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ORIGINAL ARTICLE

Early Postoperative Anti-TNF Therapy Does Not Increase Complications Following Abdominal Surgery in Crohn's Disease

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Abstract

Background The impact of postoperative anti-TNF therapy on infectious complications following Crohn's disease surgery remains controversial. Use of anti-TNF therapy 2–4 weeks postoperatively appears safe, but safety of use within 2 weeks is unknown.

Aims We sought to evaluate the effect of anti-TNF therapy initiated within 2 weeks of abdominal surgery in patients with Crohn's disease.

Methods We conducted a retrospective review of adult Crohn's disease patients undergoing abdominal surgery between 2004 and 2011. Infectious and non-infectious complications were compared between patients exposed to anti-TNF therapy within 2 weeks or between 2 and 4 weeks postoperatively and to those without exposure using chi-squared and regression analysis.

Results Three hundred thirty-one abdominal surgeries were included; 241 were without anti-TNF exposure, 46 received postoperative anti-TNF within 2 weeks of surgery, and 44 received anti-TNF therapy 2–4 weeks after surgery. Patients who received anti-TNF therapy within 2 weeks of surgery, those initiated between 2 and 4 weeks of surgery, and those who did not receive anti-TNF therapy within 4 weeks of surgery had no significant difference in rates of infectious complications (22%, 32%, 33%, $p=0.332$). Rates of non-infectious complications (4%, 9%, 14%, $p=0.143$), mortality (0%, 0%, 3%, $p=0.105$), hospital readmission (17%, 16%, 15%, $p=0.940$), and reoperation (11%, 11%, 16%, $p=0.563$) were also similar between groups.

Conclusions Use of early anti-TNF therapy within 2 weeks or between 2 and 4 weeks following abdominal surgery did not increase risk of postoperative surgical infections in Crohn's patients.

Keywords Crohn's disease · Anti-TNF · Postoperative · Complications · Infection

Introduction

Crohn's disease (CD) is an immunologically mediated, chronic, relapsing, inflammatory condition that can affect any gastrointestinal site from the oral cavity to the anus. It is most commonly thought to result from aberrant and overly aggressive T cell immune responses to commensal enteric bacteria in genetically susceptible hosts [1]. Medical therapy for CD relies on anti-inflammatory and immunomodulating agents to suppress this exaggerated immune response. Since the late 1990s, the pharmacotherapy of CD has expanded to include biologic agents, specifically anti-tumor necrosis factor (anti-TNF) medications, in addition to previously used 5-ASA compounds, steroids, and thiopurines.

Anti-TNF agents target the pro-inflammatory cytokine tumor necrosis factor α, important in the pathogenesis of CD [2]. The efficacy of anti-TNF agents, including infliximab (IFX) and adalimumab, in inducing and maintaining remission in patients with moderate-to-severe CD is well established [3–5]. More recently, anti-TNF therapy has also been found to prevent endoscopic recurrence of CD following surgery [6–9]. Despite this, nearly one-half of patients

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with CD still require a surgical resection within 10 years of diagnosis [10] and another 35% will require a second surgery over the subsequent 10 years [11]. Because of the association between long-term anti-TNF therapy and elevated risk of serious and opportunistic infections [12, 13], concern regarding their effect on postoperative complications, particularly infectious complications, exists.

Several retrospective studies have addressed postoperative morbidity as it relates to preoperative anti-TNF therapy. While some have demonstrated an increased risk of infectious complications [14–17], others have not [18, 19]. In a large meta-analysis of 21 studies, containing 6899 subjects, CD patients who received preoperative anti-TNF therapy were found to have a higher risk of postoperative infectious complications (risk ratio 1.29; 95% CI 1.07–1.55), wound infection (risk ratio 1.62; 95% CI 1.12–2.34), and septic shock (risk ratio 1.81; 95% CI 1.03–3.17) [20]. Three additional meta-analyses found similar increases in postoperative complications, particularly infectious, with preoperative anti-TNF use [21–23]. Few studies, however, have evaluated the effect of postoperative anti-TNF exposure on operative morbidity. We analyzed a large cohort of CD patients followed at the University of Maryland (UM) Inflammatory Bowel Disease (IBD) Program to compare the frequency of infectious complications following intra-abdominal surgery in CD patients exposed and not exposed to anti-TNF agents postoperatively. We hypothesized that very early use of postoperative anti-TNF therapy (within 2 weeks after surgery) would not be associated with an increase in postoperative infectious complications.

