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ORIGINAL RESEARCH—CLINICAL

Postoperative Use of Biologics Was Less Common Among Patients With Crohn's Disease With Emergent/Urgent vs Elective Intestinal Resection

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BACKGROUND AND AIMS: Given the risk of intestinal resection for Crohn's disease, postoperative treatment may be informed by several risk factors, including resection type. We compared postoperative treatment strategies for Crohn's disease between emergent/urgent vs elective resection. **METHODS:** We identified patients with intestinal resection for Crohn's disease between 2002 and 2018 using the MarketScan databases. We classified emergent/urgent resections as those occurring after emergency department admission or after the second day of admission. We estimated adjusted risk differences for the association between resection type (emergent/urgent vs elective) and 6-month postoperative medication strategy (biologic monotherapy, biologic combination therapy with an immunomodulator, immunomodulator monotherapy, other nonbiologic medication for Crohn's [5-aminosalicylates, antibiotics, and corticosteroids], or no medications for Crohn's). **RESULTS:** During 6 months after resection among 4187 patients, 23% received biologic monotherapy, 6% received combination therapy, 16% received immunomodulator monotherapy, and 36% received other nonbiologics. Compared with elective resection, emergent/urgent resection was associated with more common use of "other nonbiologic" medications (risk difference 6.4%; 95% confidence interval [CI] 2.8%, 10.0%), but less common use of biologic monotherapy (risk difference −3.2%; 95% CI −6.2%, −0.1%) and no medications (risk difference −3.6%; 95% CI −6.6%, −0.6%). **CONCLUSION:** Although patients with emergent/urgent resection may benefit from more aggressive postoperative therapy, there was evidence that emergent/urgent resection was more associated than elective resection with postoperative use of nonbiologics for Crohn's disease. Future studies of treatment patterns and comparative effectiveness of postoperative treatment strategies for Crohn's patients should consider these differences between resection types, which may be important drivers of longer term outcomes.

Keywords: Crohn's Disease; Postoperative Treatment; Intestinal Resection

Introduction

Despite significant therapeutic advances for Crohn's disease (CD), including increasing availability and use of biologic therapies, up to 80% of patients with CD may still require surgical intervention.[1–4] The most common surgical procedure is an ileocolonic resection, which involves surgical removal of the intestinal area most commonly affected by chronic inflammation.[4–7] However, surgical resection is not curative; 25% of patients who experience an intestinal resection have been estimated to require a subsequent resection within 5 years.[3,5,8] Because of this high rate of recurrence, in recent years, an increased emphasis has been placed on identifying appropriate and effective strategies for the prevention of postoperative recurrence.

The American Gastroenterological Association currently recommends early pharmacological prophylaxis with anti-tumor necrosis factor (TNF)-α agents after intestinal resection; this recommendation is instead of other agents or endoscopy-guided postoperative management for patients who are considered high risk for postoperative recurrence based on provider assessment.[4] The risk factors for postoperative recurrence include age, multiple prior resections, disease phenotype, and tobacco use.[4,7] However, the clinical complexities of CD translate to heterogeneous pharmacologic and nonpharmacologic treatment strategies in real-world populations.[9,10] Emergent surgery for inflammatory bowel disease (IBD) has been associated with postoperative

Abbreviations used in this paper: **CD, Crohn's disease; CI, confidence interval; IBD, inflammatory bowel disease; RD, risk difference; TNF, tumor necrosis factor.**

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complications and mortality.[11,12] Compared with patients with elective procedures, patients who need emergent or urgent resection may have more progressive disease and may benefit from aggressive postoperative prophylaxis. Given changes in the management of CD in the last 20 years, the extent of postoperative guideline concordance is also unknown. Treatment options now include anti-integrins and anti-interleukin 12/23 biologics but are not addressed in current guidelines.[4,7,13]

The goal of this study was to investigate postoperative medication use for CD and incidence of postoperative complications, comparing patients who experienced an emergent/urgent vs elective resection, using US administrative claims data over a 17-year period. We hypothesized that emergent/urgent (vs elective) surgery would be associated with more aggressive treatment after resection, such as biologics or immunomodulators as opposed to other nonbiologics alone, and have higher risk of complications.

Materials and Methods

Study Design and Population

We analyzed US administrative claims from the IBM Watson Health MarketScan Commercial Claims and Encounters database, which contains enrollment and health care encounter data for employer-sponsored health insurance beneficiaries and their dependents.[14] We included patients aged <65 years with an intestinal resection for CD during 2002–2018 based on Current Procedural Terminology codes for small bowel resection, ileocolonic resection, and other colonic or rectal resection performed in an inpatient setting (Table A1).[15–21] We required that patients had an International Classification of Diseases, 9th or 10th Revision, Clinical Modification, diagnosis code for CD on the same claim as the resection procedure service charge (Table A2).[15,16]

Using a 24-month preresection baseline period, we required that patients had continuous enrollment with fee-for-service medical and pharmacy coverage. We also required no prior resection during this baseline period because prior resection is associated with postoperative recurrence, and patients with multiple resections may require unique postoperative management strategies.[4,7] We used a 24-month baseline period to balance our intention of only including patients at their first resection for CD against the constraints of beneficiary enrollment duration in the MarketScan databases. We further required that patients had a recorded baseline diagnosis of CD, defined by a majority of medical claims with diagnosis codes for CD over ulcerative colitis.[22,23] To reduce potential inclusion of patients who had a resection for another gastrointestinal condition, we excluded patients with a diagnosis code for ulcerative colitis, colorectal cancer, or diverticulitis during their inpatient stay associated with the resection (Table A2). Figure 1 illustrates the design for this cohort study.

