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Preoperative anemia and outcomes in patients undergoing surgery for inflammatory bowel disease

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ABSTRACT

Background: Anemia is the most common extraintestinal manifestation in patients with inflammatory bowel disease (IBD), and has been linked to severity of the disease. The aim of the study was to assess the impact of anemia on postoperative outcomes in patients with IBD.

Methods: We retrospectively reviewed patients with IBD from the NSQIP database over an 8-year period. Patients were grouped based on the presence of anemia. The impact of anemia on postoperative morbidity, mortality and length of stay was assessed.

Results: A total of 15,761 patients met our criteria. Half of the patients were anemic upon presentation. Anemic patients were more likely to have a history of steroid use, present with sepsis and require an emergency operation. In multivariate analysis, anemia was a significant predictor of overall morbidity, serious morbidity and increased length of stay.

Conclusions: Anemic patients with IBD present more often with sepsis and require emergency surgery compared to their peers. In addition, anemia serves as an independent predictor of overall complications, serious morbidity and increased length of stay following abdominal operations.

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1. Introduction

Inflammatory bowel disease (IBD), including both ulcerative colitis (UC) and Crohn's Disease (CD) is characterized by a chronic inflammatory state with frequent relapses or progression of disease, often requiring aggressive medical therapy or surgical intervention. Since the introduction of immunomodulators and biologic agents, as well as specialized care by gastroenterologists, the need for surgical intervention has dropped significantly over the last decade.[1,2] Estimated colectomy rates for UC over a 10-year period range between 3 and 17% worldwide, whereas the overall cumulative risk of surgical intervention in CD patients over the same period approaches 30%.[2,3]

IBD has several extraintestinal manifestations, of which anemia is one of the most commonly described. It has been estimated that about half of IBD patients will become anemic over a five year period,[4] resulting in a significant impact on their quality of life.[5] Anemia has been studied as potential biomarker of disease activity in IBD, and recent studies support its association with increased severity of disease and the earlier need for surgical intervention.[6,7] To date, no studies have investigated the effect of anemia on IBD patients requiring a surgical intervention.

The purpose of this study was to investigate the impact of anemia on postoperative outcomes in IBD patients, by using the National Surgical Quality Improvement Program (NSQIP) database.

2. Methods

Using the 2005–2012 NSQIP public user file (puf), we identified all patients with IBD who underwent a surgical intervention, using the following International Statistical Classification of Diseases and Related Health Problems (ICD-9) codes: 555.0–555.2, 555.9, 556.0–556.9. Patients were grouped based on presence of anemia, as defined by the World Health Organization (WHO) as a hemoglobin less than 13 g/dl in men and less than 12 g/dL in women.[8]

Patient demographics and preoperative characteristics, including age, gender, body mass index (BMI), American society of anesthesiologists (ASA) class, smoking history, presence of malnutrition, defined as albumin less than 3, history of weight loss (>10% of weight loss over the last 6 months) and regular systemic steroid or immunosuppressant use within 30 days of initial operative procedure were compared between the two study groups.

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Recent transfusion was defined as a transfusion of ≥1 Unit up to 72 h preoperatively. Patients with a BMI less than 18.5 were considered underweight as defined by the WHO classification.

The most frequently procedures based on current procedural terminology (CPT) codes were collected for CD and UC patients. Postoperative outcomes, including length of stay, 30 day overall and serious morbidity, and mortality were collected. Any length of stay over the 75th percentile was considered prolonged. Complications were grouped into the following categories based on the system involved: wound, cardiovascular, pulmonary and renal complications. Serious morbidity was defined as per Ingraham et al.[9] as having documentation of at least one of the following ACS-NSQIP complications: organ space SSI, wound dehiscence, neurologic event (cerebrovascular accident or coma lasting >24 h), cardiac arrest, myocardial infarction, pulmonary embolism, ventilator dependence >48 h, progressive or acute renal insufficiency, and sepsis or septic shock. Readmissions and reoperations within 30 days were collected and compared between the two study groups.

Univariate analysis using *t*-test and chi-square compared continuous and categorical outcomes respectively. Multivariate analysis was used to identify risk factors contributing to postoperative morbidity and mortality. Statistical analysis was performed using Intercooled Stata, version 13.1 (StataCorp, College Station, TX).

3. Results

A total of 15,761 patients were included, 50.3% (n = 7934) of which were male, with a mean age of 43 (43.3 ± 15.8). The majority (n = 8,545, 54.2%) was diagnosed with CD. Anemia was present in half of the study population (n = 7,847, 49.8%) and equally distributed between patients with CD and UC. Anemic patients were more likely to present with malnutrition (35.3% vs. 5.6%, p < 0.001), recent weight loss (14.1% vs. 4.9%, p < 0.001), be underweight (10.7% vs. 5.1%, p < 0.001) and have recent steroid or immunosuppressant use (44% vs. 36.9%, p < 0.001). Recent blood transfusions and presence of bleeding disorder were also more frequently observed in anemic patients. In addition, they were more likely to present with preoperative sepsis (13.6% vs. 4.9%, p < 0.01), ASA class ≥3 (42.3% vs. 27.7%) and require an emergent operation (9.7% vs. 4.3%, p < 0.001) (Table 1).

