Body mass index is a practical preoperative nutritional index for postoperative infectious complications after intestinal resection in patients with Crohn’s disease

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Abstract
The patients with Crohn’s disease (CD) are often accompanied with nutritional deficiencies. Compared with other intestinal benign disease, patients with CD have the higher risk of developing postoperative complications following intestinal resection. The aim of this study was to investigate the risk factors for postoperative infectious complications (PICs) after intestinal resection for CD, as well as search a practical preoperative nutritional index for PICs in patients with CD. A total of 122 patients who underwent intestinal resection for CD during 2011 to 2015 were retrospectively analyzed. After operation, 28 (22.95%) patients experienced PICs. Compared with the non-PICs group, the patients with PICs have the lower preoperative body mass index (BMI) (16.96 ± 2.33 vs 19.53 ± 2.49 kg/m\(^2\), \(P < .001\)), lower albumin (ALB) (33.64 ± 5.58 vs 36.55 ± 6.69 g/L, \(P = .013\)), higher C-reactive protein (CRP) level (30.44 ± 37.06 vs 15.99 ± 33.30 mg/L, \(P = .052\)), and longer hospital stay (22.64 ± 9.93 vs 8.90 ± 4.32 days, \(P < .001\)). By analyzing the receiver-operating characteristic (ROC) curve, BMI have better value in predicting the occurrence of PICs than ALB. The areas under the ROC curves of BMI for PICs was 0.784 (95% confidence interval 0.690–0.878, \(P < .001\)) with an optimal diagnostic cut-off value of 17.5 kg/m\(^2\). In the univariate and multivariate analysis, BMI < 17.5 kg/m\(^2\) (\(P = .001\)), ALB < 33.6 g/L (\(P = .024\)), CRP > 10 mg/L (\(P = .026\)) were risk factors for PICs. Patients with a lower preoperative BMI (< 17.5 kg/m\(^2\)) had a 7.35 times greater risk of PICs. Therefore, preoperative BMI could be regarded as a practical preoperative nutritional index for evaluating the nutritional preparation sufficiency before CD operations. Preoperative treatment with the aim of reducing CRP level and improving the patient’s nutritional status may be helpful to reduce the rate of PICs.

Abbreviations: ALB = albumin, BMI = body mass index, CD = Crohn’s disease, CRP = C-reactive protein, HB = hemoglobin, IASCs = intraabdominal septic complications, PICs = postoperative infectious complications, ROC = receiver operating characteristic, TLC = total lymphocyte count, WBC = white blood cell.

Keywords: albumin, body mass index, C-reactive protein, Crohn’s disease, postoperative complications, surgery

1. Introduction

Crohn’s disease (CD) is a nonspecific chronic inflammation bowel disease that can cause gastrointestinal symptoms such as abdominal pain, diarrhea, and bloody stool.\(^{[1,2]}\) Although the etiology is unknown, CD is thought to result from a complex interplay of multiple genetic and environmental factors.\(^{[1,2]}\) The major therapeutic approach to CD is medical treatment, however approximately 70% of CD patients should undergo operations even after active pharmacotherapy.\(^{[3–5]}\) In addition, about 70% of patients who have had operations need further surgery.\(^{[6]}\)

Compared with other benign intestinal diseases, patients with CD have the higher risk of developing postoperative complications following intestinal resection.\(^{[7]}\) According to the previous study, the risk of postoperative complications even occur in 26.6% of CD patients.\(^{[8]}\) The postoperative morbidities, especially the postoperative infectious complications (PICs), prolong the hospital stay, increase the treatment costs. More importantly, they increase the postoperative recurrence rate and decrease the patients’ quality of life.\(^{[7,9]}\) Several risk factors associated with the development of postoperative morbidities have been reported for CD, which included preoperative steroids use, presence of abscess at the time of surgery, penetrating phenotype at surgery, handsewn anastomoses, preoperative anemia, low albumin (ALB) level, emergency surgery, and preoperative C-reactive protein (CRP) level.\(^{[10–13]}\) However, the preoperative risk factors for PICs still remain controversial in patients with CD.