Methods

Study Design and Patient Identification

We conducted a retrospective study of all adult patients with CD who underwent abdominal surgery for any indication at the University of Maryland Medical Center (UMMC) and surrounding hospitals between July 1, 2004, and May 1, 2011. Patients less than 18 years old, those who underwent isolated perianal surgeries and those with incomplete records, were excluded.

Study Aims

Our primary aims were to compare likelihood of infectious and non-infectious complications with or without early postoperative anti-TNF exposure following abdominal surgery in patients with CD. Our secondary aim was to examine the association of demographic and clinical characteristics on postoperative infectious and non-infectious complications.

Study Variables

Demographic information was obtained from a prospectively maintained, IRB-approved clinical database that contains clinical information on approximately 1500 patients that are followed at our center. Chart review was utilized to determine medical and surgical therapeutic history for identified patients.

Demographic data included gender, race, age at the time of surgery, and smoking status. The diagnosis of CD was confirmed by standard clinical, histopathologic, and endoscopic criteria [24]. CD location and behavior were characterized using the Montreal classification [25]. Medication history was obtained both pre- and postsurgery. Patients were defined as being on an immunomodulator (immunosuppressant or biologic therapy) if they received 6-mercaptopurine, azathioprine, methotrexate, IFX, adalimumab, or certolizumab pegol at any dose ≤ 8 weeks prior to surgery. Steroid exposure was defined as any systemic corticosteroid use at the time of surgery. Preoperative narcotic use was also reported. We considered type and indication for surgery, urgency of surgery, and whether or not preoperative infection was present. Preoperative infection was defined as any major infection including intra-abdominal abscess, sepsis, peritonitis, active perianal abscess, pneumonia, or clostridium difficile infection that was present at the time of operation.

Postoperative anti-TNF exposure was classified as follows:

1. Anti-TNF therapy initiated less than 2 weeks after surgery.
2. Anti-TNF therapy initiated 2–4 weeks after surgery.
3. No anti-TNF therapy given within 4 weeks of surgery.

Complications occurring within 30 days of surgery or hospital discharge, whichever was longer, were collected. Complications were categorized into:

1. Infectious complications:
   (a) Superficial surgical site infection (SSSI)—wound infection, wound dehiscence.
   (b) Deep surgical site infection (DSSI)—anastomotic leak, abdominopelvic abscess, and fistula.
   (c) Extra-abdominal septic complication—sepsis, pneumonia, urinary tract infection, and bacteremia.
2. Non-infectious complications: small bowel obstruction, acute renal failure, liver failure, arrhythmia, myocardial

infection, postoperative hemorrhage, venous thromboembolism (VTE), and prolonged ileus.

Additional outcomes evaluated included hospital readmission and reoperation.

Statistical Analysis

Data analysis was performed using SPSS version 24 (Armonk, NY), and a p value of < 0.05 was considered statistically significant. Categorical variables are presented as proportions and continuous variables as mean values with standard deviations. Bivariate analyses were performed to assess for significant differences in demographic and clinical variables by timing of postoperative anti-TNF therapy. Proportions between the three exposure groups were compared using the chi-squared test. Continuous variables were compared with ANOVA. Separate bivariate analyses were conducted to assess for significant associations between baseline demographic and clinical variables with postoperative complications. Odds ratios and 95% confidence intervals were calculated to assess the association between exposure and outcome variable.

