HHS Public Access

Author manuscript

J Minim Invasive Gynecol. Author manuscript; available in PMC 2015 March 16.

Published in final edited form as:

J Minim Invasive Gynecol. 2013 ; 20(6): 766–769. doi:10.1016/j.jmig.2013.06.001.

Venous thromboembolic events in minimally invasive gynecologic surgery

Pedro T. Ramirez, MD[*], **Alpa M. Nick, MD**, **Michael Frumovitz, MD**, and **Kathleen M. Schmeler, MD**

Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas 77030, United States

Abstract

The rate of venous thromboembolic events (VTE) including deep venous thrombosis (DVT) and pulmonary embolism (PE) among women undergoing gynecologic surgery is high, particularly for women with a gynecologic malignancy. Current guidelines recommend VTE thromboprophylaxis in the immediate postoperative period for patients undergoing open surgery. However, the VTE prophylaxis recommendations for women undergoing minimally invasive gynecologic surgery are not as well established. The risk of VTE in patients undergoing minimally invasive surgery appears to be low based on retrospective analyses. To date, there are no established guidelines that specifically provide a standard of care for patients undergoing minimally invasive gynecologic surgery for benign or malignant disease.

Introduction

The most common cause of preventable deaths in hospitalized patients in the United States is venous thromboembolic events (VTEs), including deep venous thrombosis (DVT) and pulmonary embolism (PE) (1). Among women undergoing major gynecologic surgery without thromboprophylaxis, the risk of DVT ranges from 17% to 40% (2). Among women undergoing surgery for gynecologic cancer the risk of DVT is even higher without thromboprophylaxis. VTEs can develop late in the postoperative period. A study by Schmeler et al. showed that median time between surgery and VTE was 57 days prior to implementation of strict guidelines of routine treatment with 28 days of anticoagulation in the immediate postoperative period (3). Martino et al. (4) estimated the incidence of PE among 507 patients with known or suspected gynecologic cancer undergoing major intraabdominal surgery, including laparoscopy, and found that the risk of postoperative PE

[*]Corresponding author: Pedro T. Ramirez, MD, Department of Gynecologic Oncology & Reproductive Medicine, Unit 1362, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, Texas 77030. Phone: (713) 745-5498. Fax: (713) 792-7586. peramire@mdanderson.org.

Conflict of Interest: The authors report no conflict of interest.

in patients with a diagnosis of cancer was 14 times the risk of postoperative PE in those with benign disease.

It has been suggested that the risk of VTE may be reduced in patients undergoing minimally invasive gynecologic surgery compared to open surgery because minimally invasive surgery is associated with less surgical trauma, infrequent use of retractors, shorter hospital stay, and faster return to daily activities; however, to date, there are no published prospective studies evaluating this important question in gynecologic surgery.

Herein we review the recent literature on the risk of VTEs in women undergoing minimally invasive gynecologic surgery, the consequences of VTEs and the cost of thromboprophylaxis, as well as current guidelines and clinical practice with respect to thromboprophylaxis in women undergoing minimally invasive gynecologic surgery.

Risk of VTEs in Patients Undergoing Minimally Invasive Gynecologic Surgery

One of the first studies to evaluate the incidence of VTEs in patients undergoing gynecologic laparoscopy was a prospective study of 266 consecutive patients undergoing gynecologic laparoscopy for benign indications (5). The investigators used compression ultrasonography and clinical assessment to determine the incidence of clinically relevant VTEs. No patient received pharmacologic or mechanical prophylaxis. The most common indications for surgery were ovarian cysts and endometriosis. The mean duration of surgery was 60.5 minutes (range, 10–300 minutes). The investigators found that there were no episodes of DVT in any of the patients. The authors concluded that gynecologic laparoscopy in noncancer patients is associated with a low risk of postoperative VTEs.