Emergent/Urgent vs Elective Resection

To compare postoperative treatment strategies and complications across surgery types, we classified patients by whether they had an emergent/urgent or elective resection. Previous studies have identified nonelective cases of abdominal surgery for gastrointestinal conditions in claims data using various definitions, usually associated with an emergency department admission[24–26] or procedures occurring up to 1 week after admission.[27–30] We defined emergent or urgent resections as procedures that occurred either (1) after admission through the emergency department or (2) after the second day of an inpatient admission. All other resections were considered elective procedures.

Outcomes

The primary outcome was the first observed treatment strategy in the 6-month (180-day) period after the resection date, classified as (1) biologic monotherapy, (2) biologic combination therapy with an immunomodulator, (3) immunomodulator monotherapy, (4) other nonbiologics only (at least one claim for 5-aminosalicylates, oral antibiotics, or corticosteroids), or (5) no medications.[9,23] For the biologic combination therapy group, we required that patients had claims for a biologic and an immunomodulator no more than 30 days apart (see Table A3 for medication codes and Supplemental Methods for additional detail operational definitions for postoperative treatments using outpatient and prescription claims.).

Given the reported association of emergent/urgent surgery and postoperative complications,[12] we assessed secondary outcomes as the 30- and 60-day incidence of postoperative complications after resection, which included claims for medical- and surgery-related complications, as well as claims for any infection. Postoperative complications were assessed as a composite outcome occurring by 30 or 60 days after resection (see Table A4 and Supplemental Methods for additional detail on postoperative complications definitions).[17]

Covariates

We assessed baseline characteristics, including demographics, clinical variables, recent health care utilization, and baseline medication exposure as covariates. Demographics included age at resection, sex, US Census region, resection year, and health plan type.[14] We categorized year according to biologic approval dates for use in CD in the United States: 2002–2007, 2008–2013, and 2014–2018.[31] Clinical variables included the Quan-Charlson Comorbidity Index score, history of smoking, and history of other non-IBD immune-mediated conditions (rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, psoriasis, ankylosing spondylitis, multiple sclerosis, hidradenitis suppurativa, and uveitis) that are also treated with biologics approved for CD.[32–39] We further identified whether the patient had a hospitalization, emergency department visit, gastroenterologist visit, or endoscopy in the 12 months before the resection date. For prior medication exposure during the 24-month baseline period, we assessed outpatient infusion or prescription claims for medications used to treat IBD (see Tables S2–S5 for diagnosis codes for clinical covariates and Supplemental Methods for further detail on operational definitions).

Statistical Analysis

We estimated the average treatment effect in the treated, which asks, "how much would postoperative treatment and outcomes change among patients who had emergent/urgent

