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Incidence of symptomatic deep vein thrombosis after gynecological surgery: a retrospective study in Chinese population

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Summary

Objective: Patients undergoing gynecological surgery have a high risk of developing deep vein thrombosis (DVT). While the reason were less determined. *Materials and Methods:* A retrospective review was conducted on all gynecological surgery patients with symptomatic deep venous thromboembolism from August 2012 to July 2015 in a tertiary referral center, Wuhan, China. DVT was diagnosed using ultrasonography that was triggered by symptoms such as pain, swelling, redness, warmth, and engorged superficial veins on legs. Clinical records of patients diagnosed with DVT in this period were reviewed. *Results:* In a total of 3,992 gynecological surgeries, 107 patients were diagnosed with symptomatic DVT (2.7%), of which 96 were in the lower limbs. The incidence of DVT was highest in patients with ovarian cancer (4.51%), followed by cervical cancer (2.04%), and endometrial cancer (1.75%). Most patients (42.7%, 35/82) had identifiable thrombus in left leg, 28.0% (23/82) had identifiable thrombus in right leg and 29% (24/82) were bilateral. Of 123 affected limbs 93 (75.6%) had DVT in calf veins; 50% of DVT occurred within seven days after surgery, and 75% DVT occurred in 13.0 days. *Conclusion:* Reducing the timing of gynecologic malignancies surgeries could significantly reduce the incidence of DVT, and laparoscopic surgery could significantly reduce the incidence of DVT.

Key words: Gynecological surgery; Deep venous thromboembolism; Risk factors.

Introduction

Deep venous thrombosis (DVT) is a frequent postoperative complication after gynecological surgery and may result in potentially lethal pulmonary embolism (PE)[1, 2]. DVT and PE constitute a single disease entity known as venous thromboembolism (VTE). The annual incidence of VTE is up to one per 1,000 in European ancestry population [3-5]. Immobilization, chemotherapy, hormone therapy, surgery, and the insertion of central venous catheters are well known risk factors of VTE [5, 6].

Epidemiology of VTE is extensively studied in the Western population and national guidelines for thromboprophylaxis have been established. More than 30% of gynecological patients without thromboprophylactic treatment develop VTE and share risk factors such as malignancy, vascular compression by pelvic mass, vascular injury, advanced age, lengthy surgery, and chemotherapy [7, 8]. The rate of VTE decreases to 0-15% with appropriate thromboprophylaxis using low molecular weight heparin or heparin-natrium [8]. Several societies, the American Society of Clinical Oncology (ASCO), the National Comprehensive Cancer Net (NCCN) guidelines, the European Society for Medical Oncology (ESMO), and the International Society of Thrombosis and Hemostasis (ISTH) have published guidelines on thromboprophylaxis based on the incidence of VTE in the Western population, however, without specific recommendations for patients undergoing gynecological surgery. In Asia very limited studies on the incidence of DVT have been published and no national guideline exists. The aim of this retrospective single-center study was to investigate the incidence of DVT after gynecologic surgery in a Chinese population.

Materials and Methods

This study was performed following approval of the institutional review board of this hospital. A retrospective review was conducted on all gynecological surgery patients which complicated by DVT from August 2012 to July 2015. Data reviewed included age at surgery, body mass index (BMI), date of primary surgery and thrombosis occurrence, type of gynecologic disease, histology subtype, International Federation of Gynecology and Obstetrics (FIGO) stage of malignancy, type and duration of primary surgery, surgery type, thrombosis location, D-dimer level before and after surgery, and utilization of thromboembolism prophylaxis, including anticoagulant and compression devices.

DVT was diagnosed using ultrasound (US) that was triggered by symptoms such as pain, swelling, redness, warmth, and engorged superficial veins on legs. If thrombus was found on US, side and location of DVT was recorded. Localization of DVT was classified into six segments: iliac vein, common femoral vein, femoral vein, deep femoral vein, popliteal vein and calf vein. Calf vein referred to all the deep veins in calf, including posterior tibial

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Table 1. — *Demographics of patients.*

Diseases	Cervical cancer	Ovarian cancer	Endometrial cancer	Adenomyoma	Uterine fibroid	[c]Others
No. of patients	26	29	7	5	15	14
Incidence of DVT	2.04% (26/1277)	4.51% (29/643)	1.75% (7/400)	0.70% (5/714)	1.57% (15/958)	
Mean age (range), years	50.6±7.8 (35-66)	53.4±9.6 (38-72)	59.4±9.0 (46-70)	49.2±8.9 (38-63)	48.5±6.03 (35-58)	44.5±11.7 (25-71)
[a] BMI, kg/m^2	23.8±3.0	22.7±2.8	25.3±2.3	22.0±1.4	23.7±3.0	22.7±2.6
BMI > 24 kg/m^2	11/25	10/26	4/6	0/5	6/15	5/12
D-dimer						
Pre-operation						
Elevated	3	6	2	0	2	1
Nonelevated	3	1	0	0	0	2
Unknown	20	22	5	5	13	11
Post-operation						
Elevated	12	20	6	5	15	10
Nonelevated	0	0	0	0	0	0
Unknown	14	9	1	0	0	4
[b] FIGO Stage						
Early stage (I+II)	95.8% (23/24)	33.3% (8/24)	50% (3/6)			
Advanced stage.(III+IV)	4.2% (1/24)	66.7% (16/24)	50% (3/6)			

