HHS Public Access

Author manuscript

Ann Surg. Author manuscript; available in PMC 2016 August 23.

Published in final edited form as:

Ann Surg. 2015 March ; 261(3): 487–496. doi:10.1097/SLA.0000000000000757.

The Impact of Preoperative Serum anti-TNFα Therapy Levels on Early Postoperative Outcomes in Inflammatory Bowel Disease Surgery

Cheryl Lau, MD[*], **Marla Dubinsky, MD**[^], **Gil Melmed, MD**[+], **Eric Vasiliauskas, MD**[+], **Dror Berel**[+], **Dermot McGovern, MD PhD**[+], **Andrew Ippoliti, MD**[+], **David Shih, MD PhD**[+], **Stephan Targan, MD**[+], and **Phillip Fleshner, MD**[*]

[*]Division of Colorectal Surgery, Cedars-Sinai Medical Center, Los Angeles, CA 90048

[^]Department of Pediatrics, Cedars-Sinai Medical Center, Los Angeles, CA 90048

[+]F. Widjaja Foundation Inflammatory Bowel and Immunobiology Research Institute, Cedars-Sinai Medical Center, Los Angeles, CA 90048

Abstract

Objective—Assess the impact of preoperative serum anti-TNFα drug levels on 30-day postoperative morbidity in inflammatory bowel disease patients.

Summary Background Data—Studies on the association of anti-TNFα drugs and postoperative outcomes in IBD are conflicting due to variable pharmacokinetics of anti-TNFα drugs.. It remains to be seen whether preoperative serum anti-TNFα drug levels correlate with postoperative morbidity.

Methods—30 days postoperative outcomes of consecutive IBD surgical patients with serum drawn within 7 days pre-operatively, were studied. The total serum level of 3 anti-TNF-α drugs (infliximab, adalimumab, certolizumab) was measured, with ≥0.98 μg/ml considered as detected. Data was also reviewed according to a clinical cut off value of 3 μg/ml.

Results—217 patients (123 Crohn's disease (CD) and 94 ulcerative colitis (UC)) were analyzed. 75 of 150 (50%) treated with anti-TNFα therapy did not have detected levels at the time of surgery. In the UC cohort, adverse postoperative outcomes rates between the undetectable and detectable groups were similar when stratified according to type of UC surgery. In the CD cohort, there was a higher but statistically insignificant rate of adverse outcomes in the detectable vs undetectable groups. Using acut-off level of 3 μg/ml, postoperative morbidity (OR=2.5, p=0.03) and infectious complications (OR=3.0, p=0.03) were significantly higher in the ≥ 3 μg/ml group. There were higher rates of postoperative morbidity (p=0.047) and hospital readmissions (p=0.04) in the ≥ 8 μg/ml compared to < 3 μg/ml group.

Editorial correspondence to: Phillip Fleshner, MD, 8737 Beverly Boulevard, Suite 101, Los Angeles, CA 90048. Tel (310) 289 9224. Fax (310) 289 8995. PFleshner@aol.com.

The authors have no conflict of interest.

Podium presentation at Digestive Disease Week, Orlando, FL, May 21, 2013.

Conclusion—Increasing preoperative serum anti-TNFα drug levels are associated with adverse postoperative outcomes in CD but not UC patients.

Introduction

Tumor necrosis factor-α (TNFα) is a key pro-inflammatory cytokine playing a central role in the pathogenesis of inflammatory bowel disease (IBD). Monoclonal antibodies targeting TNFα have revolutionized the management of Crohn's disease (CD) and ulcerative colitis (UC)[123]. Despite the expanding use of anti-TNFα therapy in IBD, the long term need for surgery may not be significantly reduced[45]. More than one-third of patients do not respond to induction therapy (primary nonresponse), and even among initial responders the response wanes over time in 20% to 60% of patients[6].

Among its many actions, TNFα is implicated in regulating cells central to wound healing and protection against infection. For example, TNFα is an important mediator of neutrophil chemotaxis and adhesion during the initial phases of inflammation[7]. Experimental studies have also demonstrated that TNFα blockade is associated with significant alterations in wound healing[89]. Patients receiving anti-TNFα therapy have an increased risk of opportunistic infections with various bacterial and mycotic infections[101112]. Given its potential impact on wound healing and immunosuppressive properties, a crucial concern is whether patients undergoing major abdominal surgery after anti-TNFα drug exposure are at increased risk of early postoperative complications.

Studies reporting on the association of preoperative infliximab therapy use and postoperative outcomes in IBD have been published with conflicting results[131415161718192021]. These variable findings are attributed to a number of factors including retrospective study design, single institution experiences, dissimilar durations of anti-TNFα therapies, difficulty in controlling for disease severity, and the overlapping effect of other immunosuppressive medications, especially corticosteroids. In addition, differing time periods between the last anti-TNFα therapy infusion and date of surgery has plagued all prior studies[22].

Rather than the medical history of anti-TNFα agents use, a more accurate measure of anti-TNFα effect in the IBD patient is the absolute serum anti-TNFα drug level at the time of the operation. Increasing evidence demonstrates that despite standardized dosing, varying pharmacokinetics profiles between patients leads to a wide variation in serum anti-TNFα drug levels and by extension, clinical response. Trough infliximab levels are known to be associated with increased rates of remission, lower C-reactive protein (CRP) and improved endoscopic outcomes[2324]. We postulate that serum anti-TNFα drug levels may have an adverse surgical impact on IBD patients. Therefore, our study aims to evaluate the association of serum anti-TNFα drug levels with the risk of early postoperative complications in a cohort of IBD patients.

Methods

Study Population

Consecutive UC and CD adult patients undergoing major abdominal surgery by a single surgeon in a tertiary referral center over a 13-year period ending October 2012 were initially identified. From this group, patients who had stored serum drawn within the 7 days period before surgery comprised the study cohort. Patients with IBD-unclassified (IBDU) were excluded. Other exclusion criteria included patients in whom insufficient serum was available for analysis and IBD patients who had anorectal surgery only. This study was approved by the Cedars-Sinai Medical Center Institutional Review Board (IRB #30095).

Assessment of Clinical Characteristics

A prospectively maintained IBD registry of patient's clinical profiles including demographics and disease characteristics was retrospectively reviewed. Demographic information included patient gender, age at time of surgery, pre-operative morbidity and smoking history. Disease characteristics included type of IBD (UC or CD), type of preoperative medication use, abscesses at the time of surgery and indication for surgical intervention (medically-refractory disease vs. dysplasia/cancer). The diagnosis of UC or CD was based upon standard clinical, endoscopic, radiologic and when necessary, pathological criteria[25]. Medical therapy recorded before IBD-related surgery included steroids (intravenous or oral), immunomodulators (6-mercaptopurine, azathioprine, methotrexate or cyclosporine) and anti-TNFα agents (infliximab, adalimumab, certolizumab). Laboratory values (hemoglobin, serum albumin and C-reactive protein) within one month of surgery were also collated.

Surgical Procedures

The index surgery for UC patients was either a two-stage ileal pouch-anal anastomosis (IPAA), or a subtotal colectomy (STC) (as part of a three-stage IPAA) or total proctocolectomy (TPC) with ileostomy. A standard IPAA procedure was performed with complete mucosectomy, ileal J-pouch creation and a temporary diverting ileostomy. The decision to perform an initial STC/TPC or IPAA as the index operation was at the discretion of the operating surgeon. Reasons for STC/TPC included toxic megacolon and/or bowel perforation or patients in whom an IPAA was not technically feasible (for example, significant intra-abdominal obesity or where the tissues were found intra-operatively to be too 'fragile' to safely stretch a potential ileal pouch into the pelvis). These criteria reflect current standard of surgical practice widely used by colorectal surgeons operating on UC patients[2627].

In CD patients, the type of surgical procedure selected by the surgeon was dependent on the disease site and surgical indication. In addition, surgical approach in all CD patients was guided by a desire for maximal bowel length conservation.

Serum anti-TNFα Drug Level Measurements

Stored frozen serum samples were used for analysis. Laboratory measurements of serum anti-TNFα drug levels did not degrade over time or with multiple freeze-thaw cycles[2829].

Serum anti-TNFα drug levels were measured using the homogenous mobility shift assay, which utilizes high performance liquid phase chromatography (Prometheus Labs, Inc., San Diego, California)[30,31]. This assay measures the total serum level of all 3 anti-TNFα agents commonly used in IBD (infliximab, adalimumab and certolizumab). The serum anti-TNFα drug levels measurement's false-positive rate is 5%, with the cut point value of 0.98 μg/ml, as referenced by Prometheus Lab.

Patients were categorized into detectable levels (serum anti-TNFα drug levels more than or equal to 0.98 μg/ml) or undetectable levels (serum anti-TNFα drug levels less than 0.98 μg/ml) groups. The detectable level group was further stratified into low (≥0.98 to <3 μg/ml), medium (≥ 3 to < 8 μg/ml) and high (≥ 8 μg/ml) subgroups.

Postoperative outcomes were also analyzed according to a level of 3 μg/ml, currently the most commonly utilized cut off value for clinical efficacy[32]. All assays were performed by Prometheus Labs blinded to patients' clinical characteristics, disease type, and surgery outcomes. Similarly, the records of the postoperative outcomes were analyzed without knowledge of patients' serum anti-TNFα drug levels.

