Original

The Indicator of Nutritional Status is useful for Determining the Operative Method at the Time of Operation for Ulcerative Colitis

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SUMMARY

Objectives：The surgical method and the timing of surgical intervention for refractory ulcerative colitis (UC) remain controversial. Several studies have reported that the nutritional indicators are useful for predicting of postoperative complications. This study aimed to clarify the relationship between nutritional status and outcome of surgery for UC.

Methods：This was a single-institution, retrospective study of patients with UC who underwent surgery between 2006 and 2019, excluding those who underwent emergency surgery. The Controlling Nutritional (CONUT) score and Onodera's prognostic nutrition index (OPNI) were used as indicators of nutritional status. The moderate cut-off point was determined using the receiver operating characteristic curve.

Results：A total of 51 UC patients underwent surgery between 2006 and 2019. Thirty-five UC patients were included in this study after excluding those who underwent surgery for emergency indications such as perforation, toxic megacolon. 57%（n＝20）of the patients received three-stage surgery. Postoperative complications（Clavien-Dindo classification＞II）occurred in 40%（n＝14）of patients. The prevalence of surgical site infection was 12%. The areas under the curve for the frequency of surgical site infection were 0.72 and 0.75 for CONUT and OPNI, respectively. The cut-off value for CONUT was 8.00（sensitivity：84%, specificity：50%）and OPNI was 46.5（sensitivity：44.8%, specificity：100%）. The malnutrition cohort as identified using CONUT and OPNI had a higher rate of postoperative complications than non-malnutritionl cohort（p＝0.04, p＝0.01）.

Conclusion：Nutritional status indicators are useful for determining the operative method for the treatment of UC.

Key Words：Ulcerative colitis, Surgery, Nutritional status

INTRODUCTION

Ulcerative colitis（UC）is a chronic inflammatory disease of the intestinal tract that is characterized by repeated relapse and remission；the number of patients with UC in Japan has been increasing annual-

Table 1 The screening tool for controlling nutritional status (CONUT).

Parameter	Normal		Mild		Moderate		Severe	
Albumin (g/dl)	≥3.5	(0)	3.0-3.4	(2)	2.5-2.9	(4)	<2.5	(6)
Total lymphocyte counts (/mL)	>1,600	(0)	1,200-1,599	(1)	800-1,199	(2)	<800	(3)
Total cholesterol (mg/dL)	≥180	(0)	140-179	(1)	100-139	(2)	<100	(3)
Dysnutritional status (total)	Nomal	(0-1)	Mild	(2-4)	Moderate	(5-8)	Severe	(9-12)

ly[1]. The aims of surgery for UC can be summarized as improving the quality of life in refractory cases, saving lives in severe cases, and cases of colitic cancer. Although advances in medical treatment have increased the number of cases for which surgery can be avoided, the number of patients undergoing emergency surgery after failure of second- or third-line medication has also increased[1,2].

The timing of surgical interventions and the surgical approach for refractory UC remain debated. Laparoscopic surgery for treatment of ulcerative colitis has become popular in the last decade[3]. The standard surgical treatment of UC is proctocolectomy with ileal pouch-anal anastomosis (IPAA) or ileal pouch-anal canal anastomosis (IACA)[4].

Recently, many surgeons have used a two-stage surgical approach. However, in the acute setting, such as in patients with hemorrhage, toxic megacolon, perforation and acute severe colitis, surgeons have used a three-stage approach. Two-stage approach comprises IPAA or IACA with ileostomy during the initial surgery, followed by ileostomy closure, whereas the three-stage approach comprised a subtotal colectomy and ileostomy, proctectomy and pouch creation, and ileostomy closure[5].

Three-stage surgery has been preferred for patients not only in emergency cases but also in patients deemed at high risk of complications, such as those with medication refractory disease, those taking high-dose steroids or biologics, or those with possible Crohn's disease. The three-stage surgery allows for healthier and better nourished patients after the surgery. Three-stage surgery may reduce the risk of postoperative complications relative to that if a two-stage surgery was chosen.

