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Original Research

Risk Factor of Deep Vein Thrombosis in Gynecologic Cancer Patients at Rajavithi Hospital

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Background: Venous thromboembolism (VTE), that includes both deep vein thrombosis (DVT) and pulmonary embolism (PE), represents a significant complication after major pelvic surgery and potentially lethal disease in gynecologic cancer patients. However, its incidence and associated risk factors have not been well established.
Objectives: To evaluate risk factors that may be associated with deep vein thrombosis (DVT) in gynecologic cancer patients.
Materials and Methods: This retrospective case-control study included patients who diagnosed as gynecologic cancer with or without DVT between January 2002 and December 2016 at Rajavithi Hospital. The presence of DVT was confirmed by either color doppler ultrasonography or computed tomography scan. Patient's demographic data, type and stage of cancer, including treatment modalities were compared. Univariate analysis and multivariate logistic regression analysis were analyzed to calculate odds ratios (OR) and determine independent risk factors for DVT.
Results: Over 14 years periods, 242 patients with DVT were identified in a total 8476 gynecologic cancer patients. The incidence of DVT was 2.85% in this patient setting. Complete data were available in 468 patients, 156 (33.3%) cases with DVT diagnosed were compared with 312 (66.7%) controls without DVT. Among patients with DVT, the median time to DVT diagnosis was 4 months (IQR 2-12 months) after diagnosis of cancer, most of cases (89.5%) were symptomatic DVT, and a half of them (49%) were detected in ovarian cancer. In a multivariate analysis, 3 significant predictors of developing DVT were identified: advanced-stage cancer (OR 7.22; 95%CI 4.62-11.28, p<0.001), patient undergoing lymphadenectomy (OR 1.90; 95%CI 1.21-2.98, p=0.005), and patient with massive operative blood loss (≥1500 ml; OR 2.09; 95%CI 1.12-3.91, p=0.021).
Conclusions: Awareness of DVT is the best way to prevent the venous thromboembolism. Therefore, an appropriate prophylaxis and closed monitoring of gynecologic cancer patients with advanced-stage cancer, undergoing lymphadenectomy, and massive operative blood loss should be mandatory to against thromboembolism complications.

Introduction

Venous thromboembolism (VTE), presenting as deep vein thrombosis (DVT) and pulmonary embolism (PE), is a major cause of morbidity and mortality. The average annual incidence of VTE in all adults was 1 case per 1000 person. Its worldwide incidence; however, depends on several risk factors, including ethnicity, hereditary, and acquired risk factors [1, 2]. The incidence of VTE in the Asian populations is low; VTE is one of the concerns and a serious life-threatening event, especially during postoperative periods [3, 4].

Many adverse outcomes occurred after the thrombotic event as a vicious cycle. The worst case is patient's death (about 6 percent) after 1 month following DVT diagnosis [5]. Patients with malignancy have a six-fold increased risk of VTE and patients with gynecologic cancer have the highest risk of VTE [6].

VTE is the second leading cause of death in patients with gynecologic cancer and the risk of DVT in women underwent gynecologic surgery ranged from 17% to 40%, while the rate of PE was about 1% to 26% [7,9]. Moreover, ovarian cancer was associated with one of the highest incidence rates of VTE among all solid tumors [10].

Various clinical risk factors have been suggested to be in association with cancer-related VTE, which can be classified into patient-related, cancer-related, and treatment-related factors [11]. One prospective study on 66,329 cancer patients reported that the incidence of VTE within 6 months after cancer diagnosis was 12.4 per 1000 patients, which was higher than that in the normal person [12]. Cancer involved a combination of thrombin formation due to the procoagulant effects of tumor cells and mass compressing the vein, causing venous stasis [13, 14]. Furthermore, its treatment may increase the risk of thromboembolic events such as long operative time, immobilization, radiotherapy, and chemotherapy [15].

