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ORIGINAL ARTICLE

Glasgow prognostic score is a practical predictive index for postoperative intra-abdominal septic complications after bowel resection in Crohn's disease patients

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Abstract

Purpose Postoperative intra-abdominal septic complications (IASCs) are not uncommon in patients with Crohn's disease (CD). The appropriate index to predict postoperative IASCs in these individuals remains unknown. This study investigates whether the inflammation-based Glasgow prognostic score (GPS) is predictive in the setting of postoperative IASC CD patients who underwent elective bowel resection.

Methods A consecutive cohort of 163 CD patients who underwent elective intestinal resection from July 2012 to March 2016 was retrospectively analyzed. Patients were divided into two GPS groups, one lower and one higher. The GPS was defined by serum levels of C-reactive protein and albumin. Univariate and multivariate analyses were conducted to identify risk factors for postoperative IASCs.

Results Postoperative IASCs occurred in 25 (15.3%) patients. Compared with patients in the lower GPS group, patients with a higher GPS had a higher incidence of postoperative IASCs (9.85 vs. 38.71%, $P < 0.001$) and experienced longer postoperative hospital stay (10.53 ± 7.00 vs. 15.71 ± 9.17, $P = 0.001$). Univariate and multivariate analyses revealed preoperative GPS [odds ratio (OR) 5.016, 95% confidence interval (CI) 1.134–22.193, $P = 0.034$] and penetrating behavior (OR 4.495, 95% CI 1.377–14.670, $P = 0.013$) to be independent risk factors for postoperative IASCs.

Conclusions A preoperative GPS can serve as a useful index for predicting manifestation of postoperative IASCs after bowel resection in patients with CD. Perioperative optimization is required to improve postoperative outcomes for patients with higher GPS.

Keywords Crohn's disease · Glasgow prognostic score · Postoperative complications · Bowel resection · Penetrating disease

Introduction

Crohn's disease (CD) is a nonspecific, chronic inflammatory bowel disease that may affect any part of the gastrointestinal tract [1]. Despite active pharmacotherapy, approximately 70% of CD patients might undergo bowel surgeries during their lifetime [2–4], and nearly 70% of these patients need further surgery at some point after primary operation [5]. Compared to patients with other intestinal diseases, those suffering from CD generally experience greater and more serious postoperative complications after bowel resection, despite the fact that most patients with CD are young and have no significant comorbidities [6]. Intra-abdominal septic complications (IASCs) remain the most difficult conditions to manage among all postoperative morbidities, requiring aggressive treatment and extended hospitalization [7].

Postoperative IASCs include anastomotic leaks, fistulas, or intra-abdominal abscesses [6], with incidences ranging from 2.7 to 16% [7–15]. Patients with postoperative IASCs have previously been reported to have had higher surgical recurrence rates than those without postoperative complications

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[6]. Thus, preventing the postoperative IASCs is vital in particular for patients with CD. Several risk factors associated with postoperative IASCs have been reported in the setting of CD, including preoperative steroid use, thiopurine therapy, abscess formation, a penetrating CD phenotype, operation time > 180 min, and manually sutured anastomoses [7, 8, 12, 13]. In addition, preoperative albumin (ALB) and C-reactive protein (CRP) levels have also been recognized as possible risk factors for postoperative IASCs in these individuals [9, 14, 16, 17]. However, there are no appropriate indices to predict manifestation of postoperative IASCs or determine operative timing for CD patients.

The Glasgow prognostic score (GPS), an inflammation-based prognostic index defined by elevated CRP and hypoalbuminemia, has been shown to serve as an effective prognostic marker for postoperative outcome prediction in advanced cancer patients [18–21]. However, whether GPS can be used as a predictive index for postoperative IASCs in CD patients has not yet been reported, to the best of our knowledge. Therefore, the purpose of the present study was to evaluate whether the GPS can serve as a predictive factor for postoperative IASCs in CD patients after intestinal resection. Our findings may provide a useful foundation for clinicians to plan and execute appropriate operative strategies.

