Risk of venous thromboembolism in abdominal versus minimally invasive hysterectomy for benign conditions

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OBJECTIVE: We sought to describe the incidence of venous thromboembolism (VTE) following hysterectomy for benign conditions and to estimate if VTE incidence differs for abdominal and minimally invasive hysterectomy.

STUDY DESIGN: Data for patients who underwent hysterectomy for benign conditions from 2010 through 2012 were abstracted from the American College of Surgeons National Surgical Quality Improvement Program database. Cases of VTE were compared to those without VTE. Minimally invasive hysterectomy was defined as both vaginal and laparoscopic hysterectomy. Pearson χ² test, Student t test, and binary logistic regression were used for analysis.

RESULTS: A total of 44,167 patients underwent hysterectomy; 12,733 (28.8%) underwent open hysterectomy, 22,559 (51.1%) underwent laparoscopic hysterectomy, and 8875 (20.1%) underwent vaginal hysterectomy. The incidence of VTE for open hysterectomy was higher (0.6%, 81/12,733) than minimally invasive hysterectomy (0.2% 73/31,434, P < .001). Open surgery (P < .001), body mass index (P = .006), race (P < .001), diabetes (P = .037), preoperative functional status (P < .001), American Society of Anesthesiologists class (P < .001), total operative time (P < .001), and time from surgery to discharge (P < .001) were each associated with VTE. Age, hypertension, current smoking, pack-year history, and year operation was performed were not associated with VTE. Using binary logistic regression, open surgery (P < .001), operative time (P < .001), and length of stay (P < .001) remained associated with VTE. The odds ratio for VTE after open hysterectomy compared with minimally invasive hysterectomy was 2.45 (95% confidence interval, 1.77—3.40).

CONCLUSION: In this large quality database, a minimally invasive approach to hysterectomy was independently associated with a decreased incidence of VTE when compared with open hysterectomy.

Key words: gynecology, minimally invasive surgery, postoperative complications, pulmonary embolism, venous thromboembolism

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Venous thromboembolism (VTE) is a major cause of morbidity and mortality following surgical procedures. The incidence of VTE following major gynecologic surgery among patients not receiving thromboprophylaxis has been reported to be between 17-40%.1

Currently, the incidence of VTE following hysterectomy for benign disease is unknown as most series have focused on patients undergoing different types of gynecologic surgery and have included patients with malignancies. The incidence also varies dependent on the definition of VTE ranging from 1% if defined as a clinically recognized event2 to 14% when fibrinogen phlebography is used routinely.3

It is unknown if route of surgery alters the risk of VTE after hysterectomy performed for benign disease. A minimally invasive approach (laparoscopic or vaginal) is associated with decreased length of stay and a potentially faster return to mobility, which may decrease the risk of VTE.4 However, prolonged operative times associated with laparoscopy and decreased venous return associated with pneumoperitoneum may increase the risk of VTE.5,6 Furthermore, given the relatively low incidence of VTE following benign gynecologic surgery, it is difficult to identify sufficient cases to provide adequate power to estimate specific associated risk factors such as route of surgery.

Given this, we used a large surgical quality database to estimate the incidence of VTE following hysterectomy for benign disease and to assess if that incidence differs for open hysterectomy when compared with minimally invasive hysterectomy.

MATERIALS AND METHODS

Patients who underwent hysterectomy for benign disease from January 2010 through December 2012 and were
recorded in the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database were included in this study. Current Procedural Terminology (CPT) codes were used to identify patients who underwent hysterectomy and to classify patients by route of surgery (Figure). CPT codes that include hysterectomy along with other procedures, such as lymphadenectomy, which would indicate the hysterectomy was being performed as treatment for a malignancy, were not included. Additionally, patients were excluded if their preoperative International Classification of Diseases, Ninth Revision code indicated presence of a malignancy. Definition of route of surgery was based on the primary CPT code. There is no CPT code for conversion from laparoscopic or vaginal hysterectomy to an open procedure. Converted cases were likely recorded using an open CPT code and so we are unable to analyze conversion cases separately. Additionally, cases in which patients underwent a mini-laparotomy for specimen removal are likely recorded as laparoscopic and CPT code does not allow us to discern between these patient groups.