The most frequently performed procedures were partial colectomy with removal of terminal ileum (CPT = 44,160, n = 1,724, 20.2%) and laparoscopic total abdominal colectomy with ileal pouch-anal anastomosis and loop ileostomy (CPT = 44,211, n = 886, 12.3%), in patients with CD and UC respectively (Table 2). Interestingly, anemia rates in UC patients with pancolitis (ICD-9: 556.6) were not higher compared to the remaining study population (51.4% vs. 49.6%, P = 0.18).

Table 3 describes the postoperative outcomes between anemic and non-anemic patients using univariate analysis. Overall, anemic patients were more likely to experience postoperative complications (33.2% vs. 22.9%, P < 0.001) and prolonged hospital stay (35.4% vs. 15.1%, P < 0.001). Wound related complications accounted for the majority of postoperative morbidity (17.3% vs. 15.3%, P < 0.001). Anemic patients were about five times more likely to receive a transfusion postoperatively (11.3% vs. 2.5%, P < 0.001). In addition, mortality rates were significantly higher in anemic patients (1.6% vs. 0.5%, P < 0.001). A significant percentage of both study groups was readmitted (17.4% vs. 15.6%, P = 0.17).

In multivariate analysis, after adjusting for the following variables: malnutrition, steroid use, smoking, diabetes, CD, preoperative sepsis and emergency surgery, preoperative anemia was associated with increased risk for overall and serious morbidity, increased length of stay as well as reoperation. No significant impact on mortality was observed (Table 4).

4. Discussion

To our knowledge, this is the first study to report anemia rates in IBD patients requiring surgical intervention. In addition, we found that anemic IBD patients were more likely to develop postoperative complications, stay in the hospital longer and require reoperation compared to their non-anemic peers.

Anemia is considered the most common extra-intestinal manifestation of IBD, with reported incidence rates ranging between from 6 to 74%, and higher rates observed in hospitalized patients.[10–12] Our study reported anemia rates of fifty percent,

Table 1
Patient demographics and preoperative characteristics between anemic and non-anemic patients.

	Anemic (n = 7847)	Non-Anemic (n = 7914)	P value
Age (mean ± SD)	43.3 ± 16.7	43.3 ± 15.0	0.79
Male gender	51.6	49.1	0.002
BMI (mean ± SD)	24.8 ± 6.1	26.4 ± 6.1	<0.001
Underweight	10.7	5.1	<0.001
ASA class ≥ 3	42.2	27.6	<0.001
Functional status			
Independent	94.3	98.5	<0.001
Partially dependent	4.0	1.1	
Totally dependent	1.7	0.4	
Smoking	16.6	20.2	<0.001
Steroid use	44.0	36.9	<0.001
Weight loss	14.1	4.9	<0.001
Malnutrition	35.2	5.6	<0.001
Bleeding disorder	4.8	2.1	<0.001
Recent transfusion	2.9	0.2	<0.001
Platelet count (mean ± SD)	349.1	303.4	<0.001
Hypertension	19.1	18.8	0.67
CHF	0.5	0.08	<0.001
Diabetes	7.1	4.8	<0.001
Dialysis	0.5	0.09	<0.001
Emergency surgery	9.7	4.3	<0.001
Preoperative sepsis	13.6	4.9	<0.001
Crohn's	54.1	54.4	0.69
Ulcerative Colitis	45.9	45.6	

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Table 2
Distribution of the most frequently procedures in patients with Crohn's and Ulcerative Colitis.

Description (CPT)	N (%)
Crohn's Disease	
Colectomy with removal of terminal ileum (44,160)	1724 (20.2)
Laparoscopic colectomy with removal of terminal ileum (44,205)	1279 (15.0)
Partial colectomy with anastomosis (44,140)	755 (8.8)
Small bowel resection (44,120)	672 (7.8)
Laparoscopic partial colectomy with anastomosis (44,204)	514 (6.0)
Total	4944 (57.8)
Ulcerative Colitis	
Laparoscopic total abdominal colectomy with proctectomy, ileoanal anastomosis and loop ileostomy (44,211)	866 (12.3)
Laparoscopic total abdominal colectomy (44,210)	760 (10.5)
Total abdominal colectomy (44,150)	738 (10.2)
Total abdominal colectomy with ileal reservoir creation (44,158)	677 (9.3)
Partial proctectomy with ileal reservoir creation (45,113)	618 (8.6)
Total	3659 (50.9)

Table 3
Postoperative outcomes in anemic and non-anemic patients.

Variable	Anemic (n = 7, 847)	Non-anemic (n = 7914)	P value
Overall morbidity	33.2	22.9	<0.001
Serious morbidity	16.6	10.9	<0.001
Mortality	1.6	0.5	<0.001
Mean LOS, days (mean ± SD)	11.3 ± 0.1	7.3 ± 0.1	<0.001
Increased LOS	35.4	15.1	<0.001
Blood transfusion	11.3	2.5	<0.001
Pulmonary complications	6.0	2.8	<0.001
Cardiovascular complication	0.8	0.3	<0.001
Wound complication	17.3	15.3	<0.001
Renal complication	1.4	0.9	0.002
Postoperative sepsis	7.6	5.2	<0.001
Postoperative septic shock	2.1	1.1	<0.001
Re-operation	8.4	5.5	<0.001
Re-admission	17.4	15.6	0.17

Table 4
Adjusted postoperative outcomes in anemic versus non-anemic patients.

