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Original Article

Clinical relevance of ovarian vein thrombosis and risk of secondary venous thromboembolic events in oncology patients

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Abstract: Background: There are no existing clinical guidelines for the management of ovarian vein thrombosis (OVT). Methods: In this retrospective cohort study of patients with cancer and OVT from 2012-2020, the incidence of a secondary venous thromboembolism (VTE) and use of anticoagulation was reviewed. Descriptive statistics were performed among the group with OVT alone and OVT with secondary VTE. Radiographic analysis was performed to determine extension of the OVT into the inferior vena cava or renal veins. Results: We identified the incidence of subsequent VTE was 19%. There was no difference in the development of secondary VTE in those that were started on anticoagulation (P=0.672). Patients with a history of VTE were more likely to develop a secondary VTE (P=0.021). Patients who underwent salpingo-oophorectomy on the ipsilateral side in which OVT was diagnosed, the development of secondary venous VTE was significantly lower than patients without prior ipsilateral salpingo-oophorectomy (9.5% versus 30%, P=0.008). This likely reflects a sequelae of surgery. Extension of the OVT into the inferior vena cava or renal veins did not confer increased risk for thromboembolism (P > 0.05). Conclusions: OVT is a common sequelae of surgery and the majority of patients do not require anticoagulation. Patients with specific clinical history or findings should be considered to receive therapeutic anticoagulation.

Keywords: Gonadal vein thrombosis, iatrogenic causation, incidental identification

Introduction

Ovarian vein thrombosis (OVT) is an unusual complication typically seen in the postpartum setting [1]. Complications of untreated OVT in pregnancy can lead to sepsis, thrombus extending to the IVC, renal veins, and pulmonary embolism [1]. Postpartum OVT is consequently managed with broad spectrum antibiotics and anticoagulation [1]. OVT has increasingly been recognized in non-obstetrical settings, most commonly in patients with gynecologic malignancies after surgical staging [2]. The higher prevalence of ovarian vein thrombosis in oncology patients may be attributed to thrombogenic effects of the malignancy and diminished blood flow in the ovarian vein following major gynecologic surgery [2]. Following gynecologic surgery, OVT may be the result of iatrogenic trauma to pelvic vessels, superimposed infection as well as a result of surgical ligation [3]. Chemotherapy has a known thrombogenic effect by damage to epithelial and endothelial cells and impacting clotting mechanisms [3]. Malignancy is also known to create a hypercoagulable state by activating the coagulation cascade via expression of clot promoting properties on tumor cells [4]. In the context of postoperative patients with malignancy, OVT is typically an incidental finding with resolution of the thrombus without more serious sequelae, deeming both observation and short-term anticoagulation to be acceptable management options [5].

Presentation of OVT can range from acute symptomatology to completely asymptomatic [6]. Traditionally, OVT in the setting of pregnancy presents with fever, constitutional symptoms, and occasionally palpable abdominal masses [6]. Amongst non-pregnancy related cases, vague symptoms such as nausea, vomiting, anorexia, and malaise have been present [6]. In oncology patients, where the finding is frequently incidental, it is most commonly asymptomatic [2, 3].

Historically, OVT was more commonly diagnosed on the right side which was believed to be due to the greater length of the right gonadal vein and incompetent venous valves [1]. In pregnancy, the increased occurrence on the right may be secondary to dextro-rotation of the uterus and compression on the IVC and right ovarian vein [1]. More recent studies of OVT diagnosis outside of pregnancy have shown an equal distribution of thromboses on the left and right sides, as well as bilateral OVTs [7, 8]. Laboratory findings in OVT are typically within normal limits, with the possibility of mild anemia, thrombocytopenia, leukocytosis, and mild elevation in non-specific inflammatory markers [6]. Although D-dimer assays are useful for ruling out thromboembolism, the accuracy in diagnosis of unusual sites is not well established and therefore cannot be utilized [9].

Due to the nonspecific clinical presentation and lack of characteristic laboratory findings, a strong suspicion for OVT is needed, with imaging required to confirm the diagnosis. Multiple imaging modalities can be utilized to diagnose OVT. Ultrasound, computed tomography, and magnetic resonance imaging are modalities utilized to visualize the ovarian veins [10]. There is no consensus on a gold standard test for the diagnosis of OVT [11-13]. Although ultrasound is easily accessible, safe, and cost effective, it is often inconclusive [11]. CT findings indicative of OVT are dilation of the retroperitoneal tubular vein with an area of low attenuation that is significant for the thrombus [10]. CT has been identified as having a sensitivity of 77.8% and specificity of 62.5%, with greatest limitations in the imaging modality due to insufficient enhancement of contrast [13]. MRI is the most reliable method of imaging with a sensitivity and specificity of 100% [1]. Despite the more reliable diagnostic power of MRI, CT remains the imaging modality of choice due to greater accessibility, lower costs, and improved ability to image more critically ill patients than MRI [10].