Methods

Participants

Medical histories of CD patients who consecutively underwent elective intestinal resection at Sir Run Run Shaw Hospital, College of Medicine, Zhejiang University, from July 2012 to March 2016, were retrospectively analyzed. All operations were completed by the same surgical team, and CD diagnosis was confirmed by postoperative pathologic analysis. Patients who underwent elective intestinal resection, with or without stoma creation, were included. Patients who only underwent stoma reversal, perianal surgery, isolated strictureplasty, or reoperations for postoperative complications were excluded from our analysis. The study was approved by the ethics committee of the Sir Run Run Shaw Hospital, College of Medicine, Zhejiang University.

Patient management

Preoperative nutritional risks were routinely assessed by using the Nutritional Risk Screening 2002 on the first day of hospital admission [22]. Patients with nutritional risk scores of greater than three were defined as being at nutritional risk and received appropriate nutritional therapy either by parental or enteral routes. For patients with preexisting intra-abdominal abscesses, percutaneous drainage was performed first. Steroids were withdrawn from treatment regimens within the month prior to surgery. Indications for intestinal resection in patients with CD were discussed by a multidisciplinary team, including gastrointestinal physicians and surgeons, nutritionists, radiologists, and pathologists. Operations were conducted via either conventional open or laparoscopic approaches, with the latter as a preference. The decision to create a stoma usually depended on the severity of disease, the patient's general condition, and the surgeon's judgment. Discharge was indicated based on the following criteria: afebrile within 24 h, postoperative defecation or flatus, tolerance of a liquid diet, and effective pain control with oral medication.

Data collection and identification

We used electronic medical records to retrieve the following information concerning eligible patients: demographic data (gender, age, smoking history, duration of disease, etc.), body mass index (BMI), Montreal classification [23], previous CD-related abdominal surgical history, preoperative medical therapy, disease characteristics, preoperative laboratory data, history of prior surgical procedures, postoperative complications, and the length of post-surgical hospital stay.

Preoperative medical therapy was defined as steroid, immunomodulator, 5-aminosalicylic acid, or antitumor necrosis factor agent use within 4 weeks prior to surgery. Penetrating disease was defined as fistulas, abscesses or phlegmon manifestations, as confirmed by imaging examination, intraoperative, or postoperative pathologic findings [7, 24]. Peripheral blood samples were collected to measure white blood cell (WBC), hemoglobin (Hb), CRP, and ALB levels 1 day prior to surgery. These are routine preoperative examinations for all CD patients undergoing intestinal resection at our institution.

As described previously, we used preoperative CRP and ALB levels to calculate GPS. Patients with an elevated CRP level (≥ 10 mg/L) and concomitant hypoalbuminemia (< 35 g/L) were assigned a score of 2 and to the higher GPS group. Patients with only one or none of these abnormalities were allocated scores of 1 or 0, respectively, and assigned to the lower GPS group. Postoperative IASCs were defined as any anastomotic leaks, intra-abdominal abscesses, or fistulas that occurred within the first 30 days after surgery [8]. The diagnosis of anastomotic leakage was based on clinical findings of fecal discharge within abdominal drainage, or findings on reoperation. Abdominal abscesses were confirmed by percutaneous drainage, imaging examination, or reoperative findings.

Statistical analysis

All data were analyzed with SPSS for windows, version 19.0 (IBM, USA). Continuous variables were expressed as mean ± standard deviation (SD) or medians with ranges. Categorical variables were presented as cases and percentages (%). We

applied Student's *t* test to compare continuous variables and Pearson's chi-square or Fisher's exact probability tests for categorical variables. Factors with *P* values < 0.05 on univariate analysis were incorporated into multivariate analysis by using a multivariate logistic regression model. Statistical significance was considered as *P* value < 0.05.

Results

The clinical characteristics of patients enrolled in the study are shown in Table 1. According to our inclusion criteria, a total of 163 CD patients who underwent elective intestinal resection were included in our study. The mean age at diagnosis was 36.02 ± 11.80 years, with the median disease course of 5.0 years (range 0.1–30 years). Of all patients, more than half of them were men (63.2%), and 14.7% were smokers at the time of operation. Of patients, 84.7% underwent intestinal resection for the first time, and 25 (15.3%) patients had a history of bowel operation. In 75 (46.0%) patients, diseases were localized to the ileum, in 17 (10.4%) to the colon, and 68 (41.7%) to the ileocolon. Of patients, 69.3% had been administered immunomodulators or mesalazine before surgery, 21.5% administered steroids, and 9.2% managed with infliximab. Indications of surgery included bowel stenosis (96 patients; 58.9%) and penetrating disease (fistulas or abscesses; 67 patients). Of all patients, 52.8% underwent laparoscopic-assisted surgery successfully, and 63.2% were managed with a primary anastomosis.

