Gynecologic Oncology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Gynecologic Oncology

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

Review Article

Prevention of venous thromboembolism in gynecologic oncology surgery

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HIGHLIGHTS

- Venous thromboembolism is a major source of postoperative morbidity and mortality.
- Dual prophylaxis is recommended for gynecologic oncology laparotomy patients.
- Minimally invasive surgery requires less prophylaxis than open surgery.

ARTICLE INFO

Article history:
Received 1 September 2016
Received in revised form 13 November 2016
Accepted 21 November 2016
Available online xxxx

Keywords:
Venous thromboembolism
Pharmacologic prophylaxis
Gynecologic surgery
Deep vein thrombosis
Pulmonary embolism

ABSTRACT

Gynecologic oncology patients are at a high-risk of postoperative venous thromboembolism and these events are a source of major morbidity and mortality. Given the availability of prophylaxis regimens, a structured comprehensive plan for prophylaxis is necessary to care for this population. There are many prophylaxis strategies and pharmacologic agents available to the practicing gynecologic oncologist. Current venous thromboembolism prophylaxis strategies include mechanical prophylaxis, preoperative pharmacologic prophylaxis, postoperative pharmacologic prophylaxis and extended duration pharmacologic prophylaxis that the patient continues at home after hospital discharge. In this review, we will summarize the available pharmacologic prophylaxis agents and discuss currently used prophylaxis strategies. When available, evidence from the gynecologic oncology patient population will be highlighted.

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http://dx.doi.org/10.1016/j.ygyno.2016.11.036
0090-8258/

Disclosure statement . . . 0
Presentations . . . 0
Financial support . . . 0
References . . . 0

1. Venous thromboembolism incidence and sequelae

Venous thromboembolism is a major cause of morbidity and mortality for patients with gynecologic cancers. Patients with malignancies and those undergoing pelvic surgery are known to be at higher risk of venous thromboembolism, making gynecologic oncology patients a particularly high-risk group. This increased risk for pelvic surgery patients is secondary to emboli that can arise from the lower extremities as well as the pelvic veins. When detected by a ^{125}I-fibrinogen uptake scan, postoperative venous thromboembolism rates for patients undergoing gynecologic surgery in the absence of prophylaxis are as high as 15–40% [1]. A prospective study of 2373 patients undergoing general, gynecologic, or urologic surgery for cancer reported a 2.1% 30-day incidence of clinically recognized venous thromboembolism [2]. There was a 2.0% incidence specifically among gynecologic oncology patients, 81% of whom received in hospital chemoprophylaxis and 30% of whom received extended duration prophylaxis at home. The overall death rate within 30-days of surgery was 1.7% with 46.3% of the deaths attributable to venous thromboembolism, making it the most common cause of postoperative death in this series. National statistics also suggest that pulmonary embolism is a common cause of preventable hospital death [3]. Venous thromboembolism has recently emerged as a quality metric by which hospitals are compared to one another [4].

When patients with gynecologic cancers experience a venous thromboembolism, mortality is increased. For patients with ovarian cancer, the incidence of postoperative venous thromboembolism has been reported to be as high as 13.2%, even in the setting of prophylaxis, and postoperative VTE increases the mortality rate 2.3 times compared to patients who do not experience a venous thromboembolism [5]. Among endometrial cancer patients, venous thromboembolism also increases mortality. One study found that for endometrial cancer patients >65 years of age, the incidence of venous thromboembolism within 6 months of diagnosis was 8.1%. For patients who experienced a venous thromboembolism within 6 months of diagnosis, mortality was increased 1.5 times compared to those without a venous thromboembolism [6]. It is important to note that this study included all stages of endometrial cancer, only patients >65 and used a time period of 6 months which likely accounts for the high observed cumulative incidence. Venous thromboembolism incidence also varies by histology for endometrial cancer patients. Patients with low grade (grade 1 or 2) histology have a venous thromboembolism incidence within 6 months of diagnosis of 3.6% compared to 6.1%–9.2% for grade 3 endometrioid and other high-risk histologies. Additionally, the type of malignancy is associated with risk of venous thromboembolism with ovarian cancer patients having the highest incidence among gynecologic cancers [7,8]. Given the high incidence of venous thromboembolism among patients with gynecologic cancer and the availability of prophylaxis regimens to prevent venous thromboembolism, a structured and comprehensive plan for perioperative prophylaxis is necessary to care for these patients.