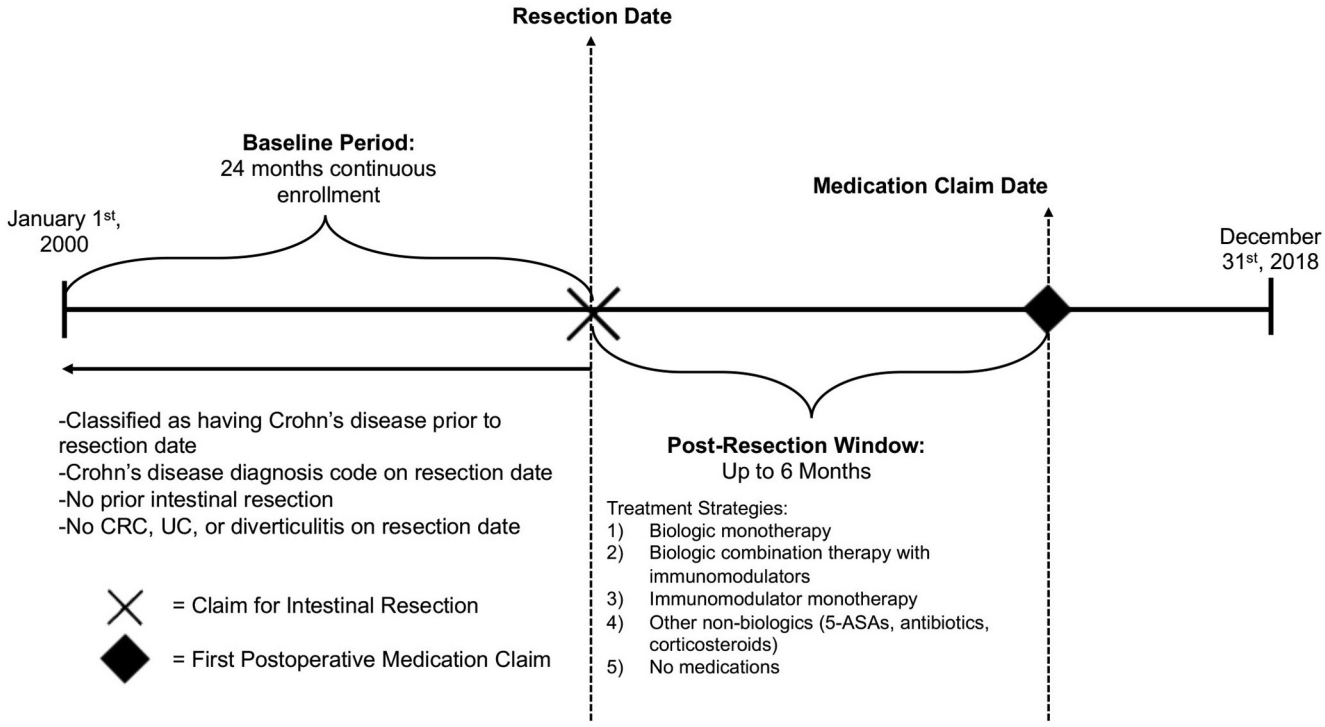

Figure 1. Study design.

resection if they instead had an elective resection?" To address this question and control for measured confounding, we used standardized mortality ratio weights based on the propensity score for emergent/urgent resection.[40–44] In addition, to account for loss-to-follow-up when individuals were disenrolled from the MarketScan database, we used inverse probability of censoring weights (see Supplemental Methods for additional detail on weighting.).[44,45] Before and after weighting, we calculated standardized mean differences to examine covariate balance between emergent/urgent and elective resection groups.[46,47]

In the crude and weighted data for each resection type, we assessed the incidence of (1) postoperative treatment strategies in the 6-month period after resection and (2) postoperative complications in the 30- and 60-day period after resection. To measure the association between emergent/urgent resection and postoperative outcomes in the weighted data, we estimated risk differences (RDs) between emergent/urgent and elective resection and 95% confidence intervals (CIs) for each treatment strategy and complication outcomes.[43]

All authors had access to the study data and reviewed and approved the final manuscript. This study was reviewed and exempted by the Institutional Review Board at the University of North Carolina at Chapel Hill (#20-1417). All analyses were conducted using SAS version 9.4 (SAS Institute, Inc, Cary, NC).

Results

There were 4187 patients who met inclusion criteria; the median age at resection was 39 years (interquartile range 26–51), 54% of patients were female, 70% were enrolled in a preferred provider organization health plan, and 59% had an ileocolonic resection (Table 1). During the 24-month preresection baseline period, 51% of patients had $\geq$1 claim for biologics and 81% had $\geq$1 claim for corticosteroids.

The prevalence of emergent/urgent resection was 27%. In the crude data, compared with patients who had elective resection, patients with emergent/urgent resection were younger and more commonly male (Table 1). In addition, patients with emergent/urgent resection had lower prevalence of (24-month) preresection claims for antibiotics (70% vs 80%), biologics (45% vs 53%), and immunomodulators (38% vs 46%), lower prevalence of (12-month) preresection gastroenterologist visit (67% vs 79%) or endoscopy visit (53% vs 75%), and higher prevalence of (12-month) preresection hospitalization (52% vs 46%) or emergency department visit (45% vs 36%). After weighting, the elective cohort was standardized to the emergent/urgent resection population and was well balanced (Table 1; see Figure A1 for standardized mean differences before and after weighting).

In the crude data, the most common treatment strategy in the 6-month postoperative period was other nonbiologics (36%), followed by biologic monotherapy (23%), no medications (19%), immunomodulator monotherapy (16%), and biologic combination therapy with an immunomodulator (6%; Table 2). Most patients (91%) in the biologic monotherapy or combination therapy groups received anti-TNF biologics (Table A6), and most patients (62%) in the other nonbiologics group received antibiotics (Table A7).

Figure 2 illustrates time trends for postoperative treatment strategy in the crude data for the entire study cohort,

Table 1. Baseline Characteristics of Commercially Insured US Patients With Intestinal Resection for Crohn's Disease, 2002–2018

