Risk factors for venous thromboembolism after benign hysterectomy

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Background

Venous thromboembolism (VTE), presenting in deep vein thrombosis (DVT) and pulmonary embolism (PE), remains a significant cause of post-surgical morbidity and mortality. In the past three decades, a number of trials have shown that thromboprophylaxis is highly effective, both with pharmacological and mechanical methods. (1) Unfractioned heparin (UFH) and low molecular weight heparin (LMWH) are the most commonly used pharmacologic agents for thromboprophylaxis. Many clinical trials indicate that heparins are a reliable method to decrease VTE in postoperative patients. (1,2) However, decision regarding the method, dose, and timing of prophylaxis depend upon balancing a patient's risk of thrombosis versus peri-operative bleeding. (3)

Without thromboprophylaxis the incidence of VTE in patients undergoing major open gynecological surgery ranges from 15 % to 40 %, which is the same as for general surgery. (4) There is little evidence regarding the incidence of VTE in patients undergoing minimally invasive surgery. As a result, there are no specific guidelines referring to prevention of VTEs in patients undergoing minimally invasive surgery. (5) Most data are several years or even decades old and do not take into account developments in surgical techniques. The strong body of evidence in favour of VTE prophylaxis means it would be unethical to make randomized control trials that include patients undergoing gynecological surgery and not receiving VTE prophylaxis. The development of minimally invasive surgery, advances in regional anesthesia, shorter recovery times, earlier mobilization and more procedures being done as day-surgeries mean the incidence of VTE would most likely be lower if similar studies were done today. (6) On the other hand more surgeries are performed on older patients with more comorbidities and thus with higher baseline risk of VTE.

Several risk assessment models that stratify patients according to their risk of VTE have been published. (7-9) The Caprini score, which includes 39 different risk factors, is by far the most widely used tool for VTE risk assessment and has been validated in both medical and surgical populations. It is believed to be transferrable to gynecological surgery but has not been specifically validated for this sub group of patients. (10,11) The American College of Chest Physicians systematically summarized the literature related to the prevention of VTE based, in part, on evidence from general surgery, urology, and colorectal literature and from this provided recommendations for gynecological surgery. (12) However, conclusions on the efficacy and safety of various methods of thromboprophylaxis drawn from studies including men and patients undergoing nongynecological procedures may not be directly applicable to gynecological surgery populations.

Selection of VTE prophylaxis can be complex, particularly with the scarcity of VTE data specifically looking at gynecological surgery. Review of the existing literature suggests the use of thromboprophylaxis is highly variable among gynecological departments. Prevention strategies for VTE start with the identification of risk factors. The primary aim of this study is to determine risk factors specific to hysterectomy associated with postoperative VTE using the Swedish National Quality Registry of Gynecological Surgery (GynOp). Our secondary aim is to see if there are any characteristics for women undergoing hysterectomy that indicate a very low risk for VTE and therefore would not need thromboprophylaxis.

Aims of the study

1. To analyze risk factors of VTE in patients undergoing benign hysterectomy.

2. To find characteristics for women with low risk getting a VTE after hysterectomy.

Methods

Design

Prospective registry based observation study.

Selection

Hysterectomy cases for benign indication between 2008 – 2018 registered in the Swedish National GynOp Registry. Cases of DVT and PE diagnosed within 8 weeks of surgery were identified through validated patient reported questionnaires after eight weeks.

Studied variables:

- PATIENT CHARACTERISTICS: Age, BMI, history of VTE, smoking status, HRT, oral contraceptive, American Society of Anesthesiology classification (ASA).
- PERIOPERATIVE VARIABLES: Route of hysterectomy (abdominal, vaginal, conventional laparoscopic, laparoscopic-assisted vaginal, robotic-assisted laparoscopic), surgical time, estimated blood loss, major complications (in the GynOp registry, major complications were defined as injury to the bowel, urinary tract, nerves, or vessels that caused reoperation or hospitalization for more than seven days or persistent physical handicap or death, bleeding of more than 3000 ml or leading to reoperation, infection that led to readmission, deep vein thrombosis or pulmonary embolism, and any other major complication (i.e. aspiration, allergic shock, myocardial infarct, or cerebral complication), admission time, length and type of thromboprophylaxis.
- POSTOPERATIVE QUESTIONS regarding VTE are Yes/ No questions registered by the doctor and the patient.

Collection of data

Data will be extracted from the GynOp registry, which started in 1997 and contains preoperative, intraoperative and postoperative information on women undergoing gynecological surgery. Data are collected using doctors' forms, on paper or online, and validated patient questionnaires administered as part of routine medical care. Women are included in the registry before surgery by the operation planner whenever a gynecological surgery is planned.

Statistics

Categorical data is analyzed by Pearson's chi-square or Fisher's exact test. Continues variables are analyzed using the Student's t-test or ANOVA with Bonferroni's post hoc test. A p-value <0.05 will be considered to be statistically significant. Multiple linear and logistic regression analyses will be used to determine the incidence of VTE as well as pharmacologic prophylaxis. Statistical analyses will be performed using SPSS (IBM Corp, Armonk, NY, USA) or R version 3.5.2 and subversions.

Ethical approval

Ethical board of the University of Umeå, Sweden, no. 2013-236–32 M (additive to 08–120 M).

Meaning

VTE is the most common preventable cause for post-surgical mortality. Much research has been done on VTE prevention in general population as well as risk-assessment tools, but little has been published looking specifically at VTE related to gynecological procedures and even less when considering improvements in surgical techniques. Pharmacological thromboprophylaxis has been shown to decrease the risk of VTE but also increase the risk of bleeding during and immediately following surgery. Balancing the risk of bleeding with the risk of thrombosis is therefore necessary and risk-assessment tools more closely tailored to specific patient groups and surgical techniques may thus give a more accurate risk assessment and allow a more customized approached to thromboprophylaxis; minimizing the risk of VTE while lowering the risk of perioperative bleeding. This study aims to look specifically at patients undergoing hysterectomy using different surgical techniques in order to identify factors correlating to very low risk of DVT and where the use of heparins can be safely reduced, or in some instances avoided completely.

Time schedule

Time allocated for this project is 3 weeks for writing project plan and data collection starting in spring 2019. Thereafter 3 weeks is allocated for data analyzing starting in autumn 2019. The manuscript writing is estimated to 3-4 weeks late 2019.

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