A variety of risk factors associated with DVT have been reported; namely, varicose vein, bedridden more than 48 hours, an operative time greater than 3 hours, laparotomy surgery, hypertension, obesity, aged> 50 years, and adenocarcinoma [16-19]. Although the most published literature presented the characteristics of DVT in large population studies, these data were limited in the Thai patients and its incidence and its risk factors have not been well understood yet. Therefore, this retrospective case-control study was designed to evaluate the incidence of DVT and explore the risk factor associated with DVT in the gynecologic cancer patients at Rajavithi Hospital, a tertiary referral center in Thailand. Identification of such risk factors might enable earlier diagnosis of DVT and offer a proper prophylaxis for high-risk patients to prevent thromboembolic complications.

Materials and Methods

This study was a retrospective case-control study approved by the Ethics Committee of Rajavithi Hospital. The medical records of the patients diagnosed with gynecologic cancer with or without DVT between 1st January 2002 and 31st December 2016 were reviewed. The exclusion criteria were pregnancy, receiving any anticoagulant therapy, receiving VTE prophylaxis, and confirmed diagnosis of DVT or PE before the treatment of cancer. DVT was defined by the following inclusion criteria: 1) radiological evidence confirmation of DVT by either using compression ultrasonography with Doppler imaging for suspected extremities DVT or computed tomography scan (CT)/ magnetic resonance imaging (MRI) for suspected deep pelvic or abdominal veins thrombosis and 2) absence of signs and symptoms consistent with DVT in the admission history and physical examination.

The controls were selected from a patient database based upon eligible criteria, and then matched with the cases on the type of cancer (including ovarian cancer, uterine cancer, cervical cancer, and vulvar cancer) at time of DVT diagnosis. In each case, 2 controls were randomly selected using a computer generator program and by time sequence. With comprehensive review of medical records, the demographic and clinical data, including patient age, weight, height, comorbidities (i.e. hypertension, diabetes mellitus, and previous cancer), histological type of cancer, stage of cancer, details of treatment (i.e. lymphadenectomy, operative time, intraoperative blood loss, and received radiotherapy or chemotherapy), and clinical outcomes were extracted. Once patients with DVT were identified, the details of thrombotic event, including signs and symptoms consistent with DVT, timing of thrombosis from initial diagnosis of cancer, and the location and number of the thrombotic events were collected.

Statistical analysis

According to unmatched case-control formula with a reference number from Hong et al. study, the calculated sample size was 116 persons per group. [16, 20]. Assuming a 10% dropout rate, a total of at least 128 patients were required per group.

The data were exported and analyzed using SPSS (version 16.0) where p-value <0.05 was considered statistically significant. Descriptive statistic was used to define the distributions of continuous variables and frequencies of categorical variables, which were compared between the cases and controls by Mann-Whitney U and Chi-square or Fisher's exact tests. Univariate and multiple logistic regressions were performed to evaluate the unadjusted and adjusted associations between the risk factors and case/control status. The results were expressed as odds ratios (ORs) with 95% confidence intervals (95% CIs), calculated by the Wald method.

Results

Over a 14-year period, 242 patients with DVT were identified among a total 8476 gynecologic cancer patients. The incidence of DVT was 2.85% in this patient setting. Complete data were available in 468 gynecologic cancer patients who met our defined inclusion criteria. One-hundred and fifty-six cases of DVT were matched with 312 randomly selected controls without DVT with respect to type of cancer. According to patients' databases during the study period, 38 (24.2%) cases of cervical cancer, 77 (49%) cases of ovarian cancer, 37 (23.6%) cases of uterine cancer, and 4 (2.6%) cases of vulvar cancer were found in DVT group. According to the similar proportion, 75 (23.9%) cases of cervical cancer, 154 (49%) cases of ovarian cancer, 75 (23.9%) cases of uterine cancer, and 8 (2.6%) cases of vulvar cancer were observed in non-DVT group. and No significant difference was found between two groups concerning the type of cancer (p=1.00).