Nick et al. (6) estimated the incidence of DVT and PE diagnosed within 6 weeks after surgery among patients undergoing gynecologic laparoscopy. Six of 849 patients (0.7%) developed symptomatic venous thromboembolism. The median time to diagnosis was 15.5 days (range, 1–41 days). However, of the 430 patients from this cohort undergoing surgery for a gynecologic malignancy, five (1.2%) developed a postoperative VTE. Furthermore, the rate of VTE in patients who underwent high-complexity procedures, defined as radical hysterectomy, pelvic and/or para-aortic lymphadenectomy, splenectomy, or small bowel and/or colon resection, was 2.8%. In that study, the authors found that obesity or operative time was not associated with a higher risk of VTE. The authors concluded that patients undergoing high-complexity procedures may benefit from postoperative anticoagulation.

A subsequent study by Ritch et al. (7) examined the risk of VTE and the use of thromboprophylaxis in women undergoing laparoscopic hysterectomy. The investigators used a health outcomes, resource utilization, and quality database to gather data for the period from 2003 through 2007. In 60,013 women, 579 (1.0%) VTEs were noted. Venous thromboembolism was diagnosed in 2.1% of women aged 60 years or older and in 2.3% of women with cancer. Interestingly, 23,562 patients (39.3%) received no thromboprophylaxis, 29,288 (48.8%) received mechanical prophylaxis, and 7,163 (11.9%) received pharmacologic prophylaxis. The authors also noted that the number of patients in a

physician's practice was an important factor in prophylaxis, with patients treated by high-volume physicians being more likely to receive pharmacologic prophylaxis. The authors concluded that among patients undergoing laparoscopic hysterectomy, older women, women with medical comorbidities, and women with cancer are at substantial risk of VTE and that prophylaxis use is highly variable. These investigators suggested the use of pharmacologic prophylaxis in women older than 60 years of age, with medical comorbidities, and with cancer.

In a recent study, Sandadi et al. (8) specifically evaluated the incidence of postoperative VTE among patients undergoing minimally invasive surgery for endometrial cancer. A total of 573 patients were evaluated. Postoperative low-molecular-weight heparin was administered to 125 patients (22%) during their immediate postoperative hospital stay. All patients had sequential compression devices placed intraoperatively and continued during hospitalization. Seven patients (1.2%) developed symptomatic VTE. The investigators found that factors associated with increased risk of postoperative VTE were body mass index of 40 kg/m^2 or higher and an operative time of 180 minutes or more. The incidence of VTE was 9.5% in this high-risk group, compared with 0.6% in all other patients. The authors noted that postoperative low-molecular-weight heparin was administered to 45% of patients in the high-risk group compared to 20% of the other patients.

The most recent evaluation of the prevalence of VTEs after minimally invasive surgery specifically looked at patients with endometrial and cervical cancers (9). This was a retrospective multi-institutional study that determined the 30-day prevalence of VTEs following minimally invasive surgery. A total of 558 patients were included in the analysis, 90% diagnosed with endometrial cancer and 10% diagnosed with cervical cancer. The modalities of hysterectomy included robotic (88%), vaginal (9%), and laparoscopic (3%). The methods of thromboprophylaxis were sequential compression devices (100%) and heparin (39%). The authors found that there were no VTEs during the hospital stay, and the 30-day prevalence of VTEs was 0.5%. The authors stated that the existing guidelines proposed by ACOG and ASCO, as defined below, for predicting the risk of VTEs within 30 days after surgery are based on results from open surgery and may not be applicable to patients undergoing minimally invasive surgery.

Recently, the Gynecologic Oncology Group published the results of an important prospective randomized trial of open versus laparoscopic hysterectomy for endometrial cancer (GOG-LAP2) (10). Patients were randomly assigned 2:1 to laparoscopy or open surgery, and 1,248 of 1,682 patients (74%) underwent laparoscopic hysterectomy. The rate of documented PE for patients undergoing laparoscopic surgery was 1%. There were no differences in the incidence of VTE between patients undergoing open and laparoscopic hysterectomy.

Large-scale studies in other specialties have confirmed the findings in the gynecologic literature. A study that evaluated 5,951 patients from 13 referral centers in Europe and the United States who underwent radical prostatectomy via a minimally invasive approach found that the rate of DVT was 0.5% while the rate of PE was 0.2%. The median time to development of DVT was 10 days, while the median time to development of PE was 11 days

(11). Interestingly, the investigators found that the incidence of VTE did not differ according to whether surgery was performed by laparoscopy or by the robotics approach. Also of note, all patients in the study had prophylaxis with graduated compression stockings and/or pneumatic compression devices on the lower limbs; however, heparin prophylactic regimens varied substantially among institutions.

