Showa Univ J Med Sci **28**(4), 317～325, December 2016

Original

Controlling Nutritional Status is Useful for Predicting Postoperative Complications in very Elderly Patients with Colorectal Cancer : A Retrospective Study

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Abstract : Controlling Nutritional Status (CONUT) is an efficient tool for early detection of malnutrition, measured using two biochemical parameters (serum albumin and total cholesterol) and one immune indicator (total lymphocyte count). The aim of this study was to define the efficacy of CONUT for predicting postoperative complications in very elderly patients with colorectal cancer. This study enrolled 52 patients aged 85 years or older with colorectal cancer for whom we were able to measure CONUT before surgery, conducted at the Department of Gastroenterological and General Surgery of Showa University Hospital in Japan between January 2010 and December 2014. The patients were subdivided into those with complications (Group C, n = 9) and those with no complications (Group NC, n = 43), and then were retrospectively compared for clinical characteristics, CONUT, and surgical outcomes. Multivariate analysis was finally performed to identify the risk factors of complications. The percentage of patients with a CONUT score of 5 or more in Group C was significantly greater than that in Group NC (7 vs. 12 patients, 77.8% vs. 27.9%, $P = 0.0079$). No other significant difference was observed in the clinical characteristics between Group C and Group NC. Multivariate analysis identified CONUT score as the only significant predictor of complications in this patient cohort (odds ratio = 1.374 ; 95% confidence interval, 1.019–1.949 ; $P = 0.0366$). Our study suggests that CONUT score is predictive of postoperative complications in very elderly patients with colorectal cancer.

Key words : CONUT, complication, colorectal cancer, very elderly, prediction

Introduction

For this clinical study, we defined *very elderly* as 85 years or older. National Institutes of Health Global Health and Aging studies project that the number of people aged 65 or older will grow from an estimated 524 million in 2010 to nearly 1.5 billion in 2050 [1]. Thus, treating very elderly patients with colorectal cancer is likely to become more common in the future.

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Very elderly patients tend to have more concurrent diseases and are more likely to be malnourished than patients under 85 years. This often makes it more difficult to treat postoperative complications and increases hospital stays. Given these circumstances, a simple and useful predictor of postoperative complications in very elderly patients would be useful.

Preoperative malnutrition is known to delay wound healing and increase the likelihood of postoperative complications[2–5], highlighting the importance of nutritional assessment in surgical patients. Various methods can be used to determine patients' nutritional status; however, patients with colorectal cancer often need immediate treatment or surgery, depending on their condition such as perforation or ileus, thus an easy and quick method of nutritional assessment is preferred in such cases. Controlling nutritional status (CONUT), introduced by Ignacio *et al*[6], uses two biochemical parameters (serum albumin and total cholesterol) and one immune indicator (total lymphocyte count) to assess nutrition. The authors reported a significant statistical association between the evaluation of malnutrition with CONUT and the Subjective Global Assessment (SGA) method, and CONUT seemed to be an efficient tool for early detection of malnutrition[4, 7].

The aim of this study was to define the efficacy of CONUT for predicting postoperative complications in very elderly patients with colorectal cancer through a retrospective study.

Materials and methods

We retrospectively determined the CONUT score for 52 colorectal cancer patients aged 85 years or older (21 males and 31 females; median age 86 years) who were treated at the Department of Gastroenterological and General Surgery of Showa University Hospital in Japan, between January 2010 and December 2014.

The patient group was subdivided into those with (Group C) and without complications (Group NC), and then retrospectively compared for clinical characteristics, CONUT, and surgical outcomes. In addition, multivariate analysis was performed to detect the risk factors of complications.

Data were collected from medical records and pathology reports. We performed open or laparoscopic colectomy, ileocecal resection, high and low anterior resection, Hartmann's operation, colostomy, ileostomy, and bypass surgery depending on the location of cancer and the patients' condition. Similarly, depending on the patient's condition, D0-3 lymph node dissections and R0-1 (curability) surgery were performed.