Next, stepwise logistic regression was used to assess for the association between postoperative anti-TNF exposure and each of the composite postoperative complications. Patients not exposed to anti-TNF therapy in the 4 weeks after surgery were included as the reference group. Variables thought to have clinical relevance and those with a p value of less than 0.10 on bivariate analysis were included in the logistic regression to control for potential confounding effect of these variables. The final model is controlled for age, preoperative steroid use, preoperative anti-TNF exposure, preoperative infection, perforating disease and urgency of surgery.

This study was approved by the UM Human Subjects Research Protection Office on 9/24/2015.

Results

Patient Demographics and Disease Characteristics

During the study period, 331 intra-abdominal surgeries were performed in 206 CD patients. Eleven were performed outside UMMC by nine different surgeons, while the remaining 320 were performed at UMMC by 21 surgeons. Ninety surgeries (27%) were associated with postoperative anti-TNF initiated between 0 and 4 weeks after surgery. Sixty percent of patients were female, 77% were Caucasian, 23% were current smokers, and the mean age at the time of surgery was 39.1 ± 13.8 years (Table 1). Patients exposed to early postoperative anti-TNF were slightly younger ($p = 0.038$) and less likely to be smokers ($p = 0.014$) than those not exposed.

Clinical characteristics and preoperative medication exposure for the study population are described in Table 2. The majority of patients had either ileal or ileocolonic CD with strictures or perforation. Patients who received anti-TNF less than 2 weeks after surgery were more likely to have ileocolonic rather than ileal or colonic disease location, while those who received anti-TNF between 2 and 4 weeks of surgery were more likely to have ileal disease ($p = 0.034$). Patients exposed to anti-TNF within 2 weeks and between 2 and 4 weeks of surgery were more likely than those who were not to have upper tract disease involvement ($p = 0.027$). Preoperative infection was less frequent in patients who received postoperative anti-TNF 2–4 weeks after surgery compared to those who received anti-TNF < 2 weeks after surgery and those who did not receive anti-TNF ($p = 0.04$). There was no difference between groups in CD behavior or presence of perianal disease.

Table 1 Baseline demographics of study population with bivariate comparison based on timing of postoperative anti-TNF treatment initiation

Patient characteristics	Total *n* (%)	No early anti-TNF *N* (%)	Anti-TNF < 2 weeks *n* (%)	Anti-TNF 2–4 weeks *n* (%)	*p* value
Sex					
Female	199 (60)	146 (60.6)	26 (56.5)	27 (61.4)	0.862
Male	132 (40)	95 (39.4)	20 (43.5)	17 (38.6)	
Smoking					
Never smoked	161 (48.6)	104 (43.2)	28 (60.9)	29 (65.9)	0.014
Former smoker	95 (28.7)	73 (30.3)	12 (26.1)	10 (22.7)	
Current smoker	75 (22.7)	64 (26.6)	6 (13)	5 (11.4)	
Race					
Caucasian	254 (76.7)	181 (75.1)	40 (87)	33 (75)	0.210
Others	77 (23.3)	60 (24.9)	6 (13)	11 (25)	
Age at time of surgery					
Mean ± SD	39 ± 13.8	40 ± 14.6	36 ± 11.5	35 ± 10.4	0.038

Table 2 Clinical characteristics of Crohn's disease and preoperative medication exposure in the study population with bivariate comparison based on timing of postoperative anti-TNF treatment initiation