Costs of Postoperative VTE and Thromboprophylaxis

Decisions about whether to use thromboprophylaxis for patients undergoing surgery must take into account not only the risk of VTE, but also the cost of VTE and of prevention. A large study evaluating the consequences of medical injuries during hospitalization showed that the cost associated with postoperative VTE was exceedingly high: on average, more than $20,000 overall. In addition, this study showed that the diagnosis of a VTE resulted in a greater than 5 day increase in the length of hospital stay (12).

A recent study by Cain et al. (13) aimed to determine the average patient cost for filling a prescription for extended-duration enoxaparin prophylaxis. That study included women who underwent major abdominal/pelvic surgery for confirmed gynecologic malignancy. Patients who underwent minimally invasive surgery were excluded. The study included 364 patients and found that the average patient cost for 28 days of enoxaparin prophylaxis was $62 (median, $21; range, $0–$1210). The investigators concluded that at least 90% of patients filled their prescription regardless of cost.

Guidelines for Thromboprophylaxis for Patients Undergoing Open Surgery

Current guidelines for thromboprophylaxis are available from a variety of groups, including the American College of Chest Physicians (ACCP) (14), the American Society of Clinical Oncology (ASCO) (15), the National Comprehensive Cancer Network (NCCN) (16), and the American College of Obstetrics and Gynecology (ACOG) (17). All of the aforementioned guidelines support the recommendation that all patients undergoing abdominal or pelvic surgery for malignancy receive pharmacologic prophylaxis. The ASCO, NCCN, and ACOG guidelines recommend consideration of continuing prophylaxis for up to 28 days following surgery. The ACCP guidelines, which were updated in 2012, include the more definitive recommendation that VTE prophylaxis be continued for 28 days after surgery compared to the prior version of the ACCP guidelines which recommended that patients undergoing abdominal or pelvic surgery for malignancy receive VTE prophylaxis for “up to 29 days” (14).

The recommendation for extended prophylaxis in gynecologic cancer patients are derived from two randomized controlled trials indicating that prolonged thromboprophylaxis reduces the incidence of postoperative VTEs. The first study was a double-blinded, multicenter trial in which patients undergoing planned curative open surgery for abdominal or pelvic cancer received enoxaparin (40 mg subcutaneously) daily for 6 to 10 days. Patients were then randomly assigned to receive either enoxaparin or placebo for another 21 days. The results showed a 60% relative reduction and a 7% absolute reduction in the risk of postoperative VTE (18). In a subsequent study, the investigators evaluated the efficacy and safety of thromboprophylaxis with the low molecular weight heparin (dalteparin), administered for 28

days vs. 7 days following major abdominal surgery for cancer. The results showed that the cumulative incidence of VTE was reduced from 16.3% among patients receiving short-term thromboprophylaxis to 7.3% among patients receiving prolonged thromboprophylaxis (19). Interestingly, a recent survey of the Society of Gynecologic Oncology membership showed that the rate of extended prophylaxis (8–30 days) in patients who had major surgery and cancer was as low as 11% (20).

Guidelines and Current Practice regarding Thromboprophylaxis for Patients Undergoing Minimally Invasive Surgery

There is a paucity of data on the incidence of VTEs in patients undergoing minimally invasive surgery, including laparoscopic and robotic surgery. As a result, there are no definitive guidelines referring to prevention of VTEs in patients undergoing minimally invasive surgery. ACCP recommends only early ambulation for patients undergoing laparoscopic surgery, unless they have other risk factors for VTE (21). ACOG recommends thromboprophylaxis on the basis of patient and procedure risk factors, regardless of whether the procedure is open or performed laparoscopically (17). ASCO proposes that there are limited data regarding the benefit of thromboprophylaxis in patients undergoing laparoscopic surgery, and consequently propose guidelines stating that patients undergoing laparoscopy lasting longer than 30 minutes should receive pharmacologic thromboprophylaxis with either low-dose unfractionated heparin or low molecular weight heparin unless contraindicated because of high risk of bleeding or active bleeding. The ASCO guidelines also state that in the absence of prospective data, standard prophylactic regimens may be tailored according to individual patient risk factors for patients undergoing minimally invasive surgery (15).

