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Original Article

Not all cuts heal the same: elevated anastomotic leak rates after elective colectomy for inflammatory bowel disease and diverticulitis

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ABSTRACT

Background: Anastomotic leak (AL) is a severe complication of colorectal surgery. However, the association between AL and the indication for surgery remains unclear. This study aimed to assess the risk of AL among patients undergoing elective colectomy for inflammatory bowel disease (IBD), cancer, diverticulitis, and polyp, hypothesizing the highest risk in IBD.
Methods: This was a retrospective cohort study of patients who underwent elective colectomy with primary ileocolic or colocolonic anastomosis from 2011 to 2021. The primary outcome was AL occurrence. The secondary outcomes included rates of reoperation, nonoperative interventional and conservative treatments after AL, timing of reoperation, and incidence of AL after hospital discharge. Univariate analyses used analysis of variance and chi-square tests with post hoc corrections. Multivariate logistic regression analysis identified independent AL risk factors. The Kruskal-Wallis test with Dunn's test was used to assess the timing of reoperation.
Results: Among 83,992 patients, those who underwent surgery for IBD (3.4%) and diverticulitis (3.0%) had higher rates of AL than those who underwent surgery for colon cancer (2.3%) and polyps (2.0%) ($P < .001$). Multivariate analysis revealed that IBD (odds ratio [OR], 1.28 [95% CI, 1.03–1.58]) and diverticulitis (OR, 1.20 [95% CI, 1.03–1.39]) were independently associated with AL compared with colon cancer. Patients with IBD who developed AL were more likely to undergo nonoperative interventional treatment (32.4%) than those with colon cancer (18.5%) and polyps (23.8%).
Conclusion: Surgical procedures for IBD and diverticulitis are risk factors for AL after elective colectomy, with IBD having the highest risk.

Introduction

Anastomotic leak (AL) is one of the most serious complications after colorectal surgery, resulting in increased length of stay, higher hospitalization costs, and increased morbidity and mortality [1]. Previous estimates of AL rates ranged between 1% and 3% for ileocolic anastomosis and 6% and 12% for left colon anastomosis [2]. The established risk factors for developing AL include preoperative (smoking, alcohol consumption, obesity, malnutrition, and preoperative radiotherapy), intraoperative (bowel vascularization, surgical approach, suture type, diverting stoma, and anastomotic tension), and postoperative (anemia and transfusion) factors [3–6]. Previous research has shown that resection for Crohn disease may have greater complication rates than resection for colon cancer [7,8]. This may be related to microscopic inflammation at the resection margin [9,10], greater use of immunosuppressive therapy [11], poorer tissue quality, and more technically challenging surgery due to fibrosis from inflammatory bowel disease (IBD) flares or previous surgical procedures. Overall, little information is available about surgical indication as a potential risk factor for AL.

Several institutional and national studies have shown conflicting results, were limited by low numbers of AL in their cohorts, and typically did not adequately adjust for confounders of AL [12–19]. To the best of our knowledge, no national studies have specifically evaluated the effect of surgical indication on AL rates. In addition, the association of surgical indication with outcomes of AL, such as treatment modality, day of reoperation, and rates of AL after discharge, is unknown.

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The objectives of this study were to (i) determine the association of surgical indication with the risk of AL after elective colectomy and to (ii) evaluate the association of surgical indication on AL-related outcomes, including treatment modality, timing of reoperation, and the rate of AL development after hospital discharge. We hypothesized that colectomy with primary ileocolic or colocolonic anastomosis for IBD will be associated with higher AL rates than surgery for diverticulitis, colon cancer, or polyps.

Materials and methods

Study design and data source

This was a retrospective cohort study that used the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database with the associated colectomy-targeted participant use data files from 2011 to 2021. The NSQIP database, which tracks surgical outcomes across participating hospitals, is a national, multi-institutional database maintained by the American College of Surgeons. In addition, the NSQIP database provides additional procedure-targeted databases that track variables specific to various procedures, such as the colectomy-targeted participant user data files.

This study was exempt from institutional review board approval because of the retrospective deidentified nature of the database. This study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (Supplementary File) [20].

Study population

Patients who underwent open or minimally invasive colectomy with primary ileocolic or colocolonic anastomosis (primary operation Current Procedural Terminology [CPT] codes 44140, 44204, 44205, and 44160) between 2011 and 2021 were extracted from the NSQIP database (Fig. 1). Patients with no additional procedures or those with adjunct procedures only (eg, splenic flexure mobilization and sigmoidoscopy) were included (secondary CPT codes 49321, 49905, 44213, 44139, and 45330). Patients with other secondary CPT codes were excluded from the study. We decided not to include colorectal anastomosis as the CPT codes for those procedures do not track the height of anastomosis, a significant risk factor for leaks. In addition, other variables, such as neoadjuvant radiation, that play a significant role in ALs are not tracked. Moreover, patients with missing AL status, disseminated cancer, outpatient surgery, emergency surgery, or American Society of Anesthesiologists Physical Status (ASA-PS) class V or those aged > 90 or < 18 years were excluded to minimize potential confounding from those with extreme physiological derangements. To account for the omission of a potentially large number of diverticulitis patients who received colectomy with colorectal anastomosis, we performed a sensitivity analysis that included patients who underwent

