

Surgical outcomes among inflammatory bowel disease patients undergoing colectomy : results from a national database

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Abstract

Introduction : Colectomy is relatively common in inflammatory bowel diseases (IBD), occurring more in Ulcerative Colitis (UC) as compared to Crohn's disease (CD). The surgical outcomes among this mixed population of patients are not well understood. This study aims to determine the predictors of post colectomy surgical outcomes in this patient population.

Methods : Using the National Surgical Quality Improvement Project (NSQIP) demographics, preoperative and post-operative data were analyzed for all patients undergoing colectomy for either CD or UC. Multiple variables were linked to several outcomes including mortality, anastomotic leak, and reoperation post colectomy.

Results : A total of 5049 IBD patients that underwent colectomy were identified. Rate of reoperation and anastomotic leak were significantly increased with steroid intake with an Odds Ratio (OR) of 1.66 (95% Confidence Interval (CI) (1.26-2.19)) and 1.81 (95%CI (1.34-2.45)) respectively. As for 30-day mortality, it was significantly lower among patients on steroid (OR=0.41; 95%CI (0.19-0.86)).

Comparing UC to CD, anastomotic leaks were less common among UC patients (OR=0.53; 95%CI (0.37-0.76)), but 30-day mortality was significantly more prevalent among UC patients (OR=8.11; 95%CI (4.22-15.6)).

Conclusion : Among IBD patients undergoing colectomy, major surgical complications except 30-day mortality appear to increase with the use of preoperative steroids (Acta gastroenterol. belg., 2018, 81, 387-392).

Keywords : Crohn's disease, Ulcerative Colitis, Inflammatory Bowel Disease, Colectomy, Outcomes.

Introduction

Ulcerative colitis (UC) and Crohn's disease (CD) are chronic inflammatory bowel diseases of the gastrointestinal tract. The prevalence of Ulcerative colitis ranges from 28 to 238 per 100,000 and that of Crohn's disease ranges from 43 to 201 per 100,000 in the United States (1,2). They are characterized by various clinical courses, from mild to moderate to debilitating (3). Many therapeutic advances have emerged in the treatment of inflammatory bowel disease, however the response is unpredictable. Some patients respond to immunosuppressive and biologic therapies and others are poor responders and develop continuous damage of the bowel mucosa and complications that require surgical interventions (4). The ability to predict the outcome of the disease, and the predisposing factors to complications and disease progression, would be of great

value in improving the quality of life of the patients and decrease the financial burden of unnecessary medical therapy.

Colectomy is performed in Ulcerative colitis usually as a salvage treatment after failure of medical therapy. Among Crohn's disease patients, colectomy is usually performed to manage complications related to the disease course mostly obstruction, strictures and fistulas (5). A cohort study from Denmark, followed 1000 patients with ulcerative colitis over 25 years. Around 80% of patients had intermittent active disease and 11% had a chance of relapse free disease and 20% ended up with progressive disease requiring colectomy after 10 years (6). The cumulative incidence of colectomy was 25.4% at 20 years from diagnosis in another study (7). A study done in New Zealand on Crohn's disease showed that 40 % of patients develop complicated disease after 5 years, and another French study showed that 60% of patients develop complicated disease after 5 years (3,8). The requirement for surgery in referral center data ranged from 17% to 35% within 5 years after initial diagnosis in Crohn's disease patients (9). A population-based cohort study showed that 58% of Crohn's disease patients required at least one abdominal surgery within 20 years of diagnosis with total proctocolectomy accounting for 11% of these surgeries (5). Severe inflammation, younger age at diagnosis, steroid use and smoking were predictors for colectomy in patients with Ulcerative Colitis (10-12).

Despite the relatively high frequency at which colectomy is performed, there is limited data about the outcomes and complications of inflammatory bowel disease patients undergoing colectomy or data comparing the post-operative outcomes between patients with Ulcerative colitis and Crohn's disease. This study aimed to study the post colectomy complication among patients with inflammatory bowel disease and compare them between both groups.