Patients with CD are often accompanied with nutritional deficiencies,\(^{[16,17]}\) with the incidence varying from 20% to 85%.\(^{[8,18]}\) In the recent studies, some researchers have found that malnutrition increase the incidence of postoperative complications and preoperative nutritional support decrease the risk of
postoperative complications in patients with CD.\cite{19} Thus, it is important to find an useful index to assess the preoperative nutritional status in CD patients, and optimize the index to minimize the incidence of postoperative complications. However, the most effective and simple index to assess the preoperative nutritional status in CD remains controversial. Some researchers have found that lower body mass index (BMI) is a predictive index for postoperative intraabdominal septic complications (IASCs) after bowel resection in patients with CD.\cite{20} However, whether a lower preoperative BMI level is a risk factor for PICs, and whether other preoperative nutritional indexes can be used as indicators for PICs has not been fully analyzed.

In the present study, we attempted to evaluate the risk factors for PICs after intestinal resection for CD, as well as search a practical nutritional index for PICs in patients with CD. The results may provide guidance for clinicians to determine appropriate therapeutic strategies.

2. Methods

2.1. Participants and definitions

The clinical information was collected from patients who underwent intestinal operations for CD at Sir Run Run Shaw Hospital, College of Medicine, Zhejiang University between July 2011 and November 2015. The diagnosis of CD was confirmed by postoperative pathologic analyses. The patients who only underwent operations for constructing stoma or closing the stoma, isolated strictureplasty, and reoperations for postoperative complications were excluded from these analyses. The primary outcome was the incidence of PICs. PICs were defined as occurrence of infections within 30 days after operation. In our study, the PICs included wound infections, abdominal abscesses, and anastomotic leakage. Other infectious complications, such as urinary tract infections, stoma problems, pneumonia, or central line infection were excluded from analyses. Criteria for a diagnosis of wound infection were an infection that occurred in the skin, subcutaneous tissue, or deep soft tissue at the incision site. The diagnosis of anastomotic leakage was confirmed if there was fecal material discharge from the abdominal drainage or based on reoperation findings. Abdominal abscesses were confirmed by percutaneous drainage or imaging examination. CD was classified using the Montreal classification.\cite{21} The study was approved by the Ethics Committee of the Sir Run Run Shaw Hospital, College of Medicine, Zhejiang University.

2.2. Nutritional status parameters

The BMI and ALB were used to evaluate the nutritional status. The BMI was calculated according to the following formula: BMI = weight/height^2 (kg/m^2).

2.3. Data collection and observation indexes

Patients were divided into 2 groups: PICs group and non-PICs group. The following factors were collected and compared in the 2 groups: the patients’ demographics; duration of CD; disease location at surgery; disease phenotype at surgery; elective or emergency surgery; previous intestinal resection history; smoking habits; medications usage; preoperative nutritional therapy; preoperative BMI; indication for surgery; preoperative blood biochemical indexes, which included white blood cell count (WBC), ALB, total lymphocyte count (TLC), CRP, and hemoglobin (Hb); operative approach (laparoscopy or open); abscess or fistula at surgery; stoma creation; intraoperative blood loss; operation time; methods of anastomosis; number of anastomoses; and postoperative hospital stay.

For medications, antibiotic therapy was defined as preoperative antibiotic usage within 1 week before surgery; immunomodulator therapy was defined as azathioprine or methotrexate use within 4 weeks before operation; 5-aminosalicylic acid use was defined as mesalazine use within 4 weeks of operation; steroid use was defined as prednisolone use within 4 weeks of operation; and anti-tumor necrosis factor therapy was defined as using the infliximab within 4 weeks before surgery. For patients with PICs, we identified the pathogens by bacterial culture which may help us to choose appropriate antibiotics.