Demographic and clinicopathological characteristics of the patients are shown in Tabl 1 for DVT group (cases) versus non-DVT group (controls). There was no significant difference between two groups in terms of mean age, mean body mass index (BMI), comorbidities (i.e. hypertension, and diabetes), mean tumor diameter, histological type of cancer, or operative time. Compared with the controls, the incidence of DVT was significantly higher in patients developed previous cancer (p=0.047), who were in advanced stage (p=0.001), received radiotherapy (p<0.001), received chemotherapy (p<0.001), underwent lymphadenectomy (p=0.014), and in those suffering from massive operative blood loss ≥1500 ml (p=0.003). Among the patients with DVT, the median time to DVT diagnosis was 4 months (IQR 2-12) after the cancer diagnosis. Fig. 1 shows timing to DVT events after cancer diagnosis. The majority of DVT events seemed to occur within the first 12 months of cancer diagnosis (78.2%). Further peaks in incidence were seen around 1 or 2 years after the cancer diagnosis.

Characteristics	Total	DVT	Non-DVT	p-value
	(n=468)	(n=156)	(n=312)	
Age (mean, year ± SD)	52.2 ± 11.9	53.1 ± 11	51.7 ± 12.3	0/22
BMI (mean, kg/m² ± SD)	23.9 ± 4.7	23.9 ± 4.7	23.9 ± 4.8	0/979
BMI (kg/m²)				0/761
< 25	294 (62.8%)	100 (64.1%)	194 (62.2%)	
≥ 25	174 (37.2%)	56 (35.9%)	118 (37.8%)	
Comorbidities				
Hypertension	130 (27.8%)	52 (33.3%)	78 (25%)	0/063
Diabetes	56 (12%)	17 (10.9%)	39 (12.5%)	0/654
Previous cancer	15 (3.2%)	9 (5.8%)	6 (1.9%)	0.047*
Type of cancer				1
Ovary	231 (49.4%)	77 (49.4%)	154 (49.4%)	
Uterus	112 (23.9%)	37 (23.7%)	75 (24%)	
Cervix	113 (24.1%)	38 (24.4%)	75 (24%)	

Vulva	12 (2.6%)	4 (2.6%)	8 (2.6%)	
Stage of cancer				< 0.001*
I	239 (51.1%)	30 (19.2%)	209 (67%)	
II	70 (15%)	28 (17.9%)	42 (13.5%)	
III	96 (26.5%)	51 (32.7%)	45 (14.4%)	
IV	63 (13.5%)	47 (30.1%)	16 (5.1%)	
Tumor diameter (mean, cm. ± SD)	8.7 ± 6.1	9.3 ± 5.6	8.4 ± 6.4	0/146
Histologic type				0/06
Clear cell	66 (14.1%)	26 (16.7%)	40 (12.8%)	
Endometrioid	109 (23.3%)	33 (21.2%)	76 (24.4%)	
Squamous cell carcinoma	71 (15.2%)	17 (10.9%)	54 (17.3%)	
Sarcoma	11 (2.4%)	7 (4.5%)	4 (1.3%)	
Others	211 (45.1%)	73 (46.8%)	138 (44.2%)	
Treatment of cancer				
Surgery	418 (89.3%)	116 (74.4%)	302 (96.8%)	< 0.001*
Radiotherapy	98 (20.9%)	50 (32.1%)	48 (15.4%)	< 0.001*
Chemotherapy	284 (60.7%)	125 (80.1%)	159 (51%)	< 0.001*
Lymphadenectomy				0.014*
No	237 (50.6%)	66 (42.3%)	171 (54.8%)	
Yes	231 (49.4%)	90 (57.7%)	141 (45.2%)	
Operative time (hours)				0/076
< 3	200 (43.2%)	75 (49%)	125 (40.3%)	
≥ 3	263 (56.8%)	78 (51%)	185 (59.7%)	
Operative blood loss (ml.)				0.003*
< 1500	407 (87.3%)	124 (80.5%)	283 (90.7%)	
≥ 1500	59 (12.7%)	30 (19.5%)	29 (9.3%)	

Table 1: Demographic and Clinico-pathological Characteristic of Patients.