There are currently no existing clinical guidelines for the management of OVT. The need for anticoagulation has even been questioned given that there is the potential for spontaneous resolution [14]. However, the theoretical possible complications of extension of the thrombus and evolution to PE have prompted many providers to initiate anticoagulation treatment [15]. One study has recommended following the same guidelines of treatment for lower extremity above the knee DVT and PE [14]. In the case of suspected thrombophlebitis, in addition to use of anticoagulation, broad spectrum antibiotics should be administered [16]. In specific cases, ovarian and vena cava vessel ligation have been utilized [16]. Furthermore, proposed management changes with thrombus invasion into the inferior vena cava, as it is believed to be an increased risk for development of PE [17]. This includes placement of a supra-renal inferior vena cava filter, surgical management with resection of a thrombotic segment or thrombolysis [18-20]. Conversely, other studies argue that in the case of asymptomatic and incidentally discovered OVT, use of anticoagulation was not correlated to overall outcomes and is not warranted [21].

Despite the increasing appreciation that the incidence of OVT is likely higher than previously recognized, decision making on the management of OVT remains difficult and non-uniform. Data regarding the management of OVT with or without anticoagulation is not yet well established. Further, there has been no stratification on treatment depending on the type of patient that develops OVT. Most data on OVT are derived from cases in the postpartum setting where it was traditionally observed. However, the unique physiologic processes that occur in pregnancy influence future sequelae and cannot be generalized to the non-pregnant patient. Our goal was to further study the clinical consequences of OVT diagnosed in women with malignancies to determine those who would benefit from treatment with therapeutic anticoagulation. To date, studies estimating the incidence of VTE following OVT in oncology

patients are limited, and estimate a relatively broad incidence ranging from 25-80% [2, 5]. Our study aimed to investigate the incidence of subsequent VTE following OVT in oncology patients and to characterize the long-term sequelae. Although the incidence is now appreciated to be higher than previously recognized, OVT remains uncommon, therefore many of the landmark studies on OVT include relatively small sample sizes. Comparatively, this study has one of the larger cohorts of ovarian vein thrombosis cases. This study contributes to the available knowledge on the natural course of OVT and specifically evaluates patients with malignancy. Further, this study is unique in its inclusion of a radiographic analysis to determine if size and extension of OVT correlate with future sequelae. We are able to stratify patients with subclinical OVT at increased risk for secondary VTE who should be considered candidates for anticoagulation.

Materials and methods

Study design

This was a retrospective cohort study of patients diagnosed with ovarian vein thrombosis and malignancy between July 2012 and June 2020 at a large academic institution. This study was approved by the institutional review board (Northwell IRB 20-1262).

Sample

Patients were queried using the mPower clinical analytics tool [22]. Inclusion criteria included all patients who had radiology imaging across multiple hospitals within a single healthcare system with the search phrases “ovarian vein thrombosis”, “gonadal vein thrombosis”, or “pelvic thrombosis” in the study impression. Cases were eligible for inclusion in this study if they had a cancer diagnosis as well. Patients must have had at least one documented encounter within the system. Patients were excluded if imaging alone was performed in the Northwell system without any additional patient encounters to provide supplemental relevant clinical and demographic information. Data was collected and protected using REDcap (Research Electronic Data Capture) through Northwell Health [23, 24].

Outcomes

The primary outcome was the occurrence of a secondary venous thromboembolic event diagnosed concurrently or within the following two years of the initial diagnosis of OVT. Secondary venous thromboembolic events were deep vein thrombosis, pulmonary embolism, or atypical venous thrombosis. Atypical venous thrombosis included the inferior vena cava, renal veins, splenic veins, iliac veins, mesenteric veins, or cerebral venous sinuses. A sub-analysis was performed radiographically to determine if there was extension of the OVT into the inferior vena cava or left renal vein and the length of extension to determine if involvement in either location was associated with secondary venous thromboembolism. Distance of the extension into the inferior vena cava and renal veins was measured utilizing multiplanar reconstruction with coronal reformation centered on the ovarian vein. For patients that had OVT develop outside of the two year window, they were no longer considered surgical patients as this event was remote from surgery.