Outcome measure	Anemic vs. Non-anemic OR (95% CI)	P value
Overall morbidity	1.3 (1.2–1.4)	<0.001
Serious morbidity	1.2 (1.1–1.3)	0.002
Prolonged length of stay	1.8 (1.7–2.0)	<0.001
Reoperation	1.4 (1.1–1.9)	0.02
Mortality	1.3 (0.9–2.0)	0.84

Adjusted for the following: malnutrition, steroid use, smoking, diabetes, Crohn's Disease, preoperative sepsis, emergency surgery.

equally distributed between CD and UC patients, in contrary to recent studies that link CD with higher rates of anemia.[4,10] Similar five year prevalence rates have been described by a recent US study.[4] Lower rates have been published by European countries, with anemia approaching 27% and 21% in CD and UC patients respectively.[10] However, these studies included all IBD patients, recognizing that patients with active disease and those requiring IBD specific medication were at higher risk of developing anemia. Interestingly, only 40% of our patient population was on steroid or immunosuppressant medication by the time of surgery, and no significant differences in the use of immunosuppressant medications were observed between and anemic and non-anemic patients.

In our study, anemic patients were more likely to be malnourished, present with a higher ASA classification, preoperative sepsis and require emergency surgery compared to their peers. Several studies have linked anemia to active and complicated disease, worse quality of life and earlier need for surgical intervention, compared to their non-anemic peers.[4,6,7,10,13] Rieder et al. linked low Hemoglobin levels in Crohn's patients to progression to complicated disease or need for surgical intervention and recommended anemia to be used as a clinical marker of disease activity.[7] Similarly, Koutroubakis et al. found that persistent anemia is associated with higher disease activity, more frequent hospitalizations, lower quality of life and increased need for surgical intervention.[6]

Despite the presence of these significant implications, anemia still remains underestimated and untreated in IBD patients.[14] Therefore, efforts have been made to better characterize anemia and develop guidelines that target its prevention and treatment.[11,15–17] Anemia in IBD patients involves several pathophysiologic mechanisms. Although ongoing blood loss from chronically inflamed intestinal mucosa and micronutrient deficiency (iron and B12) are the main mechanisms underlying the development of anemia, chronic inflammation, hemolysis, and medication-induced myelosuppression may also play important roles in both the development of anemia and the management of this condition. IBD associated anemia is usually a result of a combination of iron deficiency and anemia of chronic disease. Current recommendations include intravenous iron supplementation in IBD patients with iron deficiency, given its superior efficacy, safety profile and less adverse events compared to oral supplementation.[11,18] In addition, Gisbert et al. found a positive correlation of correction of iron deficiency anemia with improved quality in life in IBD population.[19] Similarly, a more recent study reported improved quality of life and IBD symptoms in iron deficient patients that achieved a more than 20 g/l hemoglobin increase from baseline to 6 months.[14,20] Anemia of chronic disease is strongly correlated to active disease, since inflammatory mediators may alter iron metabolism (by retaining iron in the reticular-endothelial system), erythropoiesis, and erythrocyte survival.[11] Koutroubakis et al. assessed the use of *anti*-TNF agents on the prevalence of anemia.[21] There was only a partial therapeutic effect of *anti*-TNF treatment on hemoglobin levels in anemic IBD patients. Interestingly, patients with low inflammatory markers, good quality of life, and those on immunomodulators were more likely to correct their anemia. In contrary, Wells et al. reported improvement in quality of life with correction of anemia that was independent of disease activity.[5] These findings support the multifactorial nature of anemia.

Our anemic study population was more likely to develop postoperative complications and stay in the hospital longer compared to their non-anemic peers, even after controlling for several confounding factors. This can be attributed to underlying disease activity and a chronic inflammatory state that impacts defense mechanisms. A recent NSQIP study found anemia as an independent predictor of venous thromboembolic events after IBD related surgery that could be attributed to presence of thrombocytosis.[22]

Our study had certain limitations. Disease duration and activity markers were not available, such as Harvey–Bradshaw index (HBI) for CD and the ulcerative colitis activity index (UCAI) for UC. Despite the similar steroid use between the study groups, we did not have access to dosage and duration of steroid use, nor prior use and duration of IBD specific therapy, including aminosalicylates, immunomodulator or biologic agents that can affect postoperative complications.[23] In addition, we did not have access to prior use of iron supplementation in these patients.

5. Conclusion

Our study adds some evidence to current literature that anemia

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in IBD patients is a prevalent extraintestinal manifestation that needs to be addressed and appropriately treated. In addition, our study showed that IBD patients with anemia who require a surgical intervention are more likely to have early postoperative complications.

Therefore, anemia could potentially be used as a biomarker of disease activity and predictor of complications following IBD related surgery.

6. Disclosures

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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