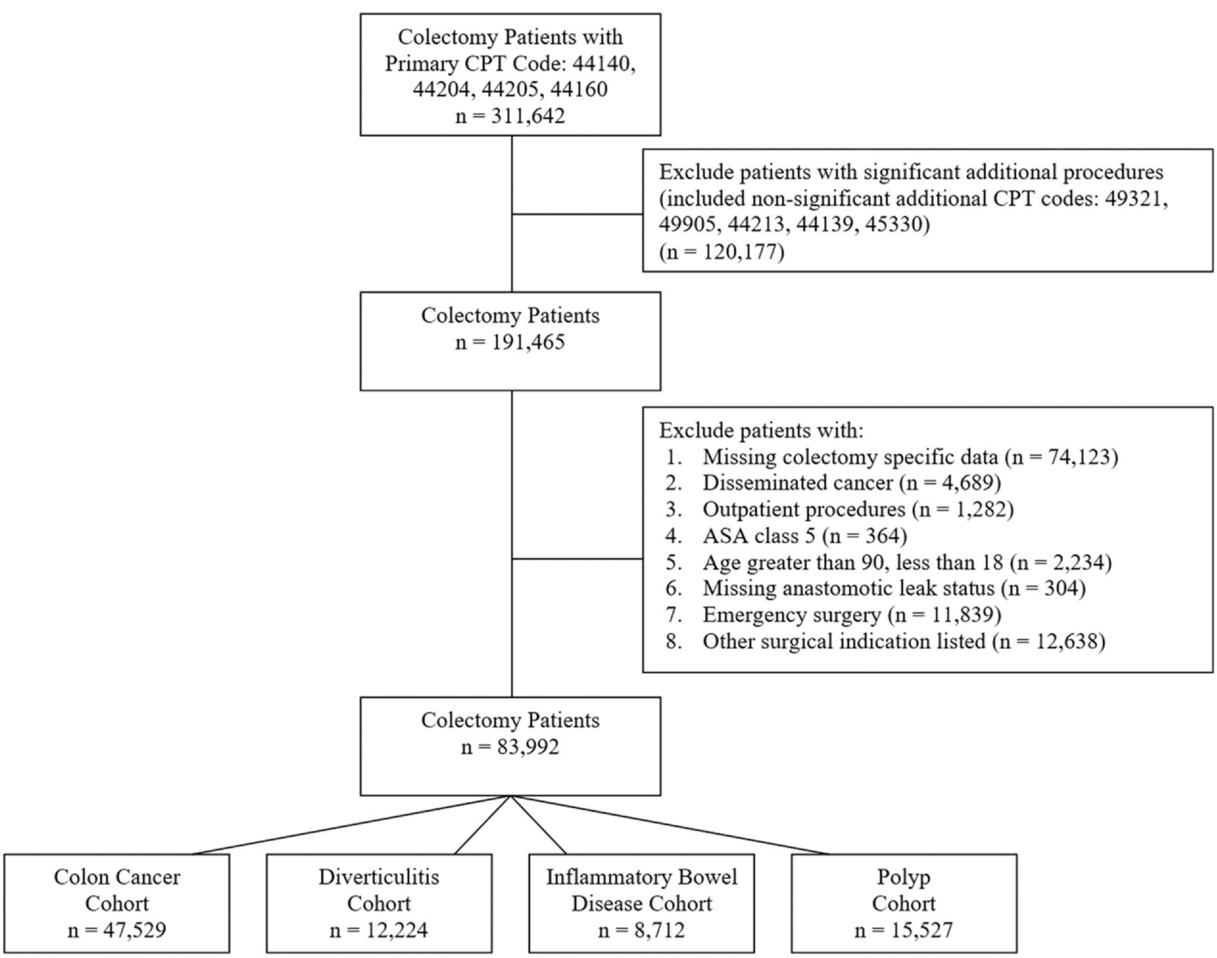

Figure 1. Patient selection flow diagram with exclusion criteria for our study population. ASA, American Society of Anesthesiologists.

colorectal anastomoses (CPT codes 44145 and 44207) as a primary indication for diverticulitis. We reassessed our main endpoints.

Patient background and surgical indication (exposure) variables

Patient characteristics that were analyzed included age, operative time, hypertension, smoking history, race, preoperative immunosuppression, ASA-PS class (I and II vs III and IV), preoperative transfusion, mechanical bowel preparation, insulin-treated diabetes mellitus, open case status, anastomosis location (ileocolic vs colocolonic), chemotherapy history, bleeding disorder history, functional status, history of chronic obstructive pulmonary disease (COPD), oral antibiotic preparation, obesity (body mass index ≥ 30 kg/m^2), preoperative hypoalbuminemia (albumin level < 3.5 g within 90 days of the primary operation), and preoperative anemia (hematocrit level < 30% within 90 days of the operation). The variable for preoperative immunosuppression in NSQIP covers the use of corticosteroids or other immunosuppressants, including the use of biologics for IBD. Further granularity in reporting the class of immunosuppressive therapy was not added until the 2021 dataset and, therefore, was not included in this study.

The independent variable of this study was surgical indication, which is coded in the colectomy-targeted participant use data file under the variable “COL_INDICATION.” We created 4 groups and identified indications with similar pathophysiology. “Ulcerative colitis” and “Crohn disease” were grouped into the IBD cohort, “colon cancer” and “colon cancer with obstruction” were grouped into the colon cancer cohort, “acute diverticulitis” and “chronic diverticular disease” were grouped into the diverticulitis cohort, and “nonmalignant polyp” was grouped into the polyp cohort.

Outcomes

The primary outcome of this study was 30-day AL rate. This variable is coded in the colectomy-targeted participant use data file under the variable “COL_ANASTOMOTIC” and includes data on the treatment modality used. All variables, including outcomes, in the NSQIP are coded and uploaded via retrospective chart review by clinically trained surgical clinical reviewers. The secondary outcomes included AL treatment modality, time to reoperation after the primary operation, and rate of AL development after discharge. The coding of AL treatment modality changed from 2012 to the following years. “Yes, reoperation,” (2012 coding) and “leak, treated with reoperation,” were grouped into the “reoperation cohort.” “Yes, percutaneous intervention,” (2012 coding) and ”leak, treated with interventional means,” were grouped into the “nonoperative interventional cohort.” “Yes, no intervention required,” (2012 coding) and “leak, treated with noninterventional/nonoperative means,” were grouped into the “conservative management” cohort. Patients with “leak, no treatment intervention documented,” were excluded from the treatment modality analyses.

