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Clinical Evaluation of Pulmonary Thromboembolism ın Gynecologic Oncology Operations: Analysis of Nine Patients ın A University Hospital

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ABSTRACT

To investigate the cases of pulmonary thromboembolism (PTE) and to analyze the risk factors in patients undergoing gynecologic oncology operations.

Material and methods: The medical records of all patients who underwent gynecologic oncology surgery from January 2015 to September 2022 were collected from the hospital's database. Cases with the diagnosis of PTE were retrieved and analyzed retrospectively.

Nine cases of clinically apparent PTE were identified in the medical records. The mean age of the patients was 56.1±3.4. The mean BMI was 27.2±1.4. The majority of the cases were advanced stage ovarian malignancy who underwent a major surgery including pelvic-paraaortic lymphadenectomy (5/9). Dyspnea and shortness of breath was the main complaint. Tachypnea was the main finding in all cases. The leukocytosis and the thrombocytosis were notable in PTE cases.

PTE remains as one of the fatal complications after gynecologic surgeries. In our case-cohort, increasing age, obesity and the complexity of surgery are significant predictors of pulmonary embolism in gynecologic oncology operations. Further multicenter studies stratifying risk factors are warranted to reach a proper prophylactic strategy and prevent PTE.

Keywords: Pulmonary thromboembolism, gynecology, malignancy, ovarian cancer

Introduction

Pulmonary thromboembolism (PTE) is one of the fatal complications after gynecologic surgeries. It has been reported to be fatal in 25% of patients undergoing the operation for malignancy (1). The most important risk factor for occurrence of PTE postoperatively is development of deep vein thrombosis (DVT). DVT may occur in up to 17-40% of gynecologic surgeries in the absence of thromboprophylaxis (2). There are several other risk factors including immobilization, obesity, presence of malignancy and older age group (3). Most of the cases of pulmonary embolism occur in the first postoperative day and there is limited time for intervention. Therefore, the determination of risk factors and early diagnosis of DVT are crucial to prevent PTE-related surgical deaths.

Most of the patients that were hospitalized for gynecologic oncology surgeries have 1 or more risk factors for development of DVT and thus PTE. These risk factors are mostly cumulative (4). The most important issue regarding PTE is the difficulty in prediction of which patient will develop DVT and fatal PTE. Another important issue is unpredicted occurrence of fatal PTE in the absence of DVT and patients with asymptomatic DVT. Although, the pulmonary angiography is the gold Standard diagnostic tool for PTE, there is an increasing trend for spiral computed tomography (CT)- pulmonary angiography (CTPA) (5). The traditional diagnostic tool for PTE was ventilation/perfusion scan (V/Q scan), however this test necessitates the further diagnostic tests in up to 50% of cases (6).

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Prevention of venous thromboembolism (VTE) is one of the most crucial strategies in gyne-oncologic patients. There are several guidelines that draw a frame for the schema. The American College of Obstetricians and Gynecologists (ACOG) reported a practice bulletin for prevention of VTE (7). The most widely used strategy is based on the risk factors as low, moderate, high, high risk-cancer surgery and these are calculated according to the caprini score (8). The prevention methods include intermittent pneumatic compression, graduated compression stockings and pharmacologic prophylaxis (9).

In this retrospective study, we aimed to determine the PTE cases developed after gyne-oncologic surgeries in our unit and to analyze the risk factors. Also, we wanted to report our experience on the diagnosis, prevention and treatment of PTE in patients with gynecologic malignancy.

Material and Methods

The medical data of all patients who underwent gynecologic oncology surgery at a university hospital between January 1, 2015 and September 1, 2022 were collected from hospital's database. The university ethical board approval was obtained before starting the data collection with date and number of 19/08/2022 and 2022/08-14?. We identified all patients with clinically diagnosed PTE following gyne-oncologic operations. Then We retrospectively evaluated their medical records for age, weight, height, body-mass index(BMI), surgical indications, surgical methods, perioperative data including operation time and laboratory data, the time passed until diagnosis, the diagnostic methods, complications, perioperative SpO2 levels, hospitalization time, clinical symptoms and other risk factors for development of PTE.

The diagnosis of PTE was done clinically and accepted as symptoms of dyspnea, tachypnea, chest pain, tachycardia, hypotension and sudden deterioration of health status. Women with these symptoms had the diagnostic test with pulmonary spiral CT-angiography (CTPA) and had confirmation for PTE. All patients had examination for venous Doppler ultrasonography of deep vein thrombosis. These results were retrieved from radiology department's database. The postoperative six weeks were accepted as the end point for development of PTE in these case group. The preventive measures for development of PTE and thrombotic complications were abstracted from data records. The routine practice in our university during gyne-oncologic surgeries is risk-based management and includes mechanical and pharmacologic prophylaxis. The exclusion criteria were as follows: patients with age under 18, the unconfirmed diagnosis of PTE, cases with suspicious death and patients who did not have pulmonology department consultation. And also, patients who were diagnosed in another hospital and sent to our intensive care unit for management were excluded from this retrospective study.