	Crude cohort			Weighted[a] cohort		
Characteristic	Elective resection (n = 3073)	Emergent resection (n = 1114)	SMD	Elective resection (n = 2992)	Emergent resection (n = 1095)	SMD
Age			−0.22			−0.04
Median (IQR)	40 (28–51)	36 (23–50)		36 (25–49)	35 (23–49)	
<18	209 (6.8%)	108 (9.7%)		298 (9.7%)	106 (9.7%)	
18–34	934 (30.4%)	422 (37.9%)		1137 (38.0%)	418 (38.2%)	
35–44	656 (21.3%)	208 (18.7%)		568 (19.0%)	205 (18.8%)	
45–54	703 (22.9%)	191 (17.1%)		505 (16.9%)	187 (17.1%)	
55–64	571 (18.6%)	185 (16.6%)		493 (16.5%)	179 (16.3%)	
Female	1685 (54.8%)	554 (49.7%)	−0.10	1580 (52.8%)	543 (49.5%)	−0.07
US geographical region			0.06			0.08
Northeast	528 (17.2%)	199 (17.9%)		566 (19.1%)	1897 (18.2%)	
Midwest	952 (31.0%)	321 (28.8%)		910 (30.7%)	318 (29.3%)	
South	1239 (40.3%)	471 (42.3%)		1150 (38.8%)	461 (42.4%)	
West	334 (10.9%)	115 (10.3%)		338 (11.4%)	111 (10.2%)	
Unknown/missing	20	8		–	–	
Resection year			0.06			0.02
2002–2007	449 (14.6%)	145 (13.0%)		407 (13.6%)	145 (13.2%)	
2008–2013	1307 (42.5%)	462 (41.5%)		1246 (41.7%)	453 (41.4%)	
2014–2018	1317 (42.9%)	507 (45.5%)		1339 (44.7%)	497 (45.4%)	
Insurance type			0.13			0.01
Comprehensive/indemnity	172 (5.6%)	36 (3.2%)		98 (3.3%)	35 (3.2%)	
EPO/PPO	2161 (70.3%)	783 (70.3%)		2132 (71.2%)	782 (71.4%)	
POS/POS with capitation	280 (9.1%)	120 (10.8%)		328 (10.9%)	122 (11.1%)	
HDHP	422 (13.7%)	156 (14.0%)		435 (14.5%)	156 (14.2%)	
Unknown/missing	38	19		–	–	
Resection type			0.12			0.01
Small bowel resection	217(7.1%)	115 (10.3%)		303 (10.1%)	115 (10.5%)	
Ileocolonic resection	1838 (59.8%)	622 (55.8%)		1692 (56.5%)	613 (56.0%)	
Other colonic or rectal resection	1018 (33.1%)	377 (33.8%)		998 (33.3%)	367 (33.6%)	
History of tobacco abuse or smoking cessation medications	528 (17.2%)	213 (19.1%)	0.05	582 (19.5%)	211 (19.2%)	−0.01
Charlson comorbidity index score			0.07			0.02
0	1906 (62.0%)	654 (58.7%)		1746 (58.3%)	645 (58.9%)	
1	700 (22.8%)	267 (24.0%)		720 (24.0%)	263 (24.1%)	
2+	467 (15.2%)	193 (17.3%)		528 (17.6%)	186 (17.0%)	
Number of Charlson comorbidity index comorbidities			0.08			0.05
1–2 conditions	1048 (34.1%)	403 (36.2%)		1126 (37.6%)	394 (36.0%)	
≥3 conditions	119 (3.9%)	57 (5.1%)		122 (4.1%)	55 (5.1%)	
Health care use in the last 12 mo						
Hospitalization	1408 (45.8%)	583 (52.3%)	0.13	1638 (54.8%)	569 (52.0%)	−0.06
Emergency department visit	1110 (36.1%)	498 (44.7%)	0.18	1411 (47.2%)	486 (44.5%)	−0.05
Gastroenterologist visit	2439 (79.4%)	751 (67.4%)	−0.27	2085 (69.7%)	738 (67.4%)	−0.05
Endoscopy visit	2289 (74.5%)	593 (53.2%)	−0.45	1617 (54.0%)	582 (53.1%)	−0.02
Medication exposure before resection						
5-ASAs	1459 (47.5%)	498 (44.7%)	−0.06	1369 (45.7%)	491 (44.8%)	−0.02
Antibiotics	2449 (79.7%)	778 (69.8%)	−0.23	2140 (71.5%)	763 (69.7%)	−0.04
Biologics	1616 (52.6%)	504 (45.2%)	−0.15	1421 (47.5%)	498 (45.5%)	−0.04
Corticosteroids	2509 (81.6%)	865 (77.6%)	−0.10	2378 (79.5%)	852 (77.8%)	−0.04
Immunomodulators or calcineurin inhibitors	1397 (45.5%)	428 (38.4%)	−0.14	1184 (39.6%)	422 (38.6%)	−0.02

Table 1. Continued

Characteristic	Crude cohort			Weighted[a] cohort		
	Elective resection (n = 3073)	Emergent resection (n = 1114)	SMD	Elective resection (n = 2992)	Emergent resection (n = 1095)	SMD
Other non-IBD immune-mediated conditions[b]	161 (5.2%)	62 (5.6%)	0.01	176 (5.9%)	62 (5.6%)	−0.01

5-ASA, 5-aminosalicylates; EPO, exclusive provider organization; HDHP, high deductible health plan; IBD, inflammatory bowel disease; IQR, interquartile range; POS, point of service; PPO, preferred provider organization; SMD, standardized mean differences.
[a]Weighted cohorts derived using standardized mortality ratio (SMR) weights to address confounding and inverse probability of censoring weights to address selection bias for patients who disenrolled before each respective follow-up period (30, 60, or 180 days). The marginal number of patients in each resection group in the weighted data are based on the weights used for analysis of the primary outcome (postoperative treatment strategy).
[b]Other non-IBD, immune-mediate conditions included rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, plaque psoriasis, ankylosing spondylitis, multiple sclerosis, hidradenitis suppurativa, and uveitis.