Statistical analysis

Continuous variables were evaluated for normality with quantile-quantile plots. Categorical variables were represented as counts with frequencies, and continuous variables were presented as medians and IQRs. Univariate analyses were performed in R (version 4.3.3; R Core Team) using chi-square tests for categorical variables and one-way analysis of variance (ANOVA) for continuous variables. Post hoc testing was performed using chi-square tests with Bonferroni correction after chi-square tests and the Tukey honestly significant difference tests after ANOVA. Multivariate logistic regression was used to identify the independent risk factors for AL. To assess for multicollinearity among predictor variables, generalized variance inflation factors (GVIFs) were calculated. For categorical variables with > 2 levels, adjusted GVIF values were computed to compare predictors. A Kruskal-Wallis test with Dunn post hoc testing was performed for comparison of day of reoperation between surgical indications. Missing data were addressed with listwise deletion under the assumption of missing at random. The only variables included with rates of missingness of > 1% were mechanical bowel preparation and oral antibiotic preparation, with rates of 13.0% and 11.9%, respectively.

Results

Patient characteristics

Our final analysis included 83,992 patients, with 47,529 patients (56.6%) in the colon cancer cohort, 12,224 patients (14.6%) in the diverticulitis cohort, 8712 patients (10.4%) in the IBD cohort, and 15,527 patients (18.5%) in the polyp cohort. On univariate analysis, all patient background factors differed significantly by indication (P < .001). On post hoc analysis, patients in the IBD cohort were more likely to be younger; had lower rates of obesity, diabetes mellitus, hypertension, and COPD; and had higher rates of preoperative immunosuppression and open surgical approach than those in the other cohorts (Table 1 and Supplementary Table 1). Patients in the colon cancer cohort had higher rates of ASA-PS class III/IV and preoperative anemia and lower rates of smoking than those in the other cohorts. The IBD cohort had primarily ileocolic anastomosis (80.2%), whereas the diverticulitis cohort had primarily colocolonic anastomosis (95.9%). The colon cancer and polyp cohorts had relatively balanced anastomosis locations (54.2% vs 49.1% colocolonic anastomoses for colon cancer vs benign polyp cohorts, respectively). The polyp cohort had a shorter operative duration than the other cohorts.

AL rates between surgical indications

On univariate analysis, the overall AL rate differed significantly by indication (Table 2). The IBD and diverticulitis cohorts (3.4% and 3.0%, respectively) were associated with significantly greater rates of AL than the colon cancer and polyp cohorts (2.3% and 2.0%, respectively) on post hoc comparisons (P < .001) (Supplementary Table 2). For both ileocolic and colocolonic anastomosis, the AL rate also differed significantly by indication (P < .001). For ileocolic anastomosis, the IBD cohort was associated with a significantly greater rate of AL than the colon cancer and polyp cohorts (3.3% vs 2.1% and 1.7%, respectively; P < .001) on post hoc analysis. For colocolonic anastomosis, IBD and diverticulitis were associated with a significantly greater rate of AL than the polyp cohort (3.9% and 3.0% vs 1.6%, respectively; P < .001), and IBD was associated with a greater rate of AL than the colon cancer cohort (3.9% vs 2.5%, respectively). Generally, colocolonic anastomosis had greater rates of AL than ileocolic anastomosis across surgical indications (2.5% vs 2.1%, respectively, for colon cancer; 3.9% vs 3.3%, respectively, for IBD; and 2.3% vs 1.7%, respectively, for polyp), except for the diverticulitis cohort (3.0% vs 3.2%, respectively). These differences were significant for polyp (P =.049) and colon cancer (P =.032) cohorts but not for IBD (P = 1.0) or diverticulitis (P =.78) cohorts. There were no differences found for IBD (3.3% vs 3.9%; P =.78) or diverticulitis (3.2% vs 3.0%; P = 1.0). Regarding the surgical approach, open procedures had higher leak rates than minimally invasive approaches across surgical indications.

Multivariate logistic regression for risk factors of AL

On multivariate logistic regression, hypertension, history of bleeding disorder, smoking, open case status, dependent functional status, male sex, preoperative immunosuppression, IBD relative to colon cancer, “other” race relative to White, diverticulitis relative to colon cancer, preoperative hypoalbuminemia, ASA-PS class III/IV

Table 1
Comparison of baseline patient characteristics between surgical indications for elective colectomy between 2011 and 2021.