The following variables were evaluated for clinical characteristics and surgical outcomes: sex, age, body mass index (BMI), clinical stage, American Society of Anesthesiologist (ASA) physical status classification, whether the operation was elective or emergent, surgical approach (open or laparoscopic), operative procedures, the existence of anastomosis, lymph node dissection, the number of lymph nodes retrieved, tumor size, operating time, blood loss, and the length of hospital stay after surgery. The following data were evaluated for postoperative complications: intra-abdominal abscess, anemia, sepsis, urinary tract infection (UTI), surgical site infection (SSI), pseudomembranous colitis, ileus, pneumonia, catheter-related bloodstream infection (CRBSI), and

Table 1. Assessment of malnutrition degree by CONUT

Parameter	Malnutrition Degree			
	Normal	Light	Moderate	Severe
Serum Albumin (g/dl)	≧ 3.5	3.0-3.4	2.5-2.9	< 2.5
Score	0	2	4	6
Total Lymphocytes/ml	≧ 1,600	1,200-1,599	800-1,199	< 800
Score	0	1	2	3
Cholesterol (mg/dl)	≧ 180	140-179	100-139	< 100
Score	0	1	2	3
Screening Total Score	0-1	2-4	5-8	9-12

anastomotic leakage. Patients were then graded based on the Clavien-Dindo classification and those with a grade higher than Grade Ⅱ were considered to have complications.

The assessment of malnutrition degree by CONUT is shown in Table 1. The levels of three parameters were scored as 0 to 6 points (by serum albumin) or 0 to 3 points (by the number of total lymphocytes and total cholesterol), and the sum of the provided score was calculated for the screening total score.

In addition, we classified all patients into two groups (Group A and Group B) according to their CONUT score to compare clinical characteristics and surgical outcomes. Group A (n = 33) included those patients whose CONUT score was 4 points or less, and in Group B (n = 19) the CONUT scores were 5 points or more.

Data are expressed as median and interquartile range. All statistical analyses were performed using JMP version 11.0 (SAS Institute Inc.). The intergroup comparisons were made using Wilcoxon rank sum test for continuous variables and Fisher's exact test for discrete variables. Binomial logistic regression analysis was performed for multivariate analysis. A P value of less than 0.05 was considered significant.

Prior to the start of the study, approval was obtained from the research ethics committee of Showa University Hospital and informed consent was obtained from all patients. All aspects of the study were conducted in accordance with the principles of the Declaration of Helsinki.

There are no conflicts of interest to declare.

Results

In our patient cohort, 9 patients (17.3%) had postoperative complications (Group C) and 43 patients had no complications (Group NC). Table 2 details each complication. Two patients whose CONUT score was 5 points or more died in hospital within 28 days after surgery, one at 1 day after surgery due to sepsis caused by colonic perforation, and the other developed pneumonia and died 28 days after surgery because of liver failure caused by liver metastasis.

Table 3 details the clinical characteristics, CONUT score, and length of hospital stay after surgery for Group C and NC. No significant difference was observed in the clinical character-

Table 2. Postoperative complications

	Patients (n = 52)
Total complications, n (%)	9 (17.3)
Intra-abdominal abscess	1 (1.9)
Anemia	1 (1.9)
Sepsis	1 (1.9)
Urinary tract infection	1 (1.9)
Surgical site infection	1 (1.9)
pseudomembranous colitis	1 (1.9)
Ileus	1 (1.9)
Pneumonia	1 (1.9)
CRBSI	1 (1.9)
Anastomotic leakage	0

CRBSI : Catheter-related bloodstream infection

istics between groups, but Group C showed a significantly greater percentage of patients whose CONUT score was 5 or more compared to Group NC (7 vs. 12 patients, 77.8% vs. 27.9%) and median length of hospital stay after surgery [21 days (interquartile range, 15–28.5 days) vs. 14 days (interquartile range, 10–19 days)] .

Table 4 shows the result of multivariate analysis to identify risk factors of postoperative complications. The only significant predictor of complications was the CONUT score (odds ratio = 1.374 ; 95% confidence interval, 1.019–1.949).

In comparing Group A and Group B patients, we observed the following significant differences. Compared to Group A, Group B patients had a lower median BMI [19.2 (interquartile ranges, 16.6–21.5) vs. 21.9 (interquartile range, 19.0–23.3)] , a higher percentage of emergent operations (63.2% vs. 6.1%), a smaller percentage of anastomosis (42.1% vs. 81.8%), greater median tumor size [50 mm (interquartile range, 40.0–70.0 mm) vs. 33.5 mm (interquartile range, 21.3–50.0mm)], a higher percentage of total complications (36.8% vs. 6.1%), and a higher percentage of infectious complications (31.6% vs. 3.0%). There was no other difference in the clinical characteristics or the surgical outcomes between Group A and Group B patients (Table 5).

Discussion

The results of our study suggest that CONUT can be used to predict postoperative complications in very elderly patients with colorectal cancer.

