

Incidence and Risk Factors of Venous Thromboembolism in Colorectal Surgery

Does Laparoscopy Impart an Advantage?

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Objectives: Laparoscopy is increasingly used in colon and rectal procedures. However, little is known regarding the incidence of venous thromboembolism (VTE) in laparoscopic colorectal (LC) compared with that in open colorectal (OC) procedures. We aimed to compare the incidences and to highlight the risk factors of developing VTE after LC and OC surgery.

Design: Analysis of the Nationwide Inpatient Sample data from 2002 through 2006.

Setting: National database.

Patients: Patients who underwent elective LC and OC surgery from 2002 through 2006.

Main Outcomes Measure: Incidence of VTE during initial hospitalization after LC and OC surgery; VTE classified by surgical site, pathology type, and at-risk patient population.

Results: Over a 60-month period, 149 304 patients underwent LC or OC resection. Overall, the incidence of VTE was significantly higher in OC cases (2036 of 141 456 [1.44%]) compared with the incidence in LC cases (65 of 7848 [0.83%]) ($P < .001$). When stratified according to pathologic condition and surgical site, the overall rate of VTE was highest in patients with inflammatory bowel disease and in those undergoing rectal resections. Patients who underwent OC surgery were almost twice as likely to develop VTE compared with patients who underwent LC surgery. We also identified malignancy, obesity, and congestive heart failure as statistically significant ($P < .05$) risk factors for VTE in OC and LC surgery.

Conclusions: On the basis of data from a large clinical data set, the incidence of perioperative VTE is lower after LC than after OC surgery. These findings may help colorectal surgeons use appropriate VTE prophylaxis for patients undergoing colorectal procedures.

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VENOTHROMBOEMBOLIC events are a major cause of morbidity and mortality in patients undergoing gastrointestinal surgery. As many as 1 in 4 patients undergoing general surgical procedures and not receiving antithrombotic prophylaxis will subsequently develop postoperative venous thromboembolism (VTE),¹ which includes deep vein thrombosis and pulmonary embolism (PE). Fatal PE is associated with 0.8% to 2% of all deaths in general surgery patients.² Colorectal surgery implies a specific high risk for postoperative thromboembolic complications.³ Previous studies have shown that conventional elective colorectal resections have an incidence of deep vein thrombosis ranging from 4% to greater than 10%,⁴ and the incidence of PE in colorectal surgery patients was approximately 4-fold higher than in other surgery patients.⁵

The acceptance rate for laparoscopic surgery has been overwhelming for many general surgical procedures, and elective laparoscopic colorectal (LC) resections are becoming more commonly used as surgeons become more experienced with laparoscopy. Despite factors associated with laparoscopy that may contribute to an inherently increased risk of VTE, such as the use of intraoperative pneumoperitoneum, reverse Trendelenburg positioning, and prolonged operative times,^{6,7} laparoscopic surgery is associated with a lower incidence of VTE compared with that of open surgery in several commonly performed gastrointestinal procedures. Nguyen and colleagues⁸ demonstrated that the overall incidence of VTE after laparoscopic procedures such as cholecystectomy, appendectomy, antireflux procedures, and gastric bypass is significantly lower compared with that of the respective open procedures (0.28% vs 0.60%).

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Table 1. Characteristics of Patients Undergoing Laparoscopic and Open Colon Resection, 2002-2006^a

| Characteristic | Open (n=141 456) | Laparoscopic (n=7848) | P Value |
|--------------------------------|---------------------|--------------------------|---------|
| Age, mean (SD), y | 63.5 (0.04) | 60.6 (0.18) | <.001 |
| Female sex, % | 53.6 | 54.2 | .23 |
| White race, % | 82.8 | 83.0 | <.001 |
| Comorbidity, % | | | |
| Congestive heart failure | 6.58 | 3.38 | <.001 |
| Chronic pulmonary disease | 14.2 | 11.6 | <.001 |
| Diabetes mellitus | 13.5 | 11.3 | <.001 |
| Hypertension | 41.1 | 39.6 | .01 |
| Liver disease | 1.37 | 1.04 | .02 |
| Obesity | 4.50 | 4.27 | .35 |
| Renal failure | 1.94 | 1.10 | <.001 |
| Valvular disease | 4.29 | 4.17 | .27 |
| Metastatic cancer | 18.1 | 9.09 | <.001 |
| Pulmonary circulation disorder | 0.45 | 0.30 | <.001 |
| Peripheral vascular disorders | 2.67 | 1.90 | <.001 |