2.4. Patients management

The strategy of preoperative optimization was used in our institution. Nutritional risk of patients was routinely assessed by using the Nutritional Risk Screening 2002 on the 1st day of admission.\cite{22} Patients with a nutritional risk scores ≥3 were defined as at nutrition risk and received the parental nutrition or enteral nutrition therapy. For patients with intraabdominal abscesses, accessibility of percutaneous drainage was discussed with surgeons and radiologists. Besides nutrition therapy, steroids and biologics were attempted to withdraw within the 1 month before surgery. The indication for surgery was discussed by a multidisciplinary team, which included the gastroenterologist, the general surgeon, the nutritionist, the radiologist, and the pathologist. The main indication for surgery included intestinal obstruction, abscess or fistula, acute gastrointestinal perforation, and medical intractability. The decision to create a stoma was left to the surgeon’s judgment, with the reason usually depending on the severity of disease, such as concurrent distal lesions (colonic or perianal) or present the intraabdominal abscess at the surgery.

2.5. Statistical analysis

All statistical analyses were performed using the Statistical Package of the Social Sciences (SPSS) version 19.0 (SPSS Inc., Chicago, IL). Continuous variables between the 2 groups were compared using Student t test and expressed as mean±SD. Categorical variables are presented as cases and percentages (%), and the χ² test or Fisher exact probability test was used to compare between groups. Receiver operating characteristic (ROC) curves were used to assess the sensitivity and specificity of the estimated incidence of postoperative infectious complications by BMI and ALB. The optimum diagnostic index for predicting postoperative infectious complications was selected as the cut-off value (the maximum Youden indices) by using ROC curves. Factors with a P<.05 on univariate analysis were incorporated into multivariate analysis by using the logistic regression model. Statistical significance was defined as P<.05.

3. Results

3.1. Patients characteristics

The patients characteristics are summarized in Table 1. A total of 122 patients who underwent intestinal resection for CD were included in the study, which included 80 (65.57%) male and 42 (34.43%) female. The mean age was 36.03±11.90 years, with...
the mean disease course of 5.18 ± 4.59 years. Of the 122 patients, 14 (11.48%) received the emergency operation, and 108 (88.52%) underwent the elective surgery. Of all the patients, 101 patients (82.79%) underwent the intestinal operation for the first time, and 21 (17.21%) patients had the history of bowel resection. Thirty nine (31.97%) patients underwent an operation due to present abscesses or fistulas, and 73 (59.84%) for intestinal obstruction. The disease of 72 (59.02%) patients were in the ileum, 10 (8.20%) in the colon, 38 (31.15%) in the ileocolon, and 2 (1.64%) in upper gastrointestinal tract. Nearly half of the patients (45.8%) had penetrating behavior. Half of them underwent laparoscopic surgery, and 47 (38.52%) underwent a partial intestinal resection plus an ostomy.

In our study, there was no postoperative death. After operation, 28 (22.95%) patients experienced PICs. Of these patients, 17 had incision complications, 8 had intraabdominal abscesses, and 3 had anastomotic leakage. For patients with PICs, the positive rate of bacterial culture was 71.4% (20/28). The Staphylococcus and Escherichia coli were the dominant pathogenic bacteria. Compared with the non-PICs group, the patients with PICs have the lower preoperative BMI, lower ALB concentration, higher CRP level, and longer hospital stay (Table 2).

### 3.2. The value of clinical nutritional parameters in PICs

The analysis of the ROC curve shows that BMI and ALB have the value in predicting PICs. In addition, by comparing with the areas under the ROC curves, the BMI has the better value in predicting the occurrence of PICs than the ALB. The areas under the ROC curves of BMI and ALB for PICs were 0.784 (95% confidence interval, 0.690–0.878; \( P < .001 \)) and 0.647 (95% confidence interval, 0.529–0.765; \( P = .018 \)), respectively. The cut-off value of BMI for the PICs was 17.5 kg/m² and had a sensitivity of 79.8% and a specificity of 67.9% (maximum Youden index = 0.476; Fig. 1). The cut-off value of the ALB for the PICs was 33.6 g/L and had a sensitivity of 70.2% and a specificity of 60.7% (maximum Youden index = 0.309; Fig. 1). All of these cut-off values were used as independent variables in the univariate and multivariate analysis.