The ACS-NSQIP database is a national quality improvement database. Participating institutions employ nurses to prospectively collect variables such as patient demographics, preoperative variables, operative variables, and postoperative variables for 30 days following surgery. These variables are then deidentified of both patient-specific and hospital-specific information and placed into the national database.

Demographic variables abstracted included age, race, and body mass index (BMI). Patient-related preoperative variables abstracted included hypertension requiring medication, diabetes mellitus requiring insulin or oral therapy, smoking in the last year, total pack-years, and preoperative functional status (a standardized assessment of the patient’s ability to perform activities of daily living within the last 30 days). Operative variables abstracted included operative time, year operation was performed, surgical approach, and American Society of Anesthesiologists (ASA) score. Postoperative variables abstracted included time from operation to discharge, presence of pulmonary embolism (PE) or deep-vein thrombosis (DVT) requiring therapy, and time from operation to VTE event.

NSQIP definitions of VTE were used. A PE was defined as “a lodging of a blood clot in a pulmonary artery with subsequent obstructions of blood supply to the lung parenchyma, confirmed by a ventilation perfusion scan interpreted as high probability of PE or a positive computed tomography spiral examination, pulmonary arteriogram, or computed tomography angiogram.” A DVT was defined as “identification of a new blood clot or thrombus within the venous system, confirmed by duplex, venogram, or computed tomography. The patient must be treated with anticoagulation therapy and/or placement of a vena cava filter or clipping of the vena cava.”

Cases of VTE were compared with control patients and routes of surgery were compared to one another. VTE rates were compared for subjects with

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**FIGURE**

Patient selection flowchart

Flowchart detailing patient selection from National Surgical Quality Improvement Program (NSQIP) database for study inclusion.

CPT, Current Procedural Terminology; ICD-9, International Classification of Diseases, Ninth Revision; LH, laparoscopic hysterectomy; LSC, laparoscopic; SCH, supracervical hysterectomy; TAH, total abdominal hysterectomy; TLH, total laparoscopic hysterectomy; VH, vaginal hysterectomy.

and without previously validated risk factors for VTE (e.g., BMI, age, smoking) using Student t for continuous variables and Pearson χ² test for categorical variables. Association between VTE and variables of potential clinical significance including route of surgery were analyzed using binomial logistic regression to examine for potential confounding. A P value of < .05 was considered significant for all analyses. SPSS, version 20.0 (IBM Corp, Armonk, NY) was used for all analyses. The institutional review board of Northwestern University approved this study and declared it exempt from formal review.

**RESULTS**

Demographic variables and known VTE risk factors are presented in Table 1 for both cases and controls. A total of 44,167 patients underwent a hysterectomy from January 2010 through December 2012. Route of surgery was open in 12,733 patients (28.8%), laparoscopic in 22,559 patients (51.1%), and vaginal in 8875 patients (20.1%). Mean age was 47.9 ± 10.7 years and mean BMI was 30.0 ± 7.9 kg/m². Of the patients, 7% were diabetic, 26.5% were hypertensive, and 18.5% had smoked within the last year. The majority of patients had an independent functional status (99.4%). Mean total operative time was 129.3 ± 68.1 minutes and mean time from surgery to discharge was 1.82 ± 2.0 days.

There were 154 cases of VTE (0.35%) among all patients who underwent a hysterectomy. Fifty-three patients had DVT alone (34.4%), 85 patients had a PE alone (55.2%), and 16 patients had both a PE and a DVT (11.7%) (Table 2). Mean time to postoperative VTE was 9.1 ± 7.0 days and did not differ dependent on surgical approach. There was also no difference between type of VTE event (PE vs DVT) dependent on route of surgery.

