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Outcomes of Bowel Resection in Patients with Crohn's Disease

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There is limited data regarding outcomes of bowel resection in patients with Crohn's disease. We sought to investigate complications of such patients after bowel resection. The Nationwide Inpatient Sample databases were used to examine the clinical data of Crohn's patients who underwent bowel resection during 2002 to 2012. Multivariate regression analysis was performed to investigate outcomes of such patients. We sampled a total of 443,950 patients admitted with the diagnosis of Crohn's disease. Of these, 20.5 per cent had bowel resection. Among patients who had bowel resection, 51 per cent had small bowel Crohn's disease, 19.4 per cent had large bowel Crohn's disease, and 29.6 per cent had both large and small bowel Crohn's disease. Patients with large bowel disease had higher mortality risk compared with small bowel disease [1.8% vs 1%, adjusted odds ratio (AOR): 2.42, $P < 0.01$]. Risks of postoperative renal failure (AOR: 1.56, $P < 0.01$) and respiratory failure (AOR: 1.77, $P < 0.01$) were higher in colonic disease compared with small bowel disease but postoperative enteric fistula was significantly higher in patients with small bowel Crohn's disease (AOR: 1.90, $P < 0.01$). Of the patients admitted with the diagnosis of Crohn's disease, 20.5 per cent underwent bowel resection during 2002 to 2012. Although colonic disease has a higher mortality risk, small bowel disease has a higher risk of postoperative fistula.

Crohn's Disease is a chronic destructive disease, which is associated with long-term disability.^{1,2} Also, Crohn's disease makes up a significant segment of inflammatory bowel diseases, which have been estimated to be responsible for more than 1.7 billion dollar costs/year in the United States.³ Despite many advances in the nonsurgical treatment of Crohn's disease, the need for bowel resection during a patient's lifetime has been estimated to be necessary in 70 to 90 per cent of patients with Crohn's disease.^{4,5} However, operation for Crohn's disease is not reliably curative, and endoscopic recurrence has been reported in 70 to 90 per cent of patients who had bowel resection within one week of operation.^{6,7} Investigation of factors associated with the need for operation, complications of patients who undergoing bowel resection, and alternative treatment methods other than operation will help advance the understanding of Crohn's disease.

A number of studies have investigated alternative treatments to decrease the need for operation in the management of Crohn's disease. Previous studies have introduced endoscopic dilation in the treatment of Crohn's strictures with a reported success rate of 86 per cent.^{8,9} Also, the impact of new medications on decreasing requirement for operation has been reported.^{10,11} Marked changes in rates of operation in the treatment of Crohn's disease from 1986 to 2003 have been reported in the United Kingdom.¹¹ However, there is limited data regarding contemporary trends of need for operation in patients who were admitted with Crohn's disease in the United States. High rates of postoperative complications of bowel resection in patients with Crohn's disease have also been cited multiple times.^{12,13} Septic intra-abdominal complications and bowel fistula are two uncommon but dreaded complications of operation in patients suffering from Crohn's disease.^{12,14} Postoperative intra-abdominal septic complications are also associated with an increased risk of recurrence and need for additional operation.¹⁵ A recent study reported that optimal perioperative care can decrease the rate of postoperative complications of patients with Crohn's disease.¹² However, there are limited data regarding identified factors associated with mortality and morbidity of Crohn's disease patients who underwent bowel resection. This study aims to report trends in the treatment of Crohn's disease in the United States, and report the rate of postoperative complications in such patients who underwent bowel resection, and investigate factors associated with mortality and morbidity of patients.

Materials and Methods

This study was derived from the Nationwide Inpatient Sample (NIS) database during 2002 to 2012. The NIS database is an inpatient care database that contains information from nearly eight million hospital stays each year across the United States with an approximately 20 per cent stratified sample of the American community, nonmilitary, and nonfederal hospitals, resulting in a sampling frame that approximates 95 per cent of all hospital discharges in the United States.¹⁶ This study evaluated patients who underwent bowel resections with the diagnosis of Crohn's disease using the appropriate codes as specified by the International Classification of Diseases, Ninth Revision, Clinical Modifications (ICD-9-CM) diagnosis codes of 555.0 to 555.9. Patients who had bowel resection were defined based on the following ICD-9-CM procedure codes: 45.61 to 45.63, 45.71 to 45.76, 45.81 to 45.83, 45.91 to 45.95, 48.50 to 48.59, and 48.62. Patients younger than 18 years were excluded from this study.

