3 (OR 0.8; 95%CI: 0.4-1.3) and Khorana score > 3 (OR 1.0; 95%CI: 0.5-1.9; $p = 0.96$) were not. Prechemotherapy platelet count showed a trend to be associated with VTE (OR 1.7; 95%CI: 1.0-3.0; $p = 0.07$). Using multivariate analysis, B-cell NHL type (OR 4.4; 95%CI: 1.4-12.5; $p = 0.01$), bulky mass > 10 cm (OR 2.2; 95%CI: 1.1-4.4; $p = 0.02$) and prechemotherapy platelet count > 350 x 10^9/L (OR 2.1; 95%CI: 1.0-4.2; $p = 0.03$) were independent predictive factors of VTE (Table 3).

The overall mortality rates among patients with and without VTE were 25.3 and 15.8%, respectively. Causes of mortality included infection (60.8%), disease progression (21.7%), and other causes (17.3%). No VTE

Table 1 Baseline characteristics of patients with lymphoma with and without venous thromboembolis

Characteristics	VTE group (n = 91)	Control group (n = 455)	*p*-value
Age, years (mean±SD)	57±18	61±16	0.09
Female sex	47 (51.6%)	223 (49.0%)	0.65
Median (IQR) BMI, kg/m^2	22.4 (19.8-25.4)	21.8 (19.5-24.2)	0.08
Pathologic type			0.02
Hodgkin disease	1 (1.1%)	29 (6.4%)	
B-cell non-Hodgkin lymphoma*	85 (93.4%)	359 (78.9%)	
T-cell non-Hodgkin lymphoma	5 (5.5%)	53 (11.7%)	
Previous VTE	0	0	
Presence of B symptoms	59/91 (64.8%)	183/407 (45.0%)	0.60
ECOG performance status > 1	23/86 (26.7%)	97/390 (24.9%)	0.001
High IPI score	40/71 (56.3%)	117/217 (53.9%)	0.79
Khorana score > 3	15/71 (21.1%)	44/215 (20.5%)	0.73
Prechemotherapy parameters			
Median (IQR) hemoglobin, g/dL	10.7 (9.3-12.3)	11.0 (9.6-12.5)	0.29
White blood cell count ($x10^9/L$) (mean±SD)	12.0±19	12.1±19.3	0.50
Mean platelet count ($x10^9/L$) (mean±SD)	318±195	250±151	0.004

Abbreviations: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; IPI, international prognostic index; IQR, interquartile range; SD, standard deviation; VTE, venous thromboembolism; *B-cell non-Hodgkin lymphoma included both high grade types (diffuse large B cell lymphoma, Burkitt lymphoma, mantle cell lymphoma) and low grade types (follicular lymphoma, small lymphocytic lymphoma, lymphoplasmacytic lymphoma, marginal zone lymphoma).