### 3.3. The risk factors associated with the incidence of PICs

The clinical factors associated with PICs were shown in Table 2. By univariate analysis, preoperative BMI < 17.5 kg/m² (\( P < .001 \)), preoperative ALB < 33.6 g/L (\( P = .008 \)), preoperative CRP ≥ 10 mg/L (\( P < .001 \)), operative approach (open surgery, \( P = .003 \)), penetrating behavior (\( P < .001 \)), present abscess (\( P < .001 \)), and present fistula (\( P < .001 \)) were associated with increased rate of PICs. By multivariate analyses, the results showed that preoperative BMI < 17.5 kg/m² (\( P = .001 \)), preoperative ALB < 33.6 g/L (\( P = .024 \)), and preoperative CRP ≥ 10 mg/L (\( P = .026 \)) were independent risk factors for PICs. Patients with a lower preoperative BMI (BMI < 17.5 kg/m²) had a 7.35 times greater risk of PICs (Table 3).

### 4. Discussion

Compared with other intestinal benign disease, patients with CD have the higher risk of developing postoperative complications following intestinal resection. In our study, the rate of PICs was 22.95%, which was comparable to the rate reported in previous studies.10,11,13 PICs are difficult to manage. However, the
Table 2
Comparison of the clinical characteristics between the PICs and non-PICs groups.

