Preoperative hypoalbuminemia is associated with an increased risk for intra-abdominal septic complications after primary anastomosis for Crohn’s disease

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Abstract

Objective: The aim of this study was to evaluate the impact of preoperative hypoalbuminemia on the development of intra-abdominal septic complications (IASCs) after primary anastomosis for patients with Crohn’s disease (CD).

Methods: All CD patients undergoing bowel resection with a primary anastomosis during the study period from 2007 to 2015 were enrolled. The association of preoperative hypoalbuminemia (<30 g/L) with the risk for IASCs were assessed using both univariate and multivariate analyses.

Results: A total of 124 eligible patients were included, 117 (94.4%) of whom had available preoperative albumin level. Preoperative hypoalbuminemia occurred in 13 (11.7%) patients. The duration from diagnosis to surgery was longer for patients with preoperative hypoalbuminemia than those without (p = 0.012). Patients with preoperative hypoalbuminemia were more likely to have a history of preoperative use of 5-aminosalicylic acid (p = 0.013) and have an intraoperative finding of small bowel obstruction (p = 0.015). Of all patients, 24 (19.4%) developed postoperative IASCs. Univariate analysis showed that patients with preoperative hypoalbuminemia had an increased risk for IASCs (p = 0.012). Multivariate analysis confirmed the association between preoperative hypoalbuminemia and IASCs (odds ratio 4.67, 95% confidence interval: 1.28–17.04, p = 0.02). Similar findings were also obtained when preoperative albumin level was analysed as a continuous variable (p = 0.019).

Conclusions: Preoperative hypoalbuminemia is a significant predictor for the development of postoperative IASCs in CD patients after bowel resection with a primary anastomosis. Favorable preoperative nutrition status might lessen the risk for IASCs.

Key words: Crohn’s disease; hypoalbuminemia; intra-abdominal septic complications; risk factor
Introduction
Crohn’s disease (CD) is a chronic inflammatory gastrointestinal (GI) disorder of unclear etiology. Despite increased use of immunosuppressant and anti-tumor necrosis factor (TNF) treatments, approximately 70% of the CD patients will eventually require surgery [1,2]. In patients with CD, postoperative complications, such as wound infection and intra-abdominal septic complications (IASCs), have been reported to occur more frequently than those with other disorders—a phenomena partly due to the inflammatory nature of CD and malnutrition [3]. Malnutrition is a common substantial problem of CD [4], which is considered to be an end product of complex pathophysiological processes, including decreased food intake due to postprandial pain, diarrhea, anorexia, malabsorption, previous gut resection or bypass, drug side effects and active inflammation [5-7].

IASCs not only significantly elongate hospitalization time, but also increase the postoperative relapse rate and decrease patients’ quality of life [8]. Since postoperative IASCs are often difficult to be treated, it is of great importance to evaluate the associated predictors to monitor patients who are at risk [1,8-10]. Several studies have reported possible risk factors, including preoperative corticosteroid therapy, an abscess or fistula at the time of laparotomy, poor nutritional status, low albumin levels, advanced age, operating time, immune-modulating medications, hand-sewn anastomosis and so on [2,8,9,11-15].

Serum albumin is an objective marker of nutritional status and index reflecting inflammation and immune status, while it is also plays an important role in wound healing and collagen synthesis [16-19]. The serum albumin measurement is convenient and inexpensive [20], which makes it a potential candidate for practical predictive index. Although several studies have indicated the possible correlation between albumin level and the risk for IASCs, data from Asian population is scare and controversial [11,21,22]. Therefore, we designed this study, aiming to evaluate the impact of preoperative hypoalbuminemia on the development of IASCs after primary anastomosis for CD.

Patients and methods

Patients
All CD patients undergoing bowel resection with a primary anastomosis at the Sixth Affiliated Hospital of Sun Yat-sen University (Guangzhou, China) from 2007 to October 2015 were included in this study. Demographics, clinicopathological variables and outcomes were all prospectively recorded. Both paper charts and electronic medical records were carefully reviewed when necessary. This study was approved by the Institutional Review Board (IRB) of The Sixth Affiliated Hospital of Sun Yat-sen University.