Variables that were considered in the study include basic demographic data (age, sex, and race), comorbidity conditions including history of congestive heart failure within 30 days before surgery, renal failure, presence of malignancy, weight loss, fluid and electrolyte disorders, liver disease, diabetes mellitus, coagulopathy, weight loss (more than 10% in last six months), and history of chronic pulmonary disease. Operative factors analyzed include surgical approach (open versus laparoscopic), type of the procedure (ileocecectomy, right colectomy, total colectomy, proctectomy, abdominoperineal resection of rectum, left colectomy, transverse colectomy, sigmoidectomy, and small bowel resection). Complications investigated include mortality, overall morbidity, intra-abdominal abscess, deep vein thrombosis, pneumonia, respiratory failure, urinary tract infection, myocardial infarction, acute renal failure, intestinal fistula (enteroenteric or enterocutaneous), enterovaginal fistulas, enterourinary fistulas, and prolonged hospitalization (longer than 30 days). The overall rates of each complication were examined. Risk-adjusted analysis was performed to compare the outcomes of colonic disease compared with small bowel Crohn's disease.

Statistical Analysis

Data were analyzed using the SPSS® software, Version 22 (SPSS Inc., Chicago, IL). Logistic regression analysis was used to estimate the risk of each complication. The presence of postoperative complications was considered as the dependent variable whereas diabetes mellitus, presence of malignancy, fluid and electrolyte disorders, chronic pulmonary disease, congestive heart failure, site of Crohn's disease (small bowel, colon, and both), weight loss, coagulopathy, liver disease, renal failure, type of the procedure, surgical approach (open versus laparoscopic), type of admission, age, gender, and race were covariates. P values less than 0.05 were considered statistically significant. For each outcome, the adjusted odds ratio (AOR) with a 95 per cent confidence interval (CI) was calculated and reported to estimate the relative risk associated with each complication.

Results

The study population consisted of 443,950 patients who were admitted to a hospital with the diagnosis of Crohn's disease during 2002 to 2012. Overall, 91,013 (20.5%) patients needed bowel resection during the index hospitalization. The median age of patients was 44-years; the majority of patients were white (80.9%) and female (56.7%). Most common comorbidities included fluid and electrolyte disorders (28.1%) and weight loss (8.8%). Patients with small bowel Crohn's disease were greater in number than those with colonic disease. The summary of patient characteristics is shown in Table 1.

Overall, 20.5 per cent of Crohn's patients who were admitted to hospitals underwent bowel resection. Females were less likely than males to need operation during hospitalization (AOR: 0.83, CI: 0.82–0.85, P <

0.01). The number of patients who were admitted to a hospital with the diagnosis of Crohn's disease steadily increased from 36,428 in 2002 to 41,125 in 2012 (Fig. 1). However, the rate of bowel resection decreased from 24.8 per cent in 2002 to 17 per cent in 2012 (Fig. 2).

Among patients who were operated with Crohn's disease 46,399 (51%) had small bowel disease, 17,652 (19.4%) had large bowel disease, and 26,962 (29.6%) had both small bowel and large bowel disease. The most common procedure was right colectomy (34.5%) followed by ileocolectomy (26.2%) and small bowel resection (24%).

The most common postoperative complications were enteric fistula (14.8%) followed by intra-abdominal abscess (6.1%). Laparoscopic approach had significantly lower postoperative enteric fistula compared with open approach (AOR: 0.73, CI: 0.62–0.87, $P < 0.01$).

The risk-adjusted analysis for postsurgical complications by disease site is reported in Table 2. Mortality (AOR: 2.42, CI: 1.91–3.07, $P < 0.01$) and overall morbidity (AOR: 1.25, CI: 1.23–1.28, $P < 0.01$) were higher in colonic disease. However, intra-abdominal abscess (AOR: 1.37, CI: 1.22–1.54, $P < 0.01$) and bowel fistula (enteroenteric or enterocutaneous) (AOR: 1.90, CI: 1.75–2.06, $P < 0.01$) were significantly higher in small bowel Crohn's disease.