Data analysis

An initial analysis was performed using descriptive statistics. Patients were categorized into two groups: ovarian vein thrombosis alone and ovarian vein thrombosis with a secondary venous thromboembolic event. Patient clinical and demographic considerations evaluated included age, ethnicity, comorbidities, BMI, use of tobacco, site of primary malignancy, cancer staging, cancer histology, adjuvant treatment, surgery performed, modality of surgery, history of prior VTE, and extension in the inferior vena cava or renal veins. Means were used for numeric data, which were compared with the Mann-Whitney U Test. Categorical variables were described using absolute frequencies and percentages, and comparison was performed using chi-square or Fischer’s exact test. $P < 0.05$ was considered to be statistically significant. All analyses were performed in R studio [25].

Results

Incidence of OVT and recurrence

A total of 248 patients were identified with a diagnosis of OVT during the study period. Of

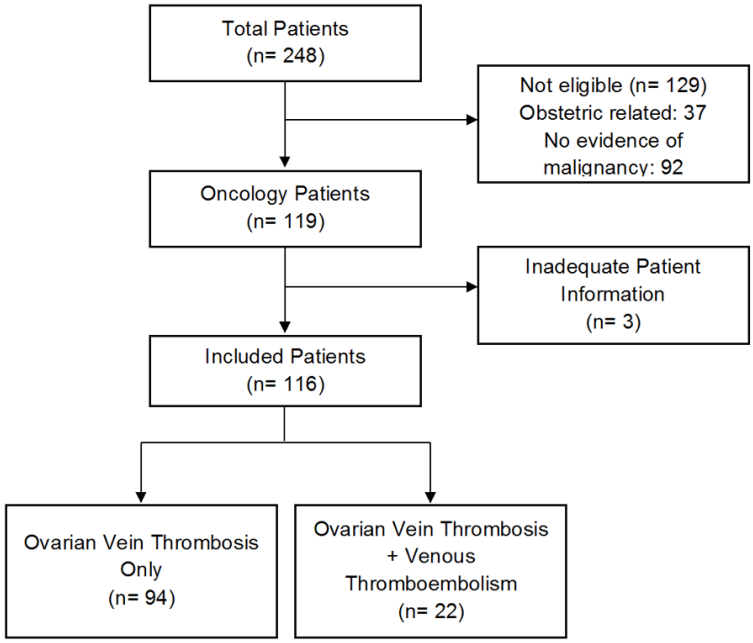

Figure 1. Flowchart of patient inclusion. Determination of patients eligible to be included within the study.

those, 129 did not have a pre-existing malignancy diagnosis and were excluded. 116 patients were included in the study, with 3 excluded due to isolated radiographic imaging without follow up patient information. In the cancer patients with OVT, there was a 19% (22 patients) incidence of secondary venous thromboembolism. The flowchart for patient eligibility is shown in **Figure 1**.

Clinical and demographic information

Patient clinical and demographic characteristics were comparable between the groups as shown in **Table 1**. There was no difference in age between patients in the OVT alone group when compared to the OVT with secondary VTE (P=0.665). There was no difference between cohorts in ethnicity, BMI, origin of cancer, or oncologic status (P=0.452, 0.579, 0.163, and 0.24 respectively). Although smoking is considered an established risk for VTE, amongst this patient population, smokers did not have a greater risk for recurrent VTE (P=0.139). The majority of the patients had malignancies that were primary gynecologic in origin, with a smaller portion of patients having non-gynecologic primary malignancies (68 gynecologic malignancies versus 48 non-gynecologic primaries). Gynecologic malignancies did not confer an increased risk of secondary venous thromboembolism compared to non-gynecologic cancers (P=0.267). The presence of medical comorbidities including hypertension, diabetes, hyperlipidemia, thyroid disease, coronary artery disease, heart failure, and anxiety or depression was also not related to subsequent VTE.

Surgery and OVT

We evaluated the impact of surgery on developing OVT as most of the patients had gynecologic or gastrointestinal malignancies with major surgical staging or cytoreductive procedures performed. Within the cohort of OVT only, salpingo-oophorectomy was performed in 60.6% of patients on the ipsilateral side to where the OVT developed (P < 0.01). Conversely, in cases of OVT with secondary VTE, a significantly smaller proportion (27.3%) had ipsilateral salpingo-oophorectomy performed on the side of OVT formation. The OVT alone cohort was more likely to have had adnexal surgery than the OVT with VTE cohort (63.8% vs. 36.8%, P=0.01). There was no difference in the cohorts in the modality of surgery performed, if a hysterectomy was performed at the coinciding time, or the type of hysterectomy performed (**Table 2**). In the OVT alone cohort, a greater proportion (59.6% vs. 50%, P=0.476) had an additional history of abdominal surgeries besides the specifically analyzed gynecologic procedures.