Participant characteristics	Colon cancer (n = 47,529)	Diverticulitis (n = 12,224)	Inflammatory bowel disease (n = 8712)	Polyp (n = 15,527)	Post hoc test
Age (y), median (IQR)	69 (18)	58 (17)	39 (25)	65 (15)	3 < 2 < 4 < 1
Female, n (%)	24,171 (50.9)	6544 (53.5)	4891 (56.1)	7907 (50.9)	1 = 4 < 2 < 3
Obesity, n (%)	16,735 (35.2)	5229 (42.8)	1873 (21.5)	6270 (40.4)	3 < 1 < 4 < 2
ASA-PS, n (%)					
Class I/II	17,412 (36.6)	7532 (61.6)	5389 (61.9)	7748 (49.9)	1 < 4 < 2 = 3
Class III/IV	30,047 (63.2)	4681 (38.3)	3318 (38.1)	7772 (50.1)	2 = 3 < 4 < 1
Insulin-treated diabetes mellitus, n (%)	3198 (6.7)	293 (2.4)	119 (1.4)	924 (6.0)	3 < 2 < 4 < 1
Hypertension, n (%)	26,764 (56.3)	5232 (42.8)	1452 (16.7)	8401 (54.1)	3 < 2 < 4 < 1
Chronic obstructive pulmonary disease, n (%)	2684 (5.7)	414 (3.4)	116 (1.3)	813 (5.2)	3 < 2 < 1 = 4
Smoking,[a] n (%)	5568 (11.7)	2307 (18.9)	1799 (20.6)	2652 (17.1)	1 < 4 < 2 < 3
Bleeding disorder, n (%)	1502 (3.2)	189 (1.6)	145 (1.7)	339 (2.2)	2 = 3 < 4 < 1
Functional status, n (%)					
Independent	46,207 (97.2)	12,137 (99.3)	8676 (99.6)	15,333 (98.8)	1 < 4 < 2 = 3
Dependent	1202 (2.5)	65 (0.5)	27 (0.3)	150 (1.0)	2 = 3 < 4 < 1
Preoperative transfusion, n (%)	1371 (2.9)	56 (0.5)	52 (0.6)	55 (0.4)	2 = 3 = 4 < 1
Preoperative chemotherapy, n (%)	791 (1.7)	43 (0.4)	40 (0.5)	66 (0.4)	2 = 3 = 4 < 1
Race, n (%)					
White	31,175 (65.6)	10,197 (83.4)	6830 (78.4)	11,427 (73.6)	1 < 4 < 3 < 2
Black or African American	4924 (10.4)	779 (6.4)	726 (8.3)	1908 (12.3)	2 < 3 < 1 < 4
Asian	2611 (5.5)	166 (1.4)	89 (1.0)	327 (2.1)	2 = 3 < 4 < 1
Other or unknown	8819 (18.6)	1082 (8.9)	1067 (12.2)	1865 (12.0)	2 < 3 = 4 < 1
Mechanical bowel preparation	30,103 (63.3)	8502 (70.0)	4692 (53.9)	9866 (63.5)	3 < 1 < 4 < 2
Oral antibiotic preparation	23,699 (49.9)	6805 (55.7)	4674 (53.7)	7869 (50.7)	1 < 3 = 4 < 2
Anastomosis type					
Colocolonic	25,748 (54.2)	11,720 (95.9)	1729 (19.8)	7617 (49.1)	3 < 4 < 1 < 2
Ileocolic	21,781 (45.8)	4504 (4.1)	6983 (80.2)	7910 (50.9)	2 < 1 < 4 < 3
Operative duration (min), median (IQR)	141.0 (82.0)	163.0 (89.0)	135.0 (75.0)	129.0 (73.8)	4 < 3 < 1 < 2
Preoperative hypoalbuminemia, n (%)	20,838 (43.8)	5904 (48.3)	3951 (45.4)	7571 (48.8)	3 = 1 < 2 = 4
Preoperative anemia, n (%)	8340 (17.5)	1246 (10.2)	1080 (12.4)	1858 (12.0)	2 < 3 = 4 < 1
Preoperative immunosuppression,[b] n (%)	1529 (3.2)	513 (4.2)	5266 (60.4)	477 (3.1)	1 = 4 < 2 < 3
Open surgical approach, n (%)	11,173 (23.5)	2398 (19.6)	2697 (31.0)	2131 (13.7)	4 < 2 < 1 < 3

ASA-PS, American Society of Anesthesiologists Physical Status.
[a] Smoking history includes any patient who has smoked within 1 year before surgery.
[b] Immunosuppression refers to regular administration of immunosuppressants (including corticosteroids, biologics, and disease-modifying antirheumatic drugs) within 30 days before the principal operation.

relative to ASA-PS class I/II, operation time, colocolonic anastomosis, lack of mechanical bowel preparation, and lack of oral antibiotic preparation were found to be independent risk factors for AL (Fig. 2). Relative to colon cancer, surgery for IBD was associated with an odds ratio (OR) of 1.28 (95% CI, 1.03–1.58), and surgery for diverticulitis was associated with an OR of 1.20 (95% CI, 1.03–1.39) (Table 3). Surgery for polyp relative to surgery for colon cancer was not a significant risk factor for AL, with an OR of 1.01 (95% CI, 0.87–1.16). All adjusted GVIF variables were below 1.4, indicating a low degree of multicollinearity (Supplementary Table 3).

Sensitivity analysis, including colorectal anastomoses for diverticulitis

In our sensitivity analysis, the number of patients with diverticulitis increased from 12,224 to 25,966 when we included patients who had colorectal anastomoses for diverticulitis. The number of patients with other indications remained the same. The AL rate for patients with diverticulitis decreased from 3.0% to 2.75% when we included colorectal anastomoses. On multivariate logistic regression, the ORs for IBD (OR, 1.28 [95% CI, 1.03–1.57]) and diverticulitis (OR, 1.20 [95% CI, 1.06–1.37]) for AL remained significant and were similar

Table 2
Comparison of rates of anastomotic leak between surgical indications for elective colectomy with ileocolic and colocolonic anastomoses between 2011 and 2021.

Outcome	Colon cancer (n = 47,529)	Diverticulitis (n = 12,224)	Inflammatory bowel disease (n = 8712)	Polyp (n = 15,527)	*P* value	Post hoc test
Anastomotic leak, n (%)	1113 (2.3)	364 (3.0)	296 (3.4)	313 (2.0)	**<.001**	3 = 2 > 1 = 4
By anastomosis location						
Ileocolic	466 (2.1)	16 (3.2)	228 (3.3)	137 (1.7)	**<.001**	3 > 4, 1
Open surgery	153 (3.1)	8 (5.7)	99 (4.6)	26 (2.6)	**.001**	3 > 1
MIS	313 (1.9)	8 (2.2)	129 (2.7)	111 (1.6)	**<.001**	3 > 4, 1
Colocolonic	647 (2.5)	348 (3.0)	68 (3.9)	176 (2.3)	**<.001**	3, 2 > 4 ǀ 3 > 1
Open surgery	224 (3.6)	99 (4.4)	34 (6.1)	29 (2.6)	**.002**	3 > 4, 1
MIS	423 (2.2)	249 (2.6)	34 (2.9)	147 (2.3)	**.04**	NA
By surgical approach						
Open	377 (3.4)	107 (4.5)	133 (4.9)	55 (2.6)	**<.001**	3, 2 > 4 ǀ 3 > 1
MIS	736 (2.0)	257 (2.6)	163 (2.7)	258 (1.9)	**<.001**	3 = 2 > 1 = 4

MIS, minimally invasive surgery; NA, not available.
Bold indicates *P* values of.05 as statistically significant.