Early Postoperative Outcomes

Postoperative morbidity and mortality were prospectively recorded during the 30-day period beginning from the date of surgery using inpatient medical records and office chart notes. In patients undergoing planned multi-staged procedures, only the complications arising from the initial surgery were analyzed. A complication was defined as any deviation from the normal expected postoperative course[33]. These complications were classified as either medical or surgical, and were further characterized as being either minor (grade 1) or major (grade 2 and 3) according to the established Clavien-Dindo classification of surgical complications[34]. In addition, all infectious complications, whether surgical or medical in nature, were specifically examined. Postsurgical length of hospitalization and 30-day hospital readmission rates were also noted.

Statistical Analysis

All data were prospectively entered in a standardized database computer program (Microsoft Excel, Seattle, WA). Descriptive statistics were reported as mean and standard deviation (SD) for continuous variables, frequencies for categorical variables. Categorical variables were analyzed using 2-tailed Fisher's exact test and continuous variables analyzed with Students' t-test or one-way ANOVA. A Cochrane-Armitage trend analysis was also used to investigate the relationship between increasing serum anti-TNFα drug levels and postoperative outcomes. Factors found significant on univariate analysis were included in a multivariate logistic regression model to test the effect of confounding variables. Analysis was performed using R statistical computing software. A p value of <0.05 was considered to be statistically significant.

Results

IBD Study Cohort

From December 1999 to October 2012, 217 (21%) patients satisfied study entry criteria and comprised the study cohort (Table 1). The mean age of the study cohort was 36.9 years (standard deviation, 15.5). 57% of the study cohort had CD. Anti-TNFα agents were used before surgery in 65% of the study cohort, most commonly infliximab. Almost 20% of patients had been treated with multiple courses of anti-TNFα agents before surgery. The majority of operations were performed for medical intractability. A small bowel/ileocolic resection (for CD) or an IPAA or STC (for UC) were performed in 93% of the study cohort.

Serum anti-TNFα Drug Level Profile

82% (177 out of 217) of the serum samples were drawn on the day of the surgery. Sixty-seven study cohort patients (31%) had detectable serum anti-TNFα drug levels (Table 1). Mean level in the detectable group was 18.17 ± 19.95 μg/ml (median 10.94, range, 1.53 to 99.11 μg/ml). There were no significant differences in age and gender distribution between the undetectable and detectable groups. Detectable levels were significantly more common in CD *versus* UC patients (OR 3.1; 95% CI 1.6–5.9; p=0.0005) and patients also being treated with steroids (OR 2.8; 95% CI 1.5–5.1; p=0.001). Although there was a significant association between the use of anti-TNFα agents and detection of serum anti-TNFα drug levels (p=0.001), 75 of the 142 (53%) patients with a history of anti-TNFα therapy did not have a detectable level at the time of surgery.

The detectable group included low, medium and high serum anti-TNFα drug levels, with 66% of the serum values in the high group (≥ 8 μg/ml) (Table 2). Although there was no significant association noted between levels and a single anti-TNFα agent use, patients treated with multiple courses of different anti-TNFα agents more commonly had high serum anti-TNFα drug levels. Significantly higher preoperative hemoglobin and albumin levels were noted in the high serum anti-TNFα drug level group compared to the low serum anti-TNFα drug level group.

Serum anti-TNFα drug levels and clinical characteristics of the UC and CD patients are shown in Tables 3 and 4. Although 60 out of 94 (64%) patients in the UC cohort were treated with preoperative anti-TNFα therapy, only 17 (28%) had detectable serum anti-TNFα drug levels at the time of surgery. In the UC cohort, the mean detectable serum anti-TNFα drug level was 14.00 ± 16.21 μg/ml. There were proportionately equal numbers of UC patients who underwent a 2-stage IPAA *vs.* 3-stage IPAA in both the detectable and undetectable groups. In the CD cohort, although 83 patients were treated with preoperative anti-TNFα therapy, only 50 (60%) had detected serum anti-TNFα drug levels at the time of surgery. Mean serum anti-TNFα drug level was 19.58 ± 21.03 μg/ml. Significantly more patients in the undetectable group had a small bowel/ileocolic resection compared to the detectable group (p=0.02). The incidence of intra-abdominal abscess found intra-operatively was similar between both groups.

Influence of Serum anti-TNFα Drug Levels on Early Postoperative Complications

Postoperative complications in the study cohort were noted in a total of 68 patients, representing an overall rate of 31% (Table 5). The most common postoperative complication was ileus (n = 16). Included in the 19 major surgical complications were small bowel obstruction (3/8 in the detectable group), postoperative intra-abdominal abscess (5/7 in the detectable group), anastomotic leaks (2/2 in the undetectable group), evisceration (1 in the detectable group) and intra-abdominal hemorrhage (1 in the undetectable group). The majority of infectious complications in the study cohort are surgical related (19/30 with superficial and/or intra-abdominal infections). The only death was a 32-year-old CD patient (serum anti-TNFα drug level of 3.47 μg/ml) who developed a fatal pulmonary embolism on postoperative day one after an elective laparoscopic total colectomy. Although there was an increased rate of medical and infectious complications in the detectable *vs* undetectable serum anti-TNFα drug level groups, these differences did not reach statistical significance (18% vs 9%, 19% vs 11%). In addition, although there was an increasing incidence of overall surgical complication rates and readmission rates with increasing serum anti-TNFα drug levels, these trends did not reach statistical significance.

There were no significant differences in adverse postoperative outcomes between the detectable and undetectable serum anti-TNFα drug level groups in the entire UC cohort (Table 6) or in UC patients stratified according to type of index surgery (Figures 1 and 2). Similar results were also seen with outcomes analyzed according to a serum cut off level of 3 μg/ml (data not shown). Analyzing a subgroup of UC patients with a preoperative history of anti-TNFα agent use (n = 60), the infectious complication risk between the undetectable group (n = 43) and the detectable serum anti-TNFα drug level groups (n =17) was not significantly different (4/43 vs 2/17, 9% vs 12%, p = 0.78). Overall postoperative morbidity risk (17/43 vs 8/17, 40% vs 47%, p = 0.59) and readmissions (8/43 vs 4/17, 19% vs 24%, p = 0.67) were also not significantly different.

In the CD cohort, there was a higher rate of overall postoperative morbidity, infectious complications and readmissions in the detectable serum anti-TNFα drug level group (Figure 3). None of these trends however reached statistical significance. As the majority of operations performed in the CD group were small bowel/ileocolic resections, the outcomes were also analyzed in this subgroup. Again, there was a higher but statistically insignificant higher rate of overall postoperative morbidity, infectious complications and readmissions in patients with detectable serum anti-TNFα drug levels (Figure 4). Using a clinical cut-off serum anti-TNFα drug level of 3 μg/ml, both overall postoperative morbidity (16/47 vs 13/76; OR=2.5, 95% CI 1.07–5.85, p = 0.03) and infectious complications (11/47 vs 7/76; OR=3.0, 95% CI 1.08–8.43, p = 0.03) were significantly higher in the ≥ 3 μg/ml group (Figure 5). There was a significantly higher rate of overall postoperative morbidity (p = 0.047) and readmissions (p = 0.043) in the ≥ 8 μg/ml serum anti-TNFα drug level group compared to the < 3 μg/ml serum anti-TNFα drug level group (Figure 6). However, a Cochrane Armitage trend analysis did not demonstrate significant results.

In our CD cohort, as there was a significantly higher incidence of overall postoperative morbidity and infectious complications in the ≥ 3 μg/ml group on univariate analysis, we then focused on whether these results held true when we adjusted for the important

confounding factors such as preoperative steroids, immunomodulators and albumin. Using a multivariable logistic regression model, the effect of adding additional confounding variables was tested. Paired comparisons of ≥ 3 μg/ml serum anti-TNFα drug levels with steroids, 6-mercaptopurine and azathioprine showed that the association of ≥ 3 μg/ml serum anti-TNFα drug levels remained significant for overall postoperative morbidity and infectious complications when adjusting for these confounders. However, these serum levels did not remain significantly associated with postoperative morbidity when adjusted for albumin (Table 7). There were no statistically significant risks for adverse postoperative outcomes in association with immunomodulator use, steroid use or laboratory levels (data not shown).

Discussion

This study represents the first to specifically examine the impact of preoperative anti-TNFα drug levels on postoperative outcomes in IBD patients. A comprehensive literature review yielded a subgroup analysis in one retrospective case-control study that looked at postoperative outcomes in 19 IBD patients with preoperative serum infliximab levels[35]. Ten patients had detectable serum levels of infliximab and nine patients had undetectable infliximab levels. There were no differences in overall infectious complication rates between the two groups. Wound infections were more frequent in the group with detected infliximab (30% vs. 0%) although the results were not statistically significant and this was a small study. As there are many studies correlating clinical and endoscopic responses in IBD with anti-TNFα drug levels and recognizing the potential for adverse wound healing and serious infections with anti-TNF-α therapy usage[3637], evaluation of the association between levels and early postoperative complications represents a logical step in IBD surgical research.