Inclusion and exclusion criteria
In order to be included in the study, patients needed to meet all the following inclusion criteria: (i) CD patients; (ii) underwent bowel resection with a primary anastomosis at our institution; (iii) had a minimal follow-up period of 30 days following bowel resection. The exclusion criteria were patients who: (i) underwent bowel resection for other underlying diseases; (ii) underwent stoma creation without bowel resection (iii) were lost in follow-up.

Patient groups
Patient’s serum albumin level recorded in this study was the last routine test within 1 week before surgery. Hypoalbuminemia was defined as serum albumin level <30 g/L [9,10]. Based on whether the patients had preoperative hypoalbuminemia, the cohort was divided into two groups: patients with hypoalbuminemia (the study group) and those without (the control group).

Definition and variables

Demographic and clinicopathological variables were defined as follows: ‘Duration from diagnosis to surgery’—the time interval from the date of CD diagnosis to the date of operation; ‘Current smoking’—consumption of more than seven cigarettes per week for at least 6 months prior to operation; ‘Ex-smoking’—cessation of smoking 6 months prior to the operation; ‘Location of CD’—L1, terminal ileum; L2, colon; L3, ileocolon; L4, upper gastrointestinal tract; ‘Upper gastrointestinal involvement’—the disease occurs in the upper gastrointestinal tract as well; ‘Perianal disease’—inflammation at or near the anus, including tags, fissures, fistulae, abscesses or stenosis; ‘Disease behavior’—B1, no structuring, no penetrating; B2, structuring, B3, penetrating; Extra-intestinal manifestations (EIM)—including the presence of arthralgia or arthropathy, pyoderma, gangrenosum, erythema nodosum, primary sclerosing cholangitis (PSC), CD-related ocular lesions, thromboembolic events; autoimmune disorders-type 1 diabetes, adult-onset asthma, rheumatoid arthritis, autoimmune thyroid diseases (including Grave’s disease and Hashimoto’s thyroiditis), psoriasis, systemic lupus erythematosus, autoimmune hemolytic anemia, vitiligo, celiac disease, pernicious anemia, idiopathic thrombocytopenic purpura and multiple sclerosis; ‘Significant comorbidities’—congestive heart failure, coronary bypass surgery, chronic obstructive pulmonary diseases, renal stone of insufficiency, non-gastrointestinal cancer, stroke and liver failure; ‘Preoperative use of medicines’—the use of any dose of biologics (including infliximab, adalimumab or certolizumab pegol), immunosuppressant, steroids, 5-aminosalicylic acid (5-ASA) or antibiotics within 1 month before the operation; ‘Elevated erythrocyte sedimentation rate’—erythrocyte sedimentation rate more than 20 mm/h; ‘Elevated C-reactive protein (CRP)’—more than 10 mg/L (dry chemical method) or 3 mg/L (hypsersensitive method); ‘Low hemoglobin’—hemoglobin less than 120 g/L in blood routine test; ‘Elevated white blood cell’—white blood cells more than 10 × 10^9/L in blood routine test; ‘Low lymphocytes’—lymphocytes less than 0.8 × 10^9/L in blood routine test; ‘Elevated platelet’—platelet more than 300 × 10^9/L in blood routine test.

Outcome measurement
The primary outcome was occurrence of IASCs, which was defined as anastomotic leaks and/or intra-abdominal abscesses, within 1 month after operation. The diagnosis of IASCs was made based on relaparotomy findings, the presence of infected or fecal material in the percutaneous drainage and/or abdominal images.

Statistical analysis
Descriptive statistics were computed for all variables. These included means and standard deviations (SD) or medians and interquartile ranges (IQR) for continuous factors and frequencies for categorical factors. Comparisons of the distribution of clinicopathological characteristics between the patients with or without preoperative hypoalbuminemia were made by using the two-tail t-test (or Wilcoxon rank sum test as alternative) for continuous variables and chi-square test (or the Fisher exact
Results