**TABLE 1**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall (N = 44,167)</th>
<th>No VTE (n = 44,013)</th>
<th>VTE (n = 154)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>47.9 ± 10.8</td>
<td>47.9 ± 10.8</td>
<td>48.6 ± 10.7</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>30.1 ± 7.9</td>
<td>30.1 ± 7.6</td>
<td>32.0 ± 8.1</td>
<td>.003</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td>&lt; .001</td>
</tr>
<tr>
<td>American Indian or Alaska Native</td>
<td>228 (0.5)</td>
<td>228 (0.5)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>1315 (3.0)</td>
<td>1314 (3.0)</td>
<td>1 (0.6)</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>5689 (12.9)</td>
<td>5652 (12.8)</td>
<td>37 (24.0)</td>
<td></td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>153 (0.3)</td>
<td>152 (0.3)</td>
<td>1 (0.6)</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>31,529 (71.4)</td>
<td>31,426 (71.4)</td>
<td>103 (66.9)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>5253 (11.9)</td>
<td>5241 (11.9)</td>
<td>12 (7.8)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>11,697 (26.5)</td>
<td>11,650 (26.5)</td>
<td>47 (30.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3093 (7.0)</td>
<td>3075 (7.0)</td>
<td>18 (11.7)</td>
<td>.037</td>
</tr>
<tr>
<td>Current smoking</td>
<td>8150 (18.5)</td>
<td>8128 (18.5)</td>
<td>22 (14.3)</td>
<td>NS</td>
</tr>
<tr>
<td>ASA score</td>
<td>2.04 ± 0.58</td>
<td>2.04 ± 0.58</td>
<td>2.2 ± 0.69</td>
<td>.002</td>
</tr>
<tr>
<td>Preoperative functional status</td>
<td></td>
<td></td>
<td></td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Independent</td>
<td>43,901 (99.4)</td>
<td>43,751 (99.4)</td>
<td>150 (97.4)</td>
<td></td>
</tr>
<tr>
<td>Partially dependent</td>
<td>166 (0.4)</td>
<td>163 (0.4)</td>
<td>3 (1.9)</td>
<td></td>
</tr>
<tr>
<td>Totally dependent</td>
<td>21 (0.05)</td>
<td>20 (0.05)</td>
<td>1 (0.6)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>79 (0.2)</td>
<td>79 (0.2)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Year operation performed</td>
<td></td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>2010</td>
<td>8997 (20.4)</td>
<td>8964 (20.4)</td>
<td>33 (21.4)</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td>14,817 (33.5)</td>
<td>14,768 (33.6)</td>
<td>49 (31.8)</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>20,353 (46.1)</td>
<td>20,281 (46.1)</td>
<td>72 (46.8)</td>
<td></td>
</tr>
<tr>
<td>Total operative time, min</td>
<td>129.3 ± 68.1</td>
<td>129.2 ± 68.3</td>
<td>158.6 ± 89.5</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Days from operation to discharge</td>
<td>1.82 ± 2.0</td>
<td>1.8 ± 2.0</td>
<td>4.5 ± 6.4</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

All data are presented at n (%) for categorical variables and mean ± SD for continuous variables. 
ASA, American Society of Anesthesiologists; BMI, body mass index; NS, nonsignificant; VTE, venous thromboembolism.

Patients with postoperative VTE were more likely to have a high BMI (P = .003), be of African American race (P < .001), have diabetes (P = .037), and have a higher ASA score (P = .002), and were less likely to have an independent preoperative functional status (P < .001). Patients with VTE also had surgeries that were 29 minutes longer than those without VTE (P < .001) and had operation-to-discharge times that were 2.7 days longer (P < .001). Patients with VTE did not differ from those without VTE with respect to age, hypertension, smoking status, or the year the operation was performed (Table 1).

To identify variables associated with the route of surgery that may have influenced VTE rates, patients who underwent open surgery were compared with those that underwent minimally invasive surgery (MIS) (Table 3). First, surgical approaches within the minimally invasive and open groups were compared to one another and no significant difference was found in VTE rates between vaginal and laparoscopic procedures or abdominal and open supracervical hysterectomies (data not shown). As VTE rates were not different, the groups were then combined into a MIS group and an open hysterectomy group. Patients receiving MIS were thinner (P < .001) and more likely to be Caucasian (P < .001), had lower rates of diabetes mellitus (P < .001) and hypertension (P < .001), were more likely to have an independent functional status (P < .001), and fewer were current smokers (P < .001). They were also slightly older than those receiving open surgery (P < .001). Patients were more likely to receive MIS as the year of the operation progressed from 2010 through 2012 (P < .001). MIS patients also had longer operative times (P < .001), driven by the length of the laparoscopic cases, and shorter operation-to-discharge times (P < .001).