The observation that over one-half of patients treated with anti-TNFα therapy before surgery did not have detectable levels at the time of surgery was intriguing. The half-life of infliximab demonstrates a wide range from 7 to 18 days[3839]. Marked inter-individual differences in drug pharmacokinetics and immunogenicity lead to differences in observed clinical efficacy despite standardized dosing[40]. The poor correlation between preoperative anti-TNFα therapy use and detectable levels in our study also demonstrates that merely using a medication record of anti-TNFα drug exposure is not rigorous enough as a factor for analysis in postoperative morbidity studies. Existing studies on the effect of anti-TNFα therapy on early postoperative complications in IBD patients demonstrate a wide disparity in the timing of drug infusion to surgery date. A recent meta-analysis on anti-TNFs and postoperative complications in IBD included prior studies with infliximab infusions varying from 4 to 12 weeks before surgery[41]. Conflicting results from these studies may in part reflect different anti-TNFα drug levels at the time of surgery.

There was a higher proportion of UC patients compared to CD patients in the undetectable serum anti-TNFα drug level group. UC disease-specific factors might stimulate earlier formation of immune complexes in anti-TNFα agent treated UC patients and lead to a reduction in serum infliximab levels[24]. This effect appears to be largely dependent on the severity of disease as a larger volume of inflamed intestinal surface leads to increased drug

clearance[42]. This observation might explain the overall poorer clinical response to anti-TNFα in hospitalized *vs.* ambulatory UC patients[434445].

Significant associations were noted between a number of laboratory values and serum anti-TNFα drug levels in this surgical cohort. Notably, mean hemoglobin and albumin levels trended higher and CRP trended lower with increasing drug levels. Anemia in IBD can be a result of the inhibitory effects of cytokines such as TNFα on erythropoiesis and as such an improvement in hemoglobin levels is expected following anti-TNFα therapy[4647]. Hepatic synthetic function and nutritional status are also known to improve with clinical response to anti-TNFα therapy, as reflected in our study's laboratory values[48]. A decrease in CRP levels is seen with increasing anti-TNFα drug levels secondary to anti-TNF blockade on the inflammatory cascade[49]. It is possible the associations between these laboratory values and anti-TNFα drug levels could favorably influence the purported deleterious effects anti-TNFα therapy have on early postoperative outcomes.

Some surgeons advocate that UC patients exposed to anti-TNF drug therapy in the preoperative period should undergo a three-stage rather than two-stage IPAA; the first operation would be a STC and end ileostomy, allowing the patient to be withdrawn from anti-TNFα therapy before creation of a ileal pouch. This surgical approach is supported by two studies showing UC patients exposed to anti-TNFα agents were significantly more likely to have postoperative anastomotic leak and pelvic infections after IPAA[1418]. Other UC studies, including a recent meta-analysis, however have found no such association[20215051]. The variable results noted in all these studies may reflect that they are all retrospective, patients are undergoing varying percentages of two-stage and three-stage IPAA, and are not uniformly based on a single surgeon experience resulting in variations in surgical techniques confounding postoperative outcomes. Additionally, as these studies included varying anti-TNFα drug dosing and intervals between dosing and surgery, the diverse results may reflect differing serum anti-TNFα drug levels between patients. In our UC cohort, there was no significant difference in adverse postoperative outcomes between the undetectable and undetectable serum anti-TNFα drug level groups. In addition, we analyzed the STC/TPC group and the IPAA group separately in order to standardize our results according to the complexity of UC surgery performed. The results again showed no significant disparity, even when patients were stratified according to a clinical cut off value at 3 μg/ml. Measurements of anti-TNFα drug levels may not have a role in the prognostication of postoperative morbidity in UC patients. More importantly though, the lack of effect of serum anti-TNFα drug levels on patients undergoing two-stage IPAA suggests that a universal policy of using a three-stage IPAA in anti-TNFα exposed patients espoused by some surgeons may be unnecessary.

The use of anti-TNFα therapy can simply be a surrogate marker for more severe disease and inherently sicker UC patients. It is plausible that undetected serum anti-TNFα drug levels in this group represent treatment failure due to the higher inflammatory disease burden, and that it is the severity of the underlying disease rather than the medications per se that potentially contribute to worse surgical outcomes. With this in mind, we looked at subgroup analysis of postoperative outcomes in undetected *vs.* detected serum anti-TNFα drug levels

in UC patients exposed to anti-TNFα therapy only. No significant differences in outcomes were seen between groups.

In our CD group, overall postoperative morbidity and infectious complications were significantly higher in the ≥ 3 μg/ml group compared to the < 3 μg/ml group. Our data also demonstrated a significantly increased overall postoperative morbidity and readmissions with levels ≥ 8 μg/ml. Taken together, these results suggest that rising values of serum anti-TNFα drug levels are associated with adverse postoperative outcomes in this population set. Our findings confirm and extend the observations from a prior study in our institution that analyzed the association between prior anti-TNFα therapy use and postoperative morbidity in 458 CD patients[52]. A recent meta-analysis of eight studies in CD patients also indicated that preoperative infliximab treatment was associated with an increased risk of postoperative infectious complications, and a trend towards an increased risk of both noninfectious and overall complications[41].

There were many factors that account for differences in morbidity outcomes between our UC and the CD groups. The type of surgical procedure was a crucial consideration. For example, all our UC patients who underwent a pelvic anastomosis have temporary protective stomas and this surgical factor would have minimized the adverse sequelae of anastomotic leaks and/or pelvic sepsis. The proportion of patients with detectable serum anti-TNFα drug levels in the UC group was also much lower than in the CD group. Finally, our CD patients frequently had additional risk factors for adverse surgical outcomes such as multiple intra-abdominal fistulae, multiple bowel anastomoses, past surgeries, and urgent indications for surgery.

Limitations of this study are a lack of adjustment for disease severity in UC patients, steroid dosage, nutritional deficiency such as body mass index and disease duration prior to operation, all of which might be predictive of developing postsurgical morbidity[5354]. We also do not have accurate information on the time period from date of last anti-TNFα drug dosage to the date of surgery. As this is a study spanning over 12 years, improved surgical technique and postoperative care such as the introduction of enhanced recovery pathways may have impacted our results. We also have no prospective information on surgery-specific factors such as intraoperative operating time and blood loss. It still remains unknown whether these factors could have confounded our results or whether such factors differ among anti-TNFα therapy exposed and unexposed patients. Lastly, our results reflect the experience of a single high-volume tertiary referral center and thus may not be generalizable to other settings.

The challenge that surgeons face is the balance between the timing of surgical intervention and preoperative anti-TNFα therapies' perceived infectious risk profile. Our series is the first study to date specifically looking at the relationship between serum anti-TNFα drug levels and early surgical complications. There is an association of increasing preoperative levels and postoperative infectious outcomes for CD patients but not UC patients. Although our study results need to be validated, the potential surgical practice-changing implications of this study suggest that especially among CD patients, preoperative serum anti-TNFα drug levels measurement should be considered to optimize preoperative counseling, guide

surgical practice and determine surgical prognosis. For example, a surgeon may elect to wait for the drug serum wash out period in elective CD surgery. Lastly, a blanket policy of advocating 3 stage procedures for all anti-TNFα-treated UC patients may be unfounded.

References

1. Hanauer SB, Feagan BG, Lichtenstein GR, et al. ACCENT I Study Group. Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. Lancet. 2002; 359(9317):1541–1549. [PubMed: 12047962]
2. Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2005; 353:2462–2476. [PubMed: 16339095]
3. Lawson MM, Thomas AG, Akobeng AK. Tumour necrosis factor alpha blocking agents for induction of remission in ulcerative colitis. Cochrane Database Syst Rev. 2006; 3:CD005112. [PubMed: 16856078]
4. Peyrin-Biroulet L, Oussalah A, Williet N, et al. Impact of azathioprine and tumour necrosis factor antagonists on the need for surgery in newly diagnosed Crohn's disease. Gut. 2011; 60:930–936. [PubMed: 21228429]
5. Danese S, Fiocchi C. Ulcerative colitis. N Engl J Med. 2011; 365:1713–1725. [PubMed: 22047562]
6. Colombel JF, Sandborn WJ, Rutgeerts P, et al. Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. Gastroenterology. 2007; 132(1): 52–65. [PubMed: 17241859]
7. Ulich TE, del Castillo J, Keys M, et al. Kinetics and mechanisms of recombinant human interleukin 1 and tumor necrosis factor-alpha-induced changes in circulating numbers of neutrophils and lymphocytes. J Immunol. 1987; 139:3406–3415. [PubMed: 3316383]
8. Lee R, Efron D, Udaya T, et al. Inhibition of tumor necrosis factor-alpha attenuates wound breaking strength in rats. Wound Repair Regen. 2000; 8:547–553. [PubMed: 11208182]
9. Albina J, Mastrofrancesco B, Vessella J, et al. HIF-1 expression in healing wounds: HIF-1alpha induction in primary inflammatory cells by TNF-alpha. Am J Physiol Cell Physiol. 2001; 281:C1971–C1977. [PubMed: 11698256]
10. Keane J, Gershon S, Wise RP, et al. Tuberculosis associated with infliximab, a tumor necrosis factor alpha-neutralizing agent. N Engl J Med. 2001; 345:1098–1104. [PubMed: 11596589]
11. Garcia-Vidal C, Rodriguez-Fernandez S, Teijon S, et al. Risk factors for opportunistic infections in infliximab-treated patients: the importance of screening in prevention. Eur J Clin Microbiol Infect Dis. 2009; 28:331–337. [PubMed: 18797940]
12. Lichtenstein GR, Cohen RD, Feagan BG, et al. Safety of infliximab and other Crohn's disease therapies: treat (TM) registry data with a mean of 5 years of follow-up. Gastroenterology. 2011; 140:S773-S.
13. Colombel JF, Loftus EV Jr, Tremaine WJ, et al. Early postoperative complications are not increased in patients with Crohn's disease treated perioperatively with infliximab or immunosuppressive therapy. Am J Gastroenterol. 2004; 99:878–883. [PubMed: 15128354]
14. Mor IJ, Vogel JD, da Luz Moreira A, et al. Infliximab in ulcerative colitis is associated with an increased risk of postoperative complications after restorative proctocolectomy. Dis Colon Rectum. 2008; 51:1202–1207. [PubMed: 18536964]
15. Marchal L, D'Haens G, van Assche G, et al. The risk of post-operative complications associated with infliximab therapy for Crohn's disease: a controlled cohort study. Aliment Pharmacol Ther. 2004; 19:749–754. [PubMed: 15043515]
16. Kunitake H, Hodin R, Shellito PC, et al. Perioperative treatment with infliximab in patients with Crohn's disease and ulcerative colitis is not associated with an increased rate of postoperative complications. J Gastrointest Surg. 2008; 12:1730–1736. discussion 1730–1736. [PubMed: 18709514]
17. Schluender SJ, Ippoliti A, Dubinsky M, et al. Does infliximab influence surgical morbidity of ileal pouch-anal anastomosis in patients with ulcerative colitis? Dis Colon Rectum. 2007; 50:1747–1753. [PubMed: 17704969]