indicating that biologic use in the postoperative setting increased over time (P value <.0005 from Fisher's exact test for table probability). Among patients with resections performed during 2002–2007, 4% had biologic monotherapy use after resection compared with 21% and 32% of patients with resections during 2008–2013 and 2014–2018,

Table 2. Postoperative Treatment Strategies and Postoperative Complications, 2002–2018

Characteristic	Crude cohort		Weighted[a] cohort	
	Elective resection (n = 3073)	Emergent resection (n = 1114)	Elective resection (n = 2992)	Emergent resection (n = 1095)
Postoperative treatment strategy within 6 mo				
Biologic monotherapy	750 (24.4%)	231 (20.7%)	714 (23.9%)	226 (20.7%)
Biologic combination therapy with immunomodulators	166 (5.4%)	65 (5.8%)	144 (4.8%)	65 (6.0%)
Immunomodulators as monotherapy	519 (16.9%)	167 (15.0%)	474 (15.9%)	165 (15.1%)
Other nonbiologics (antibiotics, 5-aminosalicylates, corticosteroids)	1046 (34.0%)	443 (39.8%)	1012 (33.8%)	440 (40.2%)
No medications	592 (19.3%)	208 (18.7%)	648 (21.7%)	199 (18.1%)
Postoperative complications[b] within 30 d				
Medical complications	655 (21.3%)	415 (37.3%)	647 (21.9%)	421 (37.4%)
Surgical complications	249 (8.1%)	170 (15.3%)	239 (8.1%)	172 (15.3%)
Infections	359 (11.7%)	220 (19.8%)	341 (11.5%)	225 (20.0%)
Any of above complications	830 (27.0%)	516 (46.3%)	810 (27.4%)	523 (46.4%)
Postoperative complications within 60 d				
Medical complications	797 (25.9%)	454 (40.8%)	776 (26.2%)	458 (40.9%)
Surgical complications	337 (11.0%)	202 (18.1%)	319 (10.8%)	204 (18.2%)
Infections	481 (15.7%)	268 (24.1%)	467 (15.8%)	274 (24.4%)
Any of above complications	1014 (33.0%)	567 (50.9%)	975 (32.9%)	573 (51.1%)

[a]Weighted cohorts derived using standardized mortality ratio weights to address confounding and inverse probability of censoring weights to address selection bias for patients who disenrolled before each respective follow-up period of interest (30, 60, or 180 days). The marginal number of patients in each resection group in the weighted data correspond to the weights for the primary outcome (postoperative treatment strategy), which based censoring weights on 6 months of follow-up.
[b]Medical complications defined based on ≥1 claim for fistula, abscess, sepsis, pneumonia, bacteremia, or strictures. Surgical complications defined based on ≥1 claim for wound debridement, bowel manipulation, lyses of adhesions, revision of ostomy, or other surgical-related procedures (surgical repair/removal, drainage, etc.) Infection cases defined based on ≥1 claim for any infection, not otherwise specified.

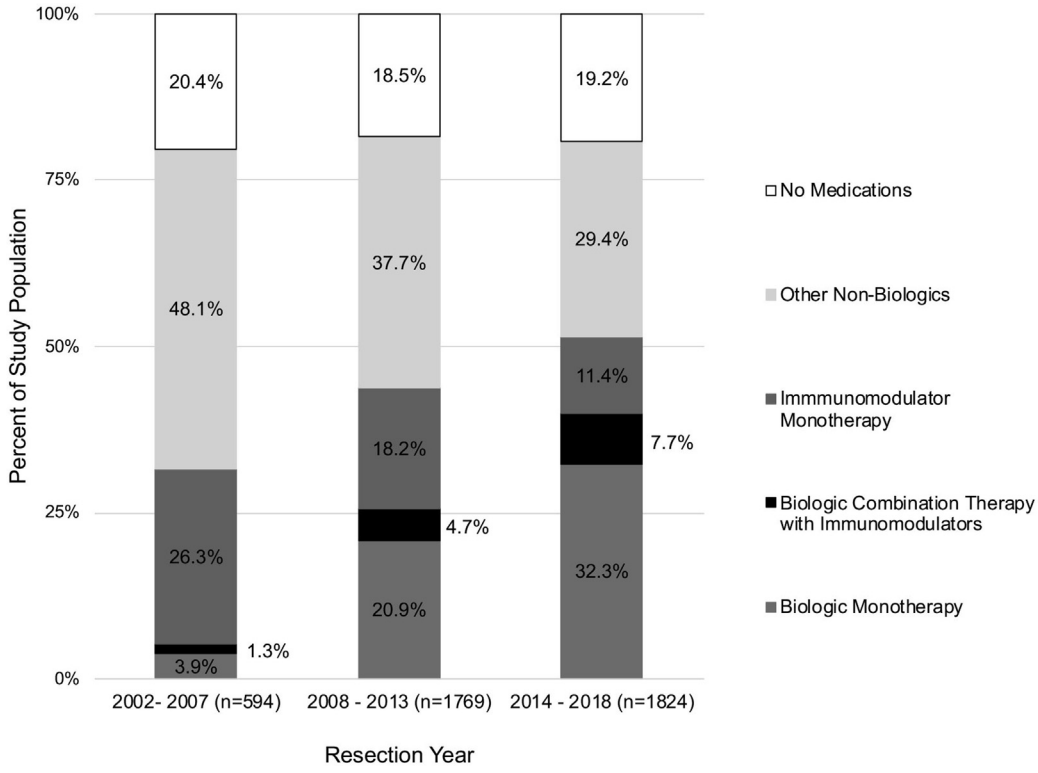

Figure 2. Time trends for postoperative treatment strategy, 2002–2018; 2-sided *P*-value from Fisher's exact test for table probability <.0005.

respectively. Similarly, the proportion of patients with biologic combination therapy with an immunomodulator increased from <2% during 2002–2007 to 5% during 2008–2013 and 8% during 2014–2018.