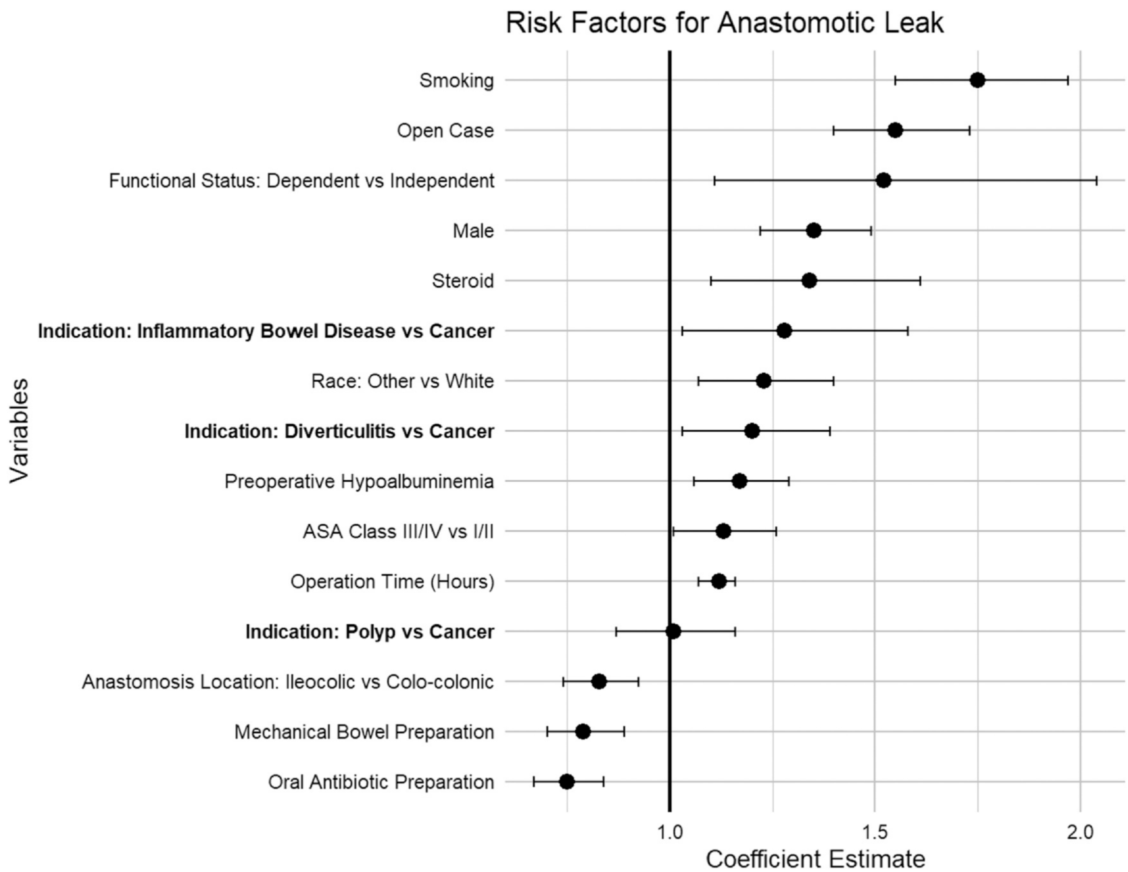

Figure 2. Independent factors associated with increased risk of anastomotic leak after elective colectomy with ileocolic and colocolonic anastomoses.

to those found in the primary analysis. In addition, all other variables that were significant in the primary multivariate regression were significant in the sensitivity analysis, with similar or identical ORs (Supplementary Table 4).

Management of AL by surgical indications

On univariate analysis, the rates of reoperation, nonoperative intervention, and conservative treatment of AL significantly differed by surgical indication (P =.026, P ≤.001, and P =.003, respectively) (Table 4). On post hoc pairwise comparisons with Bonferroni correction, we found no significant associations for rates of reoperation between surgical indications (Supplementary Table 5). The diverticulitis, colon cancer, IBD, and polyp cohorts had reoperation rates of 65.8%, 62.2%, 57.3%, and 55.5%, respectively (Table 4). On post hoc comparisons with Bonferroni correction for nonoperative interventional treatment, the IBD cohort had a significantly greater rate of nonoperative interventional treatment than the colon cancer and polyp cohorts (32.4% vs 18.5% and 23.8%, respectively). Post hoc pairwise comparisons with Bonferroni correction revealed that the IBD cohort had a significantly decreased rate of conservative treatment compared with the colon cancer and polyp cohorts (10.3% vs 19.3% and 20.7%, respectively) (Table 4).

Time to reoperation and postdischarge AL rate between surgical indications

On univariate analysis, the time to reoperation significantly differed by surgical indication (P < .001). On post hoc testing, the IBD cohort had a significantly decreased time to reoperation (median, 5 days [IQR, ± 4]) compared with the colon cancer, diverticulitis, and polyp cohorts (median: 7 days [IQR, ± 5] for colon cancer and diverticulitis and 7 days [IQR, ± 6] for polyp) (Fig. 3) (Supplementary Table 6). In addition, the proportion of patients who developed AL after discharge before requiring reoperation significantly differed by surgical indication (P < .001). On post hoc testing, the IBD cohort had significantly decreased rates of AL after discharge (26.7%) compared with the colon cancer (39.0%; P =.047), diverticulitis (49.5%; P < .001), and polyp (44.4%; P =.014) cohorts (Supplementary Tables 7 and 8).