Several recent studies have reported the uses of nutritional indicators for predicting postoperative complications. The poor preoperative nutritional status, such as low serum albumin and weight loss, were also found to be adversely associated with increase of postoperative complications. The low albumin levels may reflect an inflammatory response related to disease severity[6,7].

This study aimed to use indicators of nutritional status to determine the optimal timing of surgical treatment for UC.

METHODS

We reviewed the data of patients with UC who had been received radical surgery between March 2006 and April 2019, retrospectively. The indicators of nutritional status were body weight, body mass index, serum albumin level, Onodera's prognostic nutritional index (OPNI) and controlling nutritional score (CONUT). The OPNI was initially designed to assess the risk of postoperative complications using the serum albumin and the lymphocyte count. The OPNI is calculated as follows : OPNI = 10 × serum albumin level (g/dL) + 0.005 × the lymphocyte count (/mm^3). Patients with an OPNI of >45, or <40 were categorized in the high and low OPNI groups, respectively[8]. CONUT is calculated from the serum albumin level, the lymphocyte counts, total cholesterol level. (Table 1)[9]. All blood samples were collected two day prior to surgery. The treatment date was retrospectively obtained from the medical records of each patients. Postoperative complications and their grade were defined according to the Clavien-Dindo classification system. The Clavien-Dindo classification is a simple and feasible grading system of postoperative complications. Postoperative complications included surgical site infection, bleeding, intraabdominal abscess, anastomotic leakage, and obstruction. The use of clinical data was approved by the Human Ethics Review Board of Dokkyo Medical University (Protocol # R-27-9J).

Table 2　The background information of the patients undergoing surgery for ulcerative colitis. The data are shown as the median and range.

Factors		N = 35
Age（y）		42（24–81）
Gender	Male	19
	Female	16
Disease duration（y）		5（1–26）
Reason	Refractory	16
	Acute severe colitis	19
Range	Pancolitis	29
	Left-sided colitis	6
Total steroid dose（mg）	≥10000	16
	＜10000	19
Body weight（kg）		47.6（34.4–82）
BMI		18.5（14.7–31.3）
Total lymphocyte count		1200（201–3087）
Albumin（g/dL）		2.4（1.2–4.6）
OPNI		32（17.2–53.1）
CONUT		4（0–11）

＊OPNI：Onodera's prognostic nutritional index, CONUT：controlling nutritional score

All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). Significance was evaluated by performing the Student's t-test, analysis of variance, Mann-Whitney U test, and chi squared test as appropriate. The optimal cut-off point was selected according to the receiver operating curve (ROC) analysis. Differences were considered to be significant if the p-value was less than 0.05. Individual consent was not required because of the retrospective and anonymous nature of the study.

RESULTS

Patient characteristics

Between March 2006 and April 2019, a total of 51 patients with UC underwent surgery at the First Department of Surgery, Dokkyo Medical university. Of these, thirty-five patients were included in this study after excluding the patients who underwent surgery for emergency indications, such as hemorrhage, perforation, toxic megacolon. The main clinical characteristics of the included patients are shown in Table 2. The study included 19（54%）men and 17（49 %）women with a median age of 42 years（range 21 – 80 years）. The median disease duration was 5 years （range 1 –26 years）.

Surgical outcome

Of the 35 patients included in this study, 25 patients underwent open surgery and 10 patients underwent laparoscopic surgery. 57 %（n = 20）of the patients received three-stage surgery. Postoperative complications（Clavien-Dindo classification＞II） occurred in 40%（n = 14）of patients. The prevalence of surgical site infection（SSI）was 12%（Table 3）. The three-stage surgery group had a significantly lower serum albumin level, OPNI and CONUT. But the three-stage surgery group had none of the severe complications（Table 4）. The area under the curve for the frequency of complication was 0.72 and 0.78 for CONUT and OPNI, respectively. The cut-off value for CONUT was 8.00（sensitivity：84%, specificity：50%） and OPNI was 46.5（sensitivity：44.8%, specificity：100%）（Figure 1）. The malnutrition cohort as identified using CONUT and OPNI had a higher rate of postoperative complications than the non-malnutrition cohort（p = 0.04 and p = 0.01, respectively）（Table 5）.