In our study, there were no postoperative deaths. After operation, postoperative IASCs occurred in 25 (15.3%) patients. Of these patients, 5 (20%) were found to have an anastomotic leak, 17 (68%) were found to suffer intra-abdominal abscesses, and 3 (12%) were diagnosed with enterocutaneous fistulas.

Comparisons of clinicopathological factors between the higher and lower GPS groups are indicated in Table 2. There were 132 (81%) patients in the lower and 31 (19%) in the higher GPS groups, respectively. For parameters of gender, age, smoking habits, disease duration, BMI, disease location, previous CD-related abdominal surgery, penetrating characteristics of the disease, and medication, there were no differences between the two groups. However, a higher GPS was associated with a higher postoperative incidence of IASCs ($P < 0.001$) and a longer postoperative hospital stay ($P = 0.001$). The incidence of stoma creation or open operation was more common in the higher GPS group, though the difference was not significant. Less than 10% of patients in the lower GPS group suffered postoperative IASCs, while 38.7% in the higher GPS group did ($P < 0.001$).

The univariate and multivariate analyses of factors associated with postoperative IASCs are presented in Table 3. Univariate analysis revealed that a higher GPS ($P < 0.001$), BMI < 18.5 kg/m^2 ($P = 0.042$), ALB < 35 g/L ($P = 0.029$), open surgical management ($P < 0.001$), and penetrating disease characteristics ($P < 0.001$) were associated with increased risk of postoperative IASCs. However, results of multivariate analysis indicated that only higher GPS ($P = 0.034$) and penetrating disease ($P = 0.013$) were independent risk factors for postoperative IASCs. If the patients had neither a higher GPS or penetrating disease, the possibility of postoperative IASCs was 3.7%; in patients who had only one risk factor (either higher GPS or penetrating disease), the possibilities of postoperative IASCs were 14.3 and 16.7%, respectively; when both risk factors were present, postoperative IASC rates reached 58%.

Table 1 Demographic and clinical characteristics of CD patients with elective bowel resection

Characteristics	Patients, mean ± SD or *n* (%)
Gender	
Male	103 (63.2)
Female	60 (36.8)
Age (years)	36.02 ± 11.80
Smokers	24 (14.7)
BMI (kg/m^2)	18.95 ± 2.81
Disease duration (years)	5.00 ± 4.87
Previous abdominal surgery	25 (15.3)
Montreal classification of age	
A1 (< 16 years)	0 (0)
A2 (17–40 years)	112 (68.7)
A3 (> 40 years)	51 (31.3)
Montreal classification of disease location	
L1 (ileal)	75 (46.0)
L2 (colonic)	17 (10.4)
L3 (ileocolonic)	68 (41.7)
L4 (isolated upper disease)	3 (1.8)
Medication before surgery	
Antibiotic	74 (45.4)
Mesalazine	62 (38.0)
Immunomodulator	51 (31.3)
Steroids use within 1 month	35 (21.5)
Infliximab	15 (9.2)
Penetrating behaviors (fistulas/abscesses)	
Yes	67 (41.1)
No	96 (58.9)
GPS	
Lower GPS	132 (81)
Higher GPS	31 (19)
Laparoscopy-assisted surgery	86 (52.8)
Stoma creation	60 (36.8)
With postoperative IASCs	25 (15.3)
Postsurgical hospital stay (days)	11.52 ± 7.70

BMI body mass index, *GPS* Glasgow prognostic score, *IASCs* intra-abdominal septic complications, *SD* standard deviation

Table 2 Comparisons of clinical characteristics between the higher GPS group and lower GPS group

