Prevalence of Perioperative Asymptomatic Proximal Deep Vein Thrombosis in Thai Gynecologic Cancer Patients


* Division of Vascular Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkoknoi, Bangkok 10700, Thailand.
** Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Background: Thromboprophylaxis of deep vein thrombosis in gynecologic cancer surgery in Thai patients is not routinely performed.

Objective: The prevalence of perioperative asymptomatic proximal deep vein thrombosis of 100 patients with gynecologic cancer was identified.

Material and Method: Duplex ultrasonography of proximal vein of legs was performed in each patient, seven to 14 days, before and after surgery.

Results: The prevalence of perioperative asymptomatic proximal deep vein thrombosis was 7%. The prevalence of preoperative asymptomatic proximal deep vein thrombosis of legs was 5% and postoperative incidence of asymptomatic proximal deep vein thrombosis of legs was 2.11%. Acute symptomatic pulmonary embolism was found in only one patient. All patients who developed deep vein thrombosis had adenocarcinoma of ovary or uterus, but not cervical cancer. The other risk factors of venous thromboembolism were comparable between deep vein thrombosis and non-deep vein thrombosis group.

Conclusion: The patients with adenocarcinoma of ovary and uterus seem to be the greatest risk of perioperative deep vein thrombosis. High prevalence of venous thromboembolism in gynecologic cancer surgery of Thai patients should be concerned.

Keywords: Asymptomatic disease, Deep vein thrombosis, Female genital neoplasms, Perioperative period, Prevalence

Venous thromboembolism (VTE) is one of the most common postoperative complications observed among Caucasian population(1). The prevalence of asymptomatic deep vein thrombosis (DVT) in Western population ranges from 15% to 40% in patients undergoing major general surgery and gynecologic surgery without thromboprophylaxis. The rate of perioperative fatal pulmonary embolism (PE) ranges from 0.2% to 0.9%(2). However, VTE has been regarded as a rare disease among Asian population(3,4). The long belief that VTE is rare in Asian patients has been challenged by many studies. An incidence of perioperative DVT in Asian patients undergoing general surgery ranges from 3% to 28% which is lower than those reported for the Caucasian(5). In addition, some authors reported that the incidence of VTE among Asian patients had increased(6,7).

Correspondence to:
Sermsathanasawadi N, Division of Vascular Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Prannok Road, Bangk koknoi, Bangkok 10700, Thailand.
Phone: 0-2419-8021, Fax: 0-2412-9160
E-mail: nuttawut@gmail.com
period of gynecologic malignancy in Thai patients who
did not receive VTE prophylaxis.

Material and Method
This prospective descriptive study aimed to
demonstrate the prevalence of acute asymptomatic
deep vein thrombosis and its risk factors in perioperative
gynecologic cancer patients. One hundred patients
attending Siriraj hospital, Bangkok, Thailand between
January 2011 and May 2012 for their gynecologic
cancer surgery were enrolled for this study. Once the
informed consent was obtained, the patients were
interviewed for clinical information. Demographic data
was collected including: age, sex, height, weight, body
mass index (BMI), previous diagnosis, treatment of
DVT and PE, history of irradiation and chemotherapy,
family history of VTE, recent immobilization of
lower extremities (more than 3 days), recent surgery
within three months, recent trauma within three
months, recent admission of severe medical illness,
other associated cancers, varicose vein, thrombophilia,
use of contraceptive pills, hormonal therapy, cardiac
diseases, and cerebrovascular disease.

Each participant underwent DVT screened
by color Doppler duplex ultrasound examination with
venous compression test, augmentation, color Doppler
filling in the veins and respiratory phase variation in
common femoral veins, and popliteal veins to diagnose
proximal DVT prior to surgery(15). The color Doppler
duplex ultrasonography was performed on GE
LOGIC 9, (GE Healthcare, USA) using 5 to 10 MHz
linear transducers by an experienced vascular surgeon.