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Methods

Data Source

Data were collected from the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) participant use data file from 2012 to 2014. The ACS NSQIP collects data from more than 500 institutions across the United States and Canada, and NSQIP is a validated database for measuring surgical outcomes designed to improve hospital surgical quality (13). The American University of Beirut Medical Center is listed among the institutions affiliated with the NSQIP and is eligible on using its data for research purposes. Cases are selected based on current procedural terminology (CPT) codes using a random sampling of procedures per institution. Outcomes included in NSQIP include mortality and other adverse events, demographic data, and a variety of perioperative laboratory and clinical variables collected for the purpose of risk adjustment. Further details regarding data collection and outcome variable definitions are available on the NSQIP website (<https://www.facs.org/quality-programs/acs-nsqip>).

Inclusion Criteria

Factors for inclusion in the study included all patients who underwent colectomy with a diagnosis of inflammatory bowel disease between 2012 and 2014. All cases with CPT codes specific for open and laparoscopic colectomy were retrieved from the NSQIP data file. Patients with Ulcerative Colitis were analyzed separately from patients with Crohn's disease.

Data Collected

Patient demographics were identified and categorized, included age, gender, race (white, black or African American, others), and BMI (body mass index) of the patients. We also used operative information including the operation time, days from admission to surgery, wound classification (1 : clean, 2 : clean/contaminated, 3 : contaminated, 4 : dirty/infected), and the American Society of Anesthesiologists (ASA) class (1-5) of each patient which assesses the fitness of each patient prior to surgery ranging from healthy person (class 1) and a moribund person who is not expected to live without the surgery (class 5).

The past medical and social history of the patients involved were recorded as well and this included history of severe COPD (Chronic Obstructive Lung Disease), diabetes mellitus, recent weight loss (>10% loss of body weight in last 6 months), smoking history, chronic steroid use, and pre-operative sepsis. In addition, the lab findings prior to surgery were reported as well including the levels of creatinine, white blood cell count, serum albumin, platelets and INR (international randomized ratio of prothrombin time).

Outcomes Examined

The primary surgical outcome studied was 30-days mortality of IBD patients following colectomy. The secondary post-operative outcomes that were identified included the occurrence of anastomotic leak and reoperation rate within 30 days following the surgery. These outcomes were also compared between patients with Crohn's disease and those with Ulcerative Colitis after adjusting for confounders. Using step-wise multivariate analysis, we studied the risk factors associated with post-operative complications while adjusting for the confounding variables.

Statistical Analysis

Descriptive statistics were reported using mean and standard deviation (SD) for continuous variables and frequency distributions for categorical variables. The Student's t test, chi-squared test, and Fisher's exact probability test were used as appropriate. To adjust for confounding factors, we performed multivariate analysis using logistic regression model and studied the factors associated with post-operative mortality, anastomotic leak, and reoperation among IBD patients undergoing colectomy. Independent variables for multivariate analysis included those with a significant association in univariate analysis as well as those previously reported as influencing the risk of post-operative complications (odds ratio [OR], 95% confidence interval [CI]). A P value of <0.05 was considered statistically significant.

Results

Descriptive Statistics

The demographic and clinical characteristics were listed in Table 1. A total of 5049 patients who underwent colectomy for either Ulcerative Colitis (1414, 28%) or Crohn's disease (3635, 72%) were identified. Around 52% of patients were females and 90% were white. Mean age was 41.3 years in the Crohn's disease group and 45.6 years in the Ulcerative Colitis group.

Obesity was significantly more prevalent among Ulcerative Colitis patients with 24.7% of these patients having a BMI greater than 30 Kg/m² compared to the 19.5% among Crohn's disease patients being obese. Patients with Ulcerative Colitis undergoing colectomy were more likely to have severe COPD ($P<0.001$), diabetes mellitus ($P<0.001$), and significant weight loss (<10% in 6 months) prior to surgery ($P<0.001$). In addition, Ulcerative Colitis patients had higher ASA class and almost a fifth presented with an emergent surgery which correlates with the higher prevalence of systemic diseases among this group of patients. On the other hand, smoking was more prevalent among the patients with Crohn's disease ($P<0.001$).