Table 2 shows postoperative outcome occurrence for each treatment strategy by resection type in the crude and weighted data, and Figure 3 illustrates weighted RDs for emergent/urgent vs elective resection for each postoperative outcome of interest (see Figure A2 for risk ratio estimates). Compared with elective resection, emergent/urgent resection was associated with higher 6-month postoperative incidence of other nonbiologics (RD 6.4%; 95% CI 2.8%, 10.0%). Conversely, emergent/urgent resection was associated with lower 6-month postoperative incidence of biologic monotherapy (RD −3.2%; 95% CI −6.2%, −0.1%) and no medications (RD −3.6%; 95% CI −6.6%, −0.6%). There was minimal difference between emergent/urgent and elective resection for 6-month postoperative incidence of biologic combination therapy with an immunomodulator (RD 1.2%) or immunomodulator monotherapy (RD −0.8%). More patients with emergent/urgent resection had 30- and 60-day complications (46.4% and 51.1%, respectively) compared with those in the elective resection cohort (27.4% and 32.9%, respectively). Compared with elective resection, emergent/urgent resection was associated with higher 30-day (RD 19.0%; 95% CI 15.4%, 22.6%) and 60-day postoperative risk of any complications (RD 18.2%; 95% CI 14.6%, 21.8%).

Discussion

Our analysis of health care claims for a nationwide cohort of commercially insured patients with CD provides updated data on postoperative management in the United States. Although no prior studies have investigated emergent/urgent resection and the risk of postoperative recurrence, our analysis is the first to examine whether postoperative treatment strategies differ after emergent/urgent vs elective. The most common postoperative treatment strategy was other nonbiologics and biologic monotherapy, followed by immunomodulator monotherapy and combination therapy with a biologic and an immunomodulator therapy. In addition, a higher proportion of patients with intestinal resection for CD during 2014−2018 had claims indicating biologic treatment approaches (monotherapy or combination therapy) after surgery compared with patients with resections during 2013 and earlier. We found that emergent/urgent resection was associated with more use of other nonbiologics compared with elective resection, which was measured as at least one claim for 5-ASAs, antibiotics, or corticosteroids. Contrary to our hypothesis, emergent/urgent resection was also associated with less use of biologic monotherapy and no medications as the first postoperative treatment strategy after resection, compared with elective resection. Postoperative complications, defined by a composite outcome of ≥1 claim for medical, surgical, and infection events, were commonly