For patients who underwent resection, the overall mortality rate was 1.1 per cent. After adjustment with multivariate analysis we found 11 factors associated with mortality. Mortality predictors are reported in Table 3. Patients with coagulopathy and older than 70 years had more than six times higher mortality risk. Also, open bowel resection had three times higher mortality risk compared with laparoscopic approach.

This study found 12 factors associated with morbidity of Crohn's patients who underwent bowel resection. The most important morbidity predictor was coagulopathy. Table 4 reports morbidity predictors of Crohn's patients who underwent bowel resection. The overall morbidity rate was 17.6 per cent. Colon resection had higher morbidity compared with small bowel resection (AOR: 1.34, $P < 0.01$). Also, right colectomy procedure had lower morbidity compared to ileocolectomy procedure (AOR: 0.90, $P < 0.01$).

TABLE 1. Demographics of Patients with Diagnosis of Crohn's Disease who Underwent Bowel Resection

Variables		Small Bowel Crohn's Disease (46,399)	Large Bowel Crohn's Disease (17,652)	Both Small and Large Bowel Crohn's Disease (26,962)	
Age	Mean, year	45 ± 17	48 ± 17	41 ± 16	
	Median, year	42	48	39	
Sex	Male	22,503 (48.5%)	7,735 (43.8%)	12,888 (47.8%)	
Race	White	30,772 (86.1%)	11,636 (82.5%)	17,452 (84.4%)	
	Black or African-American	2,665 (7.5%)	1,342 (9.5%)	1,846 (8.9%)	
	Asian	1,160 (3.2%)	533 (3.8%)	713 (3.4%)	
	Others	1,151 (3.2%)	587 (4.2%)	662 (3.2%)	
	Admission	Elective surgery	22,036 (47.6%)	9,587 (54.4%)	14,777 (54.9%)
Comorbidity	Nonelective surgery	24,285 (52.4%)	8,034 (45.6%)	12,143 (45.1%)	
	Fluid and electrolyte disorders	9,546 (20.8%)	4,160 (23.8%)	5,244 (19.7%)	
	Weight loss	5,262 (11.5%)	2,523 (14.4%)	3,348 (12.6%)	
	Chronic pulmonary disease	4,580 (10%)	1,874 (10.7%)	2,279 (8.6%)	
	Diabetes mellitus	2,152 (4.6%)	1,386 (7.8%)	974 (3.6%)	
	Coagulopathy	888 (1.9%)	459 (2.6%)	511 (1.9%)	
	Congestive heart failure	858 (1.9%)	590 (3.4%)	356 (1.3%)	
	Renal failure	707 (1.5%)	403 (2.3%)	261 (1%)	
	Malignancy in diagnosis	646 (1.4%)	694 (3.9%)	283 (0.9%)	
	Liver disease	523 (1.1%)	260 (1.5%)	280 (1.1%)	
	Procedure	Small bowel resection	19,714 (42.4%)	0	3,228 (12%)
		Right colectomy	13,654 (29.4%)	4,656 (26.4%)	13,080 (48.5%)
		Ileocolectomy	13,031 (28.2%)	4,485 (25.4%)	9,169 (34%)
Transverse colectomy		0	876 (5%)	168 (0.6%)	
Left colectomy		0	2,421 (13.7%)	257 (1%)	
Proctocolectomy		0	34 (0.2%)	25 (0.1%)	
Total colectomy		0	1,909 (10.8%)	546 (2%)	
Abdominoperineal resection of rectum		0	1,076 (6.1%)	242 (0.9%)	
Sigmoidectomy		0	2,195 (12.4%)	247 (0.9%)	