Figure 1: A Histogram Showing Timing of DVT Events After Cancer Diagnosis

Tabl 2 shows the baseline characteristics of the patients with DVT according to the type of cancer. Most of the DVT cases (49%) were detected in ovarian cancer, followed by cervical cancer (24.2%), uterine cancer (23.6%), and vulva cancer (2.6%). The mean age of vulva cancer patients was significantly higher than other cancers (65.5 ± 16.8 years, p=0.048). The mean tumor diameter of ovarian cancer was 12.7 ± 5.1 cm. which was significantly larger than the others (uterine cancer; 7.2 ± 2.2 cm., cervical cancer; 4.7 ± 2.3 cm., and vulvar cancer; 5.3 ± 2.2 cm., p<0.001). The majorities of the histological type were adenocarcinoma, except all vulvar cancers which were squamous cell carcinoma. On the other hand, no significant difference was detected between four groups in terms of mean of BMI, menopausal status, and stage of cancer. Most of the DVT patients (116 from 156 patients, 74.4%) received surgical treatment and 90 (57.7%) patients underwent lymphadenectomy. Four groups has significant difference considering surgery (p<0.001) and radiotherapy (p<0.001) among while chemotherapy exerted no significant difference (p=0.468). As a result, surgery and chemotherapy were seemed to be the main treatments for ovarian and uterine cancer; whereas, cervical cancer patients mostly received radiotherapy and chemotherapy.

Variables	**Ovary**	**Uterus**	**Cervix**	**Vulva**	**p-value**	
	(n=77)	**(n=37)**	**(n=38)**	**(n=4)**		
Age (mean, year	52.5 ± 10.5	55.5 ± 11.2	51.1 ± 10.6	65.5 ± 16.8	0.048*	

± SD)						
BMI (mean, kg/m2 ± SD)	23.5 ± 4.0	25.4 ± 5.7	23.4 ± 4.9	24.8 ± 4.3	0/172	
BMI (Kg/m²)					0/107	
< 25	55 (71.4%)	20 (54.1%)	24 (63.2%)	1 (25%)		
≥ 25	22 (28.6%)	17 (45.9%)	14 (36.8%)	3 (75%)		
Menopause					0/213	
Pre-menopause	30 (39%)	10 (27%)	19 (50%)	1 (25%)		
Post-menopause	47 (61%)	27 (73%)	19 (50%)	3 (75%)		
Tumor size (mean, cm. ± SD)	12.7 ± 5.1	7.2 ± 2.2	4.7 ± 2.3	5.3 ± 2.2	< 0.001*	
Histologic type					< 0.001*	
Adenocarcinoma	71 (92.2%)	31 (83.8%)	22 (57.9%)	0 (0%)		
Squamous cell CA	0 (0%)	0 (0%)	13 (34.2%)	4 (100%)		
Sarcoma	1 (1.3%)	6 (16.2%)	0 (0%)	0 (0%)		
Others	5 (6.5%)	0 (0%)	3 (7.9%)	0 (0%)		
Stage of cancer					0/079	
Early	28 (36.4%)	9 (24.3%)	18 (47.4%)	3 (75%)		
Advanced	49 (63.6%)	28 (75.7%)	20 (52.6%)	1 (25%)		
Lymphadenectomy					< 0.001*	
No	22 (28.6%)	14 (37.8%)	29 (76.3%)	1 (25%)		
Yes	55 (71.4%)	23 (62.2%)	9 (23.7%)	3 (75%)		
Treatment of cancer						
Surgery	69 (89.6%)	32 (86.5%)	12 (31.6%)	3 (75%)	< 0.001*	
Radiotherapy	3 (3.9%)	18 (48.6%)	26 (68.4%)	3 (75%)	< 0.001*	
Chemotherapy	63 (81.8%)	29 (74.8%)	31 (81.6%)	2 (50%)	0/468	
Presenting symptoms of DVT					0/075	
No	4 (5.8%)	7 (22.6%)	3(10.3%)	0 (0%)		
Yes	65 (94.2%)	24 (77.4%)	26 (89.7%)	4 (100%)		
Time to DVT diagnosis (median, months)	4	6	4	5/5	0/533	
Location of thrombosis event					0.010*	
Calf	27 (39.1%)	14 (45.2%)	12 (41.4%)	3 (75%)		
Femoral	36 (52.2%)	6 (19.4%)	10 (34.5%)	1 (25%)		
Pelvic	6 (8.7%)	7 (22.6%)	6 (20.7%)	0 (0%)		
Other	0 (0%)	4 (12.9%)	1(3.4%)	0 (0%)		
Number of vessels					0/074	
Single	27 (39.1%)	14 (46.7%)	19 (65.5%)	3 (75%)		
Multiple	42 (60.9%)	16 (53.3%)	10 (34.5%)	1 (25%)		