Furthermore, they found that patients undergoing an open procedure were twice as likely to develop a VTE than those undergoing the same laparoscopic procedure. Early ambulation and a reduction in postoperative hypercoagulability may be responsible for this reduced risk of VTE.^{9,10} However, the true incidence of VTE after LC resections is not well defined.

Recent recommendations place laparoscopic surgical procedures in the low-risk stratification, with only early ambulation recommended for prophylaxis, unless the patients have additional risk factors, in which case they should receive chemical prophylaxis.¹¹ An improved knowledge of the risk factors in the development of VTE after LC compared with open colorectal (OC) resection may help guide surgeons' selection of appropriate thromboprophylaxis in patients undergoing LC surgery. The objectives of this study were to determine the incidence of clinically evident VTE during initial hospitalization after LC and OC surgery and to identify risk factors for VTE in the LC and OC resection patient population.

METHODS

Using the Healthcare Cost and Utilization Project Nationwide Inpatient Sample (NIS) database, we performed a retrospective comparison of elective LC and OC resections from January 1, 2002, through December 31, 2006. The principal outcome measure was the incidence of VTE during initial hospitalization after LC and OC; we further classified VTE by surgical site, pathology type, and at-risk patient population.

The NIS is the largest all-payer inpatient care database in the United States and contains information from nearly 8 million hospital stays each year across the country. The data set approximates a 20% stratified sample of US community hospitals, resulting in a sampling frame that comprises approximately 90% of all hospital discharges in the United States. Researchers and policy makers can use the data set to identify, to track, and to analyze national trends in health care utilization, access, charges, quality, and outcomes. Data elements within the NIS are drawn from hospital discharge abstracts that allow determination of all procedures performed during a given hospitalization. It also contains discharge information on inpatient hospital stay, including patient characteristics, length of stay, overall and specific post-

operative morbidity, and observed and expected in-hospital mortality. The NIS database has no information available on complications occurring after discharge, even if the complication occurred within 30 days after the date of surgery. Approval for the use of the NIS patient-level data in this study was obtained from the institutional review board of the University of California-Irvine Medical Center and the NIS.

To identify hospitalizations during which a colectomy was performed, we selected all discharges with *International Classification of Diseases, Ninth Revision (ICD-9)* diagnosis and procedure codes that corresponded to either inflammatory bowel disease (IBD), diverticulitis, or malignancy and a colorectal resection. Procedure types were chosen on the basis of the procedures reviewed in previous randomized controlled trials and meta-analyses. We then selected only those admissions that the NIS database designated as elective. Because there is no distinct ICD-9 procedure code for LC, we identified procedures that were performed laparoscopically by identifying additional ICD-9 procedure codes for laparoscopy or laparoscopic lysis of adhesions (54.21 and 54.51). All procedures were performed on an inpatient basis. Unfortunately, the NIS does not contain information on the use or nonuse of thromboprophylaxis or about the type (mechanical or antithrombotics) and duration of prophylaxis.

Patient characteristics that were examined included age, sex, race, and preexisting comorbidities. We also examined differences in in-hospital mortality and length of hospital stay. Length of stay was defined as the period from the index procedure to hospital discharge. Because the NIS database contains only inpatient information, deaths occurring after hospital discharge were not included in our analysis.

We examined the overall rate of venous thrombosis and PE after LC and OC surgery and the rate of VTE by surgical site (right colon, left colon, transverse colon, sigmoid colon, or rectum), pathology type (IBD, cancer, diverticulitis, or other), and at-risk patient population. The diagnosis of venous thrombosis and PE during the hospitalization for LC or OC was based on the presence of a secondary diagnosis of an ICD-9 code for venous thrombosis and/or PE. Patients with a primary diagnosis of phlebitis, thrombophlebitis, PE, or venous thrombosis were excluded.