Discussion

Our results demonstrated that surgical indication is an important risk factor for AL after elective colectomy with primary anastomosis. We found that surgery for IBD and diverticulitis, relative to surgery for colon cancer, were independent risk factors for AL. In addition, surgical indication had significant associations with AL outcomes. Surgery for IBD was associated with increased rates of nonoperative interventional treatment of AL, decreased rates of conservative treatment of AL, decreased time to reoperation, and decreased incidence of AL after discharge that required future reoperation compared with surgery for colon cancer, diverticulitis, and polyps.

We found that surgery for IBD and diverticulitis were significant risk factors for AL compared with surgery for colon cancer. This result differed from those of Parthasarathy et al. [21] and McKenna et al. [18], who both found that resection for cancer was an independent risk factor for AL after left-sided resection in an NSQIP-derived cohort. In addition, our findings differed from those of Midura et al. [17] and Rencuzogullari et al. [19] who did not find surgical indication to be an independent risk factor for AL. However, these study populations included those who underwent coloproctostomy for cancer, which typically undergoes neoadjuvant radiation, a significant risk factor for AL. As the NSQIP database does not collect data on perioperative radiation, this may have served as a

Table 3
Final multivariate logistic regression for anastomotic leak.

Participant characteristics	Adjusted odds ratio (95% CI)	P value
Age, y	1.00 (0.99–1.00)	.47
Male	1.35 (1.22–1.49)	**<.001**
Obesity	1.05 (0.94–1.17)	.38
ASA-PS class III/IV vs I/II	1.13 (1.01–1.26)	**.033**
Insulin-treated diabetes mellitus	1.01 (0.82–1.25)	.89
Hypertension	1.12 (1.00–1.26)	**.042**
Chronic obstructive pulmonary disease	1.10 (0.89–1.35)	.36
Smoking history[a]	1.75 (1.55–1.97)	**<.001**
Bleeding disorder	1.31 (1.00–1.68)	**.043**
Dependent functional status	1.52 (1.11–2.04)	**.007**
Preoperative transfusion	1.28 (0.93–1.73)	.12
Preoperative chemotherapy	0.76 (0.43–1.23)	.30
Race (reference: White)		
Black or African American	0.93 (0.78–1.10)	.42
Asian	0.94 (0.71–1.22)	.65
Other or unknown	1.23 (1.07–1.40)	**.002**
Mechanical bowel preparation	0.79 (0.70–0.89)	**<.001**
Oral antibiotic preparation	0.75 (0.67–0.84)	**<.001**
Ileocolic anastomosis (reference: colocolonic)	0.83 (0.74–0.93)	**<.001**
Operative duration, h	1.12 (1.07–1.16)	**<.001**
Preoperative hypoalbuminemia	1.17 (1.06–1.29)	**.003**
Preoperative anemia	0.97 (0.84–1.12)	.71
Preoperative immunosuppression[b]	1.34 (1.10–1.61)	**.003**
Open surgical approach	1.55 (1.40–1.73)	**<.001**
Surgical indication (reference: colon cancer)		
Polyp	1.01 (0.87–1.16)	.93
Diverticulitis	1.20 (1.03–1.39)	**.019**
Inflammatory bowel disease	1.28 (1.03–1.58)	**.027**

ASA-PS, American Society of Anesthesiologists Physical Status.
Bold indicates *P* values of.05 as statistically significant.
[a] Smoking history includes any patient who has smoked within 1 year before surgery.
[b] Immunosuppression refers to regular administration of immunosuppressants (including corticosteroids, biologics, and disease-modifying antirheumatic drugs) within 30 days before the principal operation.

confounder, which increased the risk of AL for patients with cancer. In addition, they did not include patients who underwent colectomy for IBD. Ilyas et al. [22] found that, in elective sigmoidectomy, surgery for colon cancer had a greater rate of AL than surgery for diverticular disease after propensity score matching. However, history of radiation was not accounted for in the propensity score matching. Therefore, our study focused on patients who had colon cancer resection with ileocolic or colocolonic anastomosis to eliminate neoadjuvant radiation as a potential confounder. Overall, our study aimed to isolate the effect of surgical indication on AL risk by addressing potential confounders through careful selection of our study population and multivariate logistic regression.

In addition, our results differed from those of Ilyas et al. [22], who found that diverticulitis had a higher rate of reoperation than colon cancer, and Bursztyn et al. [13], who found no difference in reoperation rates between Crohn disease and colon cancer. Although no significant results were observed in our post hoc testing for reoperation rates between surgical indications, an overall difference was found between the cohorts. Here, diverticulitis-associated AL had the greatest reoperation rate (65.8%), whereas polyp-associated AL had the least reoperation rate (55.5%). In addition, we found that surgery for IBD required greater rates of nonoperative interventional treatment, had decreased time to reoperation, and had decreased incidence of AL after discharge. We propose that these findings stem from more severe AL associated with IBD, necessitating nonoperative interventional treatment and reducing the time to reoperation. Furthermore, we suspect that the extended hospitalization often required for patients with IBD contributes to the lower incidence of AL once they are discharged. More research is needed to determine whether these results are driven by differences in AL-associated infectious complications, AL severity, or patient background comorbidity between surgical indications [23]. It has previously been shown that surgery for IBD was independently associated with greater infectious complications and increased return to the operating room compared with other indications [24,25]. In addition, the average patient comorbidity burden greatly varies by indication. Patients with IBD are often malnourished; are immunosuppressed [26]; have additional unaccounted for comorbidities, such as ankylosing spondylitis and autoimmune hepatitis; and often require more technically challenging surgical procedures [27]. To address these discordant results, future investigations should focus on prospective, multicenter analyses that incorporate patient comorbidity profiles, AL severity classifications, and AL associated outcomes. Such efforts would further clarify the relationship between surgical indication, use of postoperative interventions, and AL-associated outcomes.