Patient demographics

A total of 124 eligible patients were studied, 117 (94.4%) of whom had available preoperative albumin level. Ninety-eight patients (79.0%) were males. The mean ages at the time of diagnosis of CD and at surgery were 31.6 ± 11.9 years and 33.8 ± 12.1 years, respectively, with a median duration from diagnosis to surgery of 0.5 (0.1–2.2) years. Preoperative body mass index (BMI) was 18.0 ± 2.9 kg/m² (Table 1). Based on Montreal Classification by disease location, 28 (22.6%) patients had L1 (ileal) disease or L2 (colonic) disease, and 94 (75.8%) had L3 (ileocolic) disease. Upper gastrointestinal involvement was identified in 5 patients (4.0%) and 33 (26.6%) patients had perianal disease. With respect to disease behavior, 52 patients (41.9%) had B1 (non-stricturing and non-penetrating) disease or B2 (stricturing) disease and 70 (56.5%) patients had B3 (penetrating) disease. Thirty-eight (30.6%) patients had a history of bowel resection and 22 (17.7%) patients had significant comorbidity (Table 1). The indications for surgical treatment in CD patients were: fibrostenotic segment (n = 51, 41.1%), fistula (n = 66, 53.2%), perforation (n = 4, 3.2%), abscess (n = 1, 0.8%), dysplasia or cancer (n = 1, 0.8%) and others (n = 1, 0.8%).

According to the preoperative albumin level, 13 (11.7%) patients were grouped as cases and the remaining 104 (88.9%) were controls. Six patients (46.2%) with preoperative hypoalbuminemia versus 16 patients (15.4%) without preoperative hypoalbuminemia experienced postoperative IASCs (p = 0.016). The duration from diagnosis to surgery was longer for patients with preoperative hypoalbuminemia than those without (t = 0.1 (0–5.0) vs 0.5 (0–2.0), p = 0.012). Patients with preoperative hypoalbuminemia were more likely to have a history of preoperative use of 5-ASA [7 (53.8%) vs 21 (20.2%), p = 0.013] and have an intraoperative finding of small bowel obstruction [10 (76.9%) vs 43 (41.3%), p = 0.015] (Table 1).

Risk factors associated with postoperative IASCs

Univariate analysis showed that postoperative IASCs were significantly associated with preoperative hypoalbuminemia (p = 0.012), intraoperative finding of fistula (p = 0.026), preoperative use of anti-TNF biologics (p = 0.036) and duration from diagnosis to surgery (p = 0.029) (Table 2). No other clinical factor was associated with an increased risk of postoperative IASCs, including patient age, gender, BMI, smoking history, history of any drug allergy, history of bowel resection, significant comorbidities, history of diagnosis of ulcerative colitis (UC) or indeterminate colitis (IC), extra-intestinal manifestation, location of CD, upper GI involvement, perianal disease, disease behavior, preoperative use of immunosuppressants, steroids, 5-ASA or antibiotics, elevated erythrocyte sedimentation rate, low hemoglobin, elevated white blood cell, chronic fistula as the indication for surgery, laparoscopic surgery, type of anastomosis, number of anastomosis and stoma creation.

The factors detected in univariate analysis that associated with the development of postoperative IASCs were then included into a multivariate analysis model, and only preoperative hypoalbuminemia was found to be an independent risk factor for IASCs [odds ratio (OR) 4.67, 95% confidence interval (CI): 1.28–17.04, p = 0.02]. The impact of preoperative hypoalbuminemia was shown to have similar results when preoperative albumin level was analysed as a continuous variable (OR 0.89, 95% CI: 0.82–0.98, p = 0.019) (Table 3).

Discussion

CD is a chronic inflammatory gastrointestinal disorder. Approximately 70% of the CD patients will undergo operations [1,2] and have markedly high rates of postoperative IASCs, probably because of the inflammatory nature and decreased nutritional status [3,22-24]. In the current study, 24 (19.4%) patients experienced IASCs—a frequency that is consistent with the reported rates ranging from 5% to 20% [1,8,9]. In this series of 124 CD patients receiving a primary Anastomosis, a significant association between preoperative hypoalbuminemia and postoperative IASCs was revealed in the univariate analysis. Furthermore, this finding was also confirmed in the multivariate analysis after adjusting for other potential confounding factors.