All statistical analyses were conducted using SAS, version 9.2 (SAS Institute, Inc, Cary, North Carolina), incorporating recommended discharge and hospital weights. Population characteristics were explored using graphs and charts to describe the distribution of each variable. Descriptive statistics were performed using χ^2 , *t* tests, and trend tests as appropriate. Bivariate and multivariate models were used to determine the measure of association (odds ratio [OR]) between our primary outcome (odds of VTE) and putative predictive variables in both LC and OC. In addition, the multivariate regression models were tested for goodness of fit and C statistics. Statistical significance was set at *P* values greater than .05 and ORs and 95% confidence intervals (CIs) that excluded 1.

RESULTS

From January 1, 2002, through December 31, 2006, there were 149 304 patients who underwent elective LC or OC surgery nationwide. During this period, 7848 (5.3%) of all cases were performed laparoscopically. The overall mean age of patients undergoing colectomy was 63.5 years, and many patients were female (53.6%) and white (82.8%). **Table 1** shows patient demographic characteristics. In general, patients undergoing LC procedures had fewer comorbidities than did OC patients. However, the most common comorbidities in both groups were hypertension

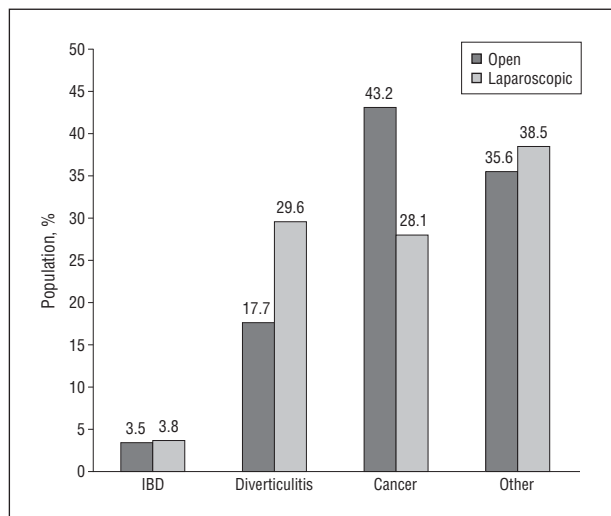


Figure 1. Comparison of pathologic conditions for colectomy between open and laparoscopic colorectal resection, 2002-2006. IBD indicates inflammatory bowel disease.

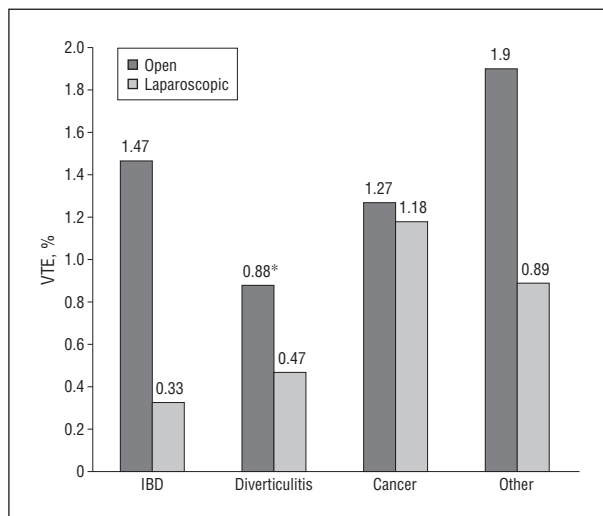


Figure 3. Incidence of venous thromboembolism (VTE) in patients undergoing open vs laparoscopic colorectal resection stratified by disease pathology, 2002-2006. IBD indicates inflammatory bowel disease. * $P < .05$.