There is no consensus on the use of preoperative thromboprophylaxis in patients undergoing minimally invasive surgery. Many concerns over intraoperative and postoperative bleeding have led many surgeons to avoid or delay the administration of pharmacologic thromboprophylaxis until the postoperative period. Administration less than 2 hours before surgery is associated with an increase in major bleeding. There are no randomized trials in gynecologic surgery that deal with the issue of timing of initiation of pharmacologic thromboprophylaxis. There is a large retrospective study of 9,949 women who underwent hysterectomy for benign conditions and it concluded that postoperative rather than preoperative administration of low-dose unfractionated heparin or low molecular weight heparin may reduce the risk of bleeding complications after hysterectomy without apparent risk of increased venous thromboembolism. (22)

A recent survey of the Society of Gynecologic Oncology membership indicated that there is significant variation in the patterns of use of thromboprophylaxis after minimally invasive surgery (23). Investigators found that most respondents (51.2%) did not routinely use preoperative pharmacoprophylaxis. Among those who did use preoperative pharmacoprophylaxis, prophylaxis was discontinued upon hospital discharge, regardless of benign (73.5%) or malignant (53.3%) pathology. The investigators noted that for laparoscopy in patients with known or suspected malignancy; combination prophylaxis (sequential compression devices and pharmacoprophylaxis) was the preferred method of

thromboprophylaxis (preferred by 71% of respondents). For low-complexity procedures, the most common form of thromboprophylaxis was sequential compression devices alone (preferred by 76% of respondents).

Conclusion

Our review of the existing literature indicates that the incidence of VTE in patients undergoing minimally invasive gynecologic surgery is low. The use of postoperative anticoagulation should be considered for patients who may be at higher risk for VTEs due to a prior history of VTE, older age (>60), malignancy or increased complexity of the procedure. We recommend that all patients should have pneumatic compression devices placed prior to surgery. When administering VTE prophylaxis, we recommend treatment for a total of 28 days postoperatively with low molecular weight heparin. The role of preoperative heparin remains elusive for patients undergoing minimally invasive surgery for gynecologic disease. Given the overall low incidence of VTE in patients undergoing minimally invasive gynecologic surgery, prospective randomized trials to determine the impact of postoperative prophylaxis on rates of VTE are unlikely to be performed. We also recommend that every institution should have a formal written policy for VTE prevention in all patients undergoing gynecologic surgery.

Acknowledgments

The authors wish to thank Ms. Stephanie Deming for the editorial contribution to this manuscript.

Financial support: The University of Texas MD Anderson Cancer Center is supported in part by the National Institutes of Health through Cancer Center Support Grant CA016672.

References

1. Heit JA, O'Fallon WM, Petterson TM, et al. Relative impact of risk factors for deep vein thrombosis and pulmonary embolism: a population-based study. Arch Intern Med. 2002; 10:1245–8. [PubMed: 12038942]
2. Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism: the Seventh Conference on Antithrombotic and Thrombolytic Therapy. Chest. 2004; 126:338S–400S. [PubMed: 15383478]
3. Schmeler KM, Wilson GL, Cain K, et al. Venous thromboembolism (VTE) rates following the implementation of extended duration prophylaxis for patients undergoing surgery for gynecologic malignancies. Gynecol Oncol. 2013; 128:204–8. [PubMed: 23200912]
4. Martino MA, Borges E, Williamson E, et al. Pulmonary embolism after major abdominal surgery in gynecologic oncology. Obstet Gynecol. 2006; 107:666–71. [PubMed: 16507939]
5. Ageno W, Manfredi E, Dentali F, et al. The incidence of venous thromboembolism following gynecologic laparoscopy: a multicenter, prospective cohort study. J Thromb Haemost. 2007; 5:503–6. [PubMed: 17092300]
6. Nick AM, Schmeler KM, Frumovitz MM, et al. Risk of thromboembolic disease in patients undergoing laparoscopic gynecologic surgery. Obstet Gynecol. 2010; 116:956–61. [PubMed: 20859161]
7. Ritch JM, Kim JH, Lewin SN, et al. Venous thromboembolism and use of prophylaxis among women undergoing laparoscopic hysterectomy. Obstet Gynecol. 2011; 117:1367–74. [PubMed: 21606747]