18. Selvasekar CR, Cima RR, Larson DW, Dozois EJ, Harrington JR, Harmsen WS, Loftus EV, Sandborn WJ, Wolff BG, Pem-berton JH. Effect of infliximab on short-term complications in patients undergoing operation for chronic ulcerative colitis. J Am Coll Surg. 2007; 204:956–962. discussion 962–963. [PubMed: 17481518]
19. Appau KA, Fazio VW, Shen B, Church JM, Lashner B, Remzi F, 37 Brzezinski A, Strong SA, Hammel J, Kiran RP. Use of infliximab within 3 months of ileocolonic resection is associated with ad- verse postoperative outcomes in Crohn's patients. J Gastrointest Surg. 2008; 12:1738–1744. [PubMed: 18709420]
20. Ferrante M, D'Hoore A, Vermeire S, Declerck S, Noman M, Van Assche G, Hoffman I, Rutgeerts P, Penninckx F. Corticosteroids but not infliximab increase short-term postoperative infectious complications in patients with ulcerative colitis. Inflamm Bowel Dis. 2009; 15:1062–1070. [PubMed: 19161179]
21. Yang Z, Wu Q, Wang F, Wu K, Fan D. Meta-analysis: effect of preoperative infliximab use on early postoperative complications in patients with ulcerative colitis undergoing abdominal surgery. Aliment Pharmacol Ther. 2012; 36:922–928. [PubMed: 23002804]
22. Ali, Tauseef; Yun, Laura; Rubin, David T. Risk of post-operative complications associated with anti- TNF therapy in inflammatory bowel disease. World J Gastroenterol. 2012 Jan 21; 18(3):197–204. [PubMed: 22294822]
23. Maser EA, Villela R, Silverberg MS, Greenberg GR. Association of trough serum infliximab to clinical outcome after scheduled maintenance treatment for Crohn's disease. Clin Gastroenterol Hepatol. 2006; 4:1248–1254. [PubMed: 16931170]
24. Seow CH, Newman A, Irwin SP, et al. Trough serum infliximab: a predictive factor of clinical outcome for infliximab treatment in acute ulcerative colitis. Gut. 2010; 59(1):49–54. [PubMed: 19651627]
25. Bernstein CN, Fried M, Krabshuis JH, et al. World Gastroenterology Organization Practice Guidelines for the diagnosis and management of IBD in 2010. Inflamm. Bowel Dis. 2010; 16:112–124. [PubMed: 19653289]
26. Cohen JL, Strong SA, Hyman NH, et al. Practice parameters for the surgical treatment of ulcerative colitis. Dis Colon Rectum. 2005; 48:1997–2009. [PubMed: 16258712]
27. Metcalf AM. Elective and emergent operative managements of ulcerative colitis. Surg Clin North Am. 2007; 87:633–641. [PubMed: 17560416]
28. McGuyer, C. Infliximab and Antibodies to Infliximab (ATI) Measurement-- 27222, 2012. New York, NY: Clinical Laboratory Evaluation Program (CLEP), New York State Department of Health Services; 2012.
29. McGuyer, C. Adalimumab and Antibodies to Adalimumab (ATA) determination (AnserADA) -35169, 2013. New York, NY: Clinical Laboratory Evaluation Program (CLEP), New York State Department of Health Services; 2013.
30. Wang SL, Ohrmund L, Hauenstein S, et al. Development and validation of a homogeneous mobility shift assay for the measurement of infliximab and antibodies-to-infliximab levels in patient serum. Journal of Immunological Methods. 2012; 382(1–2):177–188. [PubMed: 22691619]
31. Hauenstein, S.; Ohrmund, L.; Salbato, J., et al. Comparison of homogeneous mobility shift assay and solid-phase ELISA for the measurement of drug and anti-drug antibody (ADA) levels in serum from patients treated with anti-TNF biologics. Presented at Digestive Disease Week; May 19–22, 2012; San Diego, California. Abstract Su1928
32. Feagan BG, Singh S, Lockton S, et al. Novel infliximab (IFX) and antibody-to infliximab (ATI) assays are predictive of disease activity in patients with Crohn's disease. Gastroenterology. 2012; 142(Suppl.1):S-565.
33. Clavien P, Sanabria J, Strasberg S. Proposed classification of complication of surgery with examples of utility in cholecystectomy. Surgery. 1992; 111:518–526. [PubMed: 1598671]
34. Dindo, Daniel, et al. Classification of Surgical Complications: A New Proposal With Evaluation in a Cohort of 6336 Patients and Results of a Survey. Ann Surg. 2004 Aug; 240(2):205–213. [PubMed: 15273542]

35. Waterman M, Wei Xu, Dinani A, et al. Preoperative biological therapy and short-term outcomes of abdominal surgery in patients with inflammatory bowel disease. Gut. 2013; 62:387–394. [PubMed: 22619367]
36. Singh, JA.; Furst, DE.; Bharat, A., et al. Arthritis Care Res. Vol. 64. Hoboken: 2012. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis; p. 625-639.
37. Grijalva CG, Chen L, Delzell E, et al. Initiation of tumor necrosis factor-alpha antagonists and the risk of hospitalization for infection in patients with autoimmune diseases. JAMA. 2011; 306(21): 2331–2339. [PubMed: 22056398]
38. Klotz U, Teml A, Schwab M. Clinical pharmacokinetics and use of infliximab. Clin Pharmacokinet. 2007; 46:645–660. [PubMed: 17655372]
39. Ternant D, Aubourg A, Magdelaine-Beuzelin C, et al. Infliximab pharmacokinetics in inflammatory bowel disease patients. Ther Drug Monit. 2008; 30:523–529. [PubMed: 18641542]
40. Bendtzen K, Ainsworth M, Steenholdt C, et al. Individual medicine in inflammatory bowel disease: monitoring bioavailability, pharmacokinetics and immunogenicity of anti-tumour necrosis factor-alpha antibodies. Scand J Gastroenterol. 2009; 44(7):774–781. [PubMed: 19140087]
41. Kopylov U, Ben-Horin S, Zmora O, et al. Anti-tumor Necrosis Factor and Postoperative Complications in Crohn's Disease: Systematic Review and Meta-analysis. Inflamm Bowel Dis. 2012; 18:2404–2413. [PubMed: 22467533]
42. Ordas I, Feagan BG, Sandborn WJ. Therapeutic drug monitoring of tumor necrosis factor antagonists in inflammatory bowel disease. Clin Gastroenterol Hepatol. 2012; 10:1079–1087. [PubMed: 22813440]
43. Regueiro M, Curtis J, Plevy S. Infliximab for hospitalized patients with severe ulcerative colitis. J Clin Gastroenterol. 2006; 40:476–481. [PubMed: 16825928]
44. Järnerot G, Hertervig E, Friis-Liby I, et al. Infliximab as rescue therapy in severe to moderately severe ulcerative colitis: a randomized, placebo-controlled study. Gastroenterology. 2005; 128:1805–1811. [PubMed: 15940615]
45. Gisbert JP, Gonzalez-Lama Y, Mate J. Systematic review: Infliximab therapy in ulcerative colitis. Aliment Pharmacol Ther. 2007; 25(1):19–37. [PubMed: 17229218]
46. Bergamaschi G, Sabatino A, Alvertini R, et al. Prevalence and pathogenesis of anemia in inflammatory bowel disease. Influence of anti-tumor necrosis factor-α treatment. Haematologica. 2010 Feb; 95(2):199–205. [PubMed: 19815838]
47. Doyle, Mittie K.; Rahman, Mahboob U., et al. Treatment with infliximab plus methotrexate improves anemia in patients with rheumatoid arthritis independent of improvement in other clinical outcome measures—A Pooled Analysis from three large, multicenter, double-blind, randomized clinical trials. Semin Arthritis Rheum. 2008; 39:123–131. [PubMed: 18823645]
48. Fasanmade AA, Adedokun OJ, Olson A, et al. Serum albumin concentration: a predictive factor of infliximab pharmacokinetics and clinical response in patients with ulcerative colitis. Int J Clin Pharmacol Ther. 2010; 48:297–308. [PubMed: 20420786]
49. Elliott MJ, Maini RN, Feldmann M, et al. Treatment of rheumatoid arthritis with chimeric monoclonal antibodies to tumor necrosis factor alpha. Arthritis Rheum. 1993; 36:1681–1690. [PubMed: 8250987]
50. Gainsbury ML, Chu DI, Howard LA, et al. Preoperative infliximab is not associated with an increased risk of short-term postoperative complications after restorative proctocolectomy and ileal pouch-anal anastomosis. J Gastrointest Surg. 2011; 15:397–403. [PubMed: 21246415]
51. Eshuis EJ, Al Saady RL, Stokkers PC, et al. Previous infliximab therapy and post-operative complications after proctocolectomy with ileum pouch anal anastomosis. J Crohns Colitis. 2013; 7:142–149. [PubMed: 22542056]
52. Lau CC, Dubinsky M, Melmed G, et al. Su1133 Influence of Biologic Agents on Short-Term Postoperative Complications in Patients With Crohn's Disease: A Prospective, Single-Surgeon Cohort Study. Gastroenterology. 144.5(2013):S-407.