Statistical Analysis: The analyses were done with the SPSS statistical package program version 22.0(SPSS Inc., Chigaco, IL). Descriptive statistics were performed, including the description of quantitative variables such as the mean, SD and range, and description of qualitative variables such as numbers and percentages.

Results

During the study time of 7 years, a total of 1543 operations were performed at our gynecologic-oncology department. 9 cases of clinically apparent PTE were identified in the medical records. The incidence of PTE following gyne-oncologic surgery was 0.58%. Two of the 9 patients with PTE died. Two patients had serious neurological and pulmonary sequelae. Five patients recovered without any serious sequelae. Thus, the mortality rate was 22 % (2/9). The surgical indications of these 9 cases are summarized in Table 1. The demographic characteristics and some clinical data of the 9 cases are summarized in Table 2. The mean age of the cases was 56.1±3.4. The mean BMI was 27.2±1.4. The history of deep vein thrombosis or thromboembolic event was two cases in 9 patients. One had DVT two years ago and ceased her treatment. The other had PTE and recovered 7 years ago.

The majority of cases were advanced stage ovarian malignancy who underwent a major surgery including pelvic-paraaortic lymphadenectomy. The operation time was longer in ovarian cancer group than the other malignant cases. One of the cases had endodermal sinus tumor (Yolk sac tumor) of ovary which was in advanced stage. All patients underwent laparotomic surgery. The mean hospitalization time was 4.2±1.3 days. The mean duration from operation to diagnosis of PTE was 2.1±1.4 days. The mean thrombocyte count was $465x10^3$. In cases with PTE. Regarding the presenting symptom of PTE, dyspnea and

Table 1. Surgical Indications of the PTE Cases

Case	Indication	Operation
Case 1.	Ovarian cancer	Hysterectomy, BSO, PPLND, Omentectomy
Case 2.	Endometrial cancer	Hysterectomy, BSO, PLND
Case 3.	Cervical cancer	Radical hysterectomy, PPLND
Case 4.	Ovarian cancer	Debulking surgery, rectosigmoid resection
Case 5.	Vulvar cancer	Vulvectomy, inguinofemoral LND
Case 6.	Ovarian cancer	Hysterectomy, BSO, peritonectomy, PPLND
Case 7.	Ovarian cancer	Debulking surgery, PPLND, diaphragma resection, peritonectomy
Case 8.	Endometrial cancer	Hysterectomy, BSO
Case 9.	Ovarian cancer	Debulking surgery, rectosigmoid resection, PPLND

BSO: Bilateral salpinngoophorectomy, PPLND: Pelvic-paraaortic lymph node dissection, PTE: pulmonary thromboembolism, LND: Lymph node dissection.

shortness of breath was the main complaint. Tachypnea was the main finding in all cases. Eight patients had CTPA and the diagnosis of PTE was confirmed in 7 cases. Two cases had positive findings in autopsy examination. None of the patients had V/Q scan due to the technical reasons. Three patients had DVT findings on Doppler ultrasonography. The standard treatment with anticoagulation was initiated by the department of pulmonology.

The laboratory findings of the cases are listed in Table 3. The leukocytosis and the thrombocytosis were notable in PTE cases. The mean (SD) SpO_2 level of the PE cases at diagnosis was 86.7% (6.1%) and the mean (SD) PO_2 level was 56.3 mm-Hg (8.2 mm Hg??). The mean blood loss during surgery in PTE cases was 520±120 ml. The mean transfused erythrocyte unit for all cases was 2.2 Unit. The main complications or co-morbidities were hypertension, DM including impaired glucose tolerance, asthma, and heart diseases.

Dıscussıon

Pulmonary embolism is one of the most ominous clinical conditions following gynecologic oncology surgeries. Our study included 9 cases of PTE that developed after gyne-oncologic operations. The well-known risk factor for development of PTE is cancer (10). The risk of death with PTE in a gynecologic cancer patient is reported to be 8% when treated and can be as high as 30% if left untreated (11). This data indicates the importance of early diagnosis and proper treatment of PTE after these complex surgeries. Our study population included 5 patients with ovarian cancers out of 9. The literature shows 6.8% incidence of PTE in ovarian cancers which is the highest risk of developing PTE (12). This was consistent with our data that majority of our PTE cases had ovarian cancer and underwent major abdominal surgery.