Hypoalbuminemia is the result of the combined effects of inflammation and malnutrition [16]. Several studies have demonstrated the association between hypoalbuminemia and surgical outcomes. In the study of a total of 54 215 major non-cardiac surgery cases from the National VA Surgical Risk Study, albumin level is found out as a good predictor of surgical outcomes, especially the mortality and morbidity for surgery, sepsis and major infections [25]. The result of a meta-analysis including 90 cohort studies and 9 prospective controlled studies also shows that hypoalbuminemia was an independent risk factor for poor outcome in the acutely diseases [26]. In patients with CD, similar findings have also been reported [9,10,27]. Yamamoto et al retrospectively analyses 343 patients underwent intestinal anastomosis operations and found that an albumin level less than 30 g/L was an independent risk factor for IASCs [9]. However, there are also several studies failed to find out the significant correlation between albumin level and the happening of IASCs [11,21,22]. Therefore, the relationship between albumin level and postoperative IASCs remains controversial and data from Chinese patients with CD are limited. We designed this retrospective study to evaluate this association and found that serum albumin level was an independent predictor for the development of postoperative IASCs.

Albumin, produced by the liver, is an acute phase protein with a half-life of approximately 20 days, subject to alteration by cytokines and proinflammatory mediators in patients with CD [28]. Recent studies have pointed out that the serum albumin measurement is a simple and convenient method for the assessment of the nutritional and immune status in inflammatory bowel disease (IBD) patients [16-19]. According to the previous studies, albumin levels were likely to be normal in the quiescent phase of the disease [29] and significantly lower levels in patients with active disease compared to those in remission [30,31]. In our study, we found that a much higher proportion of CD patients with hypoalbuminemia had a preoperative use of 5-ASA within a month before operation and had an intraoperative finding of small bowel obstruction. Besides, it has been reported that the duration of the disease was relevant as a determinant of the severity of malnutrition in IBD, which is usually longer in CD [32]. In our study, the median duration from diagnosis to surgery was actually consistent with
other studies based on the Chinese mainland [33]. We also found that the CD patients with hypoalbuminemia tended to have a longer duration from diagnosis to surgery, in accordance with the previous study.

Serum albumin is an important material for wound healing and collagen synthesis at the anastomosis site, while hypoproteinemia can give rise to tissue edema and collagen synthesis disorders, resulting in the high risk of anastomotic leakage [34,35]. The serum albumin also has an effect on immune response [36,37]. A study by Slotwinski et al. demonstrates that critically ill patients treated in the intensive care unit (ICU) had significant disturbances in the expression of genes associated with innate antimicrobial immunity, depending on nutritional status, and may have a significant impact on the clinical outcomes [36]. A study retrospectively analysed 324 patients with IBD and found that the presence of low serum albumin were shared common risk factors for a low serum IgG or IgM level [37]. All the studies aforementioned indicate that serum album plays a vital role in tissue repair and immune response.