| Characteristics and outcomes | PICs group (n = 28) | Non-PICs group (n = 94) | P |
|-----------------------------|---------------------|-------------------------|---|
| Gender                      | Male                | Female                  | .999 |
|                             | 22 (78.57)          | 6 (21.43)               |    |
|                             | 58 (61.70)          | 36 (38.30)              |    |
| Mean age at operation, y    | 34.82 ± 10.76       | 36.39 ± 12.25           | .542 |
| Smoker habit                | Yes                 | No                      | .375 |
|                             | 6 (21.43)           | 22 (78.57)              |    |
|                             | 13 (13.83)          | 81 (86.17)              |    |
| Disease duration, y         | 6.19 ± 2.33         | 4.88 ± 4.38             | .190 |
| Preoperative BMI, kg/m²     | 16.96 ± 2.33        | 19.53 ± 2.49            | <.001 |
| <17.5                      | 19 (67.86)          | 19 (20.21)              | <.001 |
| ≥17.5                      | 9 (32.14)           | 75 (79.79)              |    |
| Previous intestinal reactions history | Yes | No | .088 |
|                             | 8 (28.57)           | 20 (71.43)              |    |
|                             | 13 (13.83)          | 81 (86.17)              |    |
| Medication usage            | Antibiotic          | Mesalazine              | .099 |
|                             | 11 (39.29)          | 12 (42.86)              |    |
|                             | 29 (50.0)           | 38 (40.43)              |    |
|                             | 36 (38.30)          | 32 (34.04)              |    |
|                             | 33.64 ± 2.76        | 33.3 ± 2.76             |    |
| CRP, mg/L                   | 30.44 ± 7.09        | 37.06 ± 15.99           | .001 |
| TLC, /C2                    | 2.33 ± 0.42         | 5.58 ± 3.55             | .001 |
| Hb, g/L                     | 11.39 ± 1.69        | 4.21 ± 1.09             | .001 |
| Preoperative nutrition supplement | Yes | No | 1.000 |
|                             | 22 (78.57)          | 6 (21.43)               |    |
|                             | 59 (62.77)          | 35 (37.23)              |    |
| Indication for surgery      | Intestinal obstruction | Abscess or fistula | <.001 |
|                             | 14 (50.0)           | 12 (42.86)              |    |
|                             | 77 (85.71)          | 78 (83.00)              |    |
|                             | 20 (71.43)          | 8 (28.57)               |    |
|                             | 31 (32.14)          | 10 (33.96)              |    |
| Preoperative blood biochemical indexes | WBC, × 10⁹/L | ALB, g/L | 1.000 |
| ≥10                         | 6.95 ± 4.21         | 33.64 ± 5.58            |    |
| <10                         | 4 (14.29)           | 16 (57.14)              |    |
|                             | 9 (35.7)            | 28 (79.23)              |    |
| Albumin, g/L                | ≤33.6               | <900                    | .008 |
|                             | 12 (42.86)          | 6 (21.43)               |    |
|                             | 66 (70.21)          | 36 (38.30)              |    |
| ≥33.6                       | 11.12 ± 4.42        | 22 (78.57)              |    |
|                             | 58 (58.17)          | 58 (58.17)              |    |
| CRP, mg/L                   | <900                | ≥900                    | .999 |
|                             | 33.64 ± 7.09        | 30.44 ± 7.09            |    |
| ≥10                         | 20 (71.43)          | 20 (71.43)              |     |
|                             | 31 (32.14)          | 31 (32.14)              |     |
| Hb, g/L                     | <10                 | <10                     | .001 |
|                             | 28 (95.65)          | 8 (28.57)               |    |
|                             | 63 (66.07)          | 31 (32.14)              |    |
| Operative approach          | Emergency           | Elective                | .033 |
|                             | 4 (14.29)           | 24 (85.71)              |    |
|                             | 10 (10.64)          | 84 (95.36)              |    |
| Disease location            | Open                | Laparoscopy             | .003 |
|                             | 21 (75.0)           | 7 (25.0)                |    |
|                             | 40 (42.55)          | 54 (57.45)              |    |
| L1 (ileal)                  | 14 (50.0)           | 10                  | .001 |
| L2 (colic)                  | 2 (7.14)            | 8 (28.57)               | .001 |
| L3 (ileocecal)              | 12 (42.86)          | 26 (86.36)              |     |
| L4 (isolated upper disease) | 0 (0)               | 2 (6.67)                | .001 |
| Penetrating behavior (fistula/abscess) | Yes | No | .001 |
|                             | 21 (75.0)           | 7 (25.0)                |    |
|                             | 34 (36.17)          | 60 (63.83)              |    |
| Prevent abscess at surgery  | Yes                 | No                      | .001 |
|                             | 15 (53.57)          | 7 (25.0)                |    |
|                             | 21 (22.34)          | 60 (63.83)              |    |
| Prevent fistula at surgery  | No                  | Yes                     | .001 |
|                             | 13 (46.43)          | 17 (53.57)              |    |
|                             | 73 (76.60)          | 68 (72.34)              |    |
| Intraoperative blood loss >300mL | Yes | No | .468 |
|                             | 4 (14.29)           | 24 (85.71)              |    |
|                             | 8 (28.57)           | 86 (91.49)              |    |
| Operation time >180min      | Yes                 | No                      | .469 |
|                             | 11 (39.29)          | 17 (60.71)              |    |
|                             | 30 (31.91)          | 64 (68.09)              |    |
| Anastomosis approach        | Handsewn            | Stapled                 | 1.000 |
|                             | 3 (10.71)           | 25 (89.29)              |    |
|                             | 10 (10.64)          | 84 (95.36)              |    |
| Number of anastomoses       | Single              | multiple                | .180 |
|                             | 22 (78.57)          | 6 (21.43)               |    |
|                             | 85 (80.43)          | 9 (9.57)                |    |
| Stoma creation              | Yes                 | No                      | .155 |
|                             | 14 (50.0)           | 14 (50.0)               |    |
|                             | 33 (35.11)          | 61 (64.89)              |    |
| Postoperative hospital stay, d| 22.64 ± 9.93        | 8.90 ± 4.32             | <.001 |

Data are reported as number of patients (%) or mean ± SD. BMI = body mass index, CRP = C-reactive protein, WBC = white blood cell count, ALB = serum albumin, ALB = serum albumin, ALB = serum albumin, ALB = serum albumin, ALB = serum albumin.

Figure 1. Receiver-operating characteristic (ROC) curves used to identify the value of body mass index and serum albumin for postoperative infectious complications.