Given the association of these variables with both VTE rates and route of surgery, binary logistic regression was performed to address the possibility of confounding (Table 4). All variables that were significantly associated with either route of surgery or VTE rates on univariate analysis were placed into a binary logistic regression model. The model was able to correctly classify women 99.6% of the time. Open surgery (P < .001), operative time (P < .001), and time to discharge (P < .001) remained significantly associated with postoperative VTE within the model. The odds ratio (OR) for VTE in open hysterectomy compared with minimally invasive hysterectomy was 2.45 (95% confidence interval [CI], 1.77–3.40). The OR for time from operation to discharge was 1.07 (95% CI, 1.05–1.09), or for every additional day the risk of VTE increased by 7%. The OR for operative time was 1.004 (95% CI, 1.003–1.005) or for every additional minute of operative time, the risk of VTE increased by 0.4%.

We performed the same logistic regression model for the MIS group and the open group separately to see if the risk factors for VTE differed between the groups. We found that for open surgery, operative time (P < .0001) and length of stay (P < .0001) were significantly associated with VTE, whereas BMI, ASA score, diabetes, hypertension, and smoking were not associated with VTE. For the MIS group, we found the same results. Operative time (P = .029) and length of stay (P < .0001) were significantly associated with VTE, but BMI, ASA score, diabetes, hypertension, and smoking were not. In this study, MIS patients and open surgery patients did not have different risk factors for VTE.

### Comment

The current literature on VTE following gynecologic surgery for benign indications has also reported a low rate of VTE. Two prospective trials have followed up patients after gynecologic laparoscopy with venous duplex ultrasonography and found no DVTs among 338 patients. In a more recent study, a prospective cohort study followed up 5297 patients undergoing hysterectomy for benign indications in Finland. They found an incidence of VTE of 0.1% for patients undergoing laparoscopic or vaginal hysterectomy and 0.16% among patients undergoing open hysterectomy. Of note, 65% of these patients received pharmacologic thromboprophylaxis.

More commonly, studies have examined all patients undergoing gynecologic surgery for both benign and malignant conditions. Nick et al found a VTE rate of 0.7% among 849 patients undergoing laparoscopic surgery with half of the patients having a gynecologic malignancy. In this study, the VTE rate was 1.2% (5/430) for patients with a malignancy and 0.2% (1/419) for patients without a malignancy. Ritch et al examined 60,013 patients undergoing laparoscopic hysterectomy from 2003 through 2007 recorded in a national health outcomes, resource utilization, and quality database and found a VTE...
rate of 1.0%. Among patients with malignancy, the rate of VTE was 2.3% (53/2295) and among patients without a malignancy the rate was 0.9% (526/57,718). A number of studies have examined VTE rates among patients suffering from malignancy and have not been updated to reflect current prophylaxis practice patterns.

As can be seen from the above review, the rate of VTE and risk factors associated with VTE in patients undergoing benign hysterectomy is difficult to ascertain. Small population sizes in single institution studies and the rarity of the outcome makes it difficult to obtain sufficient statistical power to evaluate risk factors associated with VTE. Additionally, many series have included patients undergoing hysterectomy for treatment of a malignancy. Patients with malignancy are at higher VTE risk for many reasons including the cancer itself, older age, more medical comorbidities (especially obesity in endometrial cancer), and longer surgery with more retroperitoneal dissection. Thus, it is hard to extrapolate results that incorporate patients with malignancy to patients with benign indications for hysterectomy.

Our VTE rate of 0.2% for patients undergoing laparoscopic surgery agrees with the findings of the above authors who found VTE rates of 0.1-0.9% when only examining patients with benign disease. Our rate of 0.6% for patients undergoing open procedures is higher than the rate observed in the Finnish study, but much lower than the previously reported rates for patients (with both benign and malignant indications for surgery) not receiving any prophylaxis. This difference may be secondary to the high rate of pharmaceutical prophylaxis in the Finnish study. In the general surgical literature, laparoscopic surgery has been associated with decreased rates of VTE when compared with open surgery. In patients undergoing laparoscopic general surgeries, VTE rates are lower when compared with patients who underwent the open version of the procedure even when patients were matched by a severity of illness score. Additionally, among patients who underwent open vs laparoscopic colorectal procedures, open surgery was associated with an increased rate of VTE on multivariate analysis controlling for factors known to influence the rate of VTE. Our results corroborate these findings and found an OR of 2.45 for VTE in open hysterectomy when compared with laparoscopic or vaginal surgery.

