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Abstract

Objective

To describe the perioperative outcomes and survival among women with epithelial ovarian cancer (EOC) who present with venous thromboembolism (VTE) at their initial EOC diagnosis.

Methods

Women presenting with primary EOC and VTE diagnosed within 30 days prior to their EOC treatment at a single institution between 1/2/2003 and 12/30/2011 were identified. Those who underwent primary debulking surgery (PDS) as well as those managed with chemotherapy (CT) alone were included. Patient characteristics and process-of-care variables were retrospectively abstracted. VTE was defined as a clinically diagnosed pulmonary embolism (PE) and/or deep venous thrombosis (DVT). Descriptive statistics were used to summarize the cohorts. The Kaplan-Meier method was used to estimate overall survival (OS) from the time of EOC treatment.

Results

During the study period, 36 women were diagnosed with VTE within 30 days prior to their primary EOC treatment. Among them, 28 (77.8%; mean age 64.2 years) underwent PDS and 8 (22.2%; mean age 61.4 years) received CT alone. PE was diagnosed in 53.6% (n=15) within the PDS group and in 62.5% (n=5) of the CT group. Eastern Cooperative Oncology Group (ECOG) performance status (PS) was ≤ 2 in 85.7% (n=24) of those undergoing PDS and in 62.5% (n=5) of those who received CT. Advanced stage (III/IV) disease was diagnosed in 71.4% (n=20) of the PDS group and all patients in the CT group had evidence of advanced stage disease. Among those who underwent PDS, 26 (92.9%) had a preoperative inferior vena cava (IVC) filter placed; 1 (12.5%) in the CT group received an IVC filter. Perioperative bleeding complications were low in the PDS group: 1 (3.6%) developed an intra-abdominal hematoma that was surgically evacuated and 1 (3.6%) developed rectal bleeding secondary to supratherapeutic anticoagulation. Within the PDS group, median OS was 25.6 months while in the CT group, median OS was 4.5 months.

Conclusions

Preoperative management of a VTE in the newly diagnosed EOC patient can be safely done with low rates of bleeding complications. Poor OS among those that received CT alone may reflect worse overall patient health or more aggressive cancer. Median OS among those undergoing PDS was notably shorter than previously published OS; the impact of IVC filter utilization on oncologic outcomes in EOC warrants further investigation.

Background

There are a number of risk factors for venous thromboembolism (VTE) development: age over 60, previous VTE, surgery >2 hours in duration, bed rest >3 days, and advanced stage cancer¹. All of these risk factors can be present in patients diagnosed with epithelial ovarian cancer (EOC) and most of these risk factors can occur prior to surgical intervention for EOC. VTEs can be the initial presenting symptom to an underlying malignancy and the likelihood of malignancy diagnosis is significant within the first few months following a thromboembolic event^{2,3}. VTE is the most common life-threatening postoperative complication with a 1.72% mortality rate observed in cancer patients and up to 25% of newly diagnosed EOC patients have an asymptomatic concomitant VTE^{4,5}. As only a fraction of VTEs lead to death, prevention of life-threatening VTE and improvement in prophylaxis are critical.

In general, preoperative VTEs have previously been excluded from most studies; focus has been on postop VTE occurrences. Due to this paucity of data, we were interested in determining the incidence of symptomatic VTE among women undergoing EOC surgery and describing the therapeutic approach for VTE and EOC when diagnosed concomitantly. Additionally, we wished to investigate how concomitant VTE diagnosis affects EOC surgical morbidity, EOC treatment, and resulting overall survival.

Methods

- Ovarian cancer included: primary EOC, peritoneal carcinoma and fallopian tube carcinoma
- Cancers were treated at Mayo Clinic in Rochester, Minnesota between January 2nd 2003 and December 30th 2011.
- Women must have had clinically symptomatic VTE event (DVT or PE) within 30 days prior to ovarian cancer diagnosis.
- Patient demographics, tumor characteristics, treatment, and surgical details were retrospectively abstracted.
- 2 cohorts: Primary debulking surgery (PDS) and chemotherapy (CT) alone.
- Descriptive statistics and Kaplan-Meier survival estimates were utilized for analyses

Table 1: VTE Characteristics

Characteristic	PDS (N=28)	CT (N=8)
Table 1. Locations of clinically diagnosed VTEs.		
Type of VTE, N (%)		
DVT	13 (46.4)	3 (37.5)
PE	8 (28.6)	2 (25.0)
DVT and PE	7 (25.0)	3 (37.5)
DVT location, N (%)		
Calf	4 (20.0)	1 (16.7)
Knee	4 (20.0)	1 (16.7)
Thigh	8 (40.0)	2 (33.3)
Pelvis	3 (15.0)	0 (0.0)
Unknown/unclear	1 (5.0)	0 (0.0)
Abdominal vessels	0 (0.0)	2 (33.3)

