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Regular Article

High prevalence of recurrent thrombosis in subsets of cancer patients with isolated gonadal vein thrombosis: A single center retrospective study

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ABSTRACT

Purpose: Cancer patients are a high-risk population for venous thromboembolism (VTE); the natural history of gonadal vein thrombosis (GVT) occurring in cancer patients is not well described in the medical literature.
Methods: Utilizing a software program the computerized tomographic scan reports of patients at a single cancer center from January 1, 2004 to June 30, 2011 were searched for the term GVT. Patients included in this analysis had a diagnosis of cancer, an isolated GVT (i.e. no evidence of thrombosis at another site), no symptoms referable to the GVT, and at least six months of follow-up information. All subsequent recurrent VTE events were confirmed by imaging studies.
Results: 196 cancer patients with GVT were identified. The majority of patients in this analysis had metastatic disease (118, 61.2%) as well as active cancer (167, 85.2%). Twenty patients (10.8%) developed recurrent VTE (median follow-up 14.5 months); median time to recurrent VTEs was 5.5 months (range 0–19 months). When considering only patients with without a recent history of gynecologic surgery, VTE recurrence rates were 14.3%. Active cancer was the only risk factor significantly associated with recurrent VTE ($P = 0.047$).
Conclusions: Based upon the patient's risk factors for VTE, treatment of an incidentally detected GVT in cancer patients with anticoagulation, as per guidelines for other VTE sites, may be indicated in certain high risk subgroups, especially those patients with active cancer who have not had prior pelvic surgery.

Introduction

Cancer is a well-known prothrombotic condition with an overall incidence of venous thromboembolism reported in the literature to be as high as 20% [1]; this is more than double the incidence of VTE in patients without cancer [2]. The explanation for this increased risk is multifactorial, but is associated with changes in blood flow, damage to the vascular endothelium, and changes to the plasmatic clotting factors (these three factors are known as "Virchow's triad") [3]. Due to the significant morbidity associated with VTE in patients with cancer [4], and the fact that it is a common cause of death in cancer patients [5], guidelines have been developed regarding the appropriate treatment and subsequent prophylaxis of VTE [6–10].

There is significant heterogeneity in the clinical features in which a thrombotic event occurs in a patient. The site of thrombosis may impact the subsequent treatment approach of a thrombotic event. The gonadal vein is an uncommon site of thrombosis, and thrombosis in this vein is associated with pregnancy [11,12] and the postpartum period [13,14], gastrointestinal inflammation [15], pelvic infection [16], following gynecologic surgery [17], or it may be without a discernible cause (idiopathic) [18,19]. In a single institution retrospective analysis of 35 patients with GVT, 12 (34%) had a history of cancer [20]. This study compared the thrombosis recurrence rates in these patients with GVT with 114 randomly selected females with lower extremity deep venous thrombosis, and found the VTE recurrence rates to be similar.

Currently no guidelines currently exist regarding the treatment of isolated GVT occurring in the setting of patients with cancer. To better understand the natural history and rethrombosis rate in patients with radiographically detected GVT we studied the outcome of patients with a diagnosis of GVT seen at MD Anderson between 2004–2011.

Patients and Methods

Patient Selection

Following IRB expedited approval for the study (PA12 — 0730) a software program was utilized in order to search the computerized

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tomography (CT) scan reports of patients seen at University of Texas MD Anderson Cancer Center from January 1, 2004 to June 30, 2011 for the words "gonadal vein thrombosis". Patients included in this analysis had: a) a diagnosis of cancer and, b) isolated GVT (i.e. no evidence of thrombosis at another site before or at the time GVT reported). All medical records were reviewed for relevant data. All subsequent VTE events were documented by imaging studies.

Statistical Plan

IBM SPSS (version 19.0) statistical software was utilized for all statistical analysis. The $\chi 2$ or Fisher's exact test was used to compare recurrent VTE rates following GVT between the different subgroups. To analyze the associated factors for recurrent VTE in cancer patients with isolated GVT we included only patients having at least one follow-up evaluation. According to previous report of GVT being a common radiologic finding in patients following hysterectomy and oophorectomy, we compared cancer patients with or without history of hysterectomy and/or oophorectomy. For six-month recurrent VTE analysis, we included only patients with at least six month follow-up evaluations. Active cancer was defined as current cancer diagnosis, local cancer recurrence, metastatic disease (distant relapse), or treatment for cancer within the previous six months. Statistical significance would be reached if the *P* value was less than 0.05 for any comparison.

Results

Baseline Patient Characteristics

We identified 412 CT reports of GVT. After exclusion of duplication (multiple CT reports on the same patient) and ineligible cases (mostly non-isolated GVT and uncertain diagnosis of GVT), we identified 196 cancer patients with CT reported isolated GVT (Fig. 1).