Table 2 Venous thromboembolism treatment and complications

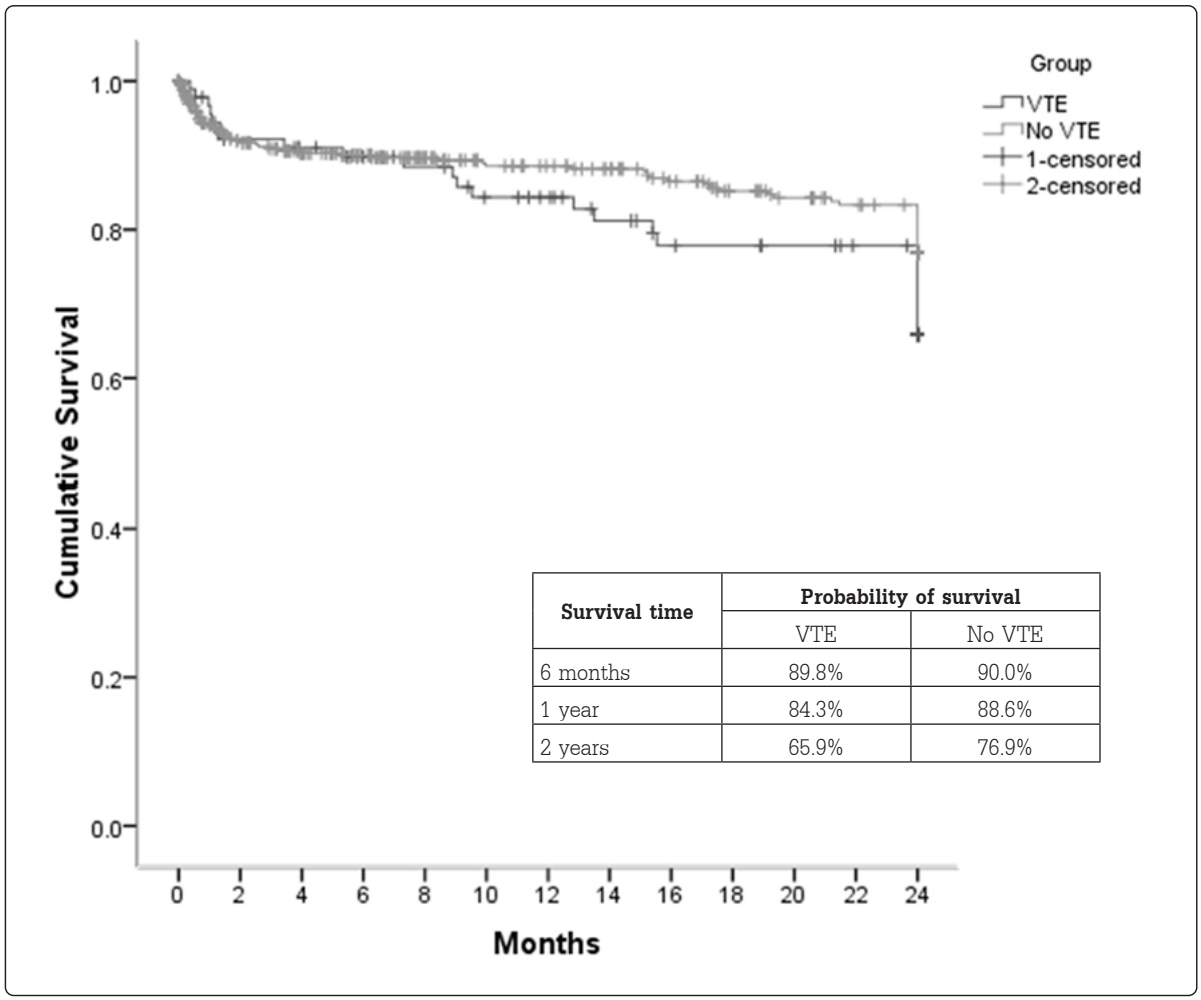
VTE Treatment and complication	VTE group (n = 91)
VTE Treatment	
Low molecular weight heparin	65/91 (71.4%)
Vitamin K antagonist	21/91 (23.1%)
Direct oral anticoagulant	2/91 (2.2%)
Inferior vena cava filter without anticoagulant therapy	1/91 (1.1%)
No treatment	2/91 (2.2%)
Treatment complications	
Major bleeding (WHO grades 3 and 4)	14/91 (15.4%)
Recurrent thrombosis	6/91 (6.6%)

Abbreviations: VTE, venous thromboembolism; WHO, World Health Organization

Table 3 Risk factors of venous thromboembolism among patients with lymphoma

Variable	Univariate analysis		Multivariate analysis	
	OR (95%CI)	*p*-value	OR (95%CI)	*p*-value
B-cell type NHL	3.2 (1.4-7.7)	0.01	4.4 (1.4-12.5)	0.01
B symptoms	2.3 (1.4-3.6)	< 0.01	1.2 (0.6-2.3)	0.69
Extranodal involvement >1 site	2.0 (1.2-3.3)	< 0.01	1.2 (0.6-2.4)	0.60
Bulky mass ≥ 10 cm	2.7 (1.6-4.7)	< 0.01	2.2 (1.1-4.4)	0.02
LDH level higher than UNL	1.9 (1.0-3.5)	0.04	1.7 (0.8-3.5)	0.20
Prechemotherapy platelet count ≥ 350 x 10^9/L	1.7 (1.0-3.0)	0.07	2.1 (1.1-4.2)	0.03