Patients characteristics	Total *n* (%)	No anti-TNF *n* (%)	Anti-TNF < 2 weeks *n* (%)	Anti-TNF 2–4 weeks *n* (%)	*p* value
Location of disease[a]					
Ileal	135 (41.3)	97 (40.8)	18 (39.1)	20 (46.5)	0.034
Colonic	48 (14.7)	36 (15.1)	2 (4.3)	10 (23.3)	
Ileocolonic	144 (44)	105 (44.1)	26 (56.5)	13 (30.2)	
Upper tract involvement					
Yes	39 (11.8)	22 (9.1)	7 (15.2)	10 (22.7)	0.027
Disease behavior					
Inflammatory disease	38 (11.5)	31 (12.9)	3 (6.5)	4 (9.1)	0.467
Stricturing	131 (39.6)	94 (39)	22 (47.8)	15 (34.1)	
Perforating	162 (48.9)	116 (48.1)	21 (45.7)	25 (56.8)	
Perianal disease					
Present	111 (33.5)	76 (31.5)	17 (37)	18 (40.9)	0.417
Preoperative infection					
Present	81 (24.5)	64 (26.6)	13 (28.3)	4 (9.1)	0.038
Preoperative medications					
Preoperative narcotics					
Taking	127 (38.4)	93 (38.6)	21 (45.7)	13 (29.5)	0.289
Preoperative anti-TNF exposure					
Yes	152 (45.9)	81 (33.6)	37 (80.4)	34 (77.3)	0.00
Preoperative immunomodulator					
Taking	120 (36.3)	83 (34)	15 (33)	22 (50)	0.122
Preoperative steroids					
Taking	124 (37.6)	90 (37.5)	14 (30.4)	20 (45.5)	0.339

[a]Four patients were missing data regarding their disease location; therefore, these patients were removed from that particular analysis and the analysis run with the remaining patient data

Preoperative Medication Exposure

Forty-six percent of patients were on preoperative anti-TNF therapy within 8 weeks of surgery, and 38% were on preoperative steroids (Table 2). Patients who received anti-TNF less than 2 weeks after surgery and between 2 and 4 weeks of surgery were more likely than those who did not receive postoperative anti-TNF within 4 weeks to have received preoperative anti-TNF ($p < 0.001$). Conversely, there was no difference in preoperative steroids, immunomodulators, and narcotics at baseline between the three groups.

Surgical Variables

Indications and characteristics of abdominal surgeries performed are described in Table 3. Forty-two (13%) of surgeries were emergent and 15% were reoperations. Two hundred thirty-nine (72%) surgeries included at least one intestinal resection, 211 (64%) of which involved creation of at least one anastomosis. Ostomies were created in 35% of cases. Patients who received anti-TNF between 2 and 4 weeks postoperatively were less likely than those who received anti-TNF less than 2 weeks after surgery and those who did not receive anti-TNF to have undergone surgery for the indication of perforation ($p = 0.009$) and more likely to have undergone surgery for an indication of "other" ($p = 0.046$). There was a trend where patients were less likely to be given anti-TNF within 4 weeks of emergent surgeries ($p = 0.056$).

Patients who did not receive postoperative anti-TNF within 4 weeks of surgery were significantly more likely to have undergone total abdominal colectomy or proctocolectomy ($p = 0.005$) and ileocolic resection ($p = 0.043$) than those who received anti-TNF within 2 weeks and between 2 and 4 weeks of surgery; they were also less likely to have undergone small bowel resection ($p = 0.008$) (Table 3).

Anti-TNF Therapy and Postoperative Complications

Postoperative complications by treatment group are described in Table 4. One hundred two (33%) surgeries were associated with infectious complications. The rate of anastomotic leak was 6% and the mortality rate was 3%. Fifty-two (16%) of patients required readmission within 30 days of surgery and 48 (15%) required reoperation. Anti-TNF use was not associated with increased risk of these events. Anti-TNF use also did not increase the risk

Table 3 Indication and characteristics of surgeries performed in the study population with bivariate comparison based on timing of postoperative anti-TNF treatment initiation