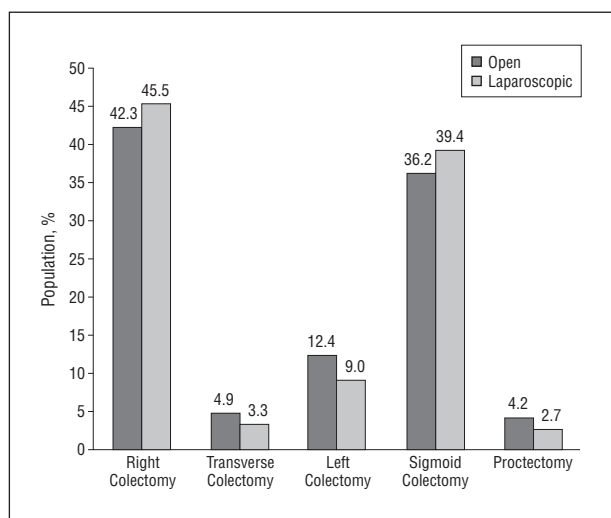


Figure 2. Comparison of surgical resection site between open and laparoscopic colorectal resection, 2002-2006.

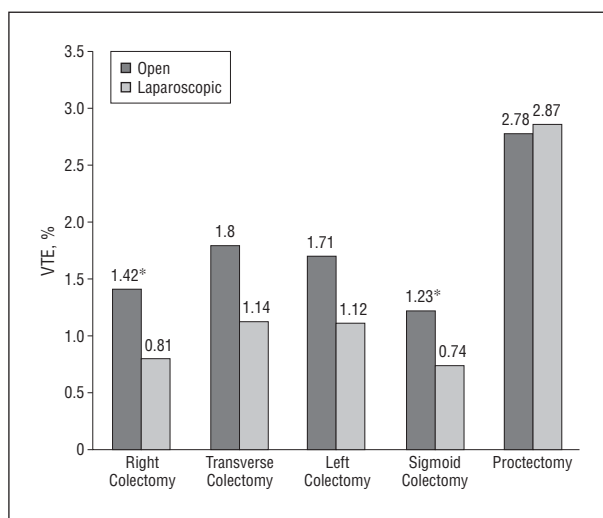


Figure 4. Incidence of venous thromboembolism (VTE) in patients undergoing open vs laparoscopic colorectal resection stratified by surgical resection site, 2002-2006. * $P < .05$.

(41.0%), metastatic cancer (17.7%), chronic pulmonary disease (14.0%), and diabetes mellitus (13.4%). The most common pathologic condition overall was cancer of any type at 42.4%. **Figure 1** shows a comparison of pathologic conditions between the LC and OC patients. In both groups, the most common surgical procedure was a right colon resection (overall, 42.5%). **Figure 2** shows the surgical resection site variations in LC and OC procedures.

Overall, VTE was diagnosed during index hospitalization in 2102 patients (1.4%). The incidence of VTE in the LC group (65 patients) was significantly lower than the corresponding incidence in the OC group (2036 patients) (0.8% vs 1.4%; $P < .001$). By pathologic condition, the IBD group experienced the highest incidence of VTE at 1.4%, followed by cancer (1.3%) and diverticulitis (0.9%). The incidence of VTE after LC and OC stratified by pathology type is illustrated in **Figure 3**. Laparoscopic colorectal surgery for diverticulitis was associated with a significantly lower rate of VTE compared with the rate of the

OC group (0.5% vs 0.9%; $P = .04$). By surgical resection site, proctectomy was associated with the greatest incidence of VTE at 2.8%, followed by transverse colectomy (1.8%), left colectomy (1.7%), right colectomy (1.4%), and sigmoid resection (1.2%). The incidence of VTE after laparoscopic and open colectomy stratified by surgical resection site is illustrated in **Figure 4**. Laparoscopic right (0.8% vs 1.4%; $P = .003$) and sigmoid (0.7% vs 1.2%; $P = .02$) colectomies were associated with a significantly lower rate of VTE compared with those of the open group.