If proximal DVT was detected, the patients
received anticoagulant immediately and the surgery
was postponed for two to four weeks. After surgery,
the patients received postoperative anticoagulant
following standard guideline(16). If the preoperative
duplex scan screening was negative for proximal
DVT, the patients underwent cancer surgery without
VTE prophylaxis.

The patients who developed symptoms and
signs of either acute DVT or acute PE after surgery
were investigated by duplex ultrasonography or
computed tomography angiography (CTA) pulmonary
immediately.

After surgery for seven to 14 days, all
asymptomatic patients were screened by duplex
ultrasound to detect postoperative acute proximal DVT.

The participants with negative duplex scan in
preoperative and postoperative period were telephone-
interviewed at one and three months postoperatively
to inquire about any clinical VTE that subsequently
developed to the duplex ultrasonography.

Hospital medical records were reviewed for
the following information: site of cancer, type of
cancer, staging of cancer and type of operation.

A sample size of 100 participants was
calculated based on an estimated 40% incidence of
VTE, using a precision 10% with the level of
confidence of 95%(2).

Descriptive data analysis was presented in
number, percentage, median, mean, and standard
deviation. For data comparison between groups, Chi-
square test and Student’s t-test were used for discrete
variables and continuous variables. A p-value <0.05
was considered to be statistically significant. Statistical
analysis was done using PASW Statistics 18.0 software.

The present study protocol and informed
consent were approved by the Institutional Review
Board, and all the patients gave informed consent.

Results
Patient characteristics
There were 100 female patients enrolled in
the study. All of the patients had gynecologic cancer
and were planned for surgical treatment. Mean age of
the patients was 54.38 (SD ±11.4) years. Mean BMI
was 24.49 (SD ±4.35) kg/m². Mean duration of hospital
stay was 8.63 (SD ±4.94) days. No patients had chest
symptoms including chest pain, dyspnea, hemoptysis
and symptoms of deep vein thrombosis prior to surgery.
No patients received any treatment for VTE prior to
enrollment.

The most common presenting symptoms were
abnormal vaginal bleeding followed by abdominal
mass (Table 1). The most common site of cancers in
the present study was endometrial cancer (42%),
followed by ovarian cancer (26%), cervical cancer:
adenocarcinoma (16%) and cervical cancer: squamous
cell carcinoma (16%) (Table 1).

Characteristics of cases of perioperative acute proximal
deep vein thrombosis
Five patients had acute asymptomatic
proximal DVT found during the screening duplex
ultrasound prior to surgery. Therefore, the prevalence
of DVT prior to surgery was 5% (5 cases of 100 cases)

Among five cases of pre-operative proximal
DVT, three cases were diagnosed as ovarian cancer and
two cases were endometrial cancer. According to
the site of acute proximal DVT, two cases had right
femoropopliteal DVT, one case had left femoropopliteal
DVT, one case had bilateral femoropopliteal DVT, and one case had right popliteal DVT and left femoropopliteal DVT.

There were two cases of post-operative DVT; one had ovarian cancer and had left femoropopliteal DVT. Another had endometrial cancer and had right popliteal DVT (Table 2). The incidence of postoperative asymptomatic proximal DVT was 2.11% (2 cases of 95 cases). Both cases of postoperative DVT were operated in supine position.

All seven cases of perioperative acute proximal DVT were asymptomatic. The authors found only one case of symptomatic acute pulmonary embolism associated with acute asymptomatic proximal DVT of lower extremities. In addition, the authors found that all seven cases of acute perioperative proximal DVT were gynecologic adenocarcinoma (Table 2).

Other patients who did not have perioperative proximal DVT were interviewed by telephone at one-month and three-month postoperatively. No one had symptoms of VTE.

### Comparing between acute perioperative proximal DVT and non DVT group

Risk factors of venous thromboembolism were compared between DVT and non-DVT groups (Table 3). There were no statistical differences in all risk factors between DVT and non-DVT groups.