Results

VTE Location and Treatment

- PE was diagnosed in 15 (53.6%) of the PDS group and in 5 (62.5%) of the CT group. Two (25.0%) patients within the CT group were diagnosed with VTE within an abdominal vessel—one within the inferior vena cava and one within the portal vein. These patients were retained in the study as the VTE diagnosis influenced their EOC management. Details of VTE locations are listed (Table 1).
- Among the PDS group, 26 (92.9%) had an IVC filter placed while only 1 (12.5%) in the CT group received an IVC filter.
- Perioperative bleeding complications within the PDS group were rare. One patient (3.6%) developed an intra-abdominal hematoma that was surgically evacuated and 1 (3.6%) developed rectal bleeding secondary to supratherapeutic anticoagulation and the presumed site of bleeding was a fresh colorectal anastomosis.

Patient Characteristics and Clinical Management

- Of the 888 patients during study period, 28 (3.2%) were diagnosed with VTE within 30 days prior to their PDS; 8 additional women were diagnosed with both biopsy-proven EOC and a new VTE within 30 days prior to the start of CT alone. Baseline characteristics are presented for comparison (Table 2).

Overall Survival & Perioperative Outcomes

- Among those who underwent PDS, overall survival was 81.3% at 1 year after surgery, (95% CI 67.8, 97.5), 53.0% (95% CI 36.6, 76.7) at 2 years, and 43.7% (95% CI 27.7, 69.0) at 5 years with median OS of 25.6 months (Figure 1).
- While 71.4% in the PDS group received chemotherapy, administration of adjuvant chemotherapy was unknown for 5 (17.9%) patients. Three (10.7%) patients did not receive adjuvant chemotherapy: one patient had a stage IA, grade 1 mixed endometrioid and serous EOC and she was treated with surgery alone and 2 died within 30 days of PDS (postoperative days 16 and 21). The 30-day mortality rate was 7.1% (2/28) in the PDS group.
- Thirty-day mortality for the CT group was 25% (2/8). At 1 year, OS in the CT group was only 25.0% (95% CI 7.5, 83.0), median OS was 4.5 months; all patients died within 3 years of EOC diagnosis (Figure 1).

Figure 1: Overall Survival

Figure 1. Kaplan-Meier estimate of overall survival among patients diagnosed with concomitant VTE and primary EOC who underwent PDS or CT.

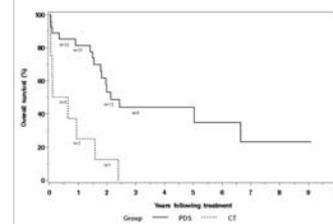


Table 2: Patient Demographics

Characteristic	PDS (N=28)	CT (N=8)
Age (years), mean (SD) [†]	64.2 (11.5)	61.4 (5.0)
BMI (kg/m ²), mean (SD)	28.2 (5.4)	30.3 (7.3)
Mode of EOC diagnosis, N (%)		
Surgical debulking		
Paracentesis	28 (100.0)	0 (0.0)
Thoracentesis	-	2 (25.0)
Image-guided biopsy	-	1 (12.5)
Advanced FIGO stage (III/IV), N (%)	20 (71.4)	8 (100.0)
FIGO grade, N (%)		
1	3 (10.7)	0 (0.0)
2	2 (7.1)	0 (0.0)
3	23 (82.1)	8 (100.0)
Histology, N (%)		
Serous	13 (46.4)	1 (12.5)
Endometrioid	4 (14.3)	0 (0.0)
Mucinous	1 (3.6)	1 (12.5)
Clear cell	6 (21.4)	0 (0.0)
Carcinosarcoma	1 (3.6)	1 (12.5)
Adenocarcinoma, not defined	0 (0.0)	4 (50.0)
Mixed [‡]	3 (10.7)	1 (12.5)
Ascites, N (%)	13 (46.4)	6 (75.0)
Number of primary CT cycles, median (IQR)	-	9 (1, 12)
IVC filter placed, N (%)	26 (92.9)	1 (12.5)
ECOG PS > 2, N (%)	4 (14.3)	3 (37.5)

Conclusions

- Median OS was notably shorter than previously published; IVC filter utilization on oncologic outcomes in EOC warrants further investigation.
- However, poor OS in CT group may reflect worse overall health or more aggressive cancer.
- Perioperative management of a preoperative VTE in the newly-diagnosed EOC patient can be safely done with low rates of bleeding complications.
- In the setting of concomitant new EOC and VTE diagnoses, if PDS is not clinically feasible, quality of life outcomes should be addressed.

References

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