A multivariate regression analysis was also performed to identify any predictive variables (patient comorbidities or pathologic condition) leading to an increased risk of VTE in patients undergoing LC and OC surgery. In general, patients undergoing OC surgery were at significantly increased risk of VTE compared with the risk of the LC group (OR, 1.8; 95% CI, 1.4-2.2). In the LC group, obesity (OR, 2.3; 95% CI, 1.3-4.0), congestive heart failure (2.0; 1.3-

Table 2. Independent Risk Factors for VTE in Laparoscopic and Open Colorectal Surgery

| Risk Factor | Laparoscopic | | Open | |
|--------------------------------|---------------|---------|---------------|---------|
| | OR (95% CI) | P Value | OR (95% CI) | P Value |
| Congestive heart failure | 2.0 (1.3-3.2) | .003 | 1.1 (1.1-1.2) | .001 |
| Obesity | 2.3 (1.3-4.0) | .004 | 1.9 (1.7-2.1) | .001 |
| Malignancy | 1.5 (1.1-2.1) | .03 | NA | NA |
| Chronic pulmonary disease | NA | NA | 1.1 (1.1-1.2) | .001 |
| Metastatic cancer | NA | NA | 1.9 (1.8-2.0) | .001 |
| Pulmonary circulation disorder | NA | NA | 1.5 (1.2-2.0) | .002 |
| Inflammatory bowel disease | NA | NA | 1.5 (1.3-1.8) | .001 |

Abbreviations: CI, confidence interval; NA, not applicable; OR, odds ratio; VTE, venous thromboembolism.

3.2), and malignancy (1.5; 1.1-2.1) were identified as statistically significant risk factors for VTE. In the OC group, congestive heart failure (OR, 1.1; 95% CI, 1.1-1.2), chronic pulmonary disease (1.1; 1.1-1.2), obesity (1.9; 1.7-2.1), metastatic cancer (1.9; 1.8-2.0), pulmonary circulation disorders (1.5; 1.2-2.0), and IBD (1.5; 1.3-1.8) were identified as statistically significant risk factors for VTE (**Table 2**). The mean length of hospital stay was significantly shorter in the LC group compared with that of the OC group (6.5 vs 9.5 days; $P < .001$). Finally, mortality was significantly lower in the LC group compared with that of the OC group (0.8% vs 3.0%; $P < .001$).

COMMENT

The risk of a thromboembolic event in the general surgery patient who does not receive prophylaxis is estimated at 15% to 40%.¹ Venous thromboembolism is associated with significant cost, including the cost of treatment and complications associated with treatment, the increased risk of VTE in the future, and death from fatal pulmonary emboli. Current hospital readmission rates after VTE range from 5% to 14% within the first year.¹² Furthermore, there is a significant risk of recurrence with VTE because a patient undergoing a general surgical procedure has a 40-fold increased risk of recurrence after a first thromboembolic event.¹³ With each recurrent deep vein thrombosis or PE, there is also an increased risk of a fatal event. In addition, chronic thromboembolic pulmonary hypertension occurs in 0.8% to 3.8% of patients with a previous PE, and postthrombotic syndrome develops in 20% to 50% of patients after initial deep vein thrombosis.¹⁴ The risk of anticoagulation-associated bleeding must also be considered. The need to avoid such consequences is motivation for the surgeon to reduce the risk of VTE whenever possible.

To date, there have been no large studies examining the incidence of VTE after LC compared with the incidence of VTE after OC surgery. In this study, we used the NIS database to evaluate the incidence and to highlight the risk factors of developing VTE in a large cohort of patients who underwent LC or OC surgery. Our data demonstrated a significantly decreased incidence of VTE with LC (0.8%) compared with that with OC (1.4%) surgery. These findings persisted even when the groups were stratified according to pathologic condition and resection site. Laparoscopic colorectal surgery for diverticulitis was associated with a significantly lower rate of VTE compared with that

of the OC group. The rate of VTE for IBD and malignancy was lower for LC than for OC surgery, but this difference was not statistically significant. We also found that a rectal resection was associated with a greater incidence of VTE (2.8%) than was any other resection site, which may be attributable to the extensive pelvic dissection required with resultant surrounding inflammatory involvement of the pelvic veins. Laparoscopic right and sigmoid colectomies were associated with a significantly lower rate of VTE compared with those of the OC group. Of note, the incidence of VTE was slightly higher in the LC group undergoing rectal resection. However, this difference was not statistically significant.