### Discussion

Perioperative VTE prophylaxis for Asian patients is usually neglected by most physicians. Some reports exhibited the high prevalence\(^5\); however, the others showed that VTE in Asian population were rare\(^17\). In addition, perioperative unexpected death was reported frequently in cancer surgery patients without definite etiology. Acute pulmonary embolism in these patients was reported as the silent killer. No previous clinical research was performed to identify the exact prevalence and risk factor of DVT in gynecologic malignancy surgery in Asia.

The present study, the authors prospectively observed the prevalence of perioperative asymptomatic proximal DVT of patients with gynecologic cancer patients who did not receive medical thromboprophylaxis for VTE. The authors found that the total prevalence of perioperative asymptomatic proximal DVT was 7%, the preoperative 5% and the postoperative 2.1%. Symptomatic pulmonary embolism was observed in one case of postoperative asymptomatic proximal DVT.

From the results, all perioperative proximal DVT had no symptom and sign of acute DVT at the time of diagnosis. It is very dangerous to perform surgery in the proximal DVT patients without medical VTE prophylaxis. It is also dangerous to observe and

### Table 1. Presenting symptoms, sites and histological type of cancer of 100 gynecologic cancer patients

<table>
<thead>
<tr>
<th>n (%)</th>
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<tbody>
<tr>
<td>Chief complaint</td>
<td></td>
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<tr>
<td>Vaginal bleeding</td>
<td>51 (51.0)</td>
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<tr>
<td>Pelvic mass</td>
<td>9 (9.0)</td>
<td></td>
<td></td>
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<tr>
<td>Abnormal pap smear</td>
<td>8 (8.0)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Abdominal pain</td>
<td>7 (7.0)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ascites</td>
<td>2 (2.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Site and histology of cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical cancer (SCC)</td>
<td>16 (16.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical cancer (Adeno CA)</td>
<td>16 (16.0)</td>
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<td></td>
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<tr>
<td>Ovarian cancer (Adeno CA)</td>
<td>26 (26.0)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Endometrial cancer (Adeno CA)</td>
<td>41 (41.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinomatosis peritonei</td>
<td>1 (1.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCC = squamous cell carcinoma; Adeno CA = adenocarcinoma</td>
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</table>

### Table 2. Characteristic cases of perioperative acute asymptomatic proximal DVT

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Time of Dx</th>
<th>Organ</th>
<th>Type</th>
<th>Staging</th>
<th>Site of DVT</th>
<th>Symptomatic PE</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>56</td>
<td>Pre-op</td>
<td>Ovary</td>
<td>Adeno CA</td>
<td>IV</td>
<td>Bilateral CFV + Pop V</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>51</td>
<td>Pre-op</td>
<td>Ovary</td>
<td>Adeno CA</td>
<td>I</td>
<td>Rt CFV + Pop V</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>68</td>
<td>Pre-op</td>
<td>Ovary</td>
<td>Adeno CA</td>
<td>I</td>
<td>Lt CFV + Lt Pop V</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>56</td>
<td>Pre-op</td>
<td>Endometrium</td>
<td>Adeno CA</td>
<td>III</td>
<td>Lt CFV + Bilat Pop V</td>
<td>Yes</td>
</tr>
<tr>
<td>5</td>
<td>55</td>
<td>Pre-op</td>
<td>Endometrium</td>
<td>Adeno CA</td>
<td>III</td>
<td>Rt Pop V</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>80</td>
<td>Post-op</td>
<td>Ovary</td>
<td>Adeno CA</td>
<td>III</td>
<td>Lt CFV + Pop V</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>65</td>
<td>Post-op</td>
<td>Endometrium</td>
<td>Adeno CA</td>
<td>I</td>
<td>Rt Pop V</td>
<td>No</td>
</tr>
</tbody>
</table>