8. Sandadi S, Lee S, Walter A, et al. Incidence of venous thromboembolism after minimally invasive surgery in patients with newly diagnosed endometrial cancer. Obstet Gynecol. 2012; 120:1077–83. [PubMed: 23090525]
9. Kumar S, Al-Wahab Z, Sarangi S, et al. Risk of postoperative venous thromboembolism after minimally invasive surgery for endometrial and cervical cancer is low: a multi-institutional study. Gynecol Oncol. 2013 (In press).
10. Walker JL, Piedmonte MR, Spirtos NM, et al. Laparoscopy compared with laparotomy for comprehensive surgical staging of uterine cancer: Gynecologic Oncology Group Study LAP2. J Clin Oncol. 2009; 27:5331–6. [PubMed: 19805679]
11. Secin FP, Jiborn T, Biartelli AS, et al. Multi-institutional study of symptomatic deep venous thrombosis and pulmonary embolism in prostate cancer patients undergoing laparoscopic or robotic-assisted laparoscopic radical prostatectomy. Eur Urol. 2008; 53:134–45. [PubMed: 17597288]
12. Zhan C, Miller MR. Excess length of stay, charges, and mortality attributable to medical injuries during hospitalization. JAMA. 2003; 290:1868–74. [PubMed: 14532315]
13. Cain K, Schmeler KM, Langley G, Max O, Ramirez PT, Levenback CF. Patient cost associated with filling a prescription for extended-duration venous thromboembolism (VTE) prophylaxis following surgery for gynecologic cancer. Gynecol Oncol. 2012; 127:18–21. [PubMed: 22813886]
14. Gould MK, Garcia DA, Wren SM, et al. Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012; 141(2 suppl):e227S–77S. [PubMed: 22315263]
15. Lyman GH, Khorana AA, Kuderer NM, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2013
16. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology; venous thromboembolic disease v. 1.2010. www.nccn.org
17. ACOG Practice Bulletin No. 84: Prevention of deep vein thrombosis and pulmonary embolism. Obstet Gynecol. 2007; 110:429–40. [PubMed: 17666620]
18. Bergqvist D, Agnelli G, Cohen AT, et al. Duration of prophylaxis against venous thromboembolism with enoxaparin after surgery for cancer. N Engl J Med. 2002; 346:975–80. [PubMed: 11919306]
19. Rasmussen MS, Jorngensen LN, Wille-Jorgensen P, et al. Prolonged prophylaxis with dalteparin to prevent late thromboembolic complications in patients undergoing major abdominal surgery: a multicenter randomized open-label study. J Thromb Haemost. 2006; 4:2384–90. [PubMed: 16881934]
20. Martino MA, Williamson E, Rajaram L, et al. Defining practice patterns in gynecologic oncology to prevent pulmonary embolism and deep venous thrombosis. Gynecol Oncol. 2007; 106:439–45. [PubMed: 17599396]
21. Geerts WH, Bergqvist D, Pineo GF, et al. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest. 2008; 133(6 suppl):381S–453S. [PubMed: 18574271]
22. Hansen CT, Kehlet H, Moller C, Morch L, et al. Timing of heparin prophylaxis and bleeding complications in hysterectomy: a nationwide prospective cohort study of 9,949 Danish women. Acta Obstet Gynecol Scand. 2008; 87:1039–47. [PubMed: 18792841]
23. Worley MJ, Rauh-Hain A, Sandberg EM, et al. Venous thromboembolism prophylaxis for laparoscopic surgery: a survey of members of the Society of Gynecologic Oncology. Int J Gynecol Cancer. 2013; 23:208–15. [PubMed: 23221603]