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SHORT COMMUNICATION

Extended venous thromboembolism prophylaxis after abdominopelvic cancer surgery: a retrospective review

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ABSTRACT

Objective Extended prophylaxis against venous thromboembolism (VTE) after abdominal or pelvic cancer surgery with low molecular weight heparin (LMWH) is recommended by multiple guidelines. The primary objective of the present study was to assess adherence to that guideline recommendation at tertiary care centres within Hamilton Health Sciences (HHS).

Methods Given that an estimated 70% of the study population would be expected to receive extended prophylaxis, a sample size of 105 patients was calculated. Patients who had undergone abdominal or pelvic surgery for cancer from March 2012 to December 2015 were identified, and data were collected from electronic health records. The primary outcome was prescription of extended VTE prophylaxis.

Results Of 105 patients, only 3 received extended VTE prophylaxis. Those 3 patients had serous carcinoma of the uterus, transitional cell carcinoma of the bladder, and cecal cancer. Of the 3 patients, 2 were followed by the thrombosis service while in hospital; none of the other 102 patients received any form of extended VTE prophylaxis.

Conclusions Based on multiple randomized controlled trials, guidelines suggest LMWH prophylaxis for up to 4 weeks after major abdominal or pelvic cancer surgery. Despite those recommendations, postoperative extended VTE prophylaxis is not commonly prescribed at HHS facilities. Next steps will include identification of barriers and an examination of how those barriers could be addressed. Failure to use prophylaxis is not consistent with evidence-based guidelines and is placing patients at risk of VTE.

Key Words Extended prophylaxis, cancer-associated thrombosis, low molecular weight heparin

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INTRODUCTION

Venous thromboembolism (VTE) can have long-term adverse effects on patients[1], and in the case of pulmonary embolism, it can be fatal. Thrombosis is the 2nd leading cause of death in patients with cancer[2], and it places a heavy financial burden on the health care system[3].

Patients with malignancy are at higher risk for VTE because of a hypercoagulable state[4]. The risk increases further after major surgery because of trauma and immobility. A prospective observational study by Agnelli *et al.*[5] found that VTE was the leading cause of mortality 30 days postoperatively in patients undergoing cancer surgery. Most thrombotic events occurred 21 days after the initial procedure.

Three randomized controlled trials have examined the use of extended VTE prophylaxis with low molecular weight heparin (LMWH), showing that extended regimens lower the incidence of VTE without significantly increasing hemorrhagic complications[6–8]. Based on those findings, guidelines[9–11] recommend that extended VTE prophylaxis be prescribed for patients undergoing abdominopelvic surgery for cancer.

Despite the available evidence, studies have shown that VTE prophylaxis is underused[12–15]. The primary objective of the present study was to assess adherence to guideline

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recommendations for the prescription of extended VTE prophylaxis at Hamilton Health Sciences (HHS).

METHODS

Population and Data Collection

Based on strong recommendations in evidence-based guidelines for use of extended VTE prophylaxis, we estimated that at least 70% of patients undergoing major abdominopelvic surgery for cancer would be expected to receive such prophylaxis. A sample size of 105 patients was calculated using WinPepi (freeware, available from http://www.brixtonhealth.com/pepi4windows.html), with an acceptable difference of 0.1.

Patients who had undergone abdominal or pelvic surgery for cancer from March 2012 to December 2015 were identified from discharge records. Patients were excluded if they had severe renal failure (creatinine clearance: <30 mL/min), contraindications to receiving LMWH, an inpatient stay exceeding 28 days, known VTE within the preceding 3 months, central nervous system hemorrhage, or a condition requiring full anticoagulation (for example, atrial fibrillation). Data for included patients were collected from electronic health records. To assess interrater reliability, a second data abstractor individually collected data from 10 randomly selected charts. Interrater reliability was excellent (Cohen kappa 1).

Outcomes

The primary outcome for this study was the provision of extended VTE prophylaxis. "Extended prophylaxis" was defined as a period of up to 28 days and was assessed by examination of the discharge summary or outpatient prescriptions for LMWH within 1 week of discharge. Any VTE events were recorded and verified by documentation of a positive Doppler ultrasound study, positive computed tomography pulmonary angiogram, or high probability ventilation–perfusion scan.

Ethics Approval

The study protocol was approved by the Hamilton Integrated Research Ethics Board (REB 2016-2250-C).

RESULTS

Population Characteristics

In the 105 charts that were reviewed, the most common sites of malignancy were colorectal (41%) and gynecologic (36%). All patients received general anesthesia, and 38% required a central venous line. Table I shows the clinical characteristics of the study population.

Prescription of Extended VTE Prophylaxis

Only 3 patients were prescribed extended VTE prophylaxis. Those 3 patients had serous carcinoma of the uterus, transitional cell carcinoma of the bladder, and cecal cancer. Of the 3 patients, 2 were followed by the thrombosis team while in hospital.