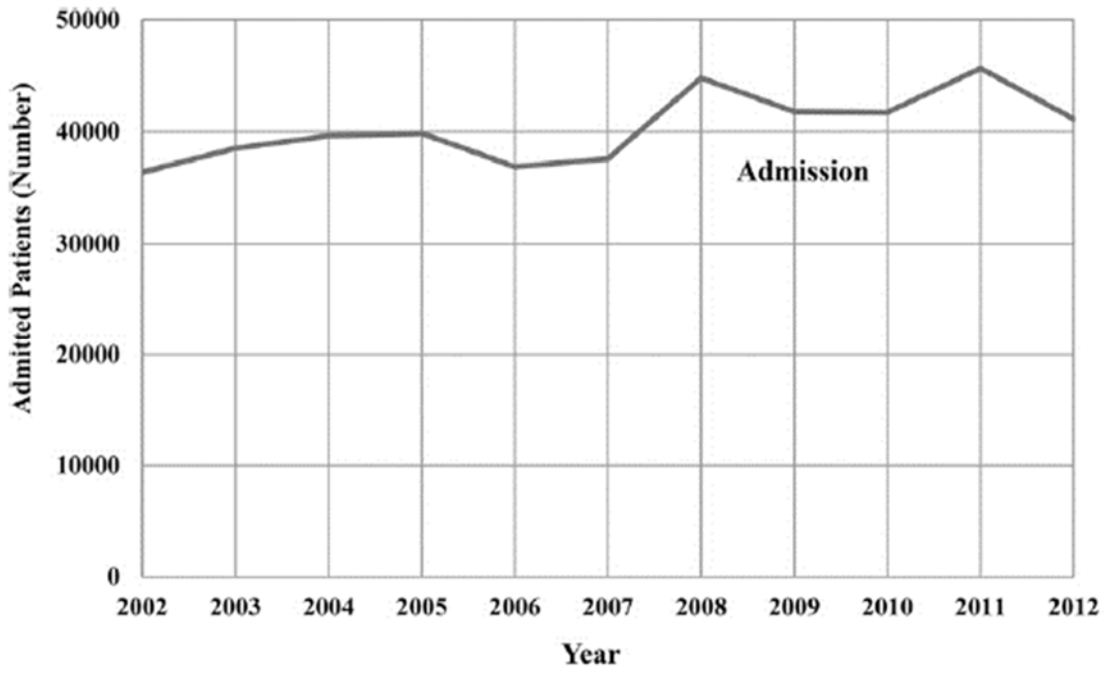


FIG. 1. Number of patients admitted with the diagnosis of Crohn's disease over time.