Table 2: Baseline Characteristics of Patients with DVT According to Type of Cancer.

a) Abbreviations: BMI = body mass index, b) DVT = deep vein thrombosis

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Most of the patients (89.5%) presented with symptoms of DVT, including swelling and painful feeling at the extremity before DVT diagnosis. The most common locations for DVT included calf (36.8%) and femoral veins (34%) and there was a significant difference between four groups (p=0.010).

Tabl 3 presents the results of the odds ratios of DVT associated with potential risk factors among all patients, from univariate and multiple logistical regressions. In the univariate analysis, the risk of DVT was significantly increased in patients who developed previous cancer, were in advanced stage cancer, underwent lymphadenectomy, or suffered from massive operative blood loss. However, in the multivariate analysis, only being in advanced stage cancer, undergoing lymphadenectomy, and suffering from massive operative blood loss were statistically significant risk factors.

Parameters	**Univariate Analysis**	**Multivariate Analysis**
	OR (95% CI)	**p-Value**
Age	1.08 (0.73-1.61)	0/689
(< 50 years vs ≥ 50 years)		
BMI	0.92 (0.62-1.37)	0/685
(< 25 kg/m² vs ≥ 25 kg/m²)		
Previous cancer	3.12 (1.09-8.94)	0.034*
(no vs yes)		
Tumor size	1.17 (0.79-1.73)	0/424
(<10 cm vs ≥10 cm)		
Cell type	1.35 (0.79-2.31)	0/272
(non-clear vs clear cell CA)		
Stage of cancer	6.81 (4.44-10.45)	<0.001*
(early vs advanced)		
Lymphadenectomy	1.65 (1.12-2.44)	0.011*
(no vs yes)		
Operative time	0.703 (0.48-1.04)	0/076

(< 3 hours vs ≥ 3 hours)		
Operative blood loss	2.36 (1.36-4.10)	0.002*
(< 1500 ml vs ≥ 1500 ml)		

Table 3:Evaluation of Risk Factors for DVT: Univariate and Multivariate Analysis.

a) Abbreviations: CI = confidence interval, b) OR = odds ratio

Subgroup analyses of risk factor profiles by the type of cancer were analyzed and the results of univariate and multivariate analysis on risk factors associated with DVT are shown in Tabl 4. For ovarian cancer, three independent variables that were identified as significant in the multivariate model were being in advanced stage cancer (p=0.001), undergoing lymphadenectomy (p<0.001), and suffering from massive operative blood loss (p=0.041). Likewise, the patients with advanced stage cancer (p=0.009) and the patients who underwent lymphadenectomy (p=0.021) appeared to develop the risk of DVT in uterine cancer. Interestingly, only chemotherapy (p=0.001) was shown to have an independent risk factor for DVT in cervical and vulvar cancers that can be due to this fact taht patients with cervical cancer had received chemotherapy, usually were in advanced stage, and experienced recurrence of the disease. Parameters Univariate Analysis Multivariate Analysis.