Characteristics and outcomes	Lower GPS group ($n = 132$)	Higher GPS group ($n = 31$)	P value
Gender			0.680
Male	82 (62.1)	21 (67.7)	
Female	50 (37.9)	10 (32.3)	
Age (years)	35.77 ± 11.98	37.13 ± 11.16	0.564
Smokers	18 (13.6)	6 (19.4)	0.408
BMI (kg/m^2)	19.04 ± 2.52	18.54 ± 3.83	0.372
Disease duration (years)	4.97 ± 5.02	5.13 ± 4.23	0.873
Previous abdominal surgery	22 (16.7)	3 (9.7)	0.417
Montreal classification of age			0.196
A1 (< 16 years)	0 (0)	0 (0)	
A2 (17–40 years)	94 (71.2)	18 (72.2)	
A3 (> 40 years)	38 (28.8)	13 (27.8)	
Montreal classification of disease location			0.519
L1 (ileal)	63 (47.7)	12 (38.7)	
L2 (colonic)	12 (9.1)	5 (16.1)	
L3 (ileocolonic)	54 (40.9)	14 (45.2)	
L4 (isolated upper disease)	3 (2.3)	0 (0)	
Medication before surgery			
Antibiotic	56 (42.4)	18 (58.1)	0.160
Mesalazine	52 (39.4)	10 (32.3)	0.540
Immunomodulator	39 (29.6)	12 (38.7)	0.390
Steroids	26 (19.7)	9 (29.0)	0.330
Infliximab	13 (9.9)	2 (6.5)	0.738
Penetrating behaviors (fistulas/abscesses)	50 (37.9)	17 (54.8)	0.105
Laparoscopy-assisted surgery	74 (56.1)	12 (38.7)	0.109
Laboratory indices			
WBC (× 10^9/L)			0.341
≥ 10	13 (9.9)	5 (16.1)	
< 10	119 (90.2)	26 (83.9)	
CRP (mg/L)			< 0.001
≥ 10	29 (22.0)	31 (100)	
< 10	103 (78.0)	0 (0)	
Albumin (g/L)			< 0.001
< 35	34 (25.8)	31 (100)	
≥ 35	98 (74.2)	0 (0)	
With postoperative IASCs	13 (9.9)	12 (38.7)	< 0.001
Postsurgical hospital stay (days)	10.53 ± 7.00	15.71 ± 9.17	0.001
Stoma creation	45 (34.1)	15 (48.4)	0.152

Data are reported as number of patients (%) or mean ± SD

BMI body mass index, *GPS* Glasgow prognostic score, *IASCs* intra-abdominal septic complications, *WBC* white blood cell, *CRP* C-reactive protein

Discussion

Postoperative IASCs are difficult to manage and prevention is therefore of key importance. In the present study, we found that higher GPS values and penetrating behaviors were significant, independent risk factors for postoperative IASCs. To our knowledge, this is the first paper to compare GPS with other clinical variables in terms of postoperative outcomes of patients with CD-related bowel resection.

Preoperative nutrition status and disease activity have been demonstrated to be associated with postoperative outcomes in CD patients [9, 12, 25–27]. In addition, past studies have reported elevated CRP and hypoalbuminemia to be independent risk factors for postoperative complications in CD

Table 3 Univariate and multivariable analyses of clinical factors associated with postoperative IASCs in CD patients

Variable	IASCs		*P* value		OR	95% CI
	Yes ($n = 25$)	No ($n = 138$)	Univariate	Multivariable		
Gender (male)	18	85	0.321			
Age < 40 years	17	95	1.000			
Smokers	5	19	0.376			
BMI < 18.5 kg/m^2	16	57	0.042	0.382	1.561	0.575–4.240
Previous abdominal surgery	6	19	0.226			
Medication before surgery						
Antibiotic	14	60	0.247			
Mesalazine	10	52	0.826			
Immunomodulator	10	41	0.307			
Steroids	6	29	0.738			
Infliximab	4	11	0.252			
Penetrating behaviors	20	47	< 0.001	0.013	4.495	1.377–14.670
Preoperative laboratory indices						
WBC ≥ 10 × 10^9/L	4	14	0.484			
CRP ≥ 10 mg/L	13	47	0.114			
Albumin < 35 g/L	15	50	0.029	0.877	0.893	0.214–3.721
Higher GPS	12	19	< 0.001	0.034	5.016	1.134–22.193
Laparoscopy-assisted surgery	5	81	< 0.001	0.103	0.376	0.116–1.221
Stoma creation	13	47	0.114			