Abbreviations: CI, confidence interval; LDH, lactate dehydrogenase; NHL, non-Hodgkin lymphoma; OR, odds ratio; UNL, upper normal limit



Survival time	Probability of survival	
	VTE	No VTE
6 months	89.8%	90.0%
1 year	84.3%	88.6%
2 years	65.9%	76.9%

Figure 2 Two-year survival of patients with and without venous thromboembolism (VTE) using Kaplan-Meier analysis

was related to death in this study. Two-year survival of patients with and without VTE using Kaplan-Meier analysis is shown in Figure 2 (p = 0.12). Probabilities of survival at 6 months, 1 year, and 2 years of patients with VTE *vs.* controls were 89.8, 84.3%, and 65.9 *vs.* 90.0%, and 88.6 and 76.9%, respectively.

Discussion

We reviewed the data of VTE among Thai patients with lymphoma at a single teaching medical center over a 10-year period. The prevalence of VTE was 5.1%. B-cell NHL type, bulky mass, and high pre-chemotherapy platelet count were associated with an increased risk. Almost one half of cases occurred during treatment or up to 3 months after completing therapy. The occurrence of VTE among patients with lymphoma was associated with a poorer outcome. Our investigation constitutes the largest Thai study to determine the prevalence, risk factors, and clinical outcomes of VTE among patients with lymphoma.

The prevalence of VTE in our study population approached the worldwide prevalence rate of 6.4% reported in a meta-analysis of 29 independent cohorts.[3] Compared with related studies conducted in Asian countries, the reported incidence of VTE among patients with lymphoma in Japan and Korea was 11 and 7.9%, respectively (Table 4).[5,6] Two retrospective cohort studies from Thailand reported the prevalence of 9.3 and 4.1%, respectively.[7,8] The variation in the reported prevalence of VTE in lymphoma in different studies could be due to the different types of patients with lymphoma in the studies and study design.

Table 4 Prevalence and risk factors for venous thromboembolism among patients with lymphoma patients from Asia

Author	Yokoyama K, et al.	Park LC, et al.	Siwasaranond N, et al.	Kunawuttinankorn W, et al.	This study
Country	Japan	South Korea	Thailand	Thailand	Thailand
Published year	2012	2013	2013	2018	Present
Study design	Retrospective cohort	Prospective cohort	Retrospective cohort	Prospective and retrospective cohort	Retrospective nested case control
Study period	2006-2010	2008-2010	2007-2011	2007-2011	2005-2015
Total study population (VTE cases/total cases)	15/142	54/686	34/342	19/469	91/1,769 (Control 455)
Prevalence (%)	11	7.9	9.3	4.1	5.1
Median time for VTE events from lymphoma diagnosis	N/A	2.0 months	N/A	N/A	1.3 months
Significant risk factors	ECOG PS ≥ 2	- Age > 60 years - Primary CNS lymphoma	IPI score ≥ 3	- Monoparesis (grades 0-3) - Bed ridden state	- B-cell NHL type - Bulky mass ≥ 10 cm - Prechemotherapy platelet count ≥ 350 x 10^9/L
Survival					
Progression free	N/A	N/A	32.4% (2 years)	N/A	N/A
Overall	N/A	25.9% (Median follow up 21.8 months)	45.8% (2 years)	N/A	89.8% (6 months), 84.3% (1 year), 65.9% (2 years)

Abbreviations: CNS, central nervous system; ECOG, Eastern Cooperative Oncology Group; IPI, international prognostic index; N/A, not available; NHL, nonHodgkin lymphoma; PS, performance status; VTE, venous thromboembolism

In 2008, Khorana et al. proposed 5 predictive variables from a stage-adjusted multivariate scoring model including site of cancer, prechemotherapy platelet count > 350 x 10^9/L, hemoglobin < 10 g/dL, leukocyte count > 11 x 10^9/L, and body mass index > 35 kg/m^2.[9] Lymphoma was part of the high-risk group together with lung, gynecologic, and genitourinary cancers, with an independent OR for thrombosis of 1.5 (95%CI: 0.9-2.7). They suggested anticoagulant for VTE prophylaxis among patients with a score of 3 points or more. However, our study demonstrated that high Khorana score > 3 was not associated with VTE among patients with lymphoma (OR 1.0; 95%CI: 0.5-1.9; p = 0.96) indicating that this score might not be predictive in all types of cancer. Moreover, one study used laboratory parameters such as D-dimer to assess the VTE risk among patients with cancer, but we could not evaluate those parameters due to the lack of data from our patients.[10]