In regards to the method of risk assessment in the perioperative period, the operative severity score called, Physiological and operative severity score for the enumeration of mortality and morbidity (POSSUM), is well known in European counties, while the physiologic and surgical stress score, Estimation of physiologic ability and surgical stress (E-PASS), is known in Japan[8–10]. The efficacy of the modified POSSUM has been reported several times[11–13] ; however, both POSSUM and E-PASS are calculated based on preoperative physiological scores and surgical severity

Table 3. Clinical characteristics, CONUT, and the length of hospital stay after surgery in patients with and without complications

Characteristics	Group C (n = 9)	Group NC (n = 43)	*P* value
Sex (male/female)	5/4	16/27	0.3077
Median age, yr (range)	86 (85-87.5)	86 (85-89)	0.4189
Median BMI	19.5 (17.2-23.1)	21.3 (18.7-23.0)	0.4606
Clinical stage, n (%)			0.5475
I	0 (0.0)	10 (23.3)	
II A	4 (44.4)	14 (32.6)	
III A	1 (11.1)	3 (7.0)	
III B	1 (11.1)	7 (16.3)	
III C	0 (0.0)	1 (2.3)	
IV	3 (33.3)	8 (18.6)	
ASA, n (%)			0.9885
1	1 (11.1)	1 (2.3)	
2	5 (55.6)	29 (67.4)	
3	2 (22.2)	12 (27.9)	
4	1 (11.1)	1 (2.3)	
Operation type, n (%)			0.6453
Elective	7 (77.8)	36 (83.7)	
Emergent	2 (22.2)	7 (16.3)	
Surgical approach, n (%)			0.7280
Open	3 (33.3)	17 (39.5)	
Laparoscopic	6 (66.7)	26 (60.5)	
Anastomosis			0.6850
Anastomosis (+)	5 (55.6)	27 (62.8)	
Anastomosis (-)	4 (44.4)	16 (37.2)	
LN dissection, n (%)			0.8070
D0	2 (22.2)	7 (16.3)	
D1	2 (22.2)	6 (14.0)	
D2	4 (44.4)	24 (55.8)	
D3	1 (11.1)	6 (14.0)	
Curability, n (%)			1.0000
R0	8 (88.9)	35 (81.4)	
R1	1 (11.1)	8 (18.6)	
Median LN retrieved, n (range)	9 (0-15)	19 (7-16.5)	0.5844
Median tumor size, mm (range)	50 (28.8-65.3)	40 (28-50)	0.3087
Median operating time, min. (range)	165 (120-192.5)	135 (95-150)	0.1636
Median blood loss, g (range)	45 (1-442.5)	20 (1-50)	0.3045
CONUT			0.0079
4 points or less, n (%)	2 (22.2)	31 (72.1)	
5 points or more, n (%)	7 (77.8)	12 (27.9)	
Median hospital stay after surgery, days (range)	21 (15-28.5)	14 (10-19)	0.0430

LN : Iymph node, range: interquartile range

Table 4. Multivariate analysis for risk factor of complications

	Odds ratio	95% CI	*P* value
CONUT score	1.374	1.019-1.949	0.0366
Operating time	1.017	0.998-1.039	0.0650
Blood loss	1.001	0.996-1.005	0.4747
ASA	0.666	0.109-3.154	0.6206

ASA : American Society of Anesthesiologist

scores. This makes it impossible to assess the total scores without examining surgical parameters, which makes preoperative risk assessment difficult. Based on the present data, we suggest that postoperative complications can be simply and effectively predicted by using CONUT to assess a patient's nutritional status, simply by using a preoperative blood test. In addition, POSSUM relies on the particular patients ; however, in very elderly patients it becomes difficult to find a difference because the POSSUM scores are likely to be similar.

The malnutrition scoring by CONUT is evaluated according to four grades : normal (0-1 point), light (2-4 points), moderate (5-8 points), and severe (9-12 points). In this study, we set 5 points (moderate malnutrition degree) as the cutoff value because no significant difference was observed when we set the other points. To the best of our knowledge, there are no English language publications that report on the relationship between CONUT and postoperative complications. In Japan, Kudoh *et al*[14] reported that patients with gastric cancer and a preoperative CONUT score of 4 points or more might be at increased risk of postoperative complications, especially for remote organ infections. On the other hand, Sahara *et al*[15] observed no significant relationship between CONUT score and overall preoperative complications after gastrointestinal surgery in elderly patients, although they did find a significant relationship between the CONUT score and infectious complications. In our study, 7 of the 9 cases showing complications were infectious, and of these, 6 patients scored 5 points or more by CONUT (Table 5), suggesting that CONUT is also useful for predicting infectious complications.