OVT timing

Identification of the OVT before or after surgery was evaluated to determine the relationship of OVT formation to abdominal and pelvic surgery. We also identified instances of OVT without any history of surgery. The majority of patients with OVT alone developed the thrombus following surgery (78.7%), a smaller portion prior to surgery (3.2%), and a portion of patients had no surgery at all (18.15%). For patients with OVT and VTE, a much larger portion of patients had no surgery (45.5%). The identification of OVT in relation to surgery has

Table 1. Baseline clinical and demographic characteristics between cohorts

		Isolated OVT (n=94)	OVT with secondary VTE (n=22)	*p*-value
Average Age		67	63	0.665
Ethnicity	White	45 (47.9%)	8 (36.4%)	0.452
	Black	24 (26.6%)	6 (27.3%)	
	Hispanic	4 (4.3%)	2 (9.1%)	
	Asian	5 (5.3%)	3 (13.6%)	
	Other	15 (16%)	3 (13.6%)	
BMI	Underweight (less than 18.5)	3 (3.2%)	1 (4.5%)	0.579
	Normal (18.5-24.9)	32 (34%)	10 (45.5%)	
	Overweight (25-29.9)	26 (27.7%)	6 (27.3%)	
	Obese (above 30)	33 (35.1%)	5 (22.7%)	
Medical Comorbidities	Hypertension	49 (52.1%)	11 (50%)	1
	Diabetes	17 (18.1%)	8 (36.4%)	0.083
	Hyperlipidemia	38 (40.4%)	8 (36.4%)	0.812
	Thyroid Disease	11 (11.7%)	3 (13.6%)	0.728
	Coronary Artery Disease	2 (2.1%)	1 (4.5%)	0.471
	Chronic Kidney Disease	2 (2.1%)	1 (4.5%)	0.471
	Heart Failure	2 (2.1%)	1 (4.5%)	0.471
	Anxiety or Depression	17 (18.1%)	3 (13.6%)	0.761
Smoker	Yes	28 (29.8%)	4 (18.2%)	0.139
	No	66 (70.2%)	17 (77.3%)	
	Unknown	0 (0%)	1 (4.5%)	
Smoker Status	Former Smoker	27 (96.4%)	2 (50%)	0.035
	Active Smoker	1 (3.6%)	2 (50%)	
Primary Cancer	Ovary	16 (17%)	2 (9.1%)	0.163
	Uterus	30 (31.9%)	5 (22.7%)	
	Cervix	5 (5.3%)	2 (9.1%)	
	Primary Peritoneal	2 (2.1%)	0 (0%)	
	Vulvar	0 (0%)	1 (4.5%)	
	GTN	2 (2.1%)	0 (0%)	
	Fallopian Tube	3 (3.2%)	0 (0%)	
	Colorectal	10 (10.6%)	3 (13.6%)	
	Appendiceal	2 (2.1%)	0 (0%)	
	Pancreatic	2 (2.1%)	0 (0%)	
	Renal	1 (1.1%)	3 (13.6%)	
	Bladder	1 (1.1%)	1 (4.5%)	
	Lung	1 (1.1%)	1 (4.5%)	
	Breast	9 (9.6%)	1 (4.5%)	
	Lymphoma	2 (2.1%)	1 (4.5%)	
	Other	8 (8.5%)	2 (9.1%)	
Cancer Status	Active	72 (76.6%)	20 (90.9%)	0.24
	Remission	22 (23.4%)	2 (9.1%)	
History of prior VTE	No	86 (91.5%)	15 (71.4%)	0.021
	Yes	8 (8.5%)	6 (28.6%)	
	Unknown	0 (0%)	1 (0.6%)	

Data are expressed as n (%) unless otherwise specified. BMI, body mass index.

Table 2. Patient surgical characteristics

		Isolated OVT (n=94)	OVT with secondary VTE (n=22)	*p*-value
Was hysterectomy performed?	No	30 (31.9%)	12 (54.5%)	0.053
	Yes	64 (68.1%)	10 (45.5%)	
Mode of Hysterectomy Performed	Open	34 (53.1%)	7 (70%)	0.317
	Robotic	23 (35.9%)	1 (10%)	
	Laparoscopic	2 (3.1%)	0 (0%)	
	Vaginal	1 (1.6%)	0 (0%)	
	Unspecified	4 (6.2%)	2 (20%)	
Hysterectomy Type	Supracervical	2 (3.1%)	0 (0%)	0.136
	Total	56 (87.5%)	8 (80%)	
	Radical	4 (6.2%)	0 (0%)	
	Unspecified	2 (3.1%)	2 (20%)	
Was salpingo-oophorectomy performed?	No	31 (33%)	12 (54.5%)	0.010
	Yes	60 (63.8%)	7 (31.8%)	
	Unknown	3 (3.2%)	3 (13.7%)	
Was ipsilateral salpingo-oophorectomy performed?	No	37 (39.4%)	16 (72.7%)	0.008
	Yes	57 (60.6%)	6 (27.3%)	

Data are expressed as n (%) unless otherwise specified.