| Characteristics                                      | All cases (n= 124) | Patients with available albumin level (n=117) | Patients without hypoalbuminemia (n=104) | Patients with hypoalbuminemia (n=13) | p-value |
|-------------------------------------------------------|-------------------|---------------------------------------------|------------------------------------------|-------------------------------------|---------|
| Age at CD diagnosis, years                            | 31.6±11.9         | 31.6±12.1                                   | 31.9±12.4                                | 28.9±9.5                            | 0.4     |
| Age at surgery, years                                 | 33.8±12.1         | 33.7±12.1                                   | 33.9±12.5                                | 31.5±9.2                            | 0.49    |
| Duration from diagnosis to surgery, years             | 0.5 (0–2.2)       | 0.5 (0–2.1)                                 | 0.5 (0–2.0)                              | 1.2 (0–5.0)                         | 0.012   |
| Male gender                                           | 98                | 92                                           | 80 (76.9%)                               | 12 (92.3%)                          | 0.29    |
| Body mass index, kg/m²                                 | 18.0±2.9          | 17.8±2.9                                    | 18.0±2.9                                 | 16.3±2.6                            | 0.078   |
| Ex or current smoker                                   | 4                 | 4                                            | 2 (1.9%)                                 | 2 (15.4%)                           | 0.06    |
| History of any drug allergy                           | 22                | 22                                           | 20 (19.2%)                               | 2 (15.4%)                           | 1.0     |
| History of bowel resection                            | 38                | 35                                           | 30 (28.8%)                               | 5 (38.5%)                           | 0.53    |
| Significant comorbidity                                | 22                | 21                                           | 17 (16.3%)                               | 4 (30.8%)                           | 0.25    |
| History of diagnosis of UC or IC                      | 3                 | 3                                            | 2 (1.9%)                                 | 1 (7.7%)                            | 0.3     |
| Extra-intestinal manifestations                       | 7                 | 7                                            | 6 (5.8%)                                 | 1 (7.7%)                            | 0.57    |
| Location of CD                                        |                   |                                              |                                          |                                    | 0.27^a  |
| L1                                                    | 26                | 25                                           | 23 (22.5%)                               | 2 (15.4%)                           |         |
| L2                                                    | 2                 | 2                                            | 1 (1.0%)                                 | 1 (7.7%)                            |         |
| L3                                                    | 94                | 88                                           | 78 (76.5%)                               | 10 (76.9%)                          |         |
| Upper gastrointestinal involvement                    | 5                 | 4                                            | 4 (3.9%)                                 | 0 (0%)                              | 1.0     |
| Perianal disease                                      | 33                | 28                                           | 24 (23.1%)                               | 4 (30.8%)                           | 0.51    |
| Disease behavior                                      |                   |                                              |                                          |                                    | 0.52^b  |
| B1                                                    | 2                 | 2                                            | 2 (2.0%)                                 | 0 (0%)                              |         |
| B2                                                    | 50                | 48                                           | 41 (40.2%)                               | 7 (53.8%)                           |         |
| B3                                                    | 70                | 65                                           | 59 (57.8%)                               | 6 (46.2%)                           |         |
| Preoperative use of biologics                         | 8                 | 7                                            | 7 (4.8%)                                 | 2 (15.4%)                           | 0.17    |
| Preoperative use of steroids                          | 14                | 14                                           | 13 (12.5%)                               | 1 (7.7%)                            | 1.0     |
| Preoperative use of S-ASA                             | 29                | 28                                           | 21 (20.2%)                               | 7 (53.8%)                           | 0.013   |
| Preoperative use of antibiotics                       | 14                | 14                                           | 14 (13.5%)                               | 0 (0%)                              | 0.36    |
| Elevated erythrocyte sedimentation rate               | 65                | 62                                           | 55 (77.5%)                               | 7 (63.6%)                           | 0.45    |
| Low hemoglobin                                        | 89                | 85                                           | 73 (70.2%)                               | 12 (92.3%)                          | 0.11    |
| Elevated white blood cell                             | 18                | 15                                           | 15 (14.4%)                               | 0 (0%)                              | 0.21    |
| Elevated platelet                                     | 46                | 42                                           | 37 (35.6%)                               | 5 (38.5%)                           | 1.0     |
| Chronic fistula as the indication for surgery, n (%)  | 66                | 62                                           | 56 (53.8%)                               | 6 (46.2%)                           | 0.6     |
| Emergency surgery                                     | 2                 | 2                                            | 2 (1.9%)                                 | 0 (0%)                              | 1.0     |
| Laparoscopic surgery                                  | 27                | 25                                           | 23 (22.1%)                               | 2 (15.4%)                           | 0.73    |
| Type of anastomosis                                   |                   |                                              |                                          |                                    | 1.0     |
| Hand-sewn                                             | 26                | 22                                           | 20 (20.6%)                               | 2 (18.2%)                           |         |
| Stapled                                               | 89                | 86                                           | 77 (79.4%)                               | 9 (81.8%)                           |         |
| Number of anastomosis                                 |                   |                                              |                                          |                                    | 0.64    |
| ≥2                                                    | 109               | 104                                          | 93 (89.4%)                               | 11 (84.6%)                          |         |
| Stoma creation                                        | 15                | 13                                           | 11 (10.6%)                               | 2 (15.4%)                           |         |
| Intraoperative finding of fistula                     | 16                | 16                                           | 15 (14.4%)                               | 1 (7.7%)                            | 1.0     |
| Intraoperative finding of abscess                     | 67                | 63                                           | 56 (53.8%)                               | 7 (53.8%)                           | 1.0     |
| Intraoperative finding of perforation                 | 33                | 32                                           | 31 (29.8%)                               | 1 (7.7%)                            | 0.11    |
| Intraoperative finding of phlegmon                    | 4                 | 3                                            | 3 (2.9%)                                 | 0 (0%)                              | 1.0     |
| Intraoperative finding of small bowel obstruction     | 35                | 34                                           | 33 (31.7%)                               | 1 (7.7%)                            | 0.11    |
| Intraoperative finding of fibrostenosis               | 56                | 53                                           | 43 (41.3%)                               | 10 (76.9%)                          | 0.015   |
| Intraoperative finding of anastomosis                 | 78                | 74                                           | 63 (60.6%)                               | 11 (84.6%)                          | 0.13    |
| Postoperative intra-abdominal septic complications     | 24                | 22                                           | 16 (15.4%)                               | 6 (46.2%)                           | 0.016   |