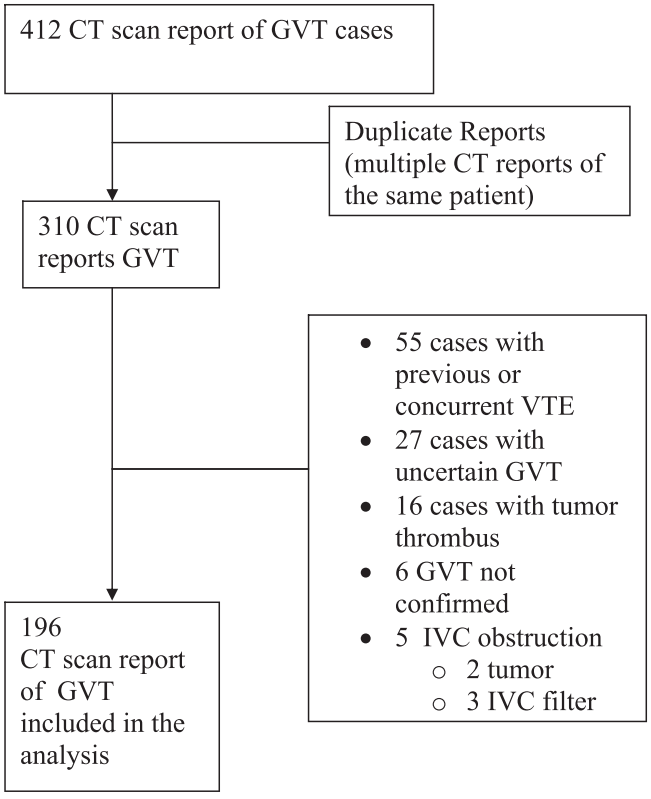

Fig. 1. Consort diagram of the study population.

Table 1
Clinical characteristics of overall cancer patients with isolated GVT.

Age	57.5 ± 12.7 years
Cancer	
-Breast	21 (10.7%)
-Hematologic malignancy	9 (4.6%)
-GI	55 (28.1%)
-GU	7 (3.6%)
-Gynecologic	87 (44.4%)
-Miscellaneous	16 (8.2%)
Chemotherapy	106 (54.1%)
Hormonal therapy	21 (10.7%)
Abdominal surgery (within 6 months prior GVT)	159 (81.1%)
Hysterectomy and/or oophorectomy history	151 (77.0%)
Cancer stage	
-Locoregional	78 (39.8%)
-Distant	118 (61.2%)
Cancer status	
-Active	29 (14.8%)
-Non-active	167 (85.2%)
GVT site	
-Right	114 (58.2%)
-Left	69 (35.2%)
-Bilateral	13 (6.6%)
Anticoagulant therapy	23 (11.7%)

Baseline patient characteristics are demonstrated in Table 1. Although gynecologic cancer was the most frequent cancer identified in this cohort, 55.6% of patients had other cancers, and of these gastrointestinal cancers accounted for the majority of cases (50.9%). Three-fourths of patients had a prior history of hysterectomy and/or oophorectomy. Most patients had active cancer (85.2%) as well as distant metastatic disease (60.2%). All reported isolated GVT were incidental CT findings without any symptoms referable to the thrombosis. More than half of patients had right sided GVT and 6.6% of cases had bilateral GVT. Only 11.7% of patients received anticoagulant therapy.

With median follow up time of 14.5 (0–71) months, recurrent VTE occurred in 20 out of 185 patients (10.8%) all of whom had at least one follow-up evaluation. The most common recurrent VTE site was pulmonary embolism (PE) present in 10 (5.4%) patients. Other sites of recurrent VTE included deep vein thrombosis of extremities (DVT) in 6 (3.2%) patients, inferior vena cava thrombosis in two (1.1%) patients, renal vein thrombosis in one (0.5%) patient and internal jugular vein thrombosis in one (0.5%) patient. The median time to event was 5.5 (0–19) months. The overall recurrent VTE rate was significantly higher in patients with active cancer (Table 2). There were no other significantly associated factors including gynecologic surgery history.

Table 2
Association between clinical characteristics and recurrent VTE incidence.

	Recurrent VTE	*P* Value
Cancer Status		
-Active cancer	20/146	
-No evidence of disease	0/28	0.047
Chemotherapy		
-Yes	13/101	
-No	7/84	0.32
Cancer Type		
-Gynecologic	7/83	
-Non-Gynecologic	13/102	0.35
Gynecologic Surgery Hx		
-Yes	14/143	
-No	6/42	0.41
Cancer Stage		
-Distant	14/112	
-Locoregional	6/73	0.36