Table 1. — Descriptive Statistics; Statistics used
(mean, standard deviation, t-test, chi-squared test, Fischer's test)

Variable	All (n=5049)		Crohn's (n=3635)		UC (n=1414)		P-value
Demographic Characteristics							
Mean age in years (SD)	42.5	(16.4)	41.3	(15.7)	45.6	(17.7)	<0.0001
Gender, female (%)	2610	(51.7)	1962	(54.0)	648	(45.8)	
Race							
White (%)	4235	(90.4)	3052	(89.7)	1183	(92.1)	
Black or African American (%)	389	(8.3)	314	(9.2)	75	(5.8)	
Others	63	(1.3)	36	(1.1)	27	(2.1)	
BMI > 30	1046	(21)	701	(19.5)	345	(24.7)	<0.0001
Operative Information							
General anesthesia	5041	(99.8)	3629	(99.8)	1412	(99.9)	1.00
ASA class (IV-V)	175	(3.5)	52	(1.4)	123	(8.7)	<0.0001
Mean total operation time in min (SD)	174.59	(85.7)	167.06	(82.0)	193.93	(91.9)	<0.0001
Days from admission to operation (SD)							
0	3343	(66.2)	2613	(71.9)	730	(51.6)	<0.0001
1	295	(5.8)	184	(5.1)	111	(7.9)	
>1	1411	(27.9)	838	(23.1)	573	(40.5)	
Emergency case	501	(9.9)	252	(6.9)	249	(17.6)	<0.0001
Wound classification							
Clean	34	(0.7)	27	(0.7)	7	(0.5)	
Clean/Contaminated	3057	(60.5)	2191	(60.2)	866	(61.2)	
Contaminated	1220	(24.2)	838	(23.1)	382	(27.1)	
Dirty/Infected	738	(14.6)	579	(15.9)	159	(11.2)	
Clinical Characteristics							
Smoking within past year	1029	(20.4)	883	(24.3)	146	(10.3)	<0.0001
Sever COPD	98	(1.9)	51	(1.4)	47	(3.3)	<0.0001
Diabetes Mellitus	274	(5.4)	144	(3.9)	130	(9.2)	<0.0001
Pre-operative Sepsis (48 hours)	571	(11.3)	309	(8.5)	262	(18.5)	<0.0001
>10% loss of body weight in last 6 months	589	(11.7)	347	(9.6)	242	(17.1)	<0.0001
Pre-operative Steroid Use	3011	(59.6)	2103	(57.9)	908	(64.2)	<0.0001
Lab Findings							
Pre-operative Creatinine (SD)	0.82	(0.48)	0.80	(0.32)	0.86	(0.74)	0.003
Pre-operative Serum albumin (SD)	3.41	(0.79)	3.56	(0.71)	3.06	(0.86)	<0.0001
Pre-operative Platelets *1000(SD)	325	(123)	319	(115)	339	(141)	<0.0001
Pre-operative INR (SD)	1.13	(0.37)	1.11	(0.30)	1.18	(0.48)	<0.0001
Pre-operative WBC *1000 (SD)	9.2	(4.5)	8.7	(4.0)	10.2	(5.6)	<0.0001

Concerning the lab findings prior to surgery, Ulcerative Colitis patients had a higher mean white blood cell count ($P<0.001$), INR ($P<0.001$), and creatinine ($P=0.003$) while Crohn's disease patients had a higher serum albumin level ($P<0.001$) (Table 1).

Outcomes

A) Mortality

The 30-day mortality rate was 1.0% among all patients under study with a higher mortality rate among Ulcerative

Table 2. — **Multivariate Analysis of Factors Associated with Post-Operative Complications ; Statistics used (multivariate analysis, Odds Ratio and 95% Confidence Interval)**

Risk Factors	OR	95% CI		p-value
30 days Mortality				
ASA class > 3	8.22	3.60	18.80	<0.0001
Age (>55)	4.46	1.91	10.40	0.0005
Functional Status	2.21	0.76	6.38	0.14
Emergency Surgery	3.04	1.25	7.39	0.01
Smoking	0.43	0.16	1.18	0.08
Weight Loss	3.41	1.48	7.89	0.004
Diabetes	2.32	0.96	5.60	0.10
Pre-operative Steroid use	0.41	0.19	0.86	0.01
Pre-operative sepsis	3.67	1.65	8.19	0.002
Pre-operative INR >1.4	3.52	1.55	8.00	0.02
Anastomotic Leak				
Crohn's vs UC	0.53	0.37	0.76	0.0005
Gender (Female vs Male)	0.66	0.50	0.87	0.003
Operation time	1.13	1.03	1.22	0.006
Emergency Surgery	1.79	1.17	2.74	0.007
Smoking	1.81	1.34	2.45	<0.0001
Pre-operative Steroid Use	1.29	0.97	1.72	0.08
Pre-operative WBC >11,000	1.33	0.98	1.82	0.07
Reoperation				
Gender (Female vs Male)	0.79	0.61	1.02	0.07
ASA class > 3	1.64	0.93	2.91	0.09
Operation time	1.11	1.02	1.20	0.01
Functional Status	2.07	0.80	5.36	0.14
Emergency Surgery	2.01	1.37	2.94	0.0003
Smoking	1.35	1.00	1.82	0.05
BMI > 30	0.57	0.39	0.83	0.003
Pre-operative Steroid use	1.66	1.26	2.19	0.0003