Multivariate regression analysis was performed to identify risk factors predisposing to VTE after LC and OC surgery. Overall, comparison of these 2 groups showed that the odds of developing an inpatient VTE are 1.75 times higher after OC compared with LC procedures. Although, to our knowledge, there are no other large-scale colorectal studies specifically examining this issue, our findings are in agreement with those of previously published studies that examined VTE after commonly performed gastrointestinal surgical procedures and that demonstrated an OR for VTE in open surgery of 1.8.⁸ Possible explanations for a decreased risk of VTE after LC surgery include decreased pain and postoperative ileus, which lend themselves to earlier ambulation, and shorter hospital stays.¹⁵ Known factors predisposing to VTE during open surgical procedures include a deficiency of antithrombin III, proteins C and S, and dysfibrinogenemia. Other risk factors include advanced age, obesity, previous history of VTE, cancer, lengthy operation (>2 hours), and immobility.¹⁶ In our study, factors associated with an increased risk of VTE in the laparoscopic group were limited to congestive heart failure, obesity, and malignancy. In addition to malignancy and obesity, congestive heart failure, chronic pulmonary disease, pulmonary circulation disorders, and IBD in the OC group were associated with increased risk for VTE. Our findings, therefore, call into question whether we should be using the same risk factors and stratification for LC procedures as we do for OC procedures because certain risk factors for VTE in a patient undergoing OC surgery do not seem to portend an increased risk of VTE in the same patient undergoing LC surgery. These study findings may be used by surgeons to more accurately assess a patient's risk for perioperative VTE as well as to select appropriate thromboprophylaxis in patients undergoing LC surgery.

Our study met with limitations similar to those of other studies making use of a large administrative database. The study population was selected from a nationwide database on the basis of ICD-9 codes between the years of 2002 and 2006. A dedicated LC ICD-9 code was not in effect until 2009. As a result, a combination of ICD-9 procedure codes was used as a surrogate for laparoscopic cases. This has the advantage of identifying cases that may have started out as laparoscopic cases but then necessitated conversion to an open resection in the laparoscopic group. However, the disadvantage is that not all cases may be captured and recorded as laparoscopic cases. The NIS database is limited to in-hospital morbidity/mortality without follow-up data. Therefore, we were able to measure only VTE occurring during a single index hospitalization. Any VTE occurring after discharge in either group was not included in the study, making the true incidence of VTE at follow-up unknown. Interestingly, Spencer et al¹⁷ demonstrated that only 26% of VTE occurred during the inpatient setting, whereas 66.4% of surgical patients with a VTE were diagnosed within a month after discharge.

Another limitation is the lack of information concerning the use and duration of thromboprophylaxis in the 2 groups. The NIS database does not record whether a patient was administered VTE prophylaxis perioperatively. Was the LC group more likely to receive adequate thromboprophylaxis throughout their hospital stay than the OC group, thereby accounting for the decreased incidence of VTE? We also noted that the OC group was more likely to include higher-risk patients with more comorbidities. Although we controlled for these risk factors, they may have predisposed the patient to VTE from the outset and possibly contributed to prolonged immobilization of the patient.

Finally, we must address the "other" category within the pathologic conditions, which included more than 30% of the population for both the LC and the OC groups and demonstrated twice the incidence of VTE in the OC group. Because there is no specification as to the nature of these pathologies, we can presume that they would include other benign processes, such as benign masses, rectal prolapse, and lower gastrointestinal bleeding. Regardless of the etiology of colorectal resection in this group, these data further validate our findings of a lower incidence of VTE in laparoscopic surgery.

CONCLUSIONS

Using a large administrative database, our study found that the overall incidence of VTE is lower after LC compared with the corresponding incidence after OC procedures. We further discovered a significantly increased rate of VTE in patients with IBD and in those patients with surgical resection involving the rectum. Compared with LC procedures, OC procedures were a significant risk factor for the development of VTE. In OC and LC surgery, congestive heart failure, obesity, and malignancy were identified as significant risk factors in the development of VTE. These findings may guide surgeons in the selection of appropriate VTE prophylaxis for patients undergoing colorectal procedures.

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