DVT = deep vein thrombosis; Dx = diagnosis; PE = pulmonary embolism; Pre-op = preoperative; Post-op = postoperative; Adeno CA = adenocarcinoma; CFV = common femoral vein; Pop V = popliteal vein; Rt = right; Lt = left
wait for VTE treatment until the symptoms and signs of acute DVT and acute PE occur. According to recent VTE practice guideline, the prevalence of perioperative VTE in the gynecologic cancer patients who do not receive anticoagulant for VTE prophylaxis is 6% or more\(^{(1)}\). These patients are classified as high-risk for perioperative VTE development. Combined medical and mechanical thromboprophylaxis is required\(^{(1)}\). Gynecologic cancer surgery in Thai patients is classified as high risk operation for VTE because the prevalence of VTE from the present study was 7%.

According to the risk factors for perioperative VTE which were reported in previous literature, we found that the risk factors including family history of VTE, recent immobilization (>3 days), previous irradiation, previous chemotherapy, recent surgery (<3 months), recent trauma (<3 months), recent admission of severe medical illness, associated other malignancy, varicose vein, use of contraceptive pills and hormone, vascular disease in family were comparable between DVT and non DVT groups. Therefore, these risk factors did not increase risk of VTE in gynecologic cancer surgery patients. Moreover, we found that acute DVT and PE occurred in patients with adenocarcinoma of ovary and uterus only, not cervix. As a result, the patients with adenocarcinoma of ovary and uterus seem to have the greatest risk of perioperative VTE.

Duplex ultrasound is a common test of acute DVT because it is noninvasive. The sensitivity of duplex ultrasound for asymptomatic proximal (femoral and popliteal) DVT is up to 95%\(^{(18)}\).

The present study’s result might make the physician concerned about the high prevalence of perioperative VTE in gynecologic cancer surgery in Thai patients. The usefulness of routine preoperative and seven to 14 day postoperative duplex scan in Thai patients to detect proximal DVT should be evaluated in the future clinical research. Moreover, routine thromboprophylaxis of VTE in Thai patients performing gynecologic cancer surgery should be investigated in randomized controlled trial.

**Conclusion**

High prevalence of venous thromboembolism in gynecologic cancer surgery of Thai patients should be concerned. The patients with adenocarcinoma of ovary and uterus seem to be the greatest risk of perioperative VTE.

**What is already known on this topic?**

The prevalence of asymptomatic perioperative proximal deep vein thrombosis is very high in gynecologic cancer surgical patients in Europe and USA. The patients must receive prophylaxis of venous thromboembolism by anticoagulant before and after surgery.

**What this study adds?**

The prevalence of venous thromboembolism in gynecologic cancer surgery of Thai patients is also high, although it is less than the prevalence of venous thromboembolism in Western countries. The patients with adenocarcinoma of ovary and uterus seem to have the greatest risk of perioperative deep vein thrombosis.

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**Table 3. Comparing risk factors between DVT group and non-DVT group**

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>DVT (n = 7), n (%)</th>
<th>Non-DVT (n = 93), n (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history of VTE</td>
<td>0 (0)</td>
<td>1 (1.1)</td>
<td>1.000</td>
</tr>
<tr>
<td>Recent immobilization (&gt;3 days)</td>
<td>0 (0)</td>
<td>1 (1.1)</td>
<td>1.000</td>
</tr>
<tr>
<td>Previous radiation</td>
<td>0 (0)</td>
<td>8 (8.6)</td>
<td>0.547</td>
</tr>
<tr>
<td>Previous chemotherapy</td>
<td>1 (14.3)</td>
<td>17 (18.3)</td>
<td>0.631</td>
</tr>
<tr>
<td>Recent surgery (&lt;3 month)</td>
<td>1 (14.3)</td>
<td>3 (3.2)</td>
<td>0.225</td>
</tr>
<tr>
<td>Recent trauma (&lt;3 month)</td>
<td>0 (0)</td>
<td>2 (2.2)</td>
<td>0.864</td>
</tr>
<tr>
<td>Recent admission of severe medical illness</td>
<td>1 (14.3)</td>
<td>2 (2.2)</td>
<td>0.197</td>
</tr>
<tr>
<td>Other malignancy</td>
<td>0 (0)</td>
<td>6 (6.5)</td>
<td>0.639</td>
</tr>
<tr>
<td>Varicose vein</td>
<td>3 (42.9)</td>
<td>18 (19.4)</td>
<td>0.159</td>
</tr>
<tr>
<td>Contraceptive pills/hormone</td>
<td>1 (14.3)</td>
<td>16 (17.2)</td>
<td>0.606</td>
</tr>
<tr>
<td>Vascular disease in family</td>
<td>1 (14.3)</td>
<td>4 (4.3)</td>
<td>0.310</td>
</tr>
</tbody>
</table>

