Master of Medicine

Impact of sarcopenia On the postoperative outcome and Recurrence in the patients with Crohn's disease

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Impact of sarcopenia On the postoperative outcome and Recurrence in the patients with Crohn's disease

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국문요약

크론병은 소화관의 모든 부위에 나타나는 만성적인, 진행성, 염증성 질환이며 영양실조와 관련이 깊은 것으로 알려져 있다. 크론병 환자들은 일생에 약 80%에서 복부수술을 받게 된다. 근감소증은 영양상태의 불량을 나타내는 하나의 지표이다. 본 연구에서는 크론병 환자에서 수술 전 근감소증이 수술 후 합병증과 재발에 끼치는 영향에 대해 분석하였다.

2006년 1월부터 2016년 12월까지 크롬 병으로 수술을 받은 환자를 대상으로 분석하였다. 수술 전 1개월이내에 있는 복부CT에서 3번째 요추 높이의 복부근육량을 측정하였다. 근감소증의 정의는 키와 총 복부근육량을 고려하여 한국기준에 맞추어 평가하였다. 총 569명의 환자 중 412명이 근감소증 환자군으로 분류되었고, 157명이 정상 환자군으로 분류되었다. 근감소증 환자군(14.8 ± 15.2)에서 정상 환자군(12.2 ± 11.4, P = 0.05)에 비해 수술 후 입원기간이 더 길었다. 다변량 분석 결과, 수술 전 항문 질환으로 수술을 받았거나(OR 2.607, P = 0.005), 수술 전 항문 주위 누공이 있는 경우에(OR 2.227, P = 0.021) 수술 후 합병증이 더 많았다. 수술 전 수혈을 시행하거나(OR 1.772, P = 0.023), 수술 전 근감소증이 있는 경우(OR 1.879, P = 0.049), 개복수술인 경우(OR 3.058, P = 0.004) 수술 후 합병증이 더 많았다. 수술 전후 근감소증 여부의 변화에 대한 하위집단 분석 따르면 수술 후 근감소증이 지속된 경우 수술 전 근감소증 유무와 상관 없이 수술적 재발 없는 생존율이 더 낮았다.

결론적으로, 크론병으로 수술을 받는 환자의 70%에서 수술 전 근감소증이 있다. 근감소증은 수술 후 발생하는 합병증의 위험요인 중 하나이며, 수술 후에도 근감소증이 지속되는 경우에는 무재발생존에 영향을 준다.

Keywords: Sarcopenia, Crohn's disease, Postoperative outcome

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Introduction

Crohn's disease (CD) is a chronic, progressive, and inflammatory condition on any sites of the alimentary tract and is well known to be associated with malnutrition, lower body mass index (BMI), and lower lean body mass[1-3]. Three-fourths of hospitalized patients with CD are malnourished and one third has a low BMI status[4] and the reasons of malnutrition in CD are associated with limited food intake, malabsorption, and treatment adverse events. Considering that up to 80% of patients with CD require abdominal surgery during their lifetime[5], surgeons easily encounter this malnourished patient with CD and worry about the patient's complications after surgery. When planning abdominal surgery, surgeons check and supplement correctable factors that associated postoperative complications, and one of the correctable factors is nutritional status[6].

Recently, the relationships between body composition and clinical outcomes have been extensively studied in the field of cancer research. Body composition parameters such as sarcopenia, visceral obesity, and muscle mass are now recognized as prognostic factor predicting toxicity and response to chemotherapy, and postoperative complications in cancer researches[7]. The patients with CD had alterations in their body composition that the simple BMI assessment may fail to detect the composition of lean and fatty body[8-10]. The altered composition in CD is associated with more severe phenotypes and may negatively impact on the clinical course of the disease, response to biologics treatment, need for surgery, and quality of life[4, 11-13].

Sarcopenia is a progressive and generalized muscle disorder that is associated with increased likelihood of adverse outcomes and sarcopenia is affected by nutritional status[14]. Patients with sarcopenia had significantly elevated costs of care during hospitalization regardless of whether they were young or old[15]. Patients with CD who require surgical intervention are relatively young, but if sarcopenia is a complication-related factor, a longer hospital stay and an increase in medical costs are also expected regardless of age. Until, now, sarcopenia is used mainly in research rather than in clinical practice, but if sarcopenia is included in nutritional factors related to postoperative complications in patients with CD, this could be a correctable factor in clinical practice.

The aims of the current study were to assess the body composition of the patients with CD underwent abdominal surgery and to investigate the association between the body composition and clinical outcomes including postoperative complications and recurrence outcomes.