53. Kasparek MS, Bruckmeier A, Beigel F, et al. Infliximab does not affect postoperative complication rates in Crohn's patients undergoing abdominal surgery. Inflamm Bowel Dis. 2012; 18:1207–1213. [PubMed: 21928373]

54. Coquet-Reinier B, Berdah SV, Grimaud JC, et al. Preoperative infliximab treatment and postoperative complications after laparoscopic restorative proctocolectomy with ileal pouch–anal anastomosis: a case-matched study. Surg Endosc. 2010; 24:1866–1871. [PubMed: 20108148]

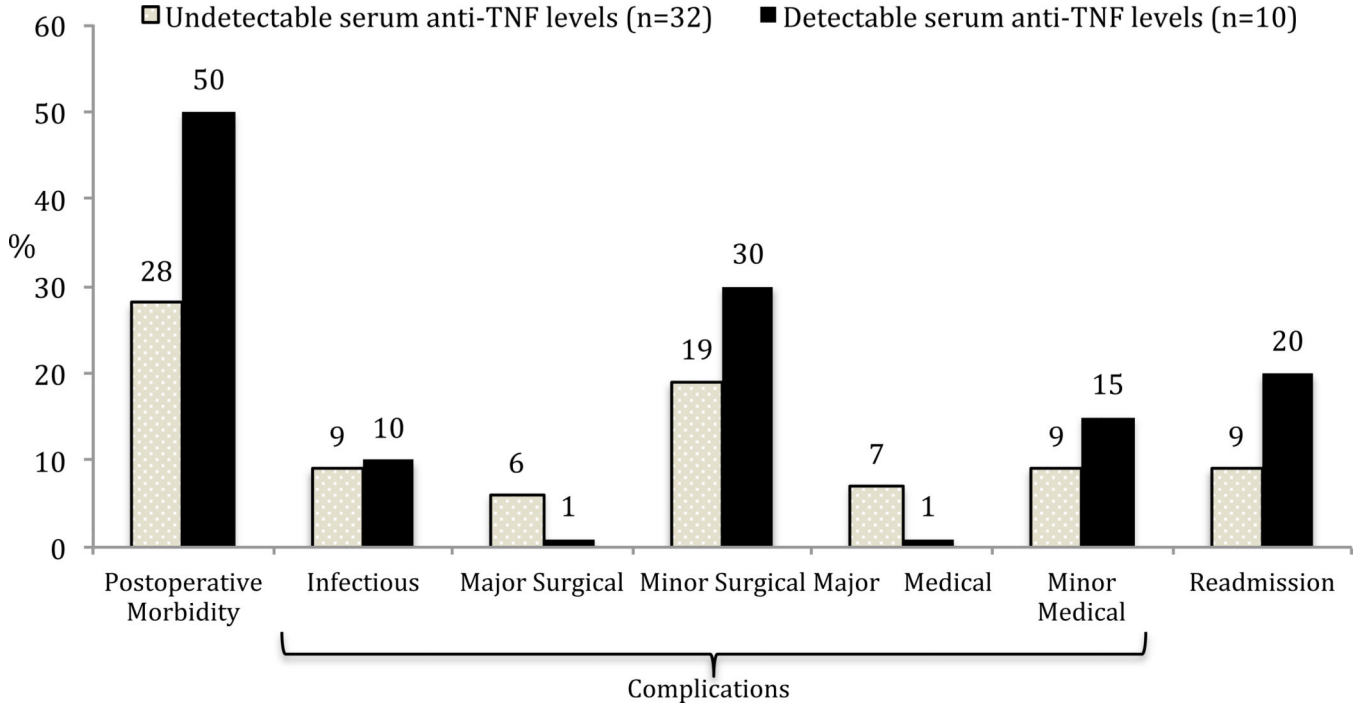

Figure 1.

Postoperative outcomes and serum anti-TNFα drug levels in ulcerative colitis patients undergoing subtotal colectomy or total proctocolectomy/end-ileostomy (all p=NS).

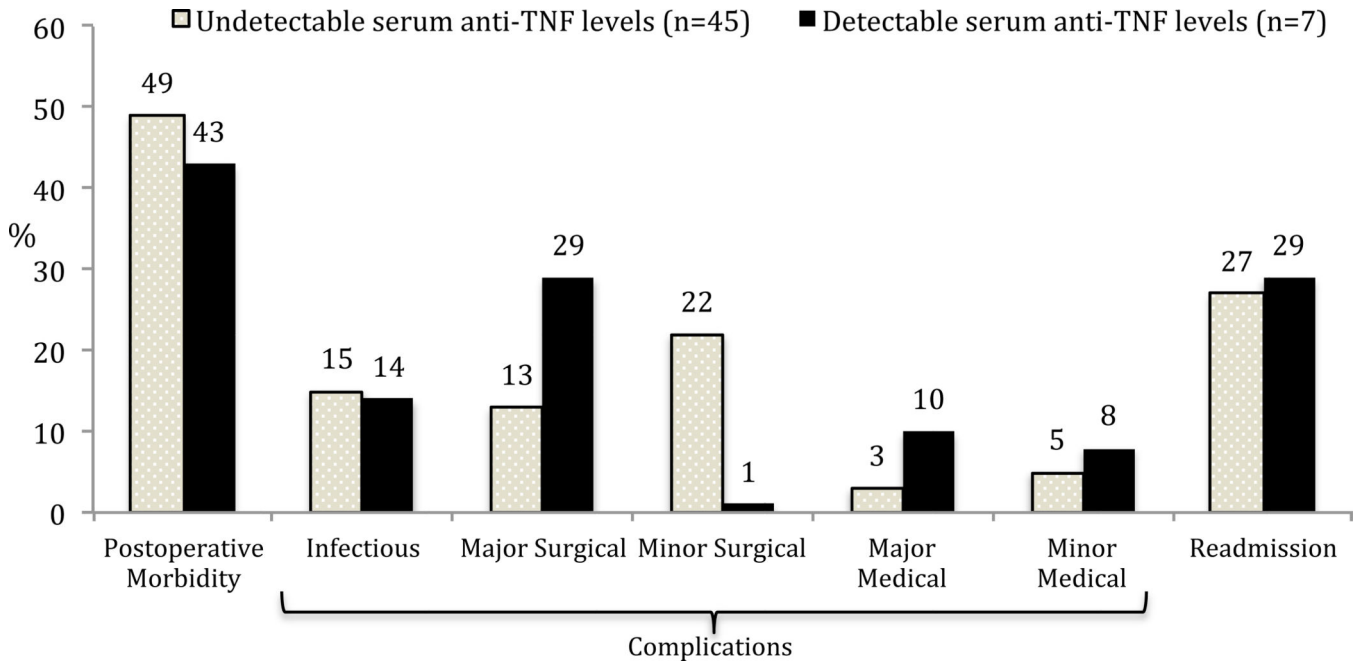

Figure 2.

Postoperative outcomes and serum anti-TNFα drug levels in ulcerative colitis undergoing ileal pouch-anal anastomosis (all p=NS).