Variables	**N (%)**	**DVT, n (%)**	**Univariate analysis**	**Multivariate analysis**
			95% CI	**p-value**
Ovarian cancer (n=231)				
Histology (adenoCA)	200 (86.6)	72 (36.0)	2.93 (1.08–7.95)	0.035*
Advanced stage cancer	86 (37.2)	49 (57.0)	5.53 (3.06–10.02)	<0.001*
Lymphadenectomy	109 (47.2)	55 (50.5	4.63 (2.55–8.39)	<0.001*
Operative blood loss ≥1500 ml.	42 (18.8)	21 (50.0)	2.77 (1.39–5.52)	0.004*
Uterine cancer (n=112)				
Advanced stage cancer	45 (40.2)	28 (62.2)	10.61 (4.21–26.78)	<0.001*
Lymphadenectomy	51 (45.5)	23 (45.1)	2.76 (1.22–6.22)	0.014*
Operative blood loss ≥1500 ml.	42 (18.8)	21 (50.0)	5.6 (1.36–23.12)	0.017*

Chemotherapy	52 (46.4)	29 (55.8)	8.20 (3.25–20.65)	<0.001*
Radiation	38 (33.9)	18 (47.4)	2.61 (1.14–5.93)	<0.023*
Cervical and vulvar cancer (n=125)				
Hypertension	26 (20.8)	13 (50.0)	2.41 (1.00–5.83)	0.050*
Advanced stage cancer	29 (23.2)	21 (72.4)	9.38 (3.64–24.17)	<0.001*
Tumor size ≥4 cm.	48 (38.4)	27 (56.2)	5.31 (2.38–11.85)	<0.001*
Operative blood loss ≥1000 ml.	42 (18.8)	21 (50.0)	3.39 (1.02–11.30)	0.047*
Chemotherapy	47 (37.6)	33 (70.2)	18.07 (7.10–46.01)	<0.001*
Radiation	56 (44.8)	29 (51.8)	4.63 (2.08–10.29)	<0.001*

Table 4: Logistic Regression Analysis of Risk Factors for Thrombosis According to Type of Cancer.

a) Abbreviations: CI = confidence interval, b) OR = odds ratio, c) CA = carcinoma

Discussion

The complication of DVT leading to VTE can be catastrophic. The decision on when and how to use medical prophylaxis against DVT in cancer patients, especially those underwent surgery, is a very challenging one. Identification of potential risk factors might enable earlier diagnosis of DVT and a mandatory method to prevent thromboembolic complications.

With a retrospective review of several kinds of literature performed in the Western countries, a higher incidence of VTE was found in gynecologic cancer patients while and the risk of VTE ranged from 4.2 - 21.6% [21, 22]. The incidence of VTE in our study appeared to be lower than that previously reported by other published literature.

The reason for the lower incidence may be the ethnicity difference; the Asian populations have a lower rates of VTE compared to Western people [23]. Furthermore, it may underestimate the true incidence, especially in the patients living in the peripheral center. Patients with early-stage disease who did not require adjuvant treatment and who did not referre to our institution were excluded.

Three significant predictors of DVT were identified in our study: advanced stage cancer, undergoing lymphadenectomy, and massive operative blood loss. Based on the results of the present study, the patients with advanced-stage cancer had increased risk of DVT due to biological aggressiveness of the tumor [21, 22].

Lymphadenectomy was significantly associated with post-op DVT, representing that lymphadenectomy was a surrogate for lymphocele formation, which might compromise venous blood flow and increased the likelihood of thrombosis [24].

Additionally, lymphadenectomy was a significant risk factor associated with DVT not only in patients with gynecological malignancy who underwent surgery, but also in the prostate cancer patients who experienced radical prostatectomy with pelvic lymphadenectomy [25]. It was also reported that an increasing number of lymph node removal was associated with symptomatic venous thromboembolic events after radical prostatectomy with pelvic lymph nodes dissection.

The other factor that was associated with DVT was massive operative blood loss. This event can be explained by Virchow's triad; blood stasis, damage in the vessel wall, and hypercoagulable state. Regarding adnexal or peritoneal cancer therapy, it was found that, advanced stage patients who received blood transfusion developed increased risk of DVT and PE [26].