BMI = body mass index; FIGO = International Federation of Gynecology and Obstetrics. a = One case of cervical cancer, three cases of ovarian cancer, and one case of endometrial cancer missed data of BMI. b = Two cases of cervical cancer, five cases of ovarian cancer, and one case of endometrial were not comprehensively staged. c = The total patients of the others were not counted.

vein, anterior tibial vein, and peroneal vein.

Chi-square (χ^2) test and Fisher's exact test were used in calculating the categorical data, Bonferroni procedure was used for multiple comparisons. Wilcoxon rank sum test was used to calculate the continuous variables. All of these statistical analyses were performed in SPSS statistics 21. The authors set α, the probability of type I error, as 0.05. A p value of < α was considered statistically significant in two-tailed tests, In multiple comparisons, α was divided by number of comparisons to achieve an adjust level of α; p < α was considered statistically significant too. SigmaPlot 12 and Coreldraw 7X were used for plotting.

Results

A total of 3,992 patients undergoing gynecological surgery during the three-year study period were identified, which contained 1,277 cases of cervical cancer, 643 cases of ovarian cancer, 400 cases of endometrial cancer, 714 cases of adenomyoma, and 958 cases of uterine fibroid. The overall incidence of DVT in malignancy was 2.67% (62/2320). In all these cases, 107 were diagnosed with DVT which comprised an incidence of 2.7%. Ninety-six of these cases formed DVT in lower limbs, and the remaining formed in other veins, such as in the portal upper limb and superficial veins.

Most cases with postoperative DVT were generated with ovarian cancer (30.2%, 29/96), followed by cervical cancer (27.1%, 26/96), uterine fibroid (15.6%, 15/96), endometrial cancer (7.3%, 7/96), adenomyoma (5.2%, 5/96), and others (14.6%, 14/96) (Table 1, Figure 1).

In the patients undergoing gynecological surgery, the authors found those undergoing operations of ovarian cancer were most likely to develop DVT events (4.51%). The ratios were significantly elevated when compared with the

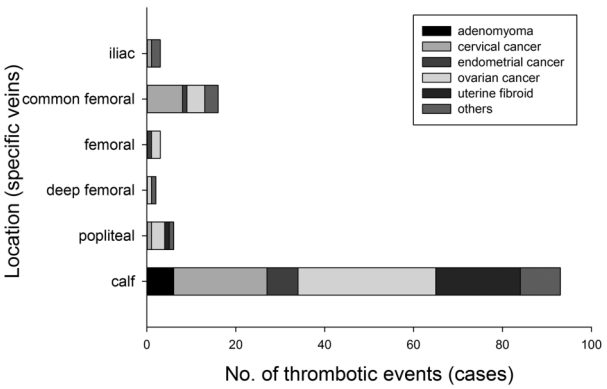

Figure 1. — Location of DVT. The deep vein of lower limb is simplified into six parts, including iliac vein, common femoral vein, femoral vein, deep femoral vein, popliteal vein, and calf vein. Calf vein refers to all the deep veins in thecalf, including posterior tibial, anterior tibial, and peroneal veins.

ones who underwent operations for cervical cancer (2.04%, p = 0.003), adenomyoma patients (0.70%, p = 0.000) or uterine fibroid patients (1.57%, p = 0.001). The postoperative DVT that have a tendency to develop in gynecologic malignancies, like ovarian and cervical cancer, may be attributed to final time of operations. Radical resection of endometrial cancer includes complete hysterectomy rather than radical hysterectomy, which reduces much time.

In the patients that formed DVT, the authors found 123 limbs in these 96 cases, and 107 in 82 cancer patients. They also found 42.7% (35/82) of malignant patients had DVT

Table 2. — *Laparotomy vs. laparoscopy.*

	Laparotomy	Laparoscopy	*p*
No. of patients	44	48	
Incidence of DVT	3.54% (44/1244)	1.73% (48/2768)	0.001
Age	52.1±10.0 (32-72)	50.1±9.1(25-71)	0.327
BMI	23.3±2.8	23.3±2.9	0.961
Stage			0.000
Benign	12	29	
Early stage (I+II)	17	16	
Advanced stage (III+IV)	15	3	
Length	291.0±101.3	207.2±80.0	0.001
Area			
Hysterectomy	29	21	0.354
Radical hysterectomy	11	17	
BSO	32	24	
Local	5	6	

BMI = body mass index; BSO = bilateral salpingoophorectomy.

in the left leg, while 28.0% (23/82) in the right leg, and 29% (24/82) had bilateral DVT . The left-sided dominance of DVT was not statistically significant ($p = 0.149$) compared to the right. These data indicated that formation of DVT prefer to develop in the legs while did not dominate any side.