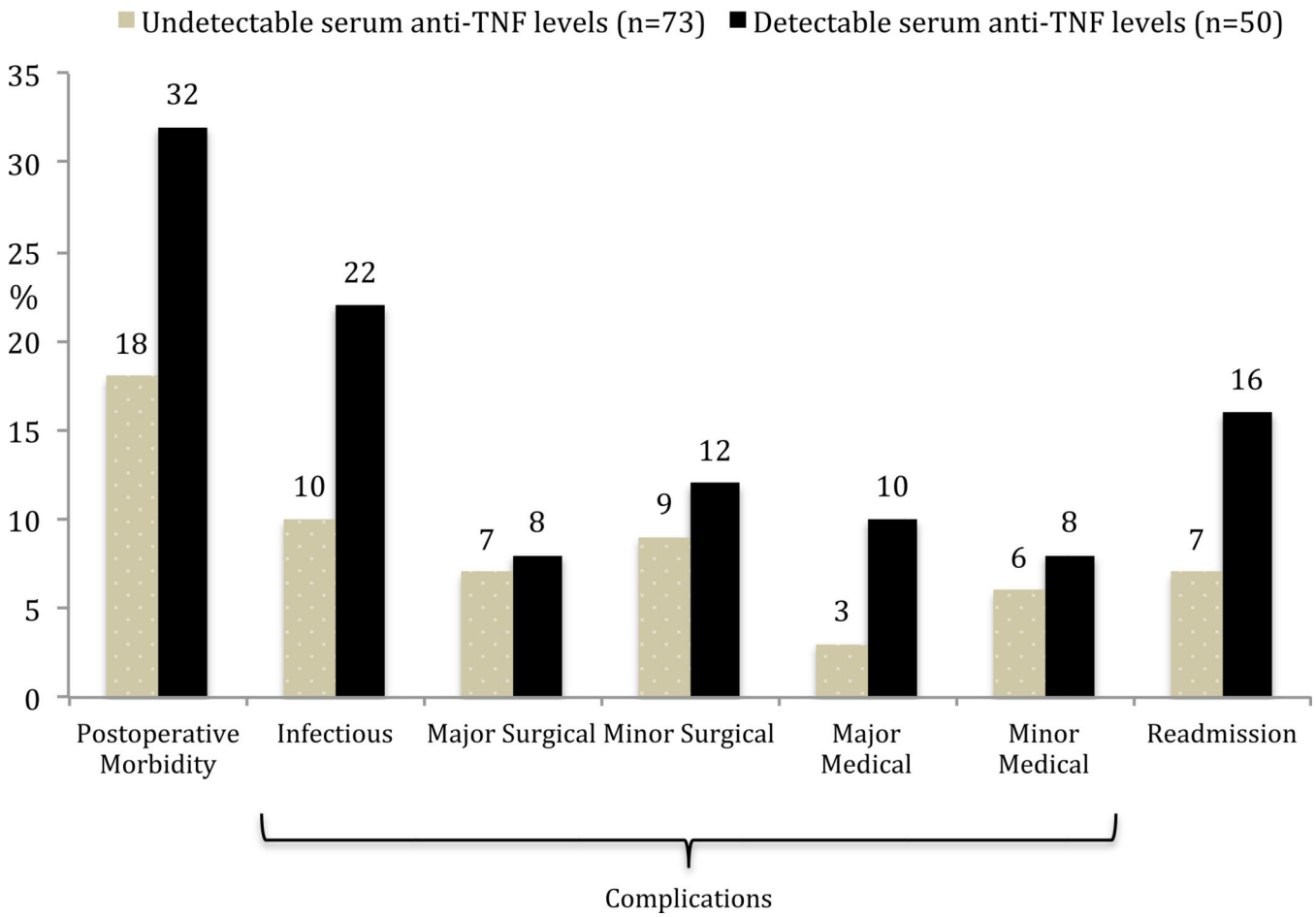

Figure 3.
Postoperative outcomes and serum anti-TNFα drug levels in Crohn's disease patients (all p=NS).

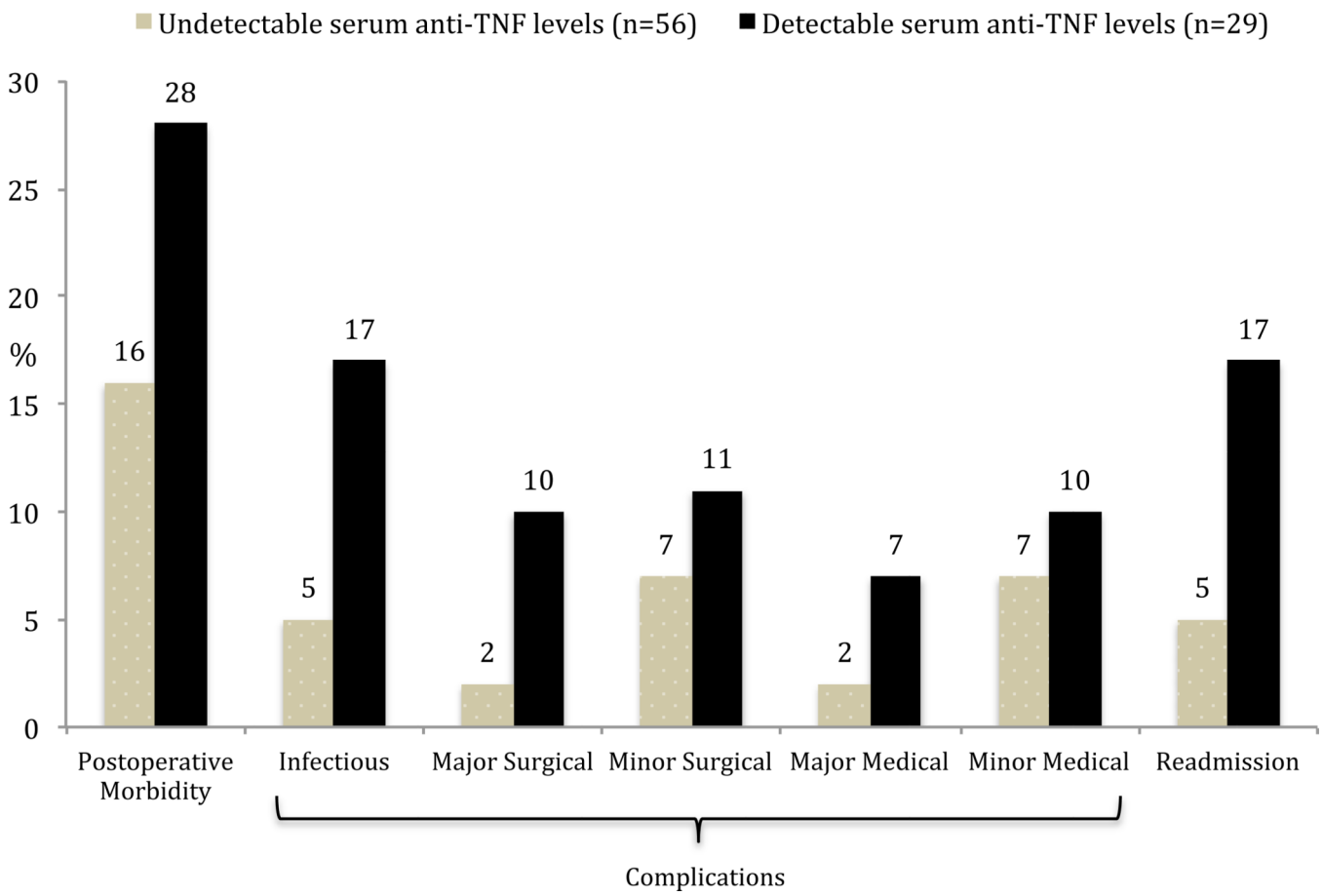

Figure 4.

Postoperative outcomes and serum anti-TNFα drug levels in Crohn's disease patients undergoing small bowel/ileocolic resection (all p=NS)

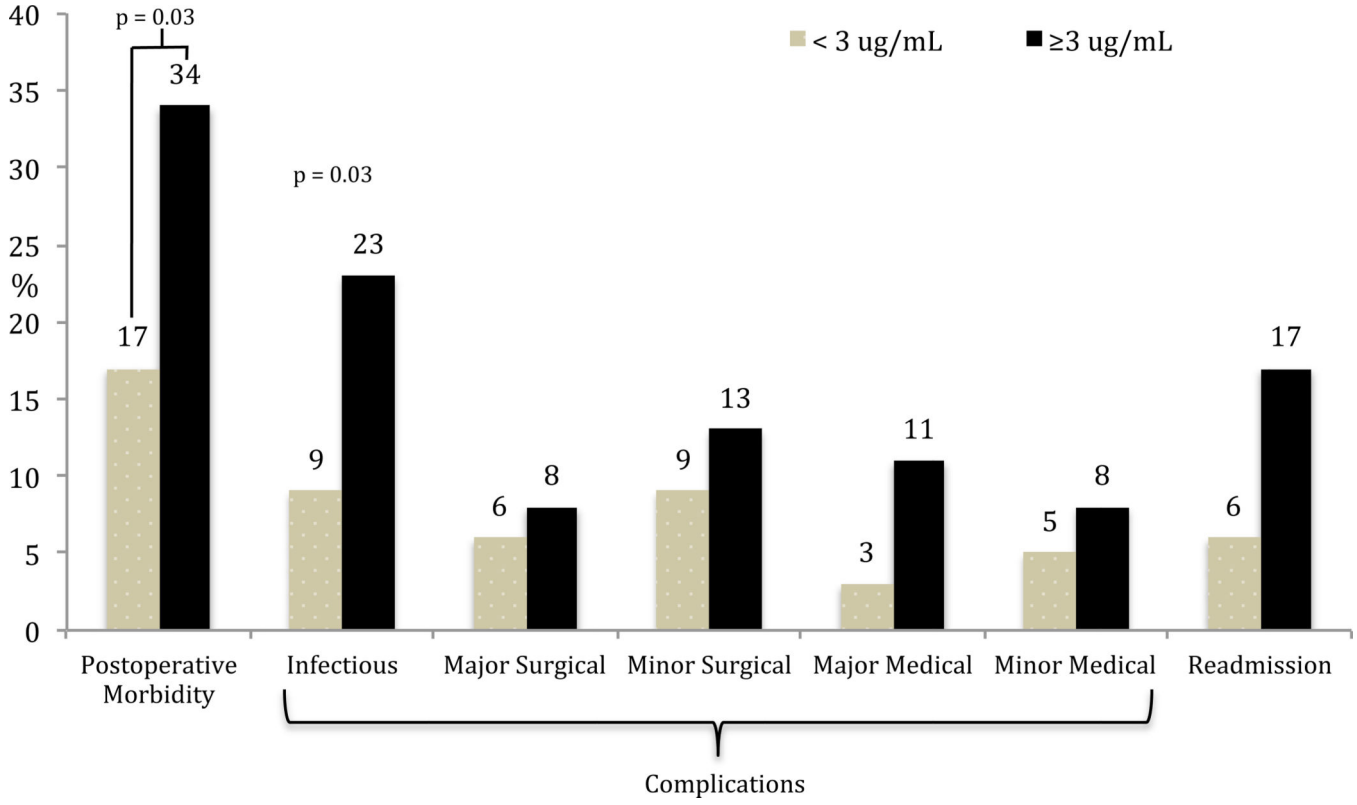

Figure 5.

