Thrombosis Research 147 (2016) 104–107

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Full Length Article

Comparison of postoperative venous thromboembolism incidence in gastrointestinal and gynecologic solid tumors

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ARTICLE INFO

Article history:
Received 25 October 2015
Received in revised form 27 August 2016
Accepted 6 October 2016
Available online 6 October 2016

Keywords:
Venous thromboembolism
Extended prophylaxis
Postoperative
Cancer
Risk factors

ABSTRACT

Introduction: Studies have shown the benefit of 28 days of extended postoperative venous thromboembolism (VTE) prophylaxis for patients undergoing major cancer surgery in the abdomen or pelvis. We retrospectively evaluated the VTE incidence at the University of Kansas Hospital between gynecologic (GYN) cancer patients, who receive extended prophylaxis, and gastrointestinal (GI) cancer patients, who do not.
Methods: Patients were evaluated between January of 2010 and December of 2013, and VTE data for eligible patients were collected for 30 and 90 days postoperatively.
Results: The study population composed of 190 GYN and 204 GI patients. Colon and endometrial cancers were the most common diagnoses. For GYN and GI patients respectively, VTE occurred in 4.2% and 5.4% at 30 days ($p = 0.584$) and 7.4% and 7.8% at 90 days ($p = 0.514$). One VTE-related death occurred in the GI group. GI patients underwent more open surgeries, 77.9% versus 66.3% ($p = 0.010$) and had longer postoperative hospital stay, median of 7 versus 4 days ($p < 0.0001$). Out of all cancer patients combined, 40% versus 17.9% had stage IV disease and 10.2% versus 0.9% had open surgery in the VTE and non-VTE groups, respectively.
Conclusions: There were no significant differences in overall VTE incidence between the two patient groups at 30 and 90 days postoperatively. A majority of VTEs occurred in stage IV patients and patients who underwent open surgeries regardless of diagnosis.

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1. Introduction

Venous thromboembolism (VTE) represents one of the most significant causes of morbidity and mortality in cancer patients [1]. The risk of VTE is estimated to be 4 to 7 times higher amongst patients with cancer [1,2]. There are many causes for this elevated risk of thrombosis, including cancer itself, older age, multiple comorbidities, obesity, primary tumor site, metastatic disease, prior history of VTEs, indwelling central venous catheters, hospitalization, and surgical interventions [1–12]. Cancer patients undergoing surgery have twice the risk of postoperative VTE and >3 times the risk of fatal pulmonary embolism (PE) compared to patients undergoing surgery for benign indications [1,9]; this risk also remains elevated for several weeks after major surgery [1,6–10].

The ENOXACAN II study was conducted in 332 patients with abdominal or pelvic cancers to determine the optimal duration of postoperative prophylaxis; results showed that extended prophylaxis with enoxaparin for 28 days significantly reduced the incidence of thrombosis without increasing bleeding risk compared with 7 days of prophylaxis. The incidence of VTE was 12% versus 4.8%, favoring the extended prophylaxis group ($p = 0.02$) [6]. This finding was also confirmed by the CANBESURE study, where 28 days of bemiparin significantly reduced major VTE events compared to 8 days of prophylaxis [9]. These findings prompted guideline updates from American Society of Clinical Oncology (ASCO), National Comprehensive Cancer Network (NCCN), and European Society for Medical Oncology (ESMO) to recommend extended pharmacological VTE prophylaxis, up to 28 days postoperatively, for patients who have had major cancer surgery in the abdomen or pelvis [1,7,12].

In the studies mentioned above, cancers of gynecologic and gastrointestinal origins have been grouped together in their assessment of VTE incidence, prompting authors of this study to question the comparative VTE risk and incidence of these two populations. Of note, both ENOXACAN II and CANBESURE had similar cancer populations in terms of malignancy type, and gastrointestinal (GI) surgery for colorectal cancer is the most common procedure performed in both studies [6,9]. In Khorana's risk stratification model for prediction of cancer-associated thrombosis, patients with gynecologic cancers are considered to be at high-risk whereas colorectal cancer is at low risk for thrombosis

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http://dx.doi.org/10.1016/j.thromres.2016.10.007
0049-3848/Published by Elsevier Ltd.

based upon their cancer alone [3,5]. At our institution, The University of Kansas Hospital (UKH), surgical patients with gynecologic cancers receive extended VTE prophylaxis with enoxaparin whereas patients with GI cancers receive VTE prophylaxis predominantly limited to the inpatient postoperative setting. This single-institution study retrospectively compares the VTE incidence of two comparable cancer populations undergoing abdominal or pelvic surgeries for tumor resection.

2. Methods

All patients aged 18 years or older who underwent abdominal or pelvic surgery for gynecologic (GYN) or GI cancers at The University of Kansas Hospital between January of 2010 and December of 2013 were considered eligible. The study protocol was approved by UKH's Institutional Review Board. Key exclusion criteria include contraindications to LMWH (defined as active bleeding or general bleeding disorders, known hypersensitivity to LMWH, history of heparin induced thrombocytopenia, cerebral thrombosis, hemorrhage, or neurosurgery within the previous 6 months), receipt of or discharge on a non-LMWH, anticoagulation treatment within 30 days of surgery, or absence of follow up. All patients received 40 mg of enoxaparin once daily per institutional protocol, adjusted for renal function and BMI as needed. A retrospective, single center chart review from the electronic medical record of eligible patients was collected for 30 days post-surgery with a follow up of 90 days post-surgery. The primary objective is to compare the incidence of symptomatic or asymptomatic VTE at 30 and 90 days amongst the GYN and GI oncology groups. The secondary objective is to compare the incidence of VTE-related deaths within 90 days of surgery date amongst the two groups. Lastly, patients were divided into VTE and non-VTE groups in an attempt to identify significant risk factors. Specifically, the following risk factors were assessed: history of VTE, obesity (defined by the World Health Organization as having a body-mass index or BMI > 30 kg/m^2), stage IV disease, age > 65 years, and open surgery. Chi-square tests and *t*-tests were used to analyze study data.

