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News and topics

The role of extended venous thromboembolism prophylaxis following urologic pelvic surgery

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Abstract

With the emergence of evidence that venous thromboembolisms (VTE) typically occurs following discharge after urologic pelvic surgery, the focus on extended VTE prophylaxis has intensified. Urologists should have a comprehensive understanding of various VTE risk factors in order to weigh the risk of postoperative hemorrhage with the possibility of fatal pulmonary embolus. Risk factors such as advanced age, obesity, and active malignancy are especially common in patient's undergoing urologic pelvic surgery, and thus this issue becomes particularly relevant to the practicing urologist. In previous years, guidelines on extended VTE prophylaxis have either been vague or not urology specific; however, the European Association of Urology has recently issued recommendations on VTE prophylaxis stratified by VTE risk and surgery type. Although these guidelines are a major advance, definitive answers on this question may prove elusive in the form of prospective randomized data given the low incidence of clinically significant postoperative VTE.

Keywords: pelvic surgery; venous thromboembolism; deep venous thrombosis; pulmonary embolism; prevention

The American Urological Association (AUA) best Practice Policy Statement (BPS) [1], American Society of Clinical Oncology clinical practice guideline [2], United Kingdom National Institute for Health and Clinical Excellence (NICE) [3], and Australian National Health and Medical Research Council (NHMRC) [4] guidelines all recommend use of thromboprophylaxis (TP) for all appropriate medical and surgical patients. In fact, the Joint Commission mandates venous thromboembolism (VTE) prophylaxis to be a patient safety goal and that the metric of compliance be tracked as a hospital's core performance measure [5].

By definition, postoperative (VTE) is venous thrombus in the deep pelvic or lower extremity vessels (DVT) or a pulmonary embolism (PE). In addition to the morbidity and mortality associated with VTE, its economic impact on health care is substantial [6]. VTE is a leading cause of death in patients with cancer and in those who undergo abdominal extirpative surgery [7]. Some estimates place the rate of VTE events following urologic pelvic cancer surgery without appropriate prophylaxis at over 20% and robust clinical data support the use of TP in reducing VTEs following cancer surgery [8]. Emerging data on patient outcomes 30 days after discharge reveal that a large proportion of symptomatic VTE events occur following hospital discharge [9]. Several professional organizations now recommend use of extended pharmacological venous thromboembolism prophylaxis (EPVTEP) for a 4-week duration following major abdominal and pelvic surgery [9–12]. Based on rigorous systematic reviews of available literature, these guidelines provide valuable resources on proper use of prophylaxis in specific management of surgical patients. Despite recommendations, there is a lack of familiarity with existing guidelines and also reluctance to apply some of these guidelines among practicing physicians [13]. This review aims to summarize the risk factors for VTE and to provide evidence, rationale, and recommendations for EPVTEP for patients undergoing urologic pelvic surgery.

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Risk Factors

When assessing a patient's risk factors for DVT, it is critical to assess the patient's predisposing clinical factors and the inherent risk factors that arise from the surgical procedure itself. Age, presence of malignancy, trauma, medication profile, history of DVT, and immobility are some of the patient-specific predisposing factors (Table 1).

In patients with cancer, the risk of VTE is significantly elevated [14]. The origin of the primary cancer has been shown to influence risk, with the highest rates of VTE seen among patients with pancreatic, stomach, bladder, kidney, and hematologic malignancies. Anemia, leukocytosis, thrombocytosis, and systemic therapies further increase the risk of VTE in patients with cancer [14–16]. These risk factors for thrombosis such as the hypercoagulable state, hemodynamic stasis, and endothelial dysfunction (Virchow's triad [17]) can last for many weeks following surgery [18]. Petterson et al. estimated VTE risk by cancer site using local county data on residents with active malignancy and incident VTE over a 13-year period. With the aid of Surveillance Epidemiology and End Results data to estimate the expected prevalence of cancer by cancer site, the age- and sex adjusted risk ratio of VTE for kidney cancer, bladder cancer, and prostate cancer were 2.16-, 2.14-, and 1.70-fold higher than reference group, respectively [19]. Based on clinical and laboratory measures, a validated risk score for cancer-associated VTE has been established [20] (Table 2).

Evidence and guidelines

Although there has been general agreement on the need for pharmacologic VTE prophylaxis in high-risk surgical patients [1–4], the role for EPVTEP in *urologic* patients had not been as clearly defined until the recent publication of the European Association of Urology (EAU) guidelines on TP [9]. For example, the American College of Chest Physicians (ACCP) guidelines pertain to "non-orthopedic surgical patients" and recommend EPVTEP for those at high-risk for VTE undergoing abdominal/pelvic cancer surgery and not at high risk for major bleeding complications [21]. The ACCP uses the validated Caprini score to risk stratify patients and the majority of patients with urologic malignancies easily fall into the high-risk group (≥5 points: 2 points for open or laparoscopic surgery ≥45 min, 2 points for malignancy, and 1 point for age 41–60). This ACCP guideline is based on multiple systematic reviews including the Cochrane Database which compared EPVTEP with limited-duration prophylaxis and found a statistically significant increased incidence of VTE after major abdominal/pelvic surgery of 14.3% in the control group as compared to 6.1% in the out-of-hospital low molecular weight heparin (LMWH) group [22]. EPVTEP was also associated with a statistically significant decreased risk of symptomatic VTE from 1.7% to 0.2% in patients receiving prolonged TP. There was no difference in major bleeding and mortality outcomes in these studies.

Much of the debate over EPVTEP studies stems from the clinical significance of an asymptomatic VTE detected on venogram. In 2010 Kakkar et al. [23] conducted a randomized double-blinded controlled trial using LMWH in patients undergoing major abdominal/pelvic cancer surgery. Patients received bemiparin for 8 days and then were randomized to receive LMWH or placebo. Bilateral venography was performed after 20 days. There was no difference in the primary outcomes which were a composite of total number of DVT, nonfatal PE, and all-cause deaths between the LMWH and placebo groups (10.1% vs. 13.3%, respectively, $P = 0.26$). Additionally, there was no difference in the risk of major bleeding between the groups. However, there was a significantly lower incidence of the secondary outcome of "major VTE" (proximal DVT, nonfatal PE, and VTE-related deaths) in the bemiparin group compared to control (4.6% vs. 0.8%, relative risk reduction 82.4%,

Table 1
Risk factors for DVT [1,30]

Risk factors for DVT
History of DVT
Immobility (surgery, trauma, or paresis)
Age
Obesity
Presence of malignancy (refer to Table 2)
Major trauma
Pregnancy (including postpartum period)
Oral contraceptives and estrogen replacement therapy
Inflammatory bowel disease
Myeloproliferative disorders
Cardiopulmonary failure
Renal failure
Central venous catheterization
Acute medical illness
Thombophila
Varicose veins

Table 2
Calculating risk score for predicting VTE in patients with cancer [20]*

Patient characteristics	Risk score
Site of cancer	
Very high risk (stomach and pancreas)	2
High risk (lung, bladder, prostate, testicular, lymphoma, and gynecologic)	1
Prechemotherapy platelet count ≥350,000/mm^3	1
Hemoglobin level < 10 g/dl or use of red cell growth factor	1
Prechomotherapy leukocyte count > 11,000/mm^3	1
Body mass index ≥35 kg/m^2	1

High-risk score ≥ 3; intermediate-risk score = 1–2; and low-risk score = 0.

Note: Primary brain tumor and myeloma and impact of prior VTE were not assessed in this study.