Caprini Risk Score

The 2012 guidelines from the American College of Chest Physicians use the modified Caprini risk score for stratification (outlined in Table II). It has been validated as an assessment tool for predicting risk of VTE in several surgical populations[16–18]. Almost all patients treated at HHS facilities (Table III provides operative details) were considered to be at high risk (score: ≥5), and most received points for major surgery, malignancy, and age. Except for 1 patient with a length of stay of 1 day, all patients received in-hospital pharmacologic VTE prophylaxis, and 41.9% had concomitant mechanical prophylaxis ordered in the form of thromboembolic-deterrent stockings or intermittent pneumatic compression (Table IV).

TABLE I Characteristics of patients undergoing abdominal or pelvic cancer surgery

Characteristic	Value	
Sex [*n* (%)]		
Men	39	(37.1)
Women	66	(62.9)
Median age (years)	62	
History of VTE [*n* (%)]	3	(2.9)
Antiplatelet use [*n* (%)]	27	(25.1)
Site of malignancy [*n* (%)]		
Gynecologic	38	(36.2)
Colorectal	43	(41)
Gastric	1	(0.9)
Hepatobiliary	2	(1.9)
Pancreatic	5	(4.8)
Urologic	6	(5.7)
Other[a]	10	(9.5)
Average BMI (kg/m^2)	28.08	
Average CrCl (mL/min)	100.1	
Caprini risk score		
Low [*n* (%)]	0	(0)
Moderate [*n* (%)]	2	(1.9)
High [*n* (%)]	103	(98.1)
Average score	7.28	

[a] Includes peritoneal carcinoma, neuroendocrine tumour, liposarcoma, adrenal cortical cancer.

VTE = venous thromboembolism; BMI = body mass index; CrCl = creatinine clearance.

Thrombotic Events

Of the patients who did not receive extended VTE prophylaxis and who were followed at HHS, 2 developed VTE after discharge. One patient developed deep vein thrombosis of the distal popliteal vein and trifurcation that required anticoagulation 6 weeks after discharge. Another patient was diagnosed with an acute right common femoral vein deep vein thrombosis approximately 7 weeks after discharge. Arterial events within 28 days of discharge occurred in 2 patients. One had right hemispheric embolic stroke, and the other had a left arm arterial thrombus requiring endarterectomy. Outcome ascertainment was incomplete because the patients could have sought care for thromboembolism outside HHS facilities; such events would have been missed in our data review.

TABLE II Modified Caprini risk score[a]

Points assigned			
1	**2**	**3**	**5**
■ Age 41–60 years ■ Minor surgery ■ BMI >25 kg/m^2 ■ Lower limb edema ■ Varicose veins ■ Pregnancy or postpartum ■ Unexplained or recurrent miscarriage or stillborn infant ■ OCP or HRT ■ Sepsis (<1 month) ■ Abnormal pulmonary function ■ Acute MI ■ CHF (<1 month) ■ IBD ■ Medical patient at bed rest	■ Age 61–74 years ■ Arthroscopic surgery ■ Major open or laparoscopic surgery (>45 min.) ■ Malignancy ■ Bed rest (>72 hours) ■ Immobilizing plaster cast ■ Central line	■ Age 75 years or older ■ Previous VTE ■ Family history of VTE ■ Factor V Leiden ■ Prothrombin 20210A ■ Lupus anticoagulant ■ Cardiolipin antibodies ■ Elevated serum homocysteine ■ Heparin-induced thrombocytopenia ■ Other congenital or acquired thrombophilia	■ Stroke (<1 month) ■ Elective arthroplasty ■ Hip, pelvis, or leg fracture ■ Acute spinal cord injury (<1 month)

Evaluation		
Very low risk	0 points	■ <0.5% risk of VTE without prophylaxis
Low risk	1–2 points	■ 1.5% risk of VTE without prophylaxis
Moderate risk	3–4 points	■ 3% risk of VTE without prophylaxis
High risk	≥5 points	■ 6% risk of VTE without prophylaxis

[a] From Gould *et al.,* 2012[9]. Reproduced with permission.
BMI = body mass index; OCP = oral contraceptive pill; HRT = hormone replacement therapy; MI = myocardial infarction; CHF = congestive heart failure; IBD = inflammatory bowel disease; VTE = venous thromboembolism.

TABLE III Admission and operative details

Variable	Value	
Length of stay (days)		
Median	5	
Quartiles 1, 3	4, 7	
Operation type [*n* (%)]		
Laparoscopic	21	(20)
Open	79	(75.2)
Converted	5	(4.8)
Median operation duration (min.)	269	
Central line insertion [*n* (%)]	40	(38)
Anesthesia type [*n* (%)]		
General anesthetic only	57	(54.3)
General anesthetic and spinal or epidural	48	(45.7)

Major Bleeding

Major bleeding was defined based on criteria outlined by the International Society on Thrombosis and Haemostasis: fatal bleeding, symptomatic bleeding in a critical area, surgical site bleeding requiring a second intervention, unexpected surgical site bleeding or extra–surgical site bleeding with a concomitant drop in hemoglobin of 20 g/L, or transfusion of 2 or more units of red cells[19]. No major bleeding occurred in the 3 patients who received extended VTE prophylaxis.