3. Results

The study population comprised a total of 394 patients, including 190 patients from the GYN cancer group and 204 patients from the GI cancer group. Characteristics of the study population are listed in Table 1. The median age is similar between the two groups: 62 and 61 years for GYN and GI patients, respectively. The GYN group had significantly more obese patients, 55.8% versus 32.4% ($p < 0.001$). The GI group had significantly more patients with stage IV disease, 28.4% versus 10.0% ($p < 0.001$). The specific breakdown of the population's malignancy and stage can be found in Table 2. Endometrial and ovarian cancers make up 82% of diagnoses in the GYN group while colorectal cancers make up 88% of diagnoses in the GI group. 77.9% of GI and 66.3% of GYN patients underwent open surgeries ($p = 0.010$), as seen in Fig. 1. GI patients also had a longer duration of postoperative hospitalization ($p < 0.0001$); the median stays were 7 days versus 4 days, as shown in Fig. 2. There were no significant differences in overall VTE incidence between the two groups at 30 and 90 days from the surgery date. For the GYN and GI groups respectively, VTE occurred in 4.2% and 5.4% at 30 days ($p = 0.584$) and 7.4% and 7.8% at 90 days ($p = 0.514$). As shown in Table 3, even though the overall incidence of VTE was similar between the two groups at 30 days, GYN patients had more PEs (3.7% versus 1.5%, $p = 0.163$) while GI patients had more DVTs (3.9% versus 0.5%, $p = 0.038$). One VTE-related death occurred in the GI group and none in the GYN group. The incidence of VTE events in relation to days post-surgery is shown in Fig. 3. For the GYN and GI groups respectively, 5 and 6 patients developed VTE during the postoperative hospitalization period.

Patients deemed at higher disease or operative VTE risk by the research group was isolated for comparison. Out of 58 GYN patients with stage III ovarian or stage IV endometrial cancer, 7 (4 PEs and 3 DVTs) VTEs were found within 90 days of surgery. Out of 51 GI patients with stage IV colorectal cancer, 8 (4 PE and 4 DVT) VTEs were found within 90 days of surgery. There was also a similar trend in the occurrence of these VTEs in regards to time from surgery.

The study population was then separated into VTE and non-VTE groups in an attempt to identify significant risk factors for developing VTE. There were 30 patients in the VTE group and 364 patients in the non-VTE group. The risk factors investigated include history of VTE, BMI > 30 kg/m^2, stage IV disease, age > 65 years, and open surgery. The distribution of the two groups in respect to the risk factors is

Table 1
Patient characteristics.

	GI ($N = 204$)	GYN ($N = 190$)	*p*-Value
Age – year			
Median	61	62	0.5497
Range	21–91	32–86	–
>65 years – no. (%)	74 (36.2)	65 (34.2)	0.668
Male sex – no. (%)	121 (59.3)	0 (0.0)	–
Body-mass index			
>30 kg/m^2 – no. (%)	66 (32.4)	106 (55.8)	<0.001
Stage IV disease – no. (%)	58 (28.4)	19 (10.0)	<0.001
History of VTE – no. (%)	6 (2.9)	2 (1.1)	0.287
HIPEC – no. (%)	16 (7.8)	0 (0)	–

Table 2
Cancer diagnosis and staging.

	No. (%)	I	II	III	IV	Unknown
GI ($N = 204$)						
Anal	1 (0.5)			1		
Appendiceal	16 (7.8)	2	1		6	7
Colon	120 (58.8)	23	22	38	34	3
GIST	3 (1.5)	1	1			1
Rectal	59 (28.9)	12	6	23	17	1
Small intestine	5 (2.5)			4	1	
GYN ($N = 190$)						
Cervical	15 (7.9)	12	2	1		
Endometrial	91 (47.9)	64	7	10	9	1
Fallopian tube	4 (2.1)		2	2		
Hydatidiform mole	1 (0.5)					1
Mullerian	1 (0.5)					1
Ovarian	65 (34.2)	10	3	38	8	6
Primary peritoneal	8 (4.2)			3	2	3
Vulvar	2 (1.1)		2			

There was a single patient each with endometrial and ovarian cancer of stages I and I, with endometrial and ovarian cancer of stages I and III, and with gynecological cancer of unknown origin and stage.

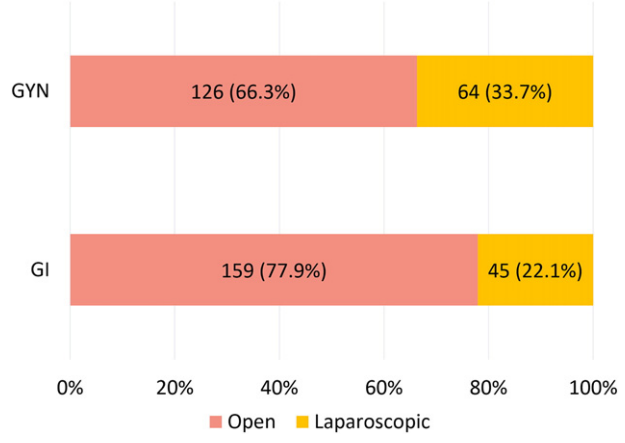

Fig. 1. Surgery type (open versus laparoscopic).