In this study, mean time to VTE was 9.1 days and was not significantly different between the minimally invasive group and the open group. For all but the most complicated postoperative course, most patients would have been discharged from the hospital when the VTE event occurred. Although we cannot know when the initial nidus of thrombus began to form, this raises the possibility that prophylaxis only in the hospital

rate of 1.0%. Among patients with malignancy, the rate of VTE was 2.3% (53/2295) and among patients without a malignancy the rate was 0.9% (526/57,718). A number of studies have examined VTE rates among patients undergoing laparoscopic surgery for treatment of endometrial cancer and found VTE rates of 1.2% and 1.0%. In terms of open gynecologic surgery, VTE rates of between 4-45% have been reported for patients undergoing major gynecologic surgery without the use of prophylaxis. However, these numbers include patients undergoing surgery for malignancy and have not been updated to reflect current prophylaxis practice patterns.

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setting may be insufficient to prevent VTE in this population. Other studies of VTE risk in patients undergoing gynecologic MIS have also found a significant time gap between surgery and VTE diagnosis with mean times from surgery to VTE of 12.9-15.5 days.3,9

We also examined other risk factors associated with VTE. On univariate analysis, African American race, higher BMI, presence of diabetes mellitus, high ASA score, a dependent functional status classification, longer time from surgery to discharge, and longer operative time were associated with VTE. However, after binary logistic regression only route of surgery, operative time, and time from operation to discharge remained significant. When we examined open patients and MIS patients separately we found that operative time and time from operation to discharge remained significant risk factors for both groups. This represents a new hierarchy in terms of which risk factors are important in development of VTE in hysterectomy performed for benign conditions. Given that most patients undergoing surgery for benign indications are relatively young and healthy when compared with patients undergoing general surgery or gynecologic oncology procedures, the relative importance of prolonged operative time and prolonged in-hospital stay with resultant immobilization play a more important role. Clinicians could use this information to guide use of prophylaxis in this higher-risk gynecologic population.

Some of the limitations of this study pertain to the use of a large national quality database. Data on select variables such as the use of hormonal therapy or use of mechanical or pharmacologic thromboprophylaxis as well as other variables that may influence VTE rates were not available. Thus we cannot comment on recommendations for mechanical or chemical prophylaxis in this population. Additionally, selection of patients was based on both International Classification of Diseases, Ninth Revision codes and CPT codes and we cannot exclude the possibility of miscoding or misclassification. However, in contrast to large databases that utilize billing and coding data only, the NSQIP database is prospectively collected by trained personnel and the purpose of the database is surgical quality and perioperative complications and thus the database is less likely to fail to record a VTE event in the postoperative period. Periodic audits are also performed on the data and reveal only a 1.8% disagreement rate confirming the accuracy of the data.16 NSQIP also only records postoperative data for the first 30 days after surgery and thus our VTE rates do not include events which occurred after that time point and may underestimate the true VTE rate. Additionally, we are unable to address the surgeon’s thought process as to why a specific route of surgery was selected. Potentially more difficult surgeries or patients with more comorbidities may have undergone open surgery. However, our multivariate analysis addressed common comorbidities such as diabetes, hypertension, and smoking, and these were not significant in the model, whereas open surgery was, suggesting that comorbidities likely do not account for the increased VTEs in the open group.

In this study, we found that among patients recorded in a large quality improvement database, patients undergoing a hysterectomy for benign indications had a low risk of VTE (0.35%). However, the risk was increased 3-fold when patients underwent open surgery compared with MIS (0.6% vs 0.2%). This difference persisted even after controlling for a number of variables that have been associated with VTE. Traditional risk factors such as race, BMI, diabetes, ASA class, and preoperative functional status were not predictive of VTE in logistic regression. However, operative time and time from surgery to discharge were predictive of VTE, with each 10-minute increase in operative time leading to a 4% increased risk of VTE. Our data help surgeons assess VTE risk in their patients and provide an accurate estimation of current VTE rates in the United States.

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