

Risk of Stroke After Colorectal Surgery for Cancerous Versus Benign Conditions

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Background: Cancer treatment, specifically surgical intervention, as a possible stroke trigger is understudied. *Methods:* Using the Nationwide Readmissions Database and validated diagnosis and procedure codes, we identified adults with index admissions for colorectal surgery for colorectal adenocarcinoma (Group A) and compared them to admissions for colorectal surgery for benign conditions (Group B) and hepatobiliary or pancreatic surgery for benign conditions (Group C). Within the colorectal cancer cohort, we further identified patients who underwent open versus laparoscopic surgery. The primary outcome was readmission for ischemic or hemorrhagic stroke up to 1 year. Cumulative risk of ischemic stroke was calculated using risk survival statistics, and hazard ratios (HR) were calculated using adjusted Cox regression. *Results:* Patients in Group A had higher 3-month readmission rates for ischemic and hemorrhagic strokes than those in Groups B and C. Higher risk of ischemic stroke (HR 1.46, 95% confidence interval [CI] 1.20-1.79) in Group A compared to Group B was eliminated following adjustments for illness severity and vascular risk factors. Comparing types of colorectal surgical intervention for cancer, there was significantly greater risk of ischemic stroke with open versus laparoscopic surgery, despite adjusting for vascular risk factors (HR 1.70, 95% CI 1.15-2.52). *Conclusions:* We found elevated risk of ischemic stroke up to 1 year following open surgery for colorectal adenocarcinoma compared to laparoscopic. More research is necessary to clarify the underlying surgery-related mechanisms that contribute to elevated risk.

Key Words: Ischemic stroke—risk factors—stroke—stroke subtypes—epidemiology—stroke prevalence

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Introduction

Both cancer and stroke contribute to significant morbidity and mortality in the United States. The association of cancer and ischemic stroke has been receiving more attention in recent days.¹⁻³ Short-term risk for ischemic stroke appears to be highest among colorectal, lung, and pancreatic cancer patients.¹ However, research on long-term risk of ischemic stroke among oncology patients report no increased risk associated with cancer.^{4,5} To further understand the nature of the

association, we chose to focus on colorectal cancer because of its rising incidence in younger patients.⁶

Several studies have investigated stroke risk following chemotherapy and radiation therapy, but fewer studies have examined surgical intervention for cancer and associated ischemic events.⁷⁻¹² An American College of Surgeons' National Surgical Quality Improvement Program publication reveals that colorectal procedures are associated with one of the highest postoperational morbidity and mortality rates compared to other general surgical

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procedures.¹³ However, reasons for this elevated morbidity and mortality are unclear, particularly with respect to stroke events.

To further explore the relationship between colorectal surgery and ischemic stroke risk, we conducted a retrospective comparative analysis of stroke outcomes up to 1 year after colorectal surgery for various conditions. We hypothesized that the risk of ischemic stroke after procedures to treat colorectal cancer is higher than the risk after several comparison procedures: (1) colorectal surgery for benign conditions; and (2) hepatobiliary or pancreatic surgery for benign conditions. We also hypothesized that the approach of the operation (open versus laparoscopic) would be associated with greater risk of stroke.

Methods

We performed a retrospective cohort study using the Nationwide Readmissions Database (NRD), a national database of readmissions for all payers, and the uninsured with data on more than 14 million U.S. admissions during the year 2013. The NRD is derived from State Inpatient Databases from 21 states, comprising data from 49.1% of all U.S. hospitalizations, excluding rehabilitation and long-term acute-care hospitalizations. The NRD allows analysis of readmissions with the use of a verified linkage identifier for each individual, which has been anonymized to comply with privacy guidelines. For this analysis, we restricted the cohort to patients aged 18 or older at the time of index event. We compared the risk of ischemic and

hemorrhagic stroke after index admission for colorectal surgery for colorectal adenocarcinoma (Group A) to 2 comparison groups: colorectal surgery for benign conditions (Group B); and hepatobiliary and pancreatic surgery for benign conditions (Group C). We chose to separate hepatobiliary and pancreatic surgery because the 2 sets of procedures involve different levels of risk. Pelvic procedures, which include colorectal surgery and gynecologic surgery, have higher rates of deep vein thrombosis (DVT) than upper abdominal surgery.^{14,15} Among those with colorectal adenocarcinoma (Group A), we explored the risk of ischemic and hemorrhagic stroke comparing laparoscopic versus open colorectal operations. The Mount Sinai review board approved this analytic plan, and all analyses comply with the Healthcare Cost and Utilization Project data use agreement.

We used International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9 CM) codes to identify index admissions for abdominal surgery for cancerous and benign conditions as well as vascular risk factors. Vascular risk factors included diabetes, hypertension, hypercholesterolemia, smoking history, and atrial fibrillation or flutter. We used ICD-9 diagnoses codes to identify cancerous and benign conditions, using codes validated in previous studies and meta-analyses^{16,17} (see Table 1). Cancer types included colorectal adenocarcinoma. Benign conditions included ulcerative colitis, diverticulosis and diverticulitis, and intestinal obstruction. We identified surgical procedures as follows: open colorectal surgery limited to colorectal

Table 1. ICD-9 diagnosis and procedure codes

Classification	Code(s)
Diagnosis	
Colorectal adenocarcinoma	153.x, 209.x, 230.3, 154.0, 154.1, 154.8
Ulcerative colitis	555.1, 555.2, 555.9, 556.x
Diverticulosis/diverticulitis	562.10-562.13
Intestinal obstruction	
With hernia	550.11-550.13, 552.0-552.03, 552.1, 552.2, 552.21, 552.29, 552.3, 552.8, 552.9
Without hernia	560.0-560.3, 560.32, 560.39, 560.80, 560.81, 560.89, 560.90
Procedure	
Colorectal	
Open surgery	45.70-45.76, 45.79, 45.80, 45.82, 45.83, 48.40-48.43, 48.49, 48.50, 48.52, 48.59, 48.60-48.65, 48.69
Laparoscopic surgery	17.30-17.36, 17.39, 45.81, 48.51
Liver	
Hepatectomy	50.22, 50.40
Lobectomy	50.30
Gallbladder and biliary tract	
Cholecystectomy	51.20-51.24
Local excision or destruction	51.60-51.69
Pancreas	
Pancreatectomy	52.50-52.53, 52.59, 52.60, 52.70
Local excision or destruction	52.20-52.22

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