Table 3. Radiographic analysis of OVT extension

		Isolated OVT (n=94)	OVT with secondary VTE (n=22)	*p*-value
Location of OVT	Right	41 (43.6%)	15 (68.2%)	0.127
	Left	31 (33%)	4 (18.2%)	
	Bilateral	22 (23.4%)	3 (13.6%)	
Did OVT extend into IVC?	No	91 (97.8%)	19 (90.5%)	0.154
	Yes	2 (2.2%)	2 (9.5%)	
Average extension into IVC (cm)		0.45 (0.38-0.52)	0.35 (0.28-0.42)	0.439
Did OVT extend into the renal veins?	No	91 (97%)	21 (95.5%)	0.574
	Yes	3 (3%)	1 (4.5%)	

Data are expressed as n (%) unless otherwise specified. IVC, inferior vena cava.

statistical significance between the group with OVT alone or OVT with a subsequent event (P=0.017). Although the interval between surgery and formation of the OVT was shorter in the group that also formed secondary VTE (120 versus 150 days), this was not statistically significant (P=0.747).

Radiographic extent

Radiographic involvement and length of extension of the OVT is summarized in **Table 3**. Extension of OVT into the inferior vena cava was a rare occurrence with 97.8% cases of OVT alone and 90.5% of OVT with VTE confined to the gonadal veins. Although a greater percentage of cases extended into the IVC in the OVT with VTE group, extension into the IVC was not a significant factor for secondary VTE both categorically and numerically (P=0.154, P=0.439 respectively). Similarly, extension into the renal veins does not appear to correlate to the risk of secondary VTE (P=0.574), however, the accuracy of this statement is limited by the rarity of involvement in the renal veins and a very small sample size where this was observed.

Use of anticoagulation

A retrospective data collection was performed on the use of anticoagulation in patients diagnosed with OVT summarized in **Table 4**. Anticoagulation was started in 38% of the women with OVT alone and 50% of the OVT with VTE

Table 4. Management of OVT

		Isolated OVT (n=94)	OVT with secondary VTE (n=22)	*p*-value
When did OVT occur?	Before surgery	3 (3.2%)	1 (4.5%)	0.017
	After surgery	74 (78.7%)	11 (50%)	
	No abdominal surgery	17 (18.1%)	10 (45.5%)	
Interval between surgery to OVT (days)		150 (65-199)	121 (33-913)	0.747
Was OVT concurrent with VTE?	No	NA	14 (63.6%)	0.515
	Yes	NA	8 (36.4%)	
Was AC started after OVT diagnosis?	Yes	38 (40.4%)	11 (50%)	0.498
	No	53 (56.4%)	10 (45.5%)	
	Unknown	3 (3.2%)	1 (4.5%)	
Anticoagulant used	ASA	6 (15.8%)	1 (9.1%)	0.092
	DOAC	8 (21.1%)	0 (0%)	
	HSQ/LWMH	19 (50%)	10 (90.9%)	
	Coumadin	5 (13.2%)	0 (0%)	

Data are expressed as n (%) unless otherwise specified. AC, anticoagulation.

groups at time of initial OVT diagnosis. This reflects the lack of established clinical guidelines for the management of OVT. The most commonly utilized anticoagulation was unfractionated or low weight molecular heparin; however, some patients received a direct-acting oral anticoagulant (DOAC) or warfarin. Patients that were started on anticoagulation continued with this practice for different intervals of time ranging from a minimum of 4 weeks to some patients remaining on anticoagulation over 1 year later, similarly highlighting the lack of uniformity in practice. All patients with secondary VTE were started on anticoagulation. In the cohort of OVT with VTE, VTE was concurrent with the diagnosis of OVT in 40% of patients. 60% of the patients had a VTE that was diagnosed in an interval following OVT.

Discussion

Principal findings

Our data suggests that for oncology patients that have undergone gynecologic surgery, OVT identified on the ipsilateral side of salpingo-oophrectomy is likely a sequelae of surgery and iatrogenically imposed. Among women who had no gynecologic surgery or had OVT identified prior to surgery, higher rates of secondary VTE were observed. Patient characteristic of prior VTE correlated with rates of secondary VTE. Although OVT were more likely to extend to the IVC or renal veins in women with secondary VTE, this was not statistically significant.