Most operations of gynecologic malignancies require longer hospital stay to acquire active treatments. The authors found that 25% DVT occurred in 5.0 days, 50% DVT occurred in seven days, and 75% DVT occurred in 13 days. These data showed that longer hospital stay may increase the incidence of DVT.

The authors also calculated the timing of surgeries in these three years. They found the average durations of surgeries were 291, 271, and 223 minutes, respectively, in three years. Furthermore, in the first two years most surgeries were exploratory laparotomy (exploratory laparotomy versus laparoscopy: 15:4 and 15:7, respectively), while 9:29 in the last year. These data indicated that with the development of laparoscopy, more Chinese gynecologist are willing to perform it, which improved the operation efficiency and reduce the timing of surgeries.

In order to evaluate that whether laparotomy could reduce the incidence of DVT, the two operations were compared. The authors found that the incidence of DVT was significantly reduced in those who progressed to laparoscopic surgery (1.73%, 48/2768), compared to those who underwent traditional laparotomy (3.54%, 44/1244) ($p = 0.001$). These data indicated that laparoscopic surgery could significantly reduce the incidence of DVT (Table 2).

Discussion

In this study, the authors identified 107 cases with postoperative DVT, 96 of which formed DVT in lower limbs. Most patients (42.7%, 35/82) had identifiable thrombus in left leg, while 28.0% (23/82) in right leg. Although the difference between left and right seems not significant, the tendency was consistence to the previous data [9]. The incidences of DVT prone to the left may due to the difference of architecture of the iliac veins, which can induce more compression on vein in the left rather than right. Anand *et al.* reported that more than 70% DVT in left leg were associated with the compression of iliac vein [10]. May-Thurner syndrome (MTS), a special iliac vein compression, can cause extensive ipsilateral DVT of the ipsilateral extremity [11].

The authors detected 123 thrombus in the 96 patients, and three-quarters of (75.6%, 93/123) thrombus occurred in calf veins. As for timing of thromboembolism, the authors found 50% DVT occurred in 7.5 days, and 75% DVT in 13.0 days. This phenomenon may due to the symptomatic incidence analyzed here, for the detection of DVT was triggered by symptoms such as pain, swelling, redness, and warmness, and the symptoms were not obvious in the early phase.

In this study, the total incidence of symptomatic postoperative DVT in malignancy was 2.67%, which was comparable to the previous studies based on Chinese population [10], while it was lower than analogic studies based on the Western literature [12]. The incidences of DVT were highest in ovarian cancer (4.51%), followed with cervical cancer (2.04%), and endometrial cancer (1.75%). Nevertheless, it was universal that patients with ovarian cancer had a highest incidence [13, 14]. Another study reported that patients with ovarian cancer have an increased susceptibility to VTE [15], in which have elevated concentrations of cross-linked fibrin degradation products and D dimmers [16, 17]. However, the present authors found that the radical operation of ovarian cancer includes more lengthy times than those of cervical cancer and endometrial cancer, which indicated that incidence of VTE is related with the time of the operation of the malignancy.

The present authors paid special attention to the incidence of DVT in uterine fibroid (15/958), which have a comparable incidence with those in endometrial cancer in this cohort ($p = 0.81$). Uterine fibroid is the most common benign tumor of the female genital tract; many women have significant symptoms of compression of inferior cava and distal vein, due to the large pelvic mass [18]. Shiota *et al.* reported a significant higher incidence in greater pelvic mass (11.5%, 7/61), because the greater mass may induce compression of the iliac vein, which leads to clotting [19]. Barsam *et al.* reported that biological growth factors produced by the fibroids might trigger VTE formation [20].

The present authors found that less DVT occurred after laparoscopic than with laparotomy. Along with the progress of laparoscopic surgery, this micro-wounded operation reduced bleeding, shortened the length of stay in hospital, and promoted rehabilitation. While most advanced stage ma-

lignancy cannot receive approved treatment in laparoscopic surgery because of the fewer vacuity of the operation. The present authors found that laparotomy often spent more time (291.0 ± 101.3 minutes) than laparoscopic surgery (207.2 ± 80.0 minutes) ($p = 0.001$) in the present hospital, and the incidence of DVT in laparoscopic surgery was significantly increased than with laparotomy. In a prospective randomized trial of open versus laparoscopic hysterectomy for uterine cancer, patients were randomly assigned 2:1 to laparoscopy or open surgery [21]. The rates of documented DVT and PE for patients undergoing open and laparoscopic surgery were both 1%. There were no differences in the incidence of DVT and PE between patients undergoing laparoscopy and laparotomy. In all, these data may indicated that undergo less operative time may decrease the incidence of DVT.

In this study, the authors only focused on postoperative incidence of symptomatic DVT, and neglected some potential influencing factors, like intraoperative thromboembolism prophylaxis, postoperative application of anticoagulants, and length of lying in bed. However, this study still indicated that elevation of operative efficiency and shortening of operation time may decrease thromboembolism in gynecological surgery.

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