Surgical characteristic of patients	Total *n* (%)	No post-operative anti-TNF *n* (%)	Anti-TNF < 2 weeks *n* (%)	Anti-TNF 2–4 weeks *n* (%)	*p* value
Indications for surgery					
Abscess	14 (4.3)	10 (4.2)	2 (4.3)	2 (4.5)	0.992
Cancer/dysplasia	4 (1.2)	4 (1.7)	0 (0.0)	0 (0.0)	0.278
Medically refractory disease	104 (31.6)	73 (30.5)	19 (41.3)	12 (27.3)	0.275
Perforation	30 (9.1)	24 (10.0)	6 (13.0)	0 (0.0)	0.009
Symptomatic stricture	97 (29.5)	74 (31.0)	11 (23.9)	12 (27.3)	0.618
Stoma reversal	30 (9.1)	18 (7.5)	5 (10.9)	7 (15.9)	0.180
Other	50 (15.2)	36 (15.1)	3 (6.5)	11 (25.0)	0.046
Type of surgery					
Segmental colectomy	50 (15.2)	38 (15.9)	8 (17.4)	4 (9.1)	0.470
[α]TAC/proctectomy	16 (4.9)	16 (6.7)	0 (0.0)	0 (0.0)	0.005
Ileocolic resection	57 (17.3)	49 (20.5)	5 (10.9)	3 (6.8)	0.043
Small bowel resection	86 (26.1)	52 (21.8)	19 (41.3)	15 (34.1)	0.008
Planned ostomy creation only	17 (5.2)	11 (4.6)	2 (4.3)	4 (9.1)	0.499
Hernia/stoma revision	26 (7.9)	18 (7.5)	4 (8.7)	4 (9.1)	0.913
Stoma reversal	24 (7.3)	16 (6.7)	2 (4.3)	6 (13.6)	0.227
Other	53 (16.1)	39 (16.3)	6 (13.0)	8 (18.2)	0.794
Urgency					
Urgent	88 (26.7)	59 (24.6)	15 (32.6)	14 (31.8)	0.375
Emergent	42 (12.7)	37 (15.4)	3 (6.5)	2 (4.5)	0.056
Creation of an anastomosis					
Yes	211 (63.7)	153 (63.5)	32 (69.6)	26 (59.1)	0.579
Surgical methods					
Laparoscopic	136 (41.2)	19 (43.2)	24 (52.2)	93 (38.8)	0.546
Open	150 (45.5)	113 (47.1)	17 (37)	20 (45.5)	
Laparoscopic converted to open	44 (13.3)	34 (14.2)	5 (10.9)	5 (11.4)	

[a]Two patients were missing data regarding their type of surgery; therefore, these patients were removed from that particular analysis and the analysis run with the remaining patient data. [α]TAC = total abdominal colectomy

Table 4 Bivariate comparison of postoperative outcomes in the study population based on timing of postoperative anti-TNF treatment initiation

Outcome	No anti-TNF in 4 weeks postop *n*/*N* (%)	Postop anti-TNF within 2 weeks *n*/*N* (%)	Postop anti-TNF between 2 and 4 weeks *n*/*N* (%)	*p* value
Infectious complication	78/238 (32.8%)	10/46 (21.7%)	14/44 (31.8)	0.332
Superficial surgical site infection	36/241 (14.9)	8/46 (17.4)	12/44 (27.3)	0.133
Deep surgical site infection	46/239 (19.2)	4/46 (8.7)	7/44 (15.9)	0.216
Extra-abdominal infection	38/240 (15.8)	0/46 (0.0)	4/44 (9.1)	0.009
Non-infectious complication	34/241 (14.1)	2/46 (4.3)	4/44 (9.1)	0.143
Death	7/241 (2.9)	0/46 (0.0)	0/44 (0.0)	0.105
Readmission	37/241 (15.4)	8/46 (17.4)	7/44 (15.9)	0.940
Reoperation	38/241 (15.8)	5/46 (10.9)	5/44 (11.4)	0.563

of superficial or deep surgical site infection or non-infectious complications. Patients who did not receive anti-TNF therapy had a higher likelihood of extra-abdominal infectious complications compared with those that received anti-TNF within 2 weeks of surgery ($p = 0.004$), but not those that received anti-TNF 2–4 weeks following surgery ($p = 0.247$). When adjusting for potential confounders including preoperative anti-TNF exposure in multivariable

regression, anti-TNF use within 2 weeks of surgery carried a lower risk of non-infectious complications, but there was no significant difference in any of the infectious or other non-infectious outcomes between treatment groups (Table 5).

Baseline Demographic Factors and Postoperative Complications

Multiple baseline factors increased patient risk of postoperative infectious complications including older age, preoperative steroid use, preoperative anti-TNF therapy within 8 weeks of surgery, perforating disease, and emergency surgery (Table 6). Reoperation rates were higher in patients with preoperative steroid use and emergency surgery. Finally, mortality was higher in older patients and after emergency surgery.