Data are reported as number of patients

IASCs intra-abdominal septic complications, *OR* odds ratio, *CI* confidence interval, *BMI* body mass index, *WBC* white blood cell, *CRP* C-reactive protein, *GPS* Glasgow prognostic score

patients [9, 14, 16, 17]. However, the conclusions remain controversial [7, 8, 10, 11, 27, 28]. In our study, a significant association between elevated CRP and the development of postoperative IASCs was not revealed; neither was hypoalbuminemia associated with postoperative IASCs on multivariate analysis. This may be due to postoperative IASCs being generally difficult to predict when using a single laboratory index. The GPS, which is an inflammation-based prognostic index, has been shown to be a marker for prediction of postoperative outcomes in several types of cancer patients [18, 21, 29]. GPS, however, has not yet been evaluated as a predictive index for postoperative outcomes in patients with CD. In the present study, we demonstrated a statistically significant difference in postoperative IASCs among the patients with different GPS values. The rate of postoperative IASCs approached 40% if the patient had an elevated CRP and concomitant hypoalbuminemia at the time of surgery. In addition, these patients had a higher incidence of stoma creation, open laparotomy, and longer postoperative hospital stay.

The precise mechanisms underlying the role of GPS in predicting postoperative outcomes is still unclear. Previous studies suggested that systemic inflammatory responses are of value in predicting cancer-specific survival and might be involved in the mechanisms behind postoperative complications [30–32]. Furthermore, it has been reported that elevated CRP is associated with the clinical disease activity in inflammatory bowel disease [33]. A previous study also found that a higher CRP level during relapse indicates a more severe clinical course in patients with CD [34]. Therefore, the GPS not merely reflects ongoing systemic inflammation, but also reflects the severity of disease in patients with CD. This may be the main reason why the GPS was valuable of predicting the postoperative outcomes in CD patients. A larger prospective study is required to verify whether improvement of preoperative GPS value optimizes postoperative outcomes.

Penetrating disease is a common phenotype of CD. Of patients, 41.1% suffered penetrating disease in this study, and our results were consistent with previous reports [35]. Some studies demonstrated that penetrating disease correlated with postoperative complications [7, 36, 37]. We also recognized that penetrating behavior was an independent risk factor for postoperative IASCs as shown by multivariate analysis. Patients with penetrating disease often present with intra-abdominal abscesses or fistulas, which may explain why the postoperative outcome was poor in this

cohort of patients. Furthermore, it has been reported that manifestations of penetrating characteristics is associated with an increased risk of clinical recurrence in these patients [35, 38, 39].

Although previous studies had reported postoperative IASCs to be significantly associated with preoperative corticosteroid therapy [11, 12, 40], our findings differed, perhaps because steroids were withdrawn within 1 month prior to surgery. The findings of this study did not demonstrate a significant association between preoperative anti-TNFα therapy and the development of postoperative IASCs. Consistent with our reports, some literature also reported preoperative anti-TNFα therapy to have no effect on risk of postoperative IASCs [37, 41–44]. This issue, however, remains controversial [8, 15, 45]. A recent study had shown that perioperative anti-TNFα usage was a significant independent risk factor for postoperative IASCs [8]. In addition, a recent meta-analysis also demonstrated that preoperative anti-TNFα usage was associated with a higher rate of postoperative complications in patients with CD [46]. Randomized, prospective studies to examine whether preoperative anti-TNFα therapy can indeed exacerbate postoperative infectious complications are required.

Limitations of this study include its retrospective nature. As it was conducted at the level of a single institution and was also observational, accuracy of data in the medical records may have possessed faults. In addition, there may have been other factors affecting postoperative IASCs that we did not take into account in our retrospective analysis. Obviously, further prospective investigations are required to counter such potential limitations. The number of patients managed with biologic treatments preoperatively was small in our study; this also may have impacted the significance of the association between preoperative anti-TNFα therapy and the development of postoperative IASCs. Despite these limitations, to the best of our knowledge, this article is the first to report that preoperative GPS is an independent predictor of postoperative IASCs in CD patients who underwent bowel resection.

In conclusion, the results of this study suggest that higher GPS values and penetrating behaviors were independent risk factors for postoperative IASCs. Preoperative GPS can serve as a predictive index for postoperative IASCs after bowel resection in patients with CD. For patients with higher preoperative GPS, formulating appropriate preoperative strategies to improve patients' nutrition status and reduce preoperative CRP levels may assist in decreasing the incidence of postoperative IASCs.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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