Results

OVT is being increasingly recognized in non-obstetric settings, particularly among oncology patients who have undergone gynecologic surgery [2]. The increasing incidence may reflect more frequent radiologic imaging and technological advances that have increased the sensitivity of detection, as well as increased identification by radiologists [7]. An example of CT diagnosed right ovarian vein thrombosis is seen in **Figure 2**. Several studies have evaluated both the treatment options for findings of incidental OVT on imaging and subsequent sequelae that have followed. However, uncertainty still exists in the best course of management with no standard clinical guidelines [2, 3, 5].

In one study on OVT occurring in malignancy, six patients with OVT were identified incidentally by CT scan [3]. Following diagnosis of OVT, only 1 patient was treated with therapeutic anticoagulation for 1 week, no patients received antibiotics, and no patients had further thrombotic complications such as a pulmonary embolism [3]. Of the study group, 2 patients had spontaneous resolution of the clot, 1 patient had no additional follow up imaging, and the remaining 3 women had clots that persisted during the study time period without further complications [3]. This study was significant in that it was the first to further evaluate the subject. However, it included a small sample size of 6 patients limiting its ability to be

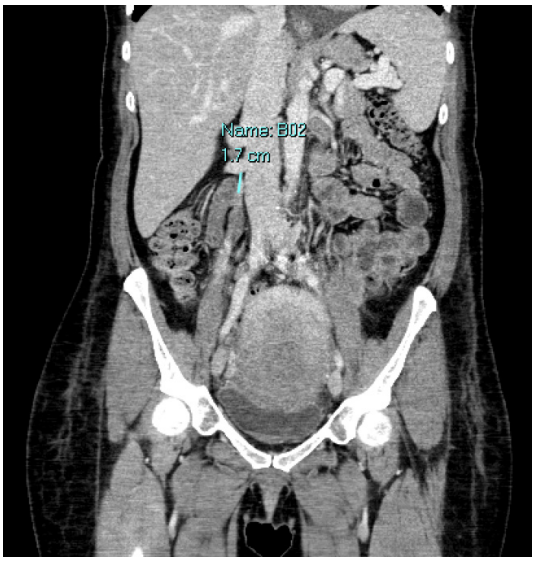

Figure 2. Right ovarian vein thrombosis. CT imaging demonstrating right sided ovarian vein thrombosis.

applied more broadly. In a similar study on OVT as an incidental postoperative finding following abdominal hysterectomy, bilateral salpingo-oophorectomy, and lymph node dissection, there were no apparent adverse clinical effects such as pulmonary embolism or thrombus extension [2]. In the cohort of patients with OVT after surgery, none were found to have complications as a result of the OVT throughout the 2-year follow up period [2]. Both studies provide an important addition to the literature on OVT, however, neither was able to aid in the treatment recommendations for OVT.

A similar study demonstrated a non-statistically significant difference in the incidence of venous thromboembolism in individuals with postoperative OVT in the 1 year following ovarian cancer cytoreductive surgery [5]. Similarly, there was no significant difference in 1-year survival with rates of 95.1% in patients with new OVT and that of 93.2% in patients without imaging evidence of OVT [5].

Another study demonstrated a VTE recurrence rate of 14.3% and found that active cancer was the only risk factor that was significant for recurrent VTE [26]. In our study, active cancer was not a significant risk factor for subsequent VTE (P=0.24). This is in alignment with two of the largest OVT studies available which showed no increased risk of VTE recurrence in cancer patients [7, 27]. These studies also recognize a history of VTE as a correlate to subsequent VTE [7, 27]. One study showed that individuals with prior VTE had a secondary VTE at twice the rate of those without prior VTE [27]. The other study also identified a personal history of VTE and prior surgery as risk factors for subsequent VTE, even with the use of anticoagulation after OVT [7]. Similarly, our findings suggest that a past personal history of VTE is a significant risk factor for subsequent VTE (P=0.021, OR 4.3, 95% CI 1.3054-14.1647). We recommend inclusion of prior VTE as an important pertinent positive when determining the need for anticoagulation.

Clinical implications

In our study of 116 oncology patients with OVT, the incidence of subsequent venous thromboembolic events was 19%. Our study was well-balanced regarding the use of anticoagulation following diagnosis of OVT with approximately half the patients in each cohort receiving anticoagulation. In all patients that received anticoagulation, the use was separate from routine use of prolonged postoperative VTE prophylactic anticoagulation. The routine use of anticoagulation does not seem to offer an advantage to patients with OVT in preventing subsequent VTE and is likely unnecessary. A smaller subsample of patients that are at higher risk for subsequent VTE due to other clinical characteristics in addition to the OVT may benefit from anticoagulation. Based on the data from our study, there was no correlation with the extent of OVT into the inferior vena cava or renal veins with VTE. Therefore, we suggest that this should not be the basis for initiating anticoagulation.