^aL3 vs L1/L2.
^bB3 vs B1/B2. Data presented as mean ± standard deviation, medians (interquartile ranges) or cases (%). CD, Crohn’s disease; UC, ulcerative colitis; IC, indeterminate colitis; S-ASA, 5-aminosalicylic acid.
disorder of the immune system, and therefore have a major impact on postoperative outcomes.

Since hypoalbuminemia is the reflection of malnutrition and immunity dysfunction and malnutrition is relevant with higher rate of postoperative complication, the nutritional management is an issue worthy of attention, especially in CD patients. Several publications have pointed out that nutritional management is of great importance to the successful clinical management of patients with gastrointestinal disease [38,39]. In a study published before, patients with preoperative enteral nutrition for 3 months had a significantly higher serum albumin level and lower CRP at operation, and suffered a lower risk of IASCs [40]. Another study also showed that no IASCs occurred in patients who received preoperative nutrition support, etc.

### Table 2. Univariate analysis of risk factors associated with intra-abdominal septic complications

| Characteristics                                      | Odds ratio | 95% confidence interval | p-value |
|------------------------------------------------------|------------|-------------------------|---------|
| Age at CD diagnosis, every 1-year increase           | 0.99       | 0.95–1.03               | 0.69    |
| Age at surgery, every 1-year increase                | 1.003      | 0.97–1.04               | 0.88    |
| Duration from diagnosis to surgery, every 1-year increase | 1.14      | 1.01–1.28               | 0.029   |
| Gender (male vs female)                              | 7.67       | 0.98–59.71              | 0.052   |
| Body mass index, every 1-kg/m² increase              | 0.99       | 0.83–1.18               | 0.94    |
| Smoking (active or ex vs never)                      | 4.46       | 0.60–33.37              | 0.15    |
| History of any drug allergy (yes vs no)             | 1.29       | 0.42–3.92               | 0.66    |
| History of bowel resection (yes vs no)              | 1.84       | 0.73–4.62               | 0.2     |
| Significant comorbidities (yes vs no)               | 0.91       | 0.28–2.99               | 0.88    |
| History of diagnosis of UC or IC (yes vs no)        | 2.13       | 0.19–24.52              | 0.54    |
| Extra-intestinal manifestation (yes vs no)          | 1.73       | 0.31–9.49               | 0.53    |
| Location of CD (L3 vs L1/L2)                         | 3.74       | 0.82–17.06              | 0.089   |
| Upper gastrointestinal involvement (yes vs no)       | 1.08       | 0.12–10.14              | 0.95    |
| Perianal disease (yes vs. no)                        | 0.33       | 0.092–1.20              | 0.093   |
| Disease behavior (B3 vs B1/B2)                       | 2.65       | 0.97–7.25               | 0.057   |
| Preoperative use of biologics (yes vs no)           | 4.80       | 1.11–20.82              | 0.036   |
| Preoperative use of immunosuppressants (yes vs no)  | 0.75       | 0.23–2.44               | 0.46    |
| Preoperative use of steroids (yes vs no)            | 0.67       | 0.14–3.20               | 0.61    |
| Preoperative use of 5-ASA (yes vs no)               | 2.40       | 0.92–6.27               | 0.074   |
| Preoperative use of antibiotics (yes vs no)         | 0.67       | 0.14–3.20               | 0.61    |
| Elevated erythrocyte sedimentation rate (yes vs no) | 1.00       | 0.29–3.50               | 1.0     |
| Low hemoglobin (yes vs no)                           | 2.25       | 0.71–7.12               | 0.17    |
| Elevated white blood cell (yes vs no)               | 1.23       | 0.37–4.13               | 0.74    |
| Elevated platelet (yes vs no)                        | 0.82       | 0.32–2.09               | 0.67    |
| Chronic fistula as the indication for surgery (yes vs no) | 2.53   | 0.96–6.63               | 0.059   |
| Laparoscopic surgery (yes vs no)                     | 0.27       | 0.06–1.24               | 0.093   |
| Type of anastomosis (stapled vs hand-sewn)          | 0.60       | 0.21–1.65               | 0.32    |
| Number of anastomosis (>2 vs 1)                      | 2.37       | 0.73–7.72               | 0.15    |
| Stoma creation (yes vs no)                           | 0.56       | 0.12–2.64               | 0.46    |
| Intraoperative finding of fistula (yes vs no)       | 3.12       | 1.14–8.52               | 0.026   |
| Intraoperative finding of abscess (yes vs no)       | 0.33       | 0.092–1.20              | 0.093   |
| Intraoperative finding of perforation (yes vs no)   | 1.41       | 0.14–14.14              | 0.77    |
| Intraoperative finding of phlegmon (yes vs no)      | 0.45       | 0.14–1.41               | 0.17    |
| Intraoperative finding of small bowel obstruction (yes vs no) | 0.84 | 0.34–2.07 | 0.7   |
| Intraoperative finding of fibrostenosis (yes vs no) | 0.64       | 0.26–1.57               | 0.33    |
| Preoperative hypoalbuminemia (yes vs no)            | 4.71       | 1.40–15.87              | 0.012   |
| Albumin level, every 1-g/L increase                  | 0.91       | 0.83–0.99               | 0.03    |