2. Risk assessment

Virchow proposed a triad of risk factors contributing to venous thromboembolism: venous stasis, endothelial injury and hypercoagulable states. Many retrospective studies have given more specific risk factors such as increasing age, extent of surgery, length of surgical procedure, and many more. A prospective study specific to women undergoing gynecologic surgery found the following were independent risk factors (when evaluated by multivariable analysis): age, personal history of venous thromboembolism, cancer, African American race, prior pelvic radiation therapy, evidence of prior venous disease (varicose veins, ankle edema), blood loss and prolonged operating time. A risk assessment model was proposed, but has never been validated [9].

Currently, the American College of Chest Physicians (ACCP) recommends using risk assessment tools to assess postoperative venous thromboembolism risk among patients undergoing surgery [10]. According to these guidelines, patients are stratified preoperatively into one of 4 risk categories: very low risk, low risk, moderate risk and high risk. These categories are based upon the relative venous thromboembolism incidence if no VTE prophylaxis is given. Specifically, very low risk patients have an incidence of <0.5%, low risk patients have an incidence of 1.5%, moderate risk patients have an incidence of 3.0%, and high-risk patients have a 6.0% incidence. The ACCP recommends that patients be categorized into these risk groups based on two different risk assessment tools, the Caprini score or the Rogers score (Table 1 and Table 2).

Both risk assessment tools provide a score based on patient and procedure risk factors that are associated with venous thromboembolism. These scores formalize the known relationships between various risk factors for venous thromboembolism that have been confirmed in large studies and assigned a relative weight to each in the form of points. Patients >60 years-old, those with cancer, those undergoing >2 h of anesthesia, those with bed-rest of >4 days, higher Charlson co-morbidity scores, longer hospital stays and a personal history of venous thromboembolism are all factors that are known to increase venous thromboembolism risk [10]. Patients who experience postoperative complications, such as blood transfusions, pneumonia, and urinary tract infections, are also more likely to experience a postoperative venous thromboembolism than those who do not [11].

The Caprini score is a risk assessment score that was developed by Joseph Caprini in the early 1990s (Table 1) [12]. It assigns points to various venous thromboembolism risk factors and each patient is categorized by their resulting score as being at low, moderate, high or very high risk of venous thromboembolism. The score has the benefit of being easy to use and it has been used in practice by many surgical specialties, including validation studies in both general surgery patients and plastic and reconstructive surgery patients [13–15]. The Caprini score has also been studied in gynecologic oncology patients. A retrospective study calculated the Caprini score for 1123 patients undergoing laparotomy with a gynecologic oncologist over a 7-year period and used the score as a predictor of venous thromboembolism. They found that 92% of patients scored in the highest risk category with a score of 5 or greater [16]. They observed a venous thromboembolism incidence of 3.3%. All patients in this study received mechanical prophylaxis and 40% received pharmacologic prophylaxis. All patients who experienced a venous thromboembolism were categorized in the highest risk group, meaning that in this population, the Caprini score was a highly specific tool for ruling out venous thromboembolism (100% of the patients with a score of <5 did not experience a thromboembolism). However, the Caprini score was not a very sensitive tool, as only 37 of the 1033 patients with a score of 5 or greater experienced a venous thromboembolism (sensitivity 3.6%). A series of 17,713 patients, all with gynecologic cancers, reported from a national quality database, confirmed this with 97% of patients scoring in the highest risk group with a Caprini score of 5 or greater [7]. When the highest risk group was sub-stratified by score, the Caprini score was useful in discriminating relative venous

Please cite this article as: E.L. Barber, D.L. Clarke-Pearson, Prevention of venous thromboembolism in gynecologic oncology surgery, Gynecol Oncol (2016), http://dx.doi.org/10.1016/j.ygyno.2016.11.036