Research implications

Our study supports the findings of Jacoby, Yassa, and Mantha et al that OVT is a common finding following cytoreductive and staging surgery, but anticoagulation is uncommonly indicated as most cases of OVT do not progress in a clinically significant way [2, 3, 5]. This was the first study to perform a radiographic analysis to correlate with clinical data. From our findings, the majority of OVT is not associated with subsequent VTE, and involvement of the IVC or renal veins does not increase the risk VTE. Based on these findings, we take the stance that only a small minority of patients require

clinical management with anticoagulation. We were able to identify high risk individuals for subsequent VTE as those with a personal history of prior VTE and would recommend therapeutic anticoagulation in this cohort, using the same guidelines for treatment as DVT. We also recommend initiating anticoagulation for patients that have an OVT that does not proceed surgery, as this is more likely to represent an atypical thrombosis and is not simply a sequelae of surgery. Further studies should continue to elucidate risk factors for secondary VTE events and best practice for treatment of OVT.

Strengths and limitations

Limitations of our study include the retrospective review which could add selection bias to our results. This study did not address the overall survival rates to determine the mortality associated with VTE recurrence. We also do not have data on complications related to anticoagulation use. The routine use of post-operative anticoagulation for DVT prophylaxis is also an emerging consideration for the impact on development of OVT. We did not include whether or not patients received postoperative prophylactic anticoagulation, what anticoagulant they had received and for how long, which may be a potential confounder. Given that the practice of prolonged post-operative chemical VTE prophylaxis has evolved, especially over the 8 year period patients were collected for this cohort, we anticipate this may impact both development of OVT and possible subsequent VTE. Although clear cell histology in both ovarian and renal cell carcinoma is a known risk factor for VTE, there were only 2 patients with this histology within our sample size, therefore it could not be investigated if this is a relevant variable. Of the cases of OVT identified among oncology patients, 3 were excluded in the final analysis due to a lack of clinical follow-up data.

Conclusions

Society recommended guidelines for initiating treatment for OVT have yet to be determined. Both clinical observation and anticoagulation have been considered options for treatment. However, outcomes from the available literature tend to indicate that anticoagulation typically appears unnecessary as OVT in this context is more likely an incidental finding and less likely to result in more adverse thromboembolic events. Based on our analysis, cancer patients with OVT who have a history of prior VTE are more likely to develop a secondary VTE event. Anticoagulation should be considered for this group. In the majority of patients with OVT, the use of anticoagulation is unnecessary. Involvement of the IVC or renal vein did not correlate with secondary VTE and should not be used as a basis for initiating anticoagulation based on this dataset. Patients with OVT diagnosed on the ipsilateral side of prior salpingo-oophorectomy are less likely to develop a secondary VTE, presumably since this reflects the sequelae of surgery rather than an underlying propensity for thromboembolism. In patients that have not had surgery and develop OVT, this likely is reflective of an atypical VTE event and therefore should be managed with therapeutic anticoagulation.

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Disclosure of conflict of interest

None.

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References

[1] Kominiarek MA and Hibbard JU. Postpartum ovarian vein thrombosis: an update. Obstet Gynecol Surv 2006; 61: 337-342.

[2] Yassa NA and Ryst E. Ovarian vein thrombosis: a common incidental finding in patients who have undergone total abdominal hysterectomy and bilateral salpingo-oophorectomy with retroperitoneal lymph node dissection. AJR Am J Roentgenol 1999; 172: 45-47.

[3] Jacoby WT, Cohan RH, Baker ME, Leder RA, Nadel SN and Dunnick NR. Ovarian vein thrombosis in oncology patients: CT detection and clinical significance. AJR Am J Roentgenol 1990; 155: 291-294.

[4] Falanga A, Marchetti M and Vignoli A. Coagulation and cancer: biological and clinical aspects. J Thromb Haemost 2013; 11: 223-233.