Based on the combination pattern of three significant risk factors of DVT in this study, the predictive model for the DVT occurrence was proposed for gynecologic cancer patients (Tabl 5). In this model, the incidence of DVT in patients with no risk factor was 15.3% (22/144). The incidence of DVT was 28.8% in patients with one risk factor and 66.1% in patients who had more than one risk factor. Our predictive model is a simple and useful method that can be applied to gynecologic cancer patients with identified thromboembolic risk.

Number of risk factors	N	DVT (%)	OR	95%Cl	p-value
None	144	22 (15.3)	1	-	-
1 risk factor	215	62 (28.8)	2/25	1.31 - 3.86	0.003*
≥ 2 risk factors	109	72 (66.1)	4/8	2.93 - 7.87	<0.001*

Table 5. *Predictive Model of DVT Based on the Combination Patterns of Three Independent Risk Factors*

a) Abbreviations: CI = confidence interval, b) OR = odds ratio

According to this risk stratification, we might be able to choose an appropriate prophylaxis and suggest color Doppler ultrasonography in high-risk patients.

To determine an appropriate duration of VTE prophylaxis, the time of incidence distribution of DVT cases should be an important issue for analysis. With respect to our findings, the highest risk of DVT events was in the first 12 months after cancer diagnosis. This peak, in part, may be due to the detection of incidental thromboembolic events during staging investigation, new disease relapse, and re-initiation of chemotherapy. Similar to the present findings, the significance of the extended use of VTE prophylactic strategies and monitoring protocols need to be evaluated, especially the time of susceptibility to DVT in gynecologic cancer patients.

The most important strengths of this study were the large sample size and long-term observation periods, which enabled us to focus on a particularly difficult group of the patients. Furthermore, we also analyzed independent factors associated with DVT according to the types of cancer and inclusion of all symptomatic and asymptomatic DVT cases.

This study had some limitations. First, the retrospective nature of this study led to incomplete data collection, including a recall bias. Second, the rate of VTE was underestimated because only VTE

cases in the database were recorded and some cases in whom it occurred later than the observational period might be missed. Third, a single institutional study might not be represented other whole country population.

In conclusion, awareness of DVT is the best way to prevent the venous thromboembolism. Therefore, a closed monitoring and immediate action of gynecologic cancer patients with advanced-stage cancer, undergoing lymphadenectomy and massive operative blood loss, should be mandatory to against thromboembolic complication.

Conflict of interest

The authors have declared no conflict of interest.

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References

[1]. White RH. The epidemiology of venous thromboembolism. Circulation. 2003;107(23):I4-8.

[2]. Tapson VF. Acute pulmonary embolism. The New England Journal of Medicine. 2008;358(10):1037-52.

[3]. White RH, Keenan CR. Effects of race and ethnicity on the incidence of venous thromboembolism. Thromb Res. 2009;123(4):S11-7.

[4]. Pruemer J. Prevalence, causes, and impact of cancer-associated thrombosis. American Journal of Health-system Pharmacy: AJHP: Official Journal of the American Society of Health- System Pharmacists. 2005;62 (22): S4-6.

[5]. Cushman M, Tsai AW, White RH, Heckbert SR, Rosamond WD, Enright P, et al. Deep vein thrombosis and pulmonary embolism in two cohorts: the longitudinal investigation of thromboembolism etiology. The American Journal of Medicine. 2004;117(1): 19-25.

[6]. Anaya DA, Nathens AB. Thrombosis and coagulation: deep vein thrombosis and pulmonary embolism prophylaxis. Surg Clin North Am. 2005;85(6):1163-77.

[7]. Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwell CW, et al. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest. 2004;126(3):338-400.

[8]. Einstein MH PE, Hartenbach EM Venous thromboembolism prevention in gynecologic cancer surgery: a systemic review. Gynecol Oncol. 2007;105(3):813-9.

[9]. Heidrich H, Konau E, Hesse P. Asymptomatic venous thrombosis in cancer patients--a problem often overlooked. Results of a retrospective and prospective study. VASA Zeitschrift fur Gefasskrankheiten. 2009;38 (2):160-6.