CD, Crohn’s disease; UC, ulcerative colitis; IC, indeterminate colitis; 5-ASA, 5-aminosalicylic acid.

### Table 3. Multivariate analysis of the risk factors associated with intra-abdominal septic complications

| Characteristics                                      | Odds ratio | 95% confidence interval | p-value |
|------------------------------------------------------|------------|-------------------------|---------|
| Albumin level as a categorical variable               |            |                         |         |
| Duration from diagnosis to surgery, every 1-year increase | 1.09   | 0.96–1.24               | 0.18    |
| Preoperative use of biologics (yes vs no)            | 1.71       | 0.28–10.43              | 0.56    |
| Intraoperative finding of fistula (yes vs no)        | 2.48       | 0.83–7.42               | 0.1     |
| Preoperative hypoalbuminemia (yes vs no)             | 4.67       | 1.28–17.04              | 0.02    |
| Albumin level as a continuous variable               |            |                         |         |
| Duration from diagnosis to surgery, every 1-year increase | 1.12   | 0.98–1.28               | 0.11    |
| Preoperative use of biologics (yes vs no)            | 1.82       | 0.32–10.39              | 0.5     |
| Intraoperative finding of fistula (yes vs no)        | 2.61       | 0.87–7.81               | 0.087   |
| Albumin level, every 1-g/L increase                  | 0.89       | 0.82–0.98               | 0.019   |
whereas 27.7% of the matched patients suffered complications [41]. All of these results indicate the importance of nutrition management in reducing the incidence of postoperative complications. However, simply albumin replacement therapy with exogenous human albumin solution did not decrease the rates of death or major complications, probably as the underlying etiology of hypoalbuminemia is not solved and exogenous albumin is rapidly degraded [20,42], so an integrated management of nutritional support to improve the serum albumin level and nutritional and physiological stabilization of patients is necessary.

The findings of the current study have several limitations. Firstly, the surgeon’s assessment of the state of inflammatory tissue at the time of surgery is subjective and difficult to quantify. Secondly, the situation of operation cannot be completely recorded and quantified. However, the information used in the study was the same unit by the same group of physicians, used similar guidelines and made decisions collectively, which would strengthen the consistency of our findings.

In summary, preoperative hypoalbuminemia is a significant predictor for the development of postoperative IASCs in CD patients after bowel resection with a primary anastomosis. Therefore, preoperative nutrition correction is of great importance in the clinical practice.

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