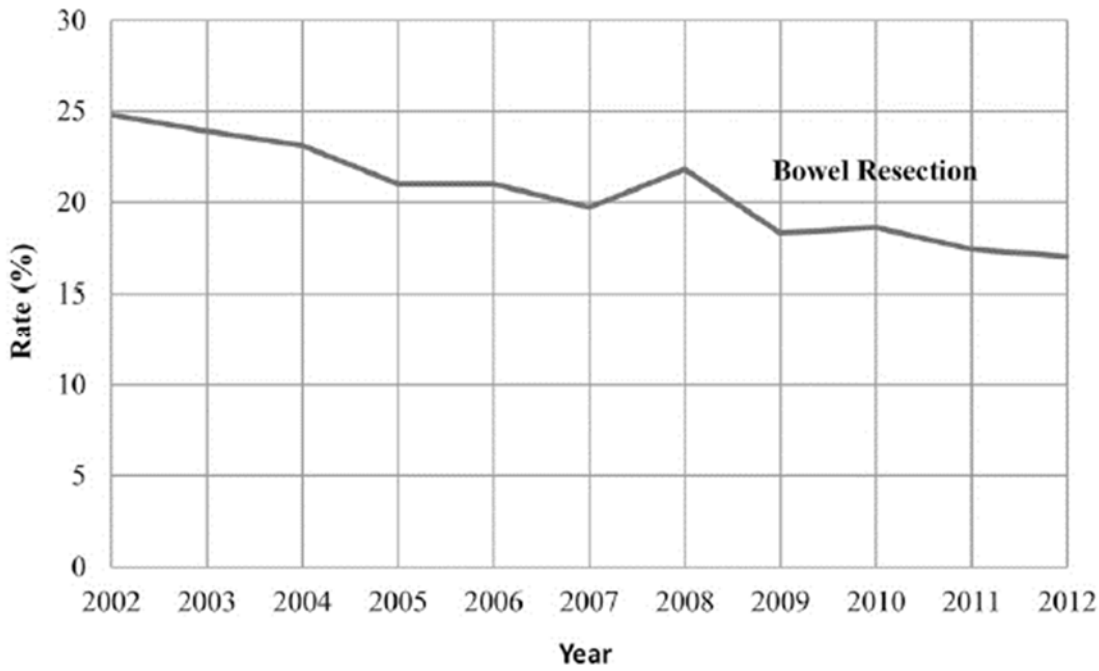


FIG. 2. Rate of need to bowel resection for patients admitted with diagnosis of Crohn's disease over time.

TABLE 2. Risk-adjusted Analysis of Outcomes of Patients with Crohn's Disease who Underwent Bowel Resection by Disease Site

Complication	Small Bowel Crohn's Disease (46,399)	Large Bowel Crohn's Disease (17,652)	AOR	95% CI	P value
Mortality	479 (1%)	320 (1.8%)	2.42	1.91–3.07	<0.01
Overall morbidity*	7569 (16.3%)	3996 (22.6%)	1.25	1.23–1.28	<0.01
Septic shock	555 (1.2%)	299 (1.7%)	1.98	1.54–2.54	<0.01
Sepsis	1577 (3.4%)	1029 (5.8%)	1.95	1.71–2.22	<0.01
Enterovaginal fistula	183 (0.4%)	430 (2.4%)	1.83	1.35–2.48	<0.01
Respiratory failure	888 (1.9%)	568 (3.2%)	1.77	1.49–2.11	<0.01
Wound infection	1079 (2.3%)	606 (3.4%)	1.65	1.42–1.92	<0.01
Hospitalization more than 30 days	1401 (3%)	741 (4.2%)	1.64	1.42–1.90	<0.01
Renal failure	1363 (2.9%)	937 (5.3%)	1.56	1.35–1.81	<0.01
Deep vein thrombosis	179 (0.4%)	153 (0.9%)	1.56	1.09–2.22	0.01
Pneumonia	1281 (2.8%)	714 (4%)	1.18	1.01–1.37	0.03
Myocardial infarction	200 (0.4%)	115 (0.6%)	1.16	0.79–1.71	0.43
Wound disruption	536 (1.2%)	291 (1.7%)	1.24	0.99–1.55	0.06
Hemorrhagic complications	632 (1.4%)	240 (1.4%)	0.93	0.75–1.15	0.53
Pulmonary embolism	275 (0.6%)	130 (0.7%)	1.18	0.86–1.62	0.28
Urinary tract infection	1832 (4%)	972 (5.5%)	1.02	0.90–1.17	0.65
Intestinal fistula†	6562 (14.1%)	1706 (9.7%)	0.55	0.51–0.60	<0.01
Enterourinary fistula	959 (2.6%)	433 (2.4%)	0.52	0.43–0.63	<0.01
Intra-abdominal abscess	2758 (5.9%)	868 (4.9%)	0.74	0.66–0.83	<0.01

* Pneumonia, sepsis, septic shock, respiratory failure, renal failure, myocardial infarction, deep vein thrombosis, hospitalization more than 30 days, wound infection, intra-abdominal abscess, wound disruption, hemorrhagic complications, pulmonary embolism, urinary tract Infection, and intestinal fistula.

† Enteroenteric or enterocutaneous.

Discussion

Our results show that patients with Crohn's disease have 1.1 per cent mortality and 17.6 per cent morbidity rates after bowel resection. Overall mortality rate after elective colon resection has been reported between 1.08 and 1.56 per cent, so patients with Crohn's disease do not have any apparent higher mortality risk.¹⁷ We found an overall morbidity rate of 17.6 per cent for Crohn's patients who underwent bowel resection, which is in line with previous reports of 12.8 to 20.2 per cent by Tan and 18 per cent reported by Zerbib.^{12, 18} Overall 17.6 per cent morbidity of Crohn's patients who underwent bowel resection is in the lower range of the 17 to 35 per cent overall morbidity rates, which have been observed for colorectal surgery patients.^{19–21} There is a steady decrease in the per cent of hospitalized patients with the diagnosis of Crohn's disease who underwent bowel resection. Although the number of patients admitted to hospitals with diagnosis of Crohn's disease increased from 36,428 patients in 2002 to 41,125 patients in 2012, the rate of need for operation