[10]. Khorana AA FC, Culakova E, et al. Frequency, risk factors, and the trends for venous thromboembolism among hospitalized cancer patients. Cancer. 2007;110:239-46.

[11]. Khorana AA, McCrae KR. Risk stratification strategies for cancer-associated thrombosis: an update. Thromb Res. 2014;133(2):S35-8.

[12]. Blom JW VJ, Oostindier MJ, et al. Incidence of venous thrombosis in a large cohort of 66,392 cancer patients: results of a record linkage study. J Thromb Haemost. 2006.4(3):529-35.

[13]. Prandoni P, Falanga A, Piccioli A. Cancer and venous thromboembolism. The Lancet Oncology. 2005;6(6):401-10.

[14]. Young A, Chapman O, Connor C, Poole C, Rose P, Kakkar AK. Thrombosis and cancer. Nature Reviews Clinical Oncology. 2012;9(8):437-49.

[15]. Ailawadi M, Del Priore G. A comparison of thromboembolic prophylaxis in gynecologic oncology patients. International Journal of Gynecological Cancer: Official Journal of the International Gynecological Cancer Society. 2001;11(5):354-8.

[16]. Qu H, Li Z, Zhai Z, Liu C, Wang S, Guo S, et al. Predicting of Venous Thromboembolism for Patients Undergoing Gynecological Surgery. Medicine (Baltimore). 2015;94(39):e1653.

[17]. Shiota M, Kotani Y, Umemoto M, Tobiume T, Tsuritani M, Shimaoka M, et al. Risk factors for deep-vein thrombosis and pulmonary thromboembolism in the benign ovarian tumor. The Tohoku Journal of Experimental Medicine. 2011;225(1):1-3.

[18]. Zhang L, Liu X, Xue Y. Analysis of deep venous thrombosis after gynecological surgery: A clinical study of 498 cases. Pakistan Journal of Medical Sciences. 2015;31(2):453-6.

[19]. Sermsathanasawadi N, Thangrod R, Hongku K, Wongwanit C, Ruangsetakit C, Chinsakchai K, et al. Prevalence of perioperative asymptomatic proximal deep vein thrombosis in Thai gynecologic cancer patients. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2014;97(2):153-8.

[20]. Schlesselman. Case-Control Studies: Design, Conduct, Analysis. New York, NY: Oxford University Press. J. 1982.

[21]. Santoso JT, Evans L, Lambrecht L, Wan J. Deep venous thrombosis in gynecological oncology: incidence and clinical symptoms study. European Journal of Obstetrics, Gynecology, and Reproductive Biology. 2009;144(2):173-6.

[22]. Metcalf RL, Fry DJ, Swindell R, McGurk A, Clamp AR, Jayson GC, et al. Thrombosis in ovarian cancer: a case-control study. British Journal of Cancer. 2014;110(5):1118-24.

[23]. Oranratanaphan S TW, Khemapech N. Incidence and clinical characteristic of venous thromboembolism in gynecologic oncology patients attending King Chulalongkorn Memorial Hospital over a 10-year period. Asian Pac J Cancer Prev. 2015;16(15): 6705-9.

[24]. Seung CP JW, Soon P, et al. The deep vein thrombosis caused by lymphocele after endoscopic extraperitoneal radical prostatectomy and pelvic lymph node dissection. Can Urol Assoc J. 2011;5(3):40-3.

[25]. Tollefson MK, Karnes RJ, Rangel L, Carlson R, Boorjian SA. Blood type, lymphadenectomy and blood transfusion predict venous thromboembolic events following radical prostatectomy with pelvic lymphadenectomy. J Urol. 2014;191(3):646-51.

[26]. Abu-Rustum NR, Richard S, Wilton A, Lev G, Sonoda Y, Hensley ML, et al. Transfusion utilization during adnexal or peritoneal cancer surgery: effects on symptomatic venous thromboembolism and survival. Gynecologic Oncology. 2005;99(2):320-6.

References