Discussion

The optimal timing of anti-TNF therapy in the postoperative Crohn's patient is not clear. In this retrospective analysis, we sought to evaluate the safety of early anti-TNF therapy initiation following abdominal surgery in patients with CD. Postoperative complications were not increased in patients treated with anti-TNF within 2 weeks or between 2 and 4 weeks of surgery as compared to those not undergoing treatment within 4 weeks. Patients who did not receive anti-TNF therapy had a higher likelihood of extra-abdominal infectious complications compared with those that received anti-TNF within 2 weeks of surgery. This difference may be explained in part by selection bias observed in retrospective studies as anti-TNF initiation was likely avoided in patients who experienced early postoperative complications.

Reasons for early postoperative anti-TNF were not specified in the database, but in our practice early postoperative

Table 5 Results of multivariable regression analysis of postoperative outcomes based on timing of early postoperative anti-TNF initiation compared to no anti-TNF treatment within 4 weeks postop

Outcome variable	Timing of early postoperative anti-TNF therapy	
	<2 weeks postop	2–4 weeks postop
Infectious complication, aOR (95% CI)	0.53 (0.23–1.24)	0.92 (0.4–1.99)
Superficial surgical site infection, aOR (95% CI)	1.29 (0.51–3.25)	2.16 (0.94–4.97)
Deep surgical site infection, aOR (95% CI)	0.36 (0.11–1.12)	0.76 (0.30–1.96)
Extra-abdominal infection, aOR (95% CI)	0.000[a]	1.22 (0.35–4.20)
Non-infectious complication, aOR (95% CI)	0.24 (0.05–1.08)	0.59 (0.18–1.91)
Readmission, aOR (95% CI)	0.93 (0.37–2.30)	0.79 (0.31–2.02)
Reoperation, aOR (95% CI)	0.69 (0.23–2.07)	0.71 (0.24–2.10)

Variables found to be significant confounders in the models that were controlled for include age, preoperative steroid use, preoperative anti-TNF exposure, preoperative infection, perforating disease, and urgency of surgery

[a]"000" one or more categories of cell do not have a value, so unable to calculate OR

Table 6 Association of baseline variables with postoperative outcomes, results from multivariable regression analysis

Outcome variable	Age > 60 years aOR (95% CI)	Preoperative steroid use aOR (95% CI)	Preoperative anti-TNF aOR (95% CI)	Preoperative infection aOR (95% CI)	Perforating disease aOR (95% CI)	Emergency surgery aOR (95% CI)
Infectious complication	**5.55 (1.49–8.46)**	**2.13 (1.26–3.61)**	**2.06 (1.18–3.61)**	1.25 (0.65–2.43)	**1.93 (1.12–3.33)**	**3.49 (1.56–7.81)**
Superficial SSI	**2.77 (1.11–6.89)**	**1.86 (1.01–3.44)**	1.36 (0.71–2.61)	0.82 (0.42–2.02)	1.39 (0.74–2.61)	1.34 (0.51–3.55)
Deep SSI	1.51 (0.58–3.93)	**1.86 (1.00–3.46)**	1.65 (0.87–3.15)	1.93 (0.93–4.01)	**1.96 (1.03–3.72)**	1.61 (0.68–3.83)
Extra-abdominal infection	**8.83 (2.96–26.30)**	**2.62 (1.17–5.86)**	0.67 (0.29–1.56)	1.39 (0.56–3.48)	**5.52 (2.20–13.88)**	**8.26 (3.00–22.74)**
Non-infectious complication	0.99 (0.30–3.24)	0.94 (0.45–1.95)	1.66 (0.8–3.44)	1.82 (0.8–4.18)	1.75 (0.83–3.67)	2.16 (0.86–5.43)
Reoperation	0.63 (0.19–2.09)	**2.61 (1.33–5.12)**	1.35 (0.67–2.71)	2.01 (0.91–4.43)	1.84 (0.91–3.72)	**2.94 (1.25–6.92)**
Death	**40.11 (2.98–539.28)**	2.06 (0.25–17)	3.97 (0.50–31.53)	3.84 (0.29–51.42)	8.33 (0.55–127.23)	**26.91 (1.55–466.30)**