TABLE 3. Risk-adjusted Analysis of Factors Associated with Mortality of Patients with Crohn's Disease after Bowel Resection

Variables	AOR	95% CI	P value
Age (years)			
≤70	Reference	Reference	Reference
>70	6.11	5.27–7.09	<0.01
Sex			
Female	Reference	Reference	Reference
Male	1.35	1.18–1.54	<0.01
Admission			
Elective	Reference	Reference	Reference
Nonelective	3.05	2.55–3.65	<0.01
Surgical technique			
Laparoscopic	Reference	Reference	Reference
Open	3.01	1.19–7.58	0.01
Comorbidity			
Chronic pulmonary disease	1.13	0.94–1.35	0.17
Coagulopathy	6.62	5.54–7.91	<0.01
Liver disease	2.91	2.14–3.97	<0.01
Renal failure	1.71	1.33–2.19	<0.01
Diabetes mellitus	0.97	0.78–1.21	0.80
Congestive heart failure	3.60	2.99–4.34	<0.01
Malignancy in diagnosis	0.88	0.59–1.31	0.53
Weight loss	1.83	1.58–2.12	<0.01
Fluid and electrolyte disorders	1.85	1.61–2.13	<0.01
Procedure			
Ileocollectomy	Reference	Reference	Reference
Right colectomy	0.83	0.68–1.01	0.06
Transverse colectomy	0.99	0.99–1	0.98
Left colectomy	0.67	0.40–1.15	0.15
Small bowel resection	1.46	1.18–1.80	<0.01
Proctectomy	0.99	0.99–1	0.99
Total colectomy	1.30	0.81–2.10	0.26
Abdominoperineal resection of rectum	0.99	0.50–1.96	0.98
Sigmoidectomy	0.72	0.46–1.14	0.16
Disease site			
Small bowel	Reference	Reference	Reference
Large bowel	2.42	1.91–3.07	<0.01

decreased significantly from 24.8 per cent in 2002 to 17 per cent in 2012. This can perhaps be explained by the improvement in nonsurgical treatment of Crohn's disease over the last decade. This is in line with previous reports of the decrease in need for operation in management of Crohn's disease in Canada and the United Kingdom.^{11, 22} Although the need for operation did not significantly decrease during 1993 to 2004 in the United States,²³ we found significant decrease in need for operation during 2002 to 2012 (24.8% vs 17%, $P < 0.01$).

Intestinal fistula (enteroenteric or enterocutaneous) is the most common complication of bowel resection in Crohn's patients. We found a rate of 14.8 per cent of postoperative intestinal fistula after bowel resection, significantly higher than other postoperative complications. The second most common complication of surgery in Crohn's patients was intra-abdominal abscess (6.1%). We found that using a laparoscopic technique in the operative treatment of Crohn's patients was associated with a decreased risk of postoperative fistula (11.8% vs 14.8%; AOR: 0.73, $P < 0.01$). Further studies are indicated to evaluate these findings.

Our study results show that the mortality and morbidity risks in patients who had colonic Crohn's disease were significantly higher than small bowel Crohn's disease. Also, complications of wound infection and wound disruption were significantly higher in colonic Crohn's patients. Among bowel fistula complications, the risk of enterovaginal fistula was significantly higher in colonic Crohn's disease compared with small bowel Crohn's disease, whereas the risk of enteroenteric, enterocutaneous, and enterourinary fistula were significantly lower in colonic Crohn's disease compared with small bowel Crohn's disease (AOR: 0.55, 0.52, $P < 0.01$). Also, we found a significantly higher risk of intraabdominal abscess in small bowel Crohn's compared to colonic Crohn's disease. Further studies are indicated to validate these findings.