Table 3 The surgical outcome of the patients undergoing surgery for ulcerative colitis.

Factors			Total (n＝35)	(％)
Method		IPAA	22	(62)
		IACA	5	(14)
		Subtotal colectomy	4	(11)
		Others	4	(11)
Procedure		1 stage	5	(14)
		2 stage	10	(29)
		3 stage	20	(57)
Approach		Laparoscopic	10	(43)
		Open	25	(57)
Complication	SSI	Wound	1	(3)
(≥ Clavien-Dindo II)		Intra-abdominal abscess	2	(6)
		Leakage	1	(3)
		Ileus	3	(9)
		High-output stoma	5	(14)
		Others	2	(6)
Clavien-Dindo		I	5	(29)
		II	5	(29)
		IIIa	5	(29)
		IIIb	2	(12)

＊IPAA：ileal pouch anal anastomosis, IACA：ileal pouch anal canal anastomosis, SSI：surgical site infection

Table 4 The three-stage surgery group had a significantly lower serum albumin level, OPNI and CONUT.

Factors		Two stage (n＝10)	Three stage (n＝20)	p-value
Body weight (kg)		56.2 (37.7–82)	50.6 (34.4–61.5)	0.10
BMI (kg/m^2)		24.8 (16.3–25.1)	20.6 (17.1–22.6)	0.09
Serum albmin (g/dL)		3.5 (1.6–4.6)	2.8 (1.3–4.3)	0.03
Lymphocyte		1411 (517–3643)	1008 (705–2280)	0.08
OPNI		44.1 (21.0–53.1)	29.7 (17.2–40.3)	＜0.01
CONUT		2.5 (0–11)	7.5 (3–11)	＜0.01
Approach	Laparoscopic	4	6	0.58
	Open	6	14	
Complication	Absense	4	0	0.02
(≥ Clavien-Dindo IIIa)	Non	6	20	

＊OPNI：Onodera's prognostic nutritional index, CONUT：controlling nutritional score
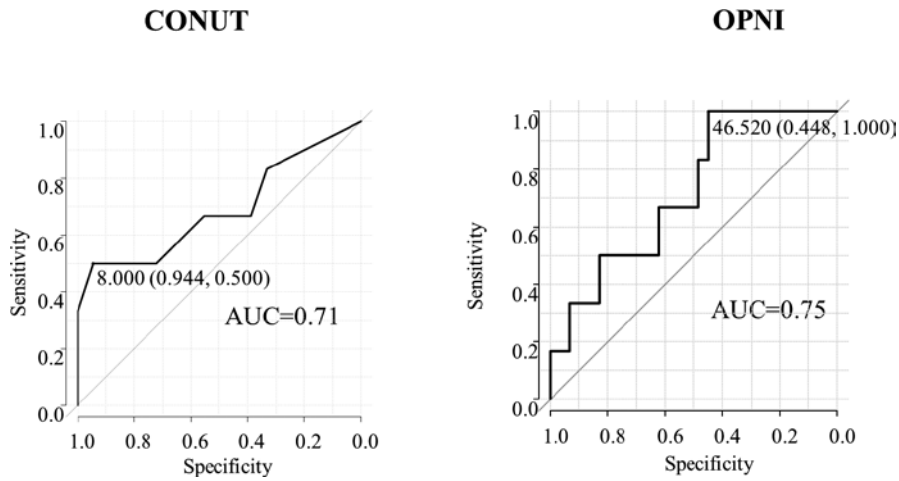
CONUT   **OPNI**

Figure1   ROC curve for CONUT and OPNI

The area under the curve for the frequency of postoperative complication was 0.72 and 0.75 for CONUT and OPNI, respectively.

＊ROC：receiver operating curve, OPNI：Onodera's prognostic nutritional index, CONUT：controlling nutritional score

Table 5   The malnutrition cohort as identified using CONUT and OPNI had a higher rate of postoperative complications than the non-malnutrition cohort（p＝0.04 and p＝0.01, respectively）.