Bolded adjusted odds ratios show significant associations after controlling for confounding

anti-TNF therapy initiation is usually done for patient convenience. Patients who were evaluated by our gastroenterologists preoperatively with plan for postoperative therapy have insurance approval prior to surgery. Postoperatively, these patients either get a dose in-hospital or are instructed to initiate therapy at their home center after discharge based on their preference. Patients new to our practice who weren't evaluated by our gastroenterologists preoperatively would not be able to receive early postoperative therapy due to time required for care coordination.

Postoperative anti-TNF therapy has been shown to reduce endoscopic recurrence rates; however, the effect on clinical recurrence is not as clear [6–9]. In their meta-analysis, Carla-Moreau et al. [7] attributed the inconsistent effect of anti-TNF therapy on clinical recurrence to subjective interpretation of recurrence. As part of a randomized, double-blind, placebo-controlled study which evaluated the effectiveness of infliximab in preventing postoperative recurrence of CD, Regueiro et al. [6] found that postoperative infliximab decreased endoscopic but not clinical recurrence. Adverse and serious events were similar between the infliximab and placebo groups; however, differences in adverse events based on timing of infliximab initiation following surgery were not reported. In an earlier pilot study, Regeuiro et al. [26] compared adverse events following ileocolonic resection in 24 patients randomized to placebo or infliximab started 2–4 weeks after surgery. Consistent with our findings, complication rates were similar between groups.

Finally, similar to prior studies, we found increased postoperative complications, particularly infectious, with preoperative steroid and anti-TNF exposure, perforating disease behavior, and emergency surgery [27, 28]. The literature regarding effect of preoperative anti-TNF therapy is mixed with some studies showing increased risk of infectious complications [14–17, 20–23], and others showing no difference [18, 19]. It is difficult to recommend the universal discontinuation of anti-TNF therapy prior to surgery based on our study given its retrospective nature and the fact that many surgeries were urgent or emergent. The potential for increased risk of postoperative infectious complications must be weighed against that of reducing inflammation preoperatively. In our practice, we typically plan surgery for when anti-TNF medication is due presuming a trough in serum levels around that time.

This study's main limitation is its retrospective design. Whether and when anti-TNF therapy was initiated was not controlled for. As mentioned previously, patients with early postoperative complications were likely started on anti-TNF therapy only after resolution of their complications. This may introduce bias as less ill patients were given anti-TNF earlier after surgery. However, the main objective of our study was to demonstrate that early anti-TNF use was safe in select patients after abdominal surgery.

Anti-TNF therapy lowers endoscopic and possibly clinical recurrence following surgery for CD. Some clinicians avoid early postoperative anti-TNF initiation due to concern regarding infectious complications. This study evaluated anti-TNF use within 2 weeks and between 2 and 4 weeks following abdominal surgery in patients with CD. No difference in postoperative complications was found. Hence, administering anti-TNF therapy within 2 weeks of an uncomplicated abdominal surgery appears to be safe. For patients who live a significant distance from the hospital, inpatient anti-TNF administration prior to discharge can decrease travel burden. Further, in those on preoperative anti-TNF, early reinstitution following surgery may prevent immunogenicity, particularly if the anti-TNF is held preoperatively to prevent postoperative complications. In the future, prospective, randomized trials assessing the effect of early anti-TNF therapy on surgical complications and clinical CD recurrence should be undertaken to corroborate this recommendation.

Compliance with ethical standards

Conflict of interest RK Cross has participated in advisory boards and has engaged in consulting with Abbvie, Janssen, Pfizer, and Takeda. RK Cross has research grants with Abbvie. No grant support was used in this project. The other authors have no potential conflicts of interest to disclose.

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