The most common procedure for Crohn's disease was right colectomy (34.5%) followed by ileocelectomy (26.2%) and small bowel resection (24%). In comparing right colectomy with ileocelectomy, although the mortality risks of the procedures were not significantly different, morbidity of patients who underwent ileocelectomy was higher than for patients who underwent right colectomy. Also, mortality and morbidity of patients who underwent small bowel resection were significantly higher than patients who underwent ileocelectomy.

We found lower risk of need for operation during hospitalization in female gender compared to male gender, which is in line with a previous report by Nguyen.²⁴

TABLE 4. Risk-adjusted Analysis of Factors Associated with Morbidity of Patients with Crohn's Disease after Bowel Resection

	Variables	AOR	95% CI	P value
Age (years)	≤70	Reference	Reference	Reference
	>70	1.55	1.46–1.64	<0.01
Sex	Male	Reference	Reference	Reference
	Female	1.03	1.001–1.07	0.04
Admission	Elective	Reference	Reference	Reference
	Nonelective	2	1.92–2.08	<0.01
Surgical Technique	Laparoscopic	Reference	Reference	Reference
	Open	1.18	1.007–1.39	0.04
Comorbidity	Chronic pulmonary disease	1.21	1.14–1.28	<0.01
	Coagulopathy	4.36	3.92–4.85	<0.01
	Liver disease	1.30	1.12–1.51	<0.01
	Renal failure	3.46	3.06–3.91	<0.01
	Diabetes mellitus	1.24	1.15–1.34	<0.01
	Congestive heart failure	2.43	2.18–2.71	<0.01
	Malignancy in diagnosis	0.91	0.79–1.05	0.20
	Weight loss	2.47	2.35–2.79	<0.01
	Fluid and electrolyte disorders	2.48	2.38–2.59	<0.01
	Procedure	Ileocelectomy	Reference	Reference
Right colectomy		0.90	0.86–0.95	<0.01
Transverse colectomy		0.91	0.75–1.11	0.39
Left colectomy		1.28	1.11–1.48	<0.01
Small bowel resection		1.15	1.08–1.22	<0.01
Proctectomy		0.54	0.24–1.25	0.15
Total colectomy		1.51	1.30–1.75	<0.01
Abdominoperineal resection of rectum		1.17	0.97–1.41	0.09
Sigmoidectomy		0.95	0.81–1.11	0.54
Disease Site	Small bowel	Reference	Reference	Reference
	Large bowel	1.34	1.25–1.44	<0.01

Study Limitations

This study is a retrospective review and is subject to typical biases for retrospective studies such as selection bias. Data in this study were collected from a national database in the United States, and there is a wide variation in hospital setting, hospital quality, and surgeons' expertise that can confound the study. Although we adjusted the results with type of the procedures, disease site, and type of admission, we did not have any information regarding indication of surgery (abscess, fistula, or perforation), which we could not adjust for our results. This study reported trends in hospitalization and need for surgical treatment in management of patients admitted to the hospital with diagnosis of Crohn's disease. However, we did not have information of readmission or reoperation of Crohn's patients, and some patients may have multiple hospitalizations. Also, coding errors in collection of data may exist because of the use of discharge data in NIS database.²⁵ Despite these limitations, this study is one of the contemporary reports on report trends and outcomes of bowel resection in Crohn's patients using multivariate analysis.

Conclusion

There is a steady decrease in need for surgery in patients who were hospitalized with the diagnosis of Crohn's disease during 2002 to 2012, despite a steady increase in the number of hospitalizations over the same period. Enteric fistula and intra-abdominal abscess are the two most common complications of bowel resection in Crohn's patients. Although overall mortality and morbidity of bowel resection are higher in colonic disease compared with small bowel disease, patients with small bowel Crohn's who underwent bowel resection had significantly higher rates of postoperative enteroenteric fistula, enterocutaneous fistula, enterourinary fistula, and intra-abdominal abscess compared with colonic disease. However, enterovaginal fistula is higher in colonic disease. Fluid and electrolyte disorders and coagulopathy are two potentially reducible mortality and morbidity risk factors of patients who underwent bowel resections. Laparoscopic approach has lower risk of mortality, overall morbidity, and postoperative enteric fistula compared with open approach.

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