Colitis patients (2.6%) compared to Crohn's disease patients (0.3%). Weight loss prior to surgery ($P=0.004$), higher ASA class ($P<0.0001$), older age ($P=0.0005$), elevated pre-operative INR ($P=0.02$), and pre-operative sepsis ($P=0.002$) were associated with a higher mortality rate among all the patients who underwent colectomy. On the other hand, patients maintained on steroids preoperatively ($P=0.01$) had lower mortality rates (Table 2).

Table 3. — **Post-operative outcomes and morbidity among Crohn's disease and ulcerative colitis patients ; statistics use (univariate and multivariate analysis, Odds ration and 95% confidence interval)**

	Univariate analysis					Multivariate Analysis			
	All Patients (N=5049)		Crohn's Disease (N = 3635)		Ulcerative Colitis (N = 1414)	p-value	OR (95% CI)	p-value	
Anastomotic Leak (%)	217	(4.3)	174	(4.8)	43	(3.0)	0.006	0.53 (0.37-0.76)	0.0005
30 Days Mortality (%)	49	(1.0)	12	(0.3)	37	(2.6)	<0.001	1.36 (0.60-3.06)	0.46
30 Days Reoperation (%)	259	(8.4)	175	(7.9)	84	(9.8)	0.08	1.08 (0.80-1.45)	0.61

B) Anastomotic Leak

The incidence of anastomotic leak among the patients was 4.3% with a higher incidence among Crohn's disease patients (4.8%) compared to Ulcerative colitis patients (3.0%). Smoking ($P<0.0001$) and longer operation time ($P=0.006$) were associated with an increased risk of post-operative anastomotic leak. Females had a lower incidence of anastomotic leak compared to males ($P=0.003$). (Table 2)

C) Reoperation Rate

The 30-day reoperation rate was 8.4% among all patients under study with a higher rate among Ulcerative Colitis patients (9.8%) compared to Crohn's disease patients (7.9%) Reoperation was more prevalent among the patients maintained on steroids preoperatively ($P=0.0003$) and smokers ($P=0.05$). Obese patients had a lower reoperation rate compared to those with lower BMI ($P=0.003$). Patients that underwent an emergent surgery had higher rates of mortality ($P=0.01$), anastomotic leak ($P=0.007$), and reoperation ($P=0.0003$) compared to those who had an elective surgery. (Table 2)

Comparing outcomes in Ulcerative Colitis Vs Crohn's Disease

The post-operative complications among both groups were listed in Table 3. Among all the patients involved in the study, a total of 49 patients (1%) died during a period of 30 days following the surgery with a mortality rate quite higher among the Ulcerative Colitis patients ($P<0.0001$).

Comparing the composite morbidity and post-operative complications between the patients with a history of Crohn's disease and those with a history of Ulcerative Colitis, the prevalence of anastomotic leak was higher among patients with Crohn's disease ($P=0.006$). The rate of reoperation was higher in Ulcerative Colitis patients ($P=0.08$) following their colectomy (Table 3). After adjusting for confounding variables, the difference in 30-days mortality between both groups became less significant with a slightly higher rate among UC patients compared to Crohn's disease patients (OR = 1.36, p-value = 0.46). Concerning other outcomes, the change in the Odds Ratio between both groups was less significant (Table 3).

Discussion

Our study showed that the rate of post-operative mortality and morbidity was significantly higher in Ulcerative Colitis compared to Crohn's disease patients but this finding became less significant after adjusting for the confounding variables. This likely reflects the severity of disease among Ulcerative Colitis patients undergoing surgery with almost 18% of these patients having emergent salvage surgery. This finding is consistent with previous studies confirming the fact that emergent surgery is one of the highest risk factors for post-operative mortality (14-16). Poor nutritional status prior to surgery reflected by preoperative weight loss was associated with increased mortality among patients with inflammatory bowel disease post-colectomy. Similarly, sepsis and elevated INR preoperatively were independent predictors of increased mortality. Elderly patients and those with higher morbidity score had increased mortality which is consistent with recent findings by Bollegala et. Al (17). In aggregate these findings suggest that sicker debilitated IBD patients with associated comorbidities have a higher mortality after colonic resection. These factors should be considered when planning and timing surgical interventions.

