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Original article

Effectiveness and safety of extended-duration prophylaxis for venous thromboembolism in major urologic oncology surgery

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Abstract

Purpose: To examine the association between extended-duration prophylaxis (EDP), low-molecular-weight heparin prophylaxis for 28 days after surgery for urologic cancer in patients at high risk of developing a venous thromboembolism (VTE), the risk of VTE, and the complications resulting from VTE prophylaxis.

Materials and methods: The cohort included 332 patients at high risk for VTE who were surgically treated for urologic cancer from June 2011 to June 2014. Adherence to VTE prophylaxis protocol, VTEs, and complications within 365 days from surgery were tracked. Patients were grouped as follows: (1) per protocol in-hospital prophylaxis with EDP ($n = 107$), (2) per protocol in-hospital prophylaxis without EDP ($n = 42$), (3) not per protocol in-hospital prophylaxis with EDP ($n = 83$), and (4) not per protocol in-hospital prophylaxis without EDP ($n = 100$). The risk of VTE was compared between the 4 groups using the Cox model, with adjustment for baseline risk factors.

Results: The rates of VTEs and median times to VTE were 7% and 58 days in group 1, 17% and 44 days in group 2, 17% and 46 days in group 3, and 21% and 15 days in group 4, respectively. Adjusted hazard ratios (HR) for VTE were HR = 0.27 (95% CI: 0.11–0.70) for groups 1 vs. 4; HR = 0.66 (95% CI: 0.25–1.60) for groups 2 vs. 4; and HR = 0.66 (95% CI: 0.29–1.26) for groups 3 vs. 4 with a trend of $P = 0.002$. The incidence of complications from VTE prophylaxis was not significantly different between the groups, with a rate of 8% in group 1, 17% in group 2, 6% in group 3, and 12% in group 4 ($P = 0.33$).

Conclusions: In high-risk urologic cancer surgery patients, a clinical protocol, with perioperative and EDP, is safe and effective in reducing VTE events.

Keywords: Venous thrombosis; Prevention and control; Pulmonary embolism; Neoplasms; Surgery

1. Introduction

Venous thromboembolism (VTE) remains a common cause of morbidity and mortality following urologic cancer surgery. VTEs, including deep vein thromboses and pulmonary embolisms (PEs), remain the most common non-surgical complication [1,2]. Given that postoperative VTE is the third most common adverse safety event in hospitalized patients, it is likely that VTE prevention initiatives will increase over time. As the need to reduce hospital-acquired VTE becomes more prominent, the concept of extended-duration prophylaxis (EDP) also is becoming more important [3,4].

Despite major reductions in VTE after surgery for urologic malignancy owing to the systematic application of some preventative recommendations, the occurrence of VTEs remains high [1]. Contemporary reports following

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specific urologic surgeries demonstrate that VTE rates vary, and similarly, so do VTE prophylaxis strategies. In the absence of VTE prophylaxis for major urologic surgeries, deep vein thrombosis incidence was estimated somewhere between 10% and 30%. The PE incidence was approximately 10%, 5% of which were reportedly fatal [5,6]. Specifically, VTE risk associated with radical cystectomy was found to be between 0.8% and 24% [6–12], nephrectomy 0.24% and 22.6% [6,9], and prostatectomy 1% and 11% [6,9,12,13].

Recently, several studies have been published reporting a reduction in VTE incidence in high-risk surgical patients with EDP and the safety associated with its use. It is estimated that after oncologic surgery, the incidence of VTE diagnosed after discharge but within 30 days is between 30.6% and 37.8% [1,14,15]. Several randomized studies have shown EDP to be more effective than limited duration prophylaxis (in-hospital only) in VTE incidence reduction after surgery for cancer [16,17]. Furthermore, a systematic review by the Cochrane group concluded that the administration of low-molecular-weight heparin (LMWH) for 4 weeks after major abdominal or pelvic surgery reduces VTE incidence without increased bleeding complications [18]. Given that the risk of VTEs remains elevated after surgery beyond discharge, there have been calls from many organizations to prescribe EDP in high-risk patients. Currently, the National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), and the American Academy of Chest Physicians (ACCP) have set forth guidelines recommending EDP in high-risk patients with LMWH for 4 weeks (Refer to Fig. 1 for exact recommendations) [19–21].

Despite these recommendations and evidence of EDP benefit, EDP employment has been suboptimal [2]. Barriers to EDP implementation have been the perceived increased complications (i.e., lymphoceles and bleeding), patients' aversions toward method of administration, and patients' costs to buy LMWH. Multiple publications refute increased bleeding and low acceptance among patients' as reasons to withhold EDP exist [1,16,22–24]. To date, there are few urology-specific recommendations for EDP. Our main objective was to evaluate a protocol instituted to achieve a reduction in VTE events and to assess the safety of its administration in high-risk urologic oncology patients undergoing major surgery.

2. Subjects and methods

2.1. VTE prevention protocol implementation

After institutional review board approval, a protocol for VTE prevention based on the ACCP, NCCN, and ASCO recommendations was implemented [21]. The protocol consisted of administration of preoperative heparin prophylaxis (within 8 h preoperatively) and postoperative pharmacologic prophylaxis (within 8 h after wound closure) in addition to intermittent pneumatic compression devices already in use. Because there has been little difference found between low-dose unfractionated heparin and LMWH in preventing VTE, low-dose unfractionated heparin as initial postoperative prophylaxis was considered per protocol if given at appropriate dose and intervals. The LMWHs, dalteparin 5,000 units or enoxaparin 40 mg, were administered subcutaneously and, if needed, doses were adjusted per manufacturer recommendations for weight and renal function. Patients were given formal self-administration training of the prophylactic medications by registered nurses at discharge.

2.2. Risk assessment

All patients undergoing major surgery for urologic cancer were evaluated using the Caprini risk assessment score (CRS) (Fig. 2) [6,22–25]. This model has been previously validated in urology patients and, retrospectively, in assigning risk scores. All elements of the CRS were evaluated at admission for surgery starting in July 2012. Retrospective risk assessment was used for patients undergoing urologic cancer surgery between June 2011 and June 2012, the charts were reviewed continuously, and those qualifying as high risk (CRS $\geq$ 8) were included for comparison analysis. A CRS $\geq$ 5 is often considered high risk; however, the version of CRS used for this study (Fig. 2) is more comprehensive,

ACCP, NCCN, ASCO Summary of Recommended VTE Prophylaxis for High-risk Patients Undergoing General and Abdominal-Pelvic Surgery

(General, Bariatric, GI, Gynecologic, Vascular, Urologic, Plastic and Reconstructive Surgery)

1. All patients undergoing major surgical intervention for malignant disease should be considered for thromboprophylaxis.
2. Patients undergoing laparotomy, laparoscopy, or thoracotomy lasting >30 minutes should receive pharmacologic thromboprophylaxis with either low-dose unfractionated heparin or low molecular weight heparin unless contraindicated because of a high-risk of bleeding or active bleeding.
3. Prophylaxis should be started preoperatively.
4. Mechanical methods should be used in addition to pharmacologic prophylaxis
5. Prolonged prophylaxis for up to 4 weeks should be considered in patients undergoing major abdominal or pelvic surgery for cancer with high-risk features.

Fig. 1. Summary of multiple organization's recommendations for VTE prophylaxis in the setting of general and abdominal-pelvic surgery in high-risk patients.