In this study, patients whose CONUT score was 5 or more had a higher incidence of postoperative complications. In addition, we chose 4 factors (CONUT score, operating time, blood loss, and ASA) with some reported association to complications, but only the CONUT score was a significant predictor of complications by multivariate analysis. These data confirm the importance of improving a patient's nutritional status before surgery. Although this is not possible in cases of emergency surgery, patients undergoing an elective operation should therefore not undergo the procedure until their nutritional status is acceptable.

Table 5 indicates that patients in Group B (CONUT score of 5 points or more) had a lower mean BMI than those in Group A (CONUT score of 4 points or less), a higher percentage of emergent operations, and a lower percentage of anastomosis. Patients with a low BMI and emergency patients tend to be malnourished, a situation we often experience and typically resulting in preparation of a stoma rather than anastomosis to reduce the risk of anastomotic

Table 5. Clinical characteristics, the percentage of complications, and the length of hospital stay after surgery in patients by comparing CONUT score

Characteristics	Group A (n = 33)	Group B (n = 19)	*P* value
Sex (male/female)	13/20	8/11	0.8478
Median age, yr (range)	86 (85-88)	87 (86-92)	0.0888
Median BMI (range)	21.9 (19.0-23.3)	19.2 (16.6-21.5)	0.0044
Clinical stage, n (%)			0.1249
I	9 (27.3)	1 (5.3)	
II A	10 (30.3)	8 (42.1)	
III A	3 (9.1)	1 (5.3)	
III B	6 (18.2)	2 (10.5)	
III C	1 (3.0)	0 (0.0)	
IV	4 (12.1)	7 (36.8)	
ASA, n (%)			0.4608
1	1 (3.0)	1 (5.3)	
2	23 (69.7)	11 (57.9)	
3	9 (27.3)	5 (26.3)	
4	0 (0.0)	2 (10.5)	
Operation type, n (%)			0.0079
Elective	31 (93.9)	7 (36.8)	
Emergent	2 (6.1)	12 (63.2)	
Surgical approach, n (%)			0.1110
Open	10 (30.3)	10 (52.6)	
Laparoscopic	23 (69.7)	9 (47.4)	
Anastomosis			0.0055
Anastomosis (+)	27 (81.8)	8 (42.1)	
Anastomosis (-)	6 (18.2)	11 (57.9)	
LN dissection, n (%)			0.3149
D0	5 (15.2)	4 (21.1)	
D1	3 (9.1)	5 (26.3)	
D2	20 (60.6)	8 (42.1)	
D3	5 (15.2)	2 (10.5)	
Curability, n (%)			0.2597
R0	29 (87.9)	14 (78.7)	
R1	4 (12.1)	5 (26.3)	
Median LN retrieved, n (range)	13.5 (7.3-16.8)	7.0 (3.8-13.3)	0.0846
Median tumor size, mm (range)	33.5 (21.3-50)	50 (40-70)	0.0051
Median operating time, min. (range)	140 (110-172.5)	125 (95-170)	0.6274
Blood loss, g (range)	15 (1-45)	37.5 (1-95)	0.3390
Total complications, n (%)	2 (6.1)	7 (36.8)	0.0079
Infectious complications, n (%)	1 (3.0)	6 (31.6)	0.0071
Median hospital stay after surgery (days)	14 (10-19.5)	16 (13-24)	0.0957

LN : Iymph node, range: interquartile range

leakage after surgery. This procedural decision accounts for Group B having a lower percentage of anastomosis than Group A, and we did not see any anastomotic leakage in this study. On the other hand, the tumor size in Group B was greater than that in Group A, and we attribute this to either cachexia causing malnutrition or ileus caused due to the fact that the tumor itself might cause appetite loss.

Complications occurred in 17.3% of patients enrolled in this study, which is greater than the incidence across all patients (of all ages) with colorectal cancer treated surgically in our department in 2013 (13.7%, 22 complications in 161 patients, unpublished data). Although this comparison highlights the difficulty in treating very elderly patients, we believe that determining a patient's preoperative CONUT score is an effective and simple way to assess nutritional status, and in turn, reduce postoperative complications.

This study is retrospective, with a small number of subjects, and limited to very elderly patients. Therefore, a prospective study with a larger number of subjects is necessary to obtain more evidence around this issue, and to demonstrate with greater confidence of the efficacy of using CONUT for all patients undergoing colorectal cancer surgery.

Conflict of interest

The authors declare no conflicts of interest.

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[Received July 25, 2016 : Accepted September 7, 2016]