In addition to surgical indication, we also found that smoking, open case status, functional status, male sex, preoperative immunosuppression, “other” race relative to White, preoperative hypoalbuminemia, ASA-PS class III/IV relative to ASA-PS class I/II, operation time, colocolonic anastomosis, lack of mechanical bowel preparation, and lack of oral antibiotic preparation were independent risk factors for AL. These results are concordant with previously described risk factors for AL [28]. We found that there were relatively low rates of mechanical bowel preparation and oral antibiotic preparation in our cohort. This may reflect the relatively lower usage of bowel preparation in the earlier years of the study period because of the lower adoption of Enhanced Recovery After Surgery protocols at the time. In addition, there may be issues with patient adherence to bowel preparation before surgery. Although most patients are recommended to use bowel preparation preoperatively, patient adherence is likely significantly less. The NSQIP database requires documentation of whether bowel preparation was performed before surgery, not whether it was prescribed. In addition, there may be an additional element of misclassification bias contributing to the missingness of these data and the low recorded rates of bowel preparation.

Although our study is unable to establish the underlying drivers of IBD as an independent risk factor for AL, the effect of IBD on poor bowel healing has been explored. Control of IBD with anti-inflammatory drugs, such as antitumor necrosis factor antibodies and

Table 4
Comparison of rates of treatment modalities for anastomotic leak between surgical indications for colectomy between 2011 and 2021.

Outcome	Colon cancer (n = 1034)	Diverticulitis (n = 348)	Inflammatory bowel disease (n = 281)	Polyp (n = 290)	P value	Post hoc test
Reoperation	643 (62.2)	229 (65.8)	161 (57.3)	161 (55.5)	**.026**	NA
Nonoperative interventional treatment[a]	191 (18.5)	58 (16.7)	91 (32.4)	69 (23.8)	**<.001**	3 > 1, 2
Conservative treatment[b]	200 (19.3)	61 (17.5)	29 (10.3)	60 (20.7)	**.003**	1, 4 > 3

NA, not available.
Bold indicates *P* values of.05 as statistically significant.
[a] Nonoperative interventional treatment was defined as treatment with percutaneous, radiological, or endoscopic interventional means.
[b] Conservative treatment was defined as treatment with nothing by mouth, antibiotics, total parenteral nutrition, or any other noninterventional or nonoperative means.

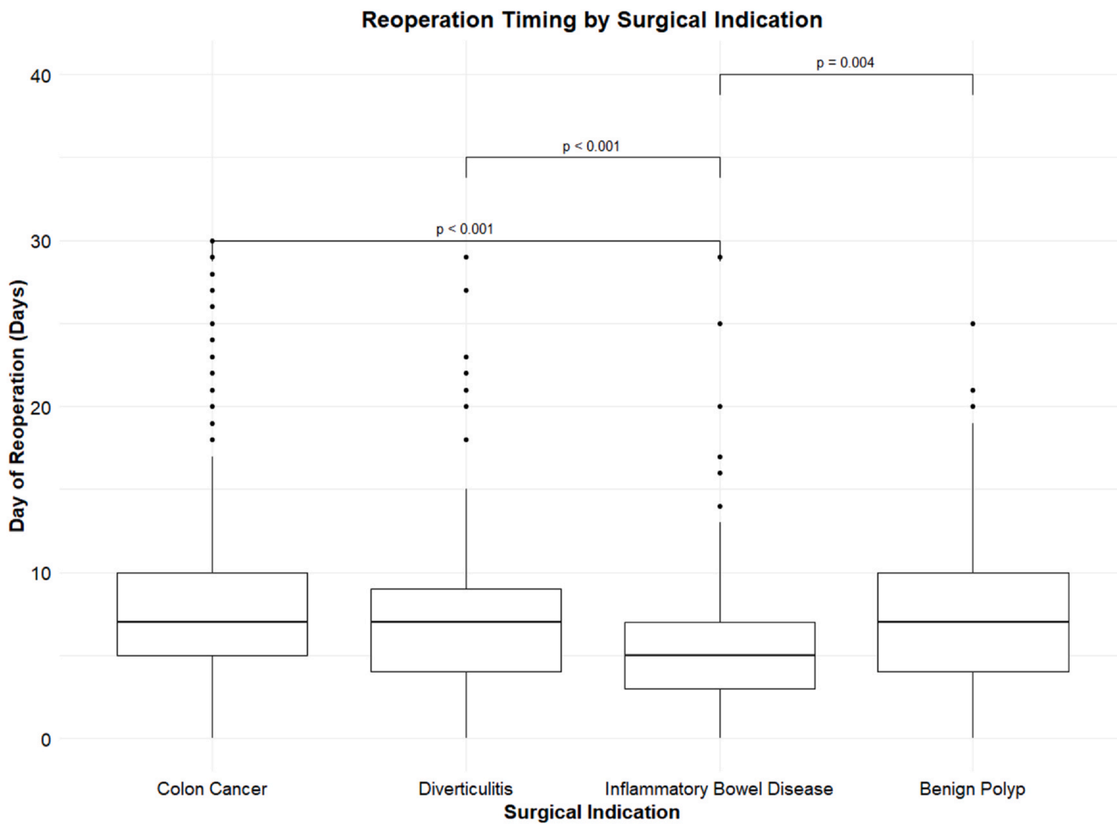

Figure 3. Comparison of time to reoperation for anastomotic leak after elective colectomy, by surgical indication.

azathioprine, induces mucosal healing and predicts lower hospitalization rates and sustained remission [29]. In addition, IBD is associated with poor tissue quality, malnutrition, and corticosteroid use, all of which inhibit tissue healing [30]. Finally, although macroscopically affected bowel can be targeted for resection, microscopic inflammation at resection margins may still be present, increasing the risk of recurrence and anastomotic complications [9,10]. We theorize that a general pathophysiological driver of our results is that the systemic inflammatory state of IBD generates microscopic inflammation in a greater area of the bowel than what is macroscopically evident, impairing healing of the anastomosis. Mechanistically, this may be related to complex inflammatory signaling associated with IBD, which interferes with the stages of anastomotic healing. For example, the levels of tumor necrosis factor alpha (TNF-α), interleukin 6, and interleukin 10, which are all associated with IBD [31], have been shown to be higher in the intraperitoneal fluid of patients who develop AL [32,33]. In contrast, resection for polyp and cancer would result in a healthier, noninflamed bowel for anastomosis surrounding the disease focus.