There are many studies that reported the older age as a risk factor for development of PTE following gynecologic surgery. A study by Chisaka et al. evaluated 88150 gynecologic and obstetric surgeries and found twenty-five cases of PTE (13). They reported that 86% of the cases were more than 40 years of age. When we analyzed our data, it was seen that majority of our cases (55%) were older than 60 years. Regarding the body weight and BMI, there is a trend toward increase in PTE cases for patients with higher body mass index. Our data showed a mean BMI higher than 25 kg/m^2.

It is reported that the clinical symptoms including tachycardia, tachypnea and dyspnea are the pivotal signs for PTE development in the early postoperative period. As consistent with the literature, dyspnea and shortness of breath with the development of dyspnea? were the main findings in our cases. And also, sudden death at the postoperative second day was seen in one of our cases due to the massive PTE. important laboratory findings that were noted in our case series were leukocytosis and thrombocytosis. Martino et al. study which evaluated 25 patients with PTE in gynecologic oncology patients reported tachycardia and leukocytosis as independently prognostics for PTE (12). There are many published laboratory tests for prediction and diagnosis of PTE (14). Another important test that is used to evaluate the PTE diagnosis is D-Dimer. The normal D-Dimer value in a case of surgical patient can lead to reliably exclusion of PTE with an accuracy of greater than 90% (15). However, this data may have some challenges

Table 2. Demographic Characteristics and Clinical Data of The Patients

	Value
Age, years (mean±SD)	56.1±3.4
Weight, kg (mean±SD)	74.6±4.2
BMI, (mean±SD)	27.2±1.4
Gravida, (mean±SD)	3.2±1.2
History of co-morbidity	
-HT, n (%)	4/9, (44%)
- DM, n (%)	3/9, (33%)
- COPD, n (%)	1/9, (11%)
-DVT, n (%)	2/9, (22%)
Hospitalization time, day, (mean±SD)	4.2±1.3
Operation time, min, (mean±SD)	141±28
Estimated intraoperative bleeding, ml	520±120
Time to diagnosis, day, (mean±SD)	2.1±1.4
Diagnostic tests	
CTPA, n/%	8/88%
X-ray, n/%	9/100%
V/Q scan, n/%	0/100
DVT presence on Doppler, n/%	3/33 %

n/%: number and percentage, SD: Standart deviation, HT:Hypertension, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary diasease, DVT: Deep vein thrombosis, CTPA: Spiral CT pulmonary angiography, V/Q: Ventilation and perfusion Scintigraphy

Table 3. Laboratory Findings of The Cases

Hgb, gr/dl	10.2±1.4
WBC x 10^3 per µl.	14.2±4.2
PLT x 10^3 per µl	465±56
D-dimer, µg/mL	7.42±4.2
SpO_2	86.7±6.1
PO_2	56.3±8.2

Hgb:Hemoglobin, WBC: White blood cell, PLT: Platelet

especially in ovarian cancer patients because of the abnormal coagulation tests and D-Dimer have been studied as prognostic biomarkers in ovarian cancer patients. In our cases, the mean D-Dimer level was 7.42±4.2, which was significantly high and predicted the PTE development.

Nick et al. evaluated the 849 patients who underwent laparoscopic gynecologic surgeries and reported a remarkably elevated number of venous thromboembolisms among cases who underwent high-complexity operations when compared to low- and intermediate- complexity surgeries (16). Our study also showed that the higher number of ovarian cancer cases and higher complexity of these surgeries may explain the higher incidence of PTE among our study cohort.

The pulmonary angiography as an invasive intervention remains to be the gold standard for diagnosis of PTE, however, there is limited use of it in many clinical settings due to the availability of resources. Therefore, the CTPA has been proved in many studies that to be effective in the diagnosis of PTE (17). It has been found in published reports that the sensitivity and specificity of CTPA to be 90% (18). In our study cohort, eight patients had examination with CTPA and 7 out of these 8 cases were confirmed with the diagnosis of PTE with CTPA which had the diagnostic accuracy of 87.5%. This data is consistent with the literature.

The first movement following postoperative 1st or 2nd day is the critical time for development of PTE and maybe for sudden death due to the massive embolism. A study by Chisaka et al reported that half of their patient developed sudden PTE following the

first walk (13). They explained this by the acute release of clot into the circulation. In our case cohort, one of the patients had sudden death at the second postoperative day following active walking and she was diagnosed with a massive embolism after autopsy examination. This case also indicated that the clinician should take in mind the importance of first walk after a long bed rest in the postoperative period.

In conclusion, PTE is one of the important complications after gynecologic surgeries with a reasonable incidence. In our case cohort, increasing age, obesity and the complexity of surgery are significant predictors of pulmonary embolism in gynecologic oncology operations. In the postoperative period, tachypnea, dyspnea and leukocytosis should be evaluated with giving attention to the PTE development. In order to prevent PTE and have a proper prophylactic strategy in patients with gynecologic malignancies, further multicenter studies stratifying risk factors are warranted.

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