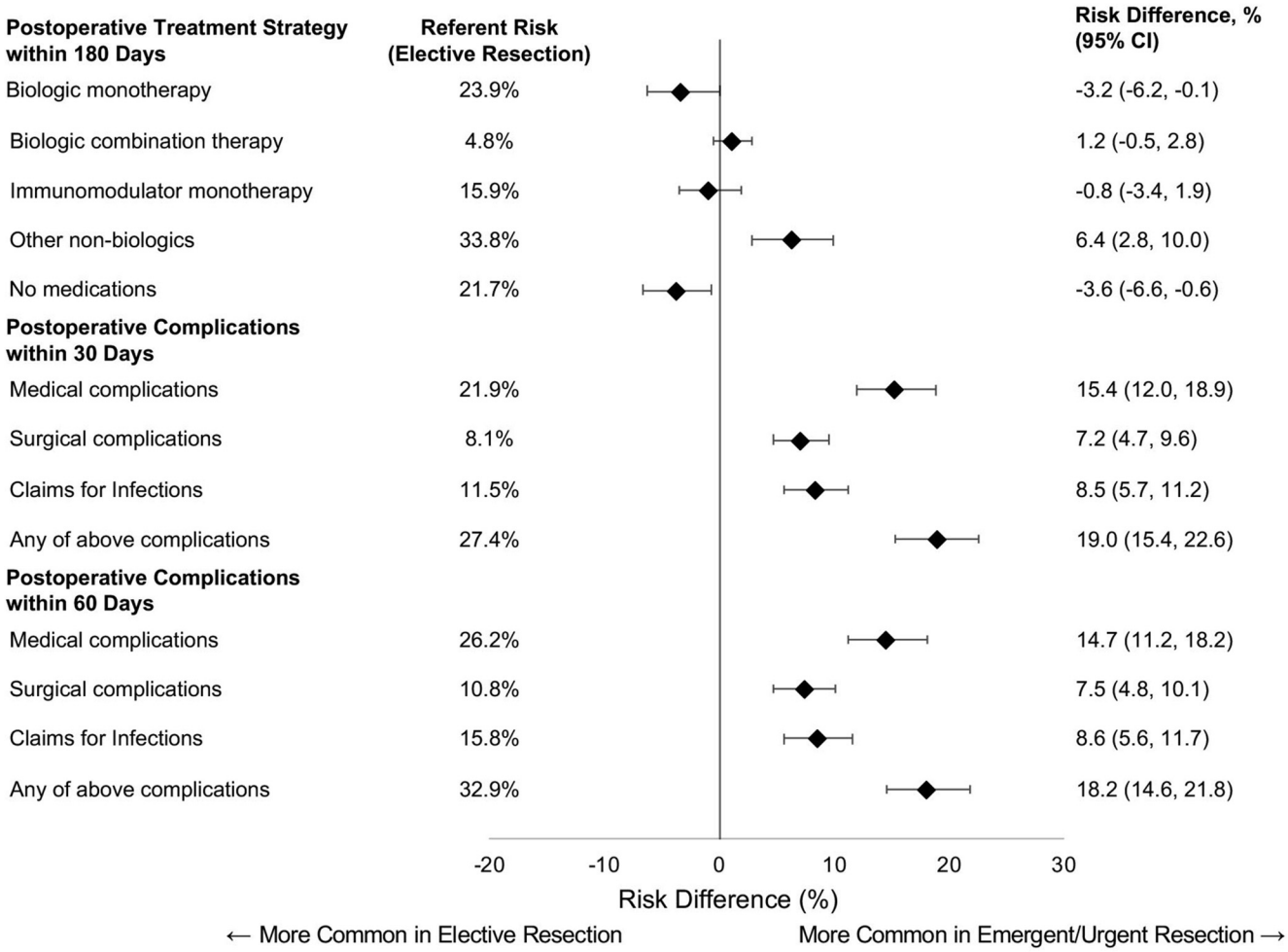

Figure 3. Weighted risk differences for emergent/urgent vs elective resection for each postoperative outcome.

observed after intestinal resection for CD. Patients with emergent/urgent resection had higher risk of any complications in the 30- and 60-day period after resection compared with patients with elective resection.

The literature on real-world postoperative treatment patterns in CD is limited, with varied findings due to differences in study design, data source, and geographic setting. In a UK single-center cohort study, 32% of patients with intestinal resection during 2009–2013 had no prophylaxis after resection, whereas 52% received thiopurine monotherapy, 9% received biologic combination therapy, and 8% received biologic monotherapy.[48] A Danish national cohort study of patients with CD between 2003 and 2013 reported that 16% of biologic-experienced and 1.3% of biologic-naïve patients received anti-TNF biologics within 6 months after their first surgery.[49] In a US claims study, more than one-third of patients with ileocolonic resection for CD between 2009 and 2012 had anti-TNF use in the 12-month postoperative period.[10] We found in our analysis that 29% of patients with intestinal resection for CD during 2002–2018 had biologic use in the 6 months after resection. In particular, 32% and 8% of patients with resections during 2014–2018 had biologic monotherapy and biologic combination therapy with an immunomodulator within 6 months after resection, respectively. Although these findings vary from previous studies, one explanation could be that as more biologic medications are approved for CD in the United States over time, more patients are using biologics as postoperative therapeutic options compared with earlier years. In addition, increased provider awareness, updated clinical guidelines, and clinical data on the benefits of biologic use in the postoperative setting could also explain increased uptake.

Current clinical guidelines highlight that patient preferences for less aggressive therapy and avoiding side effects may be considered in postoperative treatment decisions.[4] Endoscopy-guided prophylaxis by 6 months after resection is strongly recommended over no prophylaxis. In our study, 19% of patients received "no medications," which is lower than the proportions of patients with "no prophylaxis" reported in other studies.[48,50] In clinical practice, patients who do not receive prophylactic medications should at a minimum follow a monitoring-only strategy in the postoperative period, particularly for patients who do not have identified risk factors at the time of surgery.[7] Compared with some studies however, our follow-up period for examining

postoperative medication exposure was longer (6 vs 3 months), which increased the window of opportunity for classifying patients into postoperative treatment strategy groups. Furthermore, more than one-third of patients were on other nonbiologics as the first postoperative treatment strategy, which we defined as any combination of 5-ASAs, antibiotics, or corticosteroids. Although current guidelines include considerations for patient preferences for less aggressive therapy, this finding is contrary to the current recommendation of starting postoperative biologic or immunomodulator therapy over other agents.[4] Health care system factors in the United States may play a role with respect to policies of prior authorization for more aggressive therapy contingent on documented treatment failure, although a recent review of such policies found that most were outdated and not guideline concordant.[51] Clinical strategies for patients who may not be responding to biologic therapy also warrant additional investigation, particularly to identify factors that may be resulting in dependency on other nonbiologics such as corticosteroids, which are not recommended for long-term use. Our findings suggest that an increasing proportion of patients may be receiving more guideline-concordant therapeutics over time, which could be due to increasing availability of more biologics and societal guidelines with better defined treatment algorithms. However, it remains unclear whether these different strategies also lead to optimal outcomes for patients in real-world settings outside of controlled trial settings.