There are several active areas of research that explore the relationship between IBD and complications after surgery, which may help identify additional drivers of our results. The effect of biologics, such as TNF-α inhibitors on complications after colectomy, has been of great interest. The Prospective Cohort of Ulcerative Colitis and Crohn's Disease Patients Undergoing Surgery to Identify Risk Factors for Post-Operative INfection I (PUCCINI) cohort [34] and the Groupe de Recherche sur les Maladies Inflammatoires Digestives cohort [35] were prospective, multicenter studies that studied the effects of the use of TNF-α inhibitors on postoperative complications. They found that TNF-α inhibitors did not increase the risk of postoperative infections in patients with IBD and reaffirmed the increased risks associated with preoperative corticosteroid use. In addition, previous registry studies did not find any increased relative risk of AL after surgery for patients with IBD using TNF-α inhibitors [36,37]. In contrast, the Groupe d′Etude Thérapeutique des Affections Inflammatoires du Tube Digestif (GETAID) Chirurgie cohort found an increase in postoperative intra-abdominal septic and overall morbidities after surgery with TNF-α inhibitor exposure [38]. Differences in patient characteristics, practice patterns, and study methodology may have contributed to the differing outcomes between these studies. For example, the GETAID Chirurgie cohort had greater rates of surgery for stricturing disease than the PUCCINI cohort and defined biologic use based on patient-reported use. Overall, most evidence suggest that the use of TNF-α inhibitors does not increase the postoperative infectious risk after colectomy for IBD. However, further research is needed to evaluate the safety of newer biologics and small molecules perioperatively. Another area of ongoing study is the effect of the gut microbiome on outcomes of gastrointestinal diseases. For example, collagenolytic bacteria have been implicated in the pathogenesis of AL in animal models after colectomy [39–41]. In addition, dysbiosis has been shown to be present in both colon cancer and IBD and leads to inflammation and barrier disruption [42]. The relationship between gut microbiome dysbiosis and surgical indication may also be a contributing factor to the increased AL rate associated with IBD. Finally, there has been research into the use of tissue adhesives to reduce AL. Wu et al. [43] investigated the use of tissue adhesives in an experimental mouse model of IBD and found that Histoacryl Flex decreased proinflammatory macrophage accumulation at the anastomosis and increased anastomotic strength. However, Trotter et al. [44] found that the use of a hydrophilic adhesive patch on colorectal anastomoses in humans had negative effects on anastomotic healing. More research is needed to characterize how the underlying pathophysiology of IBD affects anastomosis healing, independent of malnutrition and steroid use, and the feasibility of tissue adhesive use in colectomy for IBD in humans.

This study has limitations inherent to retrospective research of a large database, such as selection bias, missing data, and patient misclassification. In addition, the large sample size increases the study power, but small, clinically insignificant differences may seem significant. Another limitation is that our study design may not have accounted for all potential confounders. The NSQIP database does not capture information on known risk factors of AL, such as intraoperative blood loss and alcohol use. In addition, although we attempted to eliminate neoadjuvant radiation as a potential confounder with our selected anastomosis types (ileocolic and colocolonic), this may still be a potential confounder in our study. Another potential confounder that could not be accounted for because of limitations in the NSQIP database is a history of previous colectomies. This would be especially relevant for cases of Crohn disease, in which patients often require multiple resections, altering the vascular supply and increasing the technical difficulty of the case. Another limitation is that our comparison of patients with AL after discharge was performed only in patients who later underwent reoperation. This is because the NSQIP database does not provide the date of AL, only the dates of the primary operation and reoperation. Therefore, we used the date of reoperation and the date of discharge to determine whether patients developed AL in the hospital. Finally, the generalizability of our findings is restricted to patients undergoing elective colectomy with primary anastomosis. In 2021, the NSQIP collected data from a wide range of United States (US) hospitals, totaling 685 participating centers. However, compared with the 2020 US census, our cohorts had a lower representation of Black and Asian patients, thereby limiting the generalizability of the results to these groups.

Conclusion

Our study demonstrated that surgical indication, specifically IBD and diverticulitis, are independent risk factors for AL compared with colon cancer. In addition, we showed that colectomy for IBD had associations with other AL outcomes, such as AL treatment modality, time to reoperation, and development of AL in the hospital. These results suggest that surgical indication is a crucial risk factor for surgeons to consider during surgical planning and patient risk stratification and that diversion should be considered in patients with IBD.

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Author contributions

K Sun: data acquisition, data analysis, data interpretation, drafting, revision, and final approval; CC Wang, M Shou, DR Habib, JL Rogers, J Sethurathnam, and D Ali: data analysis, data interpretation, drafting, and revision; A Khan: study conception, data interpretation, drafting, revision, and final approval.

Data availability

The data used for this article are from a publicly available, deidentified database from the American College of Surgeons (ACS) as part of the National Surgical Quality Improvement Program. These data can be requested after completing a Data Use Agreement, providing contact information, and completing an online questionnaire on the ACS website (https://www.facs.org/quality-programs/data-and-registries/acs-nsqip/participant-use-data-file/).

Declaration of competing interest

The authors declare no competing interests.

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Supplementary material

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.gassur.2025.102138.

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