Index	Score	Complication		p-value
		Present	Absent	
CONUT	≥ 8.00	10	2	0.04
	＜8.00	12	11	
OPNI	＜46.5	11	1	0.01
	≥ 46.5	11	12	

＊OPNI：Onodera's prognostic nutritional index, CONUT：controlling nutritional score

DISCUSSION

Despite the progress of medical therapy, which has increased the possible treatment options after failure of corticosteroids, surgery is still required in 15-35% of patients affected by UC[10]. This may reflect the increased implementation of surveillance strategies, the introduction of drugs that control inflammation more effectively, or the changing approach to maintenance therapy or colectomy. There is clear evidence that a delay in appropriate surgical treatment is detrimental to patient outcomes[11,12].

A staged proctocolectomy（with subtotal colectomy first）is considered to be wise as the first step in the surgical treatment of acute severe colitis or if patients have received prolonged steroid therapy. Subtotal colectomy with an ileostomy will spare patients from the burden of colitis.

Consequently, they will regain general health, normalized nutritional status, and have the time to consider carefully the options of an IPAA or of a permanent ileostomy. The handsewn or stapled rectosigmoid stump can be sutured as a mucosal fistula to the distal surface of the abdominal wall, closed and sutured to the subcutaneous tissue, or left unattached to the pelvis. The main reason for the creation of a mucousal fistula or the placement of a long rectal stump in the subcutaneous tissue is to avoid the destruction of the rectal stump and subsequent leakage with pelvic sepsis, especially in the case of severe colitis and tissue

thickening. The drawback of mucosal fistulas lies in the patient's dissatisfaction, which can occur with persistent secretions during a long recovery period. When performing a subtotal colectomy that leaves a rectal remnant, we always perform transanal rectal drainage for a few days to preverent a destruction of the rectal stump.

Several studies have reported a mean sepsis morbidity rate of 6.8% (4.8% during 30 days of surgery), with rates ranging between 5-24%[13~15]. Delaying definitive surgical treatment increases the risk, and patients with serious complications underwent surgery much later than those who recovered successfully. Patients who received >72 hours or more of preoperative treatment were significantly at increased risk of developing major postoperative complications. The serum albumin level and CRP have been important to assess the severity for UC. The serum albumin level is inversely related to the extent to the inflammatory response, which arises from the decreased albumin synthesis in the liver because of the hypercatabolic state associated with the inflammatory process and down regulation of synthesis by cytokines. The serum albumin level are not only evaluated as a marker of response to treatment, but also as a prognostic markers of long-term outcome. The low albumin level in acute severe UC predicts treatment failure and conversion to surgery[16~18]. Preoperative malnutrition is associated with postoperative complications and poor clinical outcomes. Albumin is the widely known indicator of nutritional status. The OPNI, which is calculated using the serum albumin level and total lymphocyte counts, was initially used to assess the immune-nutritional status. The present study shows that the OPNI is associated with outcomes in patient undergoing colorectal surgery[19].

CONUT, which is calculated using the serum albumin level, total cholesterol level, and total lymphocyte counts, is a nutritional evaluation score. The association of CONUT with postoperative complications has been previously reported[20,21]. The compositional difference between the PNI and CONUT score lies in the total cholesterol concentration. It is suggested that a lower cholesterol concentration has a detrimental effect on postoperative outcomes by affecting antioxidant reserve and inflammatory response[22]. Both of

OPNI and CONUT are obtained easily from a blood examination.

In our study, CONUT and OPNI were able to predict postoperative complications. When it is possible to predict postoperative complications before performing the surgery, surgeons may choose a method with a fewer risk such as three-stage surgery with the initial operation without anastomosis. Both of these nutritional indices were able to identify a useful prognostic marker and is cheap, reliable and readily available at the time of determination to surgery and predict the clinical course of UC.

In conclusion, it is important to assess preoperative nutritional status when deciding the timing of surgical intervention for UC.

This study has limitations in the forms of its retrospective design and that it only included patients from a single institution. Our findings warrant further consideration and validation in a large series of patients with UC.

Conflicts of Interest

There are no conflicts of interest.

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