Postoperative outcomes in Crohn's disease and serum anti-TNFα drug level cut off value at 3 μg/ml. There was a proportionately higher rate of overall postoperative morbidity and infectious complications in the ≥ 3 μg/ml serum anti-TNFα drug level group compared to the < 3 μg/ml serum anti-TNFα drug level group.

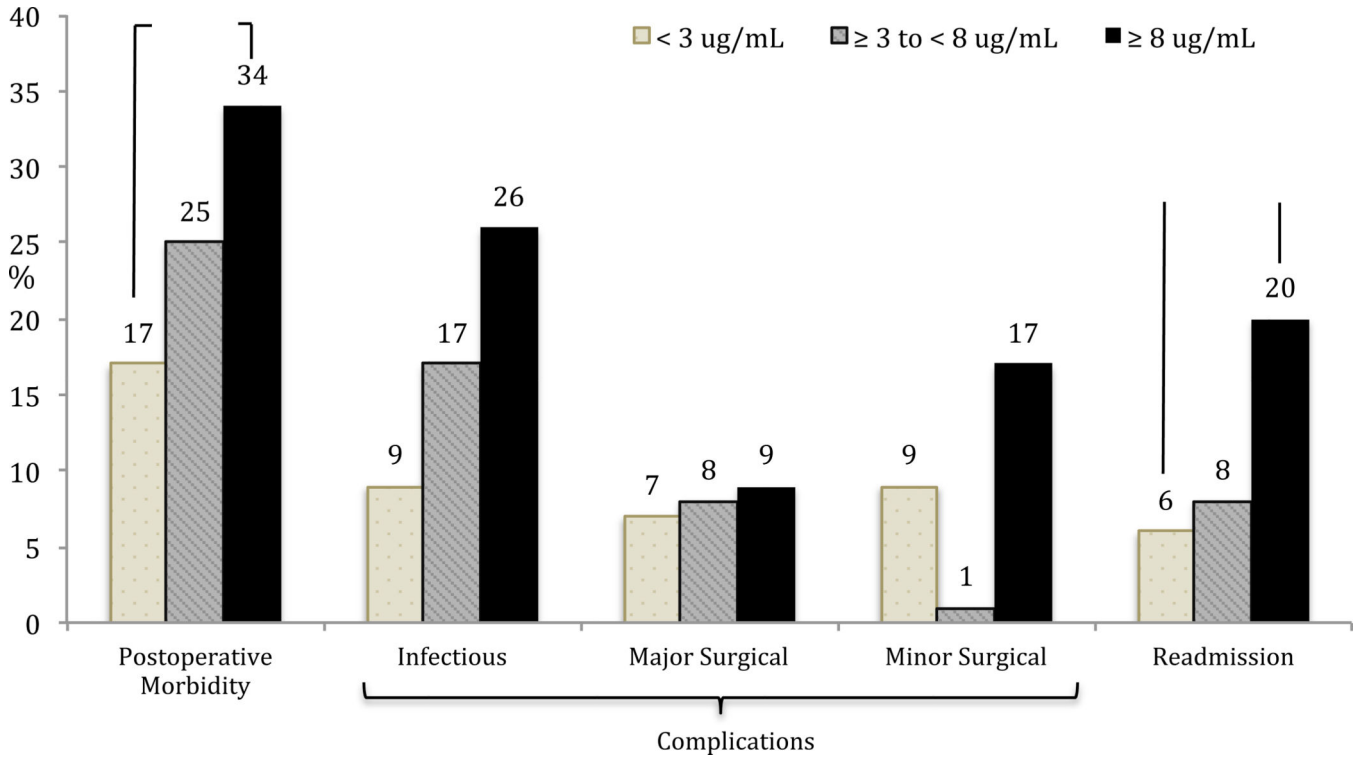

Figure 6.

Postoperative outcomes in Crohn's disease patients with increasing serum anti-TNFα drug levels. There was a proportionately higher rate of overall postoperative morbidity and readmissions in the ≥ 8 μg/ml serum anti-TNFα drug level group compared to the < 3 μg/ml serum anti-TNFα drug level group.

Table 1

Study Cohort Clinical Characteristics and Serum anti-TNFα Drug Levels

	Study Cohort (n=217)	Undetectable Level (n=150)	Detectable Level (n=67)	p
Mean Age (years)	36.9 (15.5)	36.6 (15)	37.4 (16.7)	0.74
Gender (M : F)	127 : 90	82 : 68	45 : 22	0.09
Active Smoker at Time of Surgery	12 (6)	8 (5)	4 (6)	0.85
Type of IBD				
Crohn's disease	123 (57)	73 (49)	50 (75)	0.0005
Ulcerative colitis	94 (43)	77 (51)	17 (25)	
Preoperative Steroids	116 (53)	69 (46)	47 (70)	0.001
Preoperative Immunomodulators	201 (93)	137 (91)	64 (95)	0.28
6-mercaptopurine	138 (64)	91 (61)	47 (70)	0.18
Azathioprine	15 (7)	13 (9)	2 (3)	0.15
Methotrexate	22 (10)	13 (9)	9 (13)	0.29
Cyclosporine	26 (12)	20 (13)	6 (9)	0.36
Preoperative anti-TNFα Agent	143 (66)	76 (51)	67 (100)	0.006
Infliximab	79 (36)	43 (29)	36 (54)	0.0005
Adalimumab	18 (8)	9 (6)	9 (13)	0.07
Certolizumab	5 (2)	3 (2)	2 (3)	0.66
Multiple	41 (19)	21 (14)	20 (30)	0.007
Indication for Surgery				
Medical intractability	189 (87)	130 (87)	59 (88)	0.78
Intra-abdominal abscess at surgery	15 (7)	8 (5)	7 (10)	0.18
Dysplasia/cancer	13 (6)	12 (8)	1 (1)	0.10
Mean Preoperative Lab Values				
Hemoglobin (g/dl)	11.93 (1.92)	11.83 (1.92)	12.12 (1.93)	0.36
Serum albumin (g/dl)	3.81 (0.65)	3.78 (0.64)	3.86 (0.67)	0.51
C-reactive protein (mg/dl)	2.27 (3.41)	2.23 (3.49)	2.35 (3.29)	0.84
Surgical Procedures				
Small bowel / ileocolic resection	108 (50)	65 (43)	43 (64)	0.005
Ileal pouch-anal anastomosis	52 (23)	45 (30)	7 (10)	0.003
Subtotal colectomy and ileostomy	43 (20)	32 (21)	11 (16)	0.40
Low colorectal anastomosis	10 (5)	4 (3)	6 (9)	0.06
Closure of ileostomy / colostomy	2 (1)	2 (1)	0	0.60
Total proctocolectomy/ ileostomy	2 (1)	2 (1)	0	0.60
Pelvic Anastomosis Created	62 (29)	49 (33)	13 (19)	0.048

All values in parentheses denote % except age and preoperative lab values (standard deviation) IBD inflammatory bowel disease