TABLE IV Prophylaxis for venous thromboembolism prescribed to patients postoperatively and in hospital

Variable	Dose	Value	
Extended prophylaxis [*n* (%)]		3	2.9
Dalteparin	(SC, 5000 U or 7500 U daily)	2	1.9
Enoxaparin	(SC, 40 mg daily)	1	1
In-hospital prophylaxis [*n* (%)]			
Pharmacologic			
None		1	1
Dalteparin	(SC, 5000 U daily)	53	50.5
Dalteparin	(SC, 7500 U daily)	4	3.8
Heparin	(SC, 5000 U twice daily)	30	28.6
Heparin	(SC, 5000 U three times daily)	16	15.2
Enoxaparin	(SC, 40 mg daily)	1	1
Mechanical			
None		61	58.1
TEDs		29	27.6
IPC		11	10.5
TEDs and IPC		4	3.8

SC = subcutaneously; TEDS = thromboembolic-deterrent stockings; IPC = intermittent pneumatic compression.

DISCUSSION

Upon discharge, only 3 of 105 patients who had abdominopelvic cancer surgery received extended VTE prophylaxis. The present retrospective study shows that, in this scenario and despite evidence-based guideline recommendations, extended VTE prophylaxis is underused. In contrast, almost all patients received in-hospital VTE prophylaxis with LMWH, and 41.9% of the patients had orders for additional mechanical prophylaxis. Based on the modified Caprini risk score, 98% of the patients in our study were at high risk for development of VTE (score: ≥5).

Our findings accord with those in other studies that have shown underuse of VTE prophylaxis[13,15]. A study conducted in the United States revealed that use of extended prophylaxis increased with time, but remained low. Using the Truven Health MarketScan database, the authors found that 1.7%, 18.3%, and 12.2% of patients undergoing surgery for colon, ovarian, and uterine cancer respectively were provided with extended prophylaxis[14].

Possible barriers to providing extended VTE prophylaxis include perceived cost, outpatient medication administration, and lack of awareness of evidence-based guidelines. Also, the broad description of patients who could benefit from extended prophylaxis in current guidelines might result in uneasiness. The guidelines from the American College of Chest Physicians use the Caprini risk score to recommend modalities of in-hospital prophylaxis; however, it is unclear whether the score also applies to extended prophylaxis. Iannuzzi *et al.*[20] examined the cost-effectiveness of extended prophylaxis with LMWH. Based on a quality-of-life adjusted life-year of $50,000, prophylaxis is recommended if the VTE incidence is greater than 2.39%. If the incidence falls between 0.88% and 2.39%, patient preference should be taken into account.

Limitations

Our study has several limitations that should be considered. Data collection relied on chart documentation, and prescription of extended prophylaxis was determined solely by discharge summaries and prescriptions. Factors that would have influenced a patient's calculated Caprini score might not have been rigorously documented (for example, bed rest, presence of varicose veins). Additionally, because of the focus on tertiary care centres, the population examined in this retrospective review might not be generalizable. We could not comprehensively assess rates of VTE in this population given that some patients received follow-up care at health care facilities outside HHS.

CONCLUSIONS

At HHS facilities, extended VTE prophylaxis was not commonly prescribed postoperatively for patients who underwent surgery for abdominal or pelvic cancer. In a study by Schmeler *et al.*[21], a quality improvement initiative—driven by a multidisciplinary team—that involved an educational retreat and updated postoperative order sets increased the rate of prescription for extended VTE prophylaxis and lowered the rate of VTE diagnosed after 30 days, but not after 90 days. Next steps will include the identification of barriers and an examination of how those barriers can be addressed to improve adherence to guidelines.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare the following interests: MC has sat on advisory boards for Octapharma and Bayer; he has participated in study steering committees or other research-related activities for projects involving Daiichi–Sankyo and Bayer; he holds a Career Investigator award from the Heart and Stroke Foundation of Ontario and the Leo Pharma Chair in Thromboembolism Research at McMaster University (income from which is used to support the salary of research employees); his institutions (either or both of McMaster University and St. Joseph's Healthcare) have received funding for research projects from the Heart and Stroke Foundation of Canada, Leo Pharma, and Bayer for work in which he is involved; he has received funding for preparation of educational materials or presentations (or both) from Alexion, Bristol–Myers Squibb/Pfizer alliance, Leo Pharma, Bayer, and CSL Behring; he has participated in various medicolegal activities relating to thrombosis, anticoagulant drugs, or other aspects of hematology practice, and those activities are bound by confidentiality arrangements. Further, this declaration is made to the best of MC's ability, but might be incomplete or contain material errors, given the foibles of human memory. This work was supported by a Regional Medical Associates scholarship to ML. ME has no conflicts to disclose.

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