There is limited data on the risk factors for anastomotic leak and reoperation in patients with inflammatory bowel disease. In our study, emergent surgery again carried a higher risk of return to the operation room or anastomotic leak following the intestinal resection compared to elective surgery. Several studies have reported current smoking status as an independent risk factor for anastomotic leak which agrees with the higher rate of leak among smokers in our study (4,18,19). A systematic review showed that Crohn's disease patients on corticosteroids had a 6.8% rate of anastomotic leak compared to 3.3% for those not maintained on corticosteroids which is comparable to our finding where steroid users had a slightly higher rate of a leak event (20).

The Cleveland clinic reported a 3-fold increased risk of pouch failure and reoperation post colectomy in Crohn's disease patients compared to Ulcerative Colitis while our study showed a slightly higher rate of return to the operation room among Ulcerative Colitis patients (21). Those differences could be attributed to differences in the outcomes examined (any reoperation vs pouch failure) and possibly some selection bias related to surgeries performed in a referral center compared to a large national database. Small bowel disease and upper gastrointestinal involvement were also associated with a higher risk of readmission to the hospital in another study, factors that couldn't be examined in our cohort. Among patients with Ulcerative Colitis, several studies showed that male sex, persistently elevated inflammatory markers and smoking status predict colectomy in patients with long standing Ulcerative Colitis (22-24). These same factors carried a higher risk of reoperation and

anastomotic leak in this study as well. These findings suggest that predictors of refractory disease and hence surgery could also predict complicated post-operative course.

One of the strengths of our study is the evaluation of the risk factors for 30-days reoperation using NSQIP among IBD patients and comparing this outcome between Ulcerative Colitis and Crohn's disease patients over 3 years. A recent study showed a reoperation rate of 7.1% at 30-day among IBD patients (17). Our study confirms and extends these findings from the NSQIP data and is consistent with the study by Scarpa et. Al that showed a re-laparotomy rate of 8% in Crohn's Disease patients (25). Preoperative steroids use was an independent predictor of reoperation and anastomotic leak (25). Steroids are usually sensitive to the dosing period and dose. A possible hypothesis is that the rapid suspension of steroids can cause an inflammatory flare leading to postoperative complications depending on its severity. Poor functional status and higher morbidity were also shown to be independent predictors of reoperation after bowel surgery in IBD patients. These findings should be considered by managing physicians for better understanding of the outcomes in this group of patients.

It is very important to emphasize however that the data collection process and the NSQIP data itself suffers from some deficiencies. The lack of information on pathology, exact type of surgery and specific disease characteristics and biology make any conclusions regarding the described outcomes mostly speculative. As in other large database studies and while the large number of patients helps offset some of these deficiencies, the observations made actually lead to more questions and help define future directions for research. This is evident in the current study addressing a complex IBD patient population.

In addition, and as pointed out by other researchers using the database (26), the data collection might not be very accurate especially if the initial data collection module was not designed to capture the details of specific disease entities or conditions. This might well be the case in our cohorts where detailed medical and treatment histories related to IBD will impact the way we analyze the data and the conclusions drawn. Such detailed information might also help explain some of the unexpected findings such as the lower mortality while on steroids and the more reoperation among Ulcerative Colitis patients.

Another limitation of the data is that NSQIP only measures 30-day mortality and reoperation, and long-term outcomes are not assessed. Such outcomes are important end points in this patient population.

Conclusion

Analysis of this data illustrates that in a large cohort of patients, major surgical complications except 30-day mortality appear to increase with the use of preoperative

steroids among IBD patients undergoing colectomy. Compared to Crohn's disease patients, Ulcerative Colitis patients have higher mortality rate and more surgical complications except for anastomotic leak. These findings should be kept in mind when planning surgical interventions among IBD patients. More studies are needed where the efforts should be directed towards creating an IBD module in NSQIP so that IBD specific data can be collected and studied.

Conflict of interest statement

None of the authors has any conflict of interest with respect to the presented study.

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