Table 2

Clinical Characteristics of Different Detectable Serum anti-TNFα Drug Levels

	Low Level (n=6)	Medium Level (n=17)	High Level (n= 44)	p
Mean Age (years)	32.2 (19.2)	40.1 (17.1)	37.1 (16.3)	0.60
Gender M:F	3 : 3	13 : 4	29 : 15	0.46
Type of IBD				
Crohn's disease	3 (50)	12 (71)	35 (79)	0.23
Ulcerative colitis	3 (50)	5 (29)	9 (21)	
Preoperative Steroids	3 (50)	12 (70)	32 (73)	0.58
Preoperative Immunomodulators				
6-mercaptopurine	5 (83)	9 (53)	33 (75)	0.23
Azathioprine	0	1 (6)	1 (2)	0.57
Methotrexate	1 (17)	1 (6)	7 (16)	0.53
Cyclosporine	2 (33)	1 (6)	3 (7)	0.12
Preoperative anti-TNFα Agent				
Infliximab alone	5 (83)	10 (59)	21 (48)	0.27
Adalimumab alone	1 (17)	5 (29)	3 (7)	0.06
Certolizumab alone	0	1 (6)	1 (2)	0.57
Multiple	0	1 (6)	19 (43)	0.003
Mean Preoperative Lab Values				
Hemoglobin (g/dl)	10.7 (0.97)	10.9 (1.98)	12.7 (1.75)	0.004
Serum albumin (g/dl)	3.6 (0.34)	3.42 (0.73)	4.0 (0.62)	0.03
C-reactive protein (mg/dl)	5.72 (2.03)	2.94 (4.03)	1.76 (2.91)	0.05
Indication for Surgery				
Medical intractability	6 (100)	15 (88)	38 (86)	1.0
Abscess at time of surgery	0	1 (6)	6 (14)	0.83
Dysplasia/cancer	0	1 (6)	0	0.34
Surgical Procedures				
Small bowel/ ileocolic resection	3 (50)	12 (71)	30 (68)	0.62
Ileal pouch-anal anastomosis	2 (33)	2 (12)	3 (7)	0.10
Subtotal colectomy and ileostomy	1 (17)	4 (24)	6 (14)	0.67
Low colorectal anastomosis	0	1 (6)	5 (11)	1.0
Closure of ileostomy/colostomy	0	0	0	-
Total proctocolectomy/ileostomy	0	0	0	-
Pelvic Anastomosis Created	2 (33)	3 (18)	8 (18)	0.71

All values in parentheses denote % except age and preoperative lab values (standard deviation)

IBD inflammatory bowel disease

Table 3

UC Patient Cohort Clinical Characteristics and Serum anti-TNFα Drug Levels

	UC Cohort (n = 94)	Undetectable Level (n = 77)	Detectable Level (n =17)	p
Mean Age (years)	38.4 (15.9)	37.2 (14.38)	43.8 (21.52)	0.12
Gender M: F	45 : 49	34 : 43	11 : 6	0.59
Indication for Surgery				
Medical Intractability	81 (86)	67 (87)	14 (82)	0.13
Dysplasia/Cancer	13 (14)	10 (13)	3 (18)	
Type of Surgery				
3-Stage (STC as index operation)	42 (45)	32 (41)	10 (59)	0.20
2-Stage (IPAA as index operation)	52 (55)	45 (59)	7 (41)	
Mean Preoperative lab values				
Hemoglobin (g/dl)	11.6 (1.7)	11.6 (1.8)	11.6 (1.6)	0.90
Serum albumin (g/dl)	3.7 (0.7)	3.7 (0.7)	3.5 (0.7)	0.75
C-reactive protein (mg/dl)	2.0 (3.9)	2.2 (4.2)	1.0 (2.4)	0.42
Preoperative Steroids	17 (18)	13 (17)	4 (24)	0.50
Preoperative Immunomodulators				
6-mercaptopurine	31 (33)	27 (35)	4 (23)	0.41
Azathiopurine	3 (3)	3 (4)	0	1.00
Methotrexate	6(6)	6 (8)	0	0.59
Cyclosporine	25 (26)	19 (25)	6 (35)	0.38
Preoperative anti-TNFα agent	60 (64)	43 (56)	17 (100)	0.02

All values in parentheses denote % except preoperative lab values (standard deviation)

UC ulcerative colitis; STC subtotal colectomy; IPAA ileal pouch-anal anastomosis

Table 4

CD Patient Cohort Clinical Characteristics and Serum anti-TNFα Drug Levels

	CD Cohort (n = 123)	Undetectable Level (n = 73)	Detectable Level (n = 50)	P
Disease Behavior				
Stricturing	62 (50)	37 (51)	25 (50)	0.94
Penetrating	24 (19)	15 (20)	9 (18)	0.72
Both	25 (20)	12 (16)	13 (26)	0.20
Non-stricturing/penetrating	12 (10)	9 (12)	3 (6)	0.25
Intra-abdominal Abscess	15 (12)	8 (11)	7 (14)	0.47
Small Bowel/ileocolic Resection	85 (69)	56 (77)	29 (58)	0.02
Mean Preoperative Lab Values				
Hemoglobin (g/dl)	12.2 (2.0)	12.1 (2.0)	12.3 (2.0)	0.66
Serum albumin (g/dl)	3.9 (0.61)	3.9 (0.56)	3.9 (0.67)	0.84
C-reactive protein (mg/dl)	2.45(3.11)	2.26 (2.84)	2.67 (3.42)	0.53
Preoperative Steroids	99 (80)	56 (77)	43 (86)	0.21
Preoperative Immunomodulators				
6-mercaptopurine	75 (61)	41 (56)	34 (68)	0.24
Azathiopurine	12 (10)	10 (14)	2 (4)	0.09
Methotrexate	16 (13)	7 (10)	9 (18)	0.18
Cyclosporine	1 (1)	1 (1)	0	0.65
Preoperative anti-TNFα Agent	83 (67)	33 (45)	50 (100)	0.0008

All values in parentheses denote % except preoperative lab values (standard deviation)

Table 5

Postoperative Outcomes and Serum anti-TNFα Drug Levels in Study Cohort

	Study Cohort (n=217)	Undetectable Level (n=150)	Detectable Level (n=67)	Low Level (n=6)	Medium Level (n=17)	High Level (n=44)
Postoperative morbidity	68 (31)	44 (29)	24 (36)	1 (17)	7 (41)	16 (36)
Medical complications	26 (12)	14 (9)	12 (18)	1 (17)	5 (29)	6 (14)
Major	11 (5)	5 (3)	6 (9)	0	4 (24)	2 (4)
Minor	15 (7)	9 (6)	6 (9)	1 (17)	1 (6)	4 (9)
Surgical complications	51 (24)	36 (24)	15 (22)	0	3 (18)	12 (27)
Major	19 (9)	13 (9)	6 (9)	0	2 (12)	4 (9)
Minor	32 (15)	23 (15)	9 (13)	0	1 (6)	8 (18)
Infectious complications	30 (14)	17 (11)	13 (19)	1 (17)	3 (18)	9 (20)
Postoperative mortality	1 (1)	0	1 (1)	0	1 (6)	0
Mean postoperative LOS (d)	5.6 (2.5)	5.8 (2.6)	5.2 (2.2)	5.3 (1.4)	4.7 (1.9)	5.4 (2.4)
Readmission within 30 days	32 (15)	20 (13)	12 (18)	0	3 (18)	9 (20)

All values in parentheses denote % except postoperative length of stay (standard deviation)

LOS length of stay

All p=

Table 6

Postoperative Outcomes and Serum anti-TNFα Drug Levels in UC Cohort

	UC Cohort (n=94)	Undetectable Level (n=77)	Detectable Level (n=17)	P
Postoperative morbidity	39 (41)	31 (40)	8 (47)	0.61
Medical complications	11 (12)	8 (10)	3 (18)	0.41
Major	4 (4)	3 (4)	1 (6)	0.72
Minor	7 (7)	5 (6)	2 (12)	0.46
Surgical complications	29 (31)	24 (31)	5 (29)	1.00
Major	10 (11)	8 (10)	2 (12)	0.87
Minor	19 (20)	16 (21)	3 (18)	0.77
Infectious complications	12 (13)	10 (13)	2 (12)	0.89
Mean postoperative LOS (d)	6.3 (2.1)	6.3 (2.1)	6.0 (2.3)	0.54
Readmission within 30 days	19 (20)	15 (19)	4 (23)	0.71

All values in parentheses denote % except postoperative length of stay (standard deviation)

LOS length of stay

Table 7

Model Analysis of Postoperative Outcomes in Crohn's Disease Patients using Multivariate Logistic Regression and Serum anti-TNFα Drug Level Cut-off Value of 3 μg /ml

	Variable	Odds Ratio	95% Confidence Interval	P value
Overall Postoperative Morbidity				
1.	Serum anti-TNFα drug level ≥ 3 μg/ml	2.41	1.03 – 5.68	0.04
	Steroids alone	1.47	0.45 – 4.82	0.53
2.	Serum anti-TNFα drug level ≥ 3 μg/ml	2.52	1.07 – 5.92	0.03
	6-Mercaptopurine alone	0.95	0.39 – 2.29	0.91
3.	Serum anti-TNFα drug level ≥ 3 μg/ml	2.45	1.04 – 5.78	0.04
	Azathioprine alone	0.78	0.16 – 3.91	0.76
4.	Serum anti-TNFα drug level ≥ 3 μg/ml	1.91	0.66 – 5.51	0.23
	Albumin alone	0.42	0.18 – 0.99	0.05
Infectious Complications				
1.	Serum anti-TNFα drug level ≥ 3 μg/ml	2.86	1.01 – 8.08	0.04
	Steroids alone	1.79	0.37 – 8.6	0.46
2.	Serum anti-TNFα drug level ≥ 3 μg/ml	3.34	1.16 – 9.57	0.02
	6-Mercaptopurine alone	0.5	0.17 – 1.41	0.19
3.	Serum anti-TNFα drug level ≥ 3 μg/ml	2.92	1.03 – 8.26	0.04
	Azathioprine alone	0.66	0.08 – 5.71	0.71
4.	Serum anti-TNFα drug level ≥ 3 μg/ml	3.03	0.82 – 11.21	0.09
	Albumin alone	0.63	0.24 – 1.65	0.35