[5] Mantha S, Sarasohn D, Ma W, Devlin SM, Chi DS, Roche KL, Suidan RS, Woo K and Soff GA. Ovarian vein thrombosis after debulking surgery for ovarian cancer: epidemiology and clinical significance. Am J Obstet Gynecol 2015; 213: 208, e1-4.
[6] Rottenstreich A, Da'as N, Kleinstern G, Spectre G, Amsalem H and Kalish Y. Pregnancy and non-pregnancy related ovarian vein thrombosis: clinical course and outcome. Thromb Res 2016; 146: 84-88.
[7] Lenz CJ, Wysokinski WE, Henkin S, Cohoon KP, Casanegra A, Simmons BS, Saadiq RA, Daniels PR, Wysokinska EM, Bjarnason H and McBane RD. Ovarian vein thrombosis: incidence of recurrent venous thromboembolism and survival. Obstet Gynecol 2017; 130: 1127-1135.
[8] Gakhal MS, Levy HM, Spina M and Wrigley C. Ovarian vein thrombosis: analysis of patient age, etiology, and side of involvement. Del Med J 2013; 85: 45-50; quiz 59.
[9] Ordieres-Ortega L, Demelo-Rodríguez P, Galeano-Valle F, Kremers BMM, Ten Cate-Hoek AJ and Ten Cate H. Predictive value of D-dimer testing for the diagnosis of venous thrombosis in unusual locations: a systematic review. Thromb Res 2020; 189: 5-12.
[10] Virmani V, Kaza R, Sadaf A, Fasih N and Fraser-Hill M. Ultrasound, computed tomography, and magnetic resonance imaging of ovarian vein thrombosis in obstetrical and nonobstetrical patients. Can Assoc Radiol J 2012; 63: 109-118.
[11] Riva N and Calleja-Agius J. Ovarian vein thrombosis: a narrative review. Hamostaseologie 2021; 41: 257-266.
[12] Bannow BTS and Skeith L. Diagnosis and management of postpartum ovarian vein thrombosis. Hematology Am Soc Hematol Educ Program 2017; 2017: 168-171.
[13] Kubik-Huch RA, Hebisch G, Huch R, Hilfiker P, Debatin JF and Krestin GP. Role of duplex color Doppler ultrasound, computed tomography, and MR angiography in the diagnosis of septic puerperal ovarian vein thrombosis. Abdom Imaging 1999; 24: 85-91.
[14] Wysokinska EM, Hodge D and McBane RD 2nd. Ovarian vein thrombosis: incidence of recurrent venous thromboembolism and survival. Thromb Haemost 2006; 96: 126-131.
[15] Harris K, Mehta S, Iskhakov E, Chalhoub M, Maniatis T, Forte F and Alkaied H. Ovarian vein thrombosis in the nonpregnant woman: an overlooked diagnosis. Ther Adv Hematol 2012; 3: 325-328.
[16] Duff P and Gibbs RS. Pelvic vein thrombophlebitis: diagnostic dilemma and therapeutic challenge. Obstet Gynecol Surv 1983; 38: 365-373.
[17] Radomski JS, Jarrell BE, Carabasi RA, Yang SL and Koolpe H. Risk of pulmonary embolus with inferior vena cava thrombosis. Am Surg 1987; 53: 97-101.
[18] Abujudeh H and Lim H. Emergency suprarenal inferior vena cava filter placement in ovarian vein thrombosis. Emerg Radiol 2004; 10: 270-272.
[19] Carr S and Tefera G. Surgical treatment of ovarian vein thrombosis. Vasc Endovascular Surg 2006; 40: 505-508.
[20] Angle JF, Matsumoto AH, Al Shammari M, Hagspiel KD, Spinosa DJ and Humphries JE. Transcatheter regional urokinase therapy in the management of inferior vena cava thrombosis. J Vasc Interv Radiol 1998; 9: 917-925.
[21] Plastini T, Henry D and Dunleavy K. Ovarian vein thrombus: to treat or not to treat? Blood Adv 2017; 1: 1120-1123.
[22] Nuance. mPower clinical analytics for medical imaging [Apparatus and software]. 2022.
[23] Patridge EF and Bardyn TP. Research electronic data capture (REDCap). J Med Libr Assoc 2018; 106: 142-144.
[24] Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, McLeod L, Delacqua G, Delacqua F, Kirby J and Duda SN; REDCap Consortium. The REDCap consortium: building an international community of software platform partners. J Biomed Inform 2019; 95: 103208.
[25] RStudio Team. RStudio: Integrated Development for R. Boston, MA: Rstudio, PBC; 2020.
[26] Tanasanvimon S, Garg N, Viswanathan C, Truong M, Kaur H, Kee BK, Sahin IH, Javle MM and Garrett CR. High prevalence of recurrent thrombosis in subsets of cancer patients with isolated gonadal vein thrombosis: a single center retrospective study. Thromb Res 2014; 133: 154-157.
[27] Assal A, Kaner JD, Danda N, Cohen HW and Billett HH. Risk factors and prognosis of ovarian vein thrombosis. Blood Coagul Fibrinolysis 2017; 28: 468-474.