We found that compared with elective cases, emergent/urgent resection was associated with greater use of other nonbiologics. For patients with progressive disease who require an unplanned procedure, aggressive treatment with biologics after surgery may be a more appropriate strategy to prevent disease recurrence.[7] However, emergent/urgent resection was also associated with less use of biologic monotherapy and no medications as postoperative strategies compared with elective cases. In the baseline period, we observed that a lower proportion of patients in the emergent/urgent cohort had a gastroenterologist or endoscopy visit than those in the elective cohort. These differences in health care use before resection suggest that there may also be differences related to patient health behaviors in accessing specialized care, which ultimately would impact the need/urgency of surgery and postoperative treatment approaches. Other factors such as provider characteristics, which are not measured in claims data, may also vary and may be important confounders that impact standard of care at a population level.

With respect to postoperative complications, patients with emergent/urgent resection had higher risk of having any postoperative complication compared with patients with elective resection in the first 30 and 60 days after resection, which aligns with prior literature findings.[12] Patients at higher risk of complications may opt to delay an aggressive long-term treatment strategy with biologic monotherapy to treat their underlying CD, given the risk of infection associated with anti-TNF biologics.[52] Complications resulting in readmissions requiring subsequent resection may also delay appropriate treatment with biologic therapy although we observed that rehospitalization claims for an intestinal resection within 30 days after initial discharge was rare and occurred in $<1\%$ of patients. Although the higher risk of complications in emergent/urgent cases compared with elective cases could help explain the associations with postoperative treatment strategies, we are not able to infer causality because these complication events did not necessarily precede the postoperative medication exposure for every patient.

There are several limitations in our study to consider. First, as claims data are primarily collected to record financial transactions, we did not have important clinical data that are important factors in treatment decisions. Patient perceptions of the risk-benefit profile for CD interventions may vary, and other health behaviors may impact decision-making with provider son postoperative prophylactic strategies. We hypothesized that patients with emergent/urgent resections would have more progressive disease compared with elective resections. Although we did not have baseline data on disease severity, a higher proportion of patients with emergent/urgent resection did have a hospitalization or emergency department visit in the year before resection, compared with elective cases. Furthermore, we were also unable to ascertain whether patients classified has having no medications in the first 6 months may be managing their CD outside their health plan. Approximately 31% of patients in this study were lost-to-follow-up before 6 months had elapsed after surgery. To address this loss-to-follow-up, we incorporated censoring weights in our analysis for each of the postoperative outcomes of interest. Second, although we used previously published algorithms in the general CD or overall IBD populations to reduce misclassification, postoperative CD has also been relatively understudied in real-world databases. Thus, there is a lack of robustly validated algorithms for case ascertainment specifically in the postoperative setting. In particular, approximately 80% of emergent/urgent cases were identified because they occurred after admission through the emergency department. The remaining 20% being identified as emergent/urgent because they were performed after the second day of the admission; the timing of these cases relative to the admission date would not be considered as truly elective for abdominal surgery. However, there was also overlap between the 2 definitions in 40% of cases identified as emergent/urgent surgery. As we required each resection procedure service charge to be associated with a CD diagnosis code in the primary position in the MarketScan claims data, we were unable to ascertain additional granularity on the patient's condition that might have triggered the surgical intervention. Additional research is needed to investigate the nature of these emergent/urgent cases, particularly around the timing of resections and clinical characteristics associated with procedures that appear to be unplanned,

but not explicitly documented in administrative data as emergent/urgent. Finally, we required a longer baseline period than typically used in claims analyses to identify a study population that had an extended period without needing intestinal resection. This decreased our sample size but targeted a population with at least 24 resection-free months before the resection event of interest.

In this cohort study of patients with intestinal resection for CD, we found that a higher proportion of patients have postoperative biologic use in more recent years compared with earlier years. Emergent/urgent vs elective resection was also associated with different postoperative treatment approaches as well as higher risk of postoperative complications. Key areas for future research include evaluating patterns of treatment discontinuation and switching and investigating whether different postoperative strategies in real-world settings, such as endoscopic monitoring without initial medications, are associated with better outcomes and differential costs to patients and payers. Although common real-world data courses may also be limited in measuring postoperative recurrence outcomes, there is a need to assess the effect of postoperative medications on other important CD outcomes such as hospitalization and emergency department use. Appropriate comparators are also critical in subsequent research to minimize confounding by indication. Although it is important to understand the patient population opting for routine monitoring over immediate prophylaxis with medications, these patients may differ from patients with immediate prophylaxis in terms of treatment preferences and risk for recurrence. Prospective cohort studies are especially needed to validate associations between emergent/urgent resection and postoperative treatment and to investigate patient-level and physician-level factors associated with postoperative treatment decisions. Finally, future research should consider the impact of postoperative complications on medication strategies to account for the temporality of these complications as part of treatment decision-making for patients after intestinal resection for CD.

Supplementary Materials

Material associated with this article can be found in the online version at https://doi.org/10.1016/j.gastha.2022.06.003.

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Data Transparency Statement:
Study protocol and statistical code are available from A.C.K. on request (akinlaw@unc.edu). Data (MarketScan claims) are available through data use agreements and licenses issued by IBM Watson Health.