VTE = venous thromboembolism
Acknowledgement
The authors wish to thank Dr. Suthat Chottanapund for statistical analysis.

Potential conflicts of interest
None.

References
ความชุกของการระลึกเสื่อมของหลอดเลือดอุดตันของขาในผู้ป่วยมะเร็งที่ต้องรักษาร่างกายปอดในระบบอวัยวะสืบพันธุ์

นรัฐวุฒิ เสริมนรัตน์, รัตนา เพิ่มสวัสดิ์, ชุมพล วิจนัยกิจ, เฉนียน เรืองเศรษฐกิจ, บุญทิพย์ ชีวิน, ชินศักดิ์ชัย คามิน, ชัยรัตน์ ลิปป์ คล้าย, ประภู ศิริวัฒน์

ภูมิหลัง: ในประเทศไทยยังไม่มีการให้ยาในการป้องกันภาวะลิ่มเลือดอุดหลอดเลือดดำชั้นลึกของผู้ป่วยมะเร็งทุกคนที่เข้ารับการรักษาโดยการผ่าตัด

วัตถุประสงค์: หาความชุกของการเกิดภาวะลิ่มเลือดอุดหลอดเลือดดำชั้นลึกของขาที่ไม่แสดงอาการในผู้ป่วยมะเร็งทุกคนที่เข้ารับการผ่าตัด

วัสดุและวิธีการ: ผู้ป่วยทุกรายจะได้รับการตรวจด้วยเครื่องอัลตราซาวด์ทั้งระยะก่อนผ่าตัดและหลังผ่าตัด 1-2 สัปดาห์

ผลการศึกษา: ความชุกของการเกิดภาวะลิ่มเลือดอุดหลอดเลือดดำชั้นลึกของขาที่ไม่แสดงอาการในระยะก่อนและหลังผ่าตัดรวมกัน ร้อยละ 7 โดยที่ตรวจพบในระยะก่อนผ่าตัด ร้อยละ 5 และตรวจพบหลังผ่าตัดส่งผลต่อ ร้อยละ 2 มีผู้ป่วยหนึ่งรายที่แสดงอาการเหนื่อยหอบจากลิ่มเลือดที่ขาได้หลุดไปอุดหลอดเลือดแดงที่ปอด ผู้ป่วยก่อนการexpiry. ผู้ป่วยทุกรายที่เป็นภาวะลิ่มเลือดอุดหลอดเลือดดำชั้นลึกของขาเป็นมะเร็งที่ต้องรักษาเป็นกรณีพิเศษ.

สรุป: ความชุกของการระลึกเสื่อมของหลอดเลือดอุดตันของขาในผู้ป่วยมะเร็งที่ต้องรักษาร่างกายปอดเป็นเรื่องที่ควรให้ความสนใจ และผู้ป่วยทุกคนที่ต้องรับการผ่าตัดมีความเสี่ยงสูงที่จะเกิดภาวะลิ่มเลือดอุดตันของขาอุดหลอดเลือดดำชั้นลึก