Table 3
Multivariable analysis of the risk factors for the PICs.

| Characteristics | Odds ratio | 95% Confidence interval | P |
|-----------------|------------|-------------------------|---|
| BMI < 17.5 kg/m²| 7.352      | 2.377–22.736            | .001 |
| Albumin < 33.6 g/L| 3.631      | 1.181–11.167            | .024 |
| CRP ≥ 10 mg/L   | 3.611      | 1.170–11.140            | .026 |
| Operative approach (open surgery) | 0.409 | 0.110–1.514 | .181 |
| Penetrating behavior | 0.346 | 0.027–4.425 | .415 |
| Present abscess at surgery | 4.090 | 0.324–7.902 | .561 |
| Present fistula at surgery | 6.318 | 0.848–47.048 | .072 |

BMI = body mass index, CRP = C-reactive protein, PIC = postoperative infectious complications.
greater risk of PICs. The result suggests that preoperative BMI had the better value of evaluating the nutritional status for patients with CD, and could serve as a practical index to predict the incidence of PICs.

Some researchers have investigated the effect of BMI in patients with CD. Zhang et al.[23] found that the patients with a lower preoperative BMI carried a greater risk of IASCs, and BMI was a better clinical factor to reflect the basic nutritional status of CD patients. In another study, Mijac et al.[8] found that the BMI was a simple and convenient methods for the assessment of the nutritional status in IBD patients. Thus, a larger randomized prospective study to evaluate whether improvement of preoperative BMI minimizes postoperative morbidity remains to be carried out.

CRP is a useful clinical marker for detecting the severity of inflammatory diseases due to its rapid response and short half-life. Some studies have reported the importance of CRP in CD. Solem et al.[24] reported that CRP elevation in CD patients was associated with clinical disease activity, endoscopic inflammation, and severely active histologic inflammation. Iaculli et al.[25] found that perioperative CRP levels were predictive markers for endoscopic recurrence after ileo-colonic resection for CD. Furthermore, some researchers have found that CRP could predict the surgical outcome in subgroups of patients with CD and preoperative CRP level could serve as a predictive index for postoperative IASCs in patients with CD.[11,26] The results imply that higher CRP level was associated with the poor surgical outcome in CD. In our study, we found that preoperative CRP ≥10 mg/L was an independent risk factor for PICs. The results further verify the importance of CRP in CD. Thus, taking effective clinical measure to reduce the preoperative CRP levels may help to decrease the incidence of PICs.

ALB was not only regarded as one of the clinical index to evaluate the nutritional status, but also related to the clinical outcome in CD. Suzuki et al.[27] found that the pre-escalation ALB level was a good predictor of recovering efficacy after dose escalation infliximab therapy in CD patients with loss of response to treatment for CD. Guo et al. reported that preoperative ALB level less than 35 g/L was an independent risk factor for anastomotic leakage after surgery for CD. Furthermore, some studies suggested that a lower level of ALB could increase the risk of postoperative complications in CD patients.[11,14] In our study, preoperative ALB <33.6 g/L was an independent risk factor for PICs. The results were consistent with other studies, and further indicated that preoperative ALB optimization or elevation may be helpful to reduce the occurrence of postoperative complications after intestinal resection in patients with CD.

There are several limitations in our study. First, this was a retrospective study, which may lead to potential defects in the accuracy of the date information in the medical records. In addition, there may be other factors affecting the PICs that we did not take into account through the retrospective analysis. Therefore, the further prospective investigation is required to resolve those limitations. Third, the optimal diagnostic cut-off value in our results were analyzed from a single center. Thus, multicenter studies are needed to validate the results. However, to the best of our knowledge, this article is the first to report that the BMI have the better value in predicting the PICs than ALB. In conclusion, preoperative BMI ≥17.5 kg/m², ALB <33.6 g/L, and CRP ≥10 mg/L are independent risk factors for PICs. Therefore, we recommend that preoperative treatment with the aim of reducing CRP level and improving the patient’s nutritional status would be conducive to reduce the rate of PICs. BMI has the better value in predicting the occurrence of PICs than the ALB. The preoperative BMI levels could be regarded as a practical preoperative nutritional indexes for evaluating the nutrition preparation endpoint before CD operations.

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