Limitations were encountered in our study. First, the study design was a nested case-control from a large cohort of patients with lymphoma, so the analytical data may not be totally represented in the survival analysis of the whole cohort. However, our study included 31% of the patients in the cohort and the analysis showed relevant results which were informative for clinicians treating patients with lymphoma. Second, some data such as laboratory values were unavailable because these variables were retrospectively reviewed from the medical records. Third, the evaluation of some lymphoma-related factors and transient thrombotic risk

factors which could aggravate VTE events during and after lymphoma therapy, such as immobilization > 3 days, central venous catheter insertion, recent surgery, use of mechanical ventilation and type of lymphoma treatment were undetermined in our study. Strategies to solve these limitations include a prospective design with complete clinical and complete laboratory data.

Conclusion

The prevalence of VTE among Thai patients with lymphoma was not low. B-cell NHL, bulky mass, and elevated prechemotherapy platelet count constituted predictive factors of VTE. The IPI and Khorana scores were not predictive of VTE among Thai patients with lymphoma. Survival of patients with lymphoma and VTE was lower than those without VTE. Predictive VTE risk score for Thai patients with lymphoma should be further developed. Future studies to determine the benefit of thromboprophylaxis among patients with lymphoma and high risk of developing VTE are also warranted.

Disclosure

All authors declare they have no conflict of interest.

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References

1. *Lauw MN, van Doormaal FF, Middeldorp S, Buller HR. Cancer and venous thrombosis: current comprehensions and future perspectives. Semin Thromb Hemost. 2013;39:507-14.*
2. *Angchaisuksiri P. Cancer-associated thrombosis in Asia. Thromb J. 2016;14(Suppl 1):26.*
3. *Caruso V, Di Castelnuovo A, Meschengieser S, Lazzari MA, de Gaetano G, Storti S, et al. Thrombotic complications in adult patients with lymphoma: a meta-analysis of 29 independent cohorts including 18,018 patients and 1,149 events. Blood. 2010;115:5322-8.*
4. *Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, et al. WHO classification of tumours of haematopoietic and lymphoid tissues. In: Bosman FT, Jaffe ES, Lakhani SR, Ohgaki H, eds. World Health Organization Classification of Tumours. Lyon, France: IARC; 2008.*
5. *Yokoyama K, Murata M, Ikeda Y, Okamoto S. Incidence and risk factors for developing venous thromboembolism in Japanese with diffuse large b-cell lymphoma. Thromb Res. 2012;130:7-11.*
6. *Park LC, Woo SY, Kim S, Jeon H, Ko YH, Kim SJ, et al. Incidence, risk factors and clinical features of venous thromboembolism in newly diagnosed lymphoma patients: results from a prospective cohort study with Asian population. Thromb Res. 2012;130:e6-12.*
7. *Siwasaranond N, Norasethada L, Tantiworawit A, Rattarittamrong E, Chai-adisaksopha C, Navwarawong W. Increased prevalence of thromboembolism events in Thai patients with lymphoma: the single center expreience from Maharaj Nakorn Chiang Mai Hospital. J Hematol Tranfus Med. 2013;23:33-41.*
8. *Kunawuttinankorn W, Tanyasaensook K, Rojnuckarin P. Incidence and risk factors for venous thromboembolism in Thai hospitalized lymphoma patients. Pharm Sci Asia. 2018;45(2):144-122.*
9. *Khorana AA, Kuderer NM, Culakova E, Lyman GH, Francis CW. Development and validation of a predictive model for chemotherapy-associated thrombosis. Blood. 2008;111:4902-7.*
10. *Ay C, Vormittag R, Dunkler D, Simanek R, Chiriac AL, Drach J, et al. D-dimer and prothrombin fragment 1+2 predict venous thromboembolism in patients with cancer: results from the Vienna Cancer and Thrombosis Study. J Clin Oncol. 2009;27:4124-9.*