Methods

Patients and variables

This retrospective study evaluated patients who underwent abdominal surgery for CD at the Asan Medical Center, Seoul, Korea between January 2006 and December 2016. Patients were included if they had undergone intestinal resection surgery, or strictureplasty to resolve CD pathology. Patients were excluded if they had undergone just biopsy, stoma-formation surgery, or closure of diverting stoma, and they were the age of 16 and under at the time of surgery. The following variables were collected: demographics, preoperative CD characteristics using the Montreal classification, history of previous abdominal and perineal surgery, history of perineal disease, duration of CD, preoperative medication, preoperative nutritional state (BMI, albumin, hemoglobin, replacement of fluid or feeding, sarcopenia index), operative finding [operative approach (open or laparoscopy), emergency operation, indication for surgery, method of anastomosis (hand-sewn or stapled), types of anastomosis (end-to-end, end-to-side, side-to-side), operation time, detailed operation name, and diverting ostomy], postoperative outcomes [postoperative length of hospital stay, complications (total, infection, or intra-abdominal), recurrence-free survival (clinical and surgical)].

Complications were classified as septic or non-septic complication. Septic complication included wound infection, abdominal abscess, anastomotic leak, enterocutaneous fistula, pneumonia, and urinary tract infection. Recurrence was classified into clinical and surgical recurrence. Clinical recurrence was defined as image study or colonoscopic findings, following development of patients' symptoms were indicated worsening of CD inflammation. Surgical recurrence was defined as re-operation for CD.

The study protocol was approved by the institutional review board of the Asan Medical Center (registration no.: 2020-0328), and the study was performed in accordance with the Declaration of Helsinki.

Assessment of sarcopenia and nutritional state

The visceral fat area (VFA, cm^2) and subcutaneous fat area (SFA, cm^2) were demarcated using the adipose tissue thresholds on CT. Visceral obesity (VO) was defined as a VFA $\geq$ 100 cm^2. The skeletal muscle index (SMI) was calculated as total abdominal muscle area (TAMA)/height^2 and sarcopenia was defined by an SMI of $\leq$ 49.0 cm^2/m^2 for men and $\leq$ 31.0 cm^2/m^2 for women using Korean specific cutoff value[16]. The BMI was calculated as weight (kg)/height^2 (m^2). A BMI above 25 was considered obesity and a BMI below 18.5 was considered underweight.

Preoperative anemia was defined as a hemoglobin level of less than 12 g/dL for women and 14 g/dL for men according to World Health Organization criteria. Hypoalbuminemia was defined as the level of serum albumin < 3.0 g/dL. Among the malnourished patients, patient who received nutritional support for weight maintenance during hospitalization before surgery were classified as follows; oral support (administration of the marketed oral nutritional supplements) and parenteral support. Malnourished status was defined as a state requiring nutritional support before surgery and unintentional weight low greater than 10% of the usual body weight over a period of 6 to 12 months.

To assess the effect of sarcopenia on clinical outcomes, the included patients were classified into two groups according sarcopenia; sarcopenic group (SG) and non-sarcopenic group (NSG). Besides, in this study, changes in the sarcopenia were calculated using follow-up CT performed between 6 and 18 months after intestinal resection surgery, and the effects of this changes on the outcomes of recurrences were investigated.

Statistical analysis

Discrete variables, including demographic and preoperative characteristics, operative methods, and operative details were analyzed using the χ^2 test to compare the SG group with NSG group. Continuous variables including, age at surgery, hospital stay, disease duration, and follow-up duration, were compared using unpaired Student's *t*-test. The recurrence-free survival rate was examined using the Kaplan-Meier method and compared using the log-rank test. Multivariable analyses using binary logistic regression were used to assess the risks of developing postoperative complication. Statistical significance was defined as $p < 0.05$, and all statistical analyses were performed using SPSS Statistics for Windows, version 21 (IBM Corp, Armonk, NY, USA).

Results

Baseline characteristics

A total of 569 patients were included in this study and the incidence of sarcopenia was 72.4% (412 patients). There was a significantly younger in the SG at diagnosis (SG: 25.3 ± 9.3 *vs.* NSG: 27.5 ± 10.4, $p = 0.02$) than in the NSG (25.3 ± 9.3 *vs.* 27.5 ± 10.4, $p = 0.02$). But, there was no significant differences between the SG and NSG for age at operation, the duration of disease prior to surgery, follow-up duration. The SG had higher rate of male patients (81.8% *vs.* 38.2%, $p = 0.001$), was lower

mean BMI (17.55 ± 2.52 *vs.* 20.46 ± 3.32, $p = 0.001$) and had higher rate of underweighted patients (66.0% *vs.* 35.0%, $p = 0.001$) than the NSG. There was more history of previous perianal surgery (44.8% *vs.* 33.1%, $p = 0.001$) and perianal fistula (56.3% *vs.* 40.1%, $p = 0.001$) in the SG, compared with the NSG. In the Montreal classifications, there was a difference only in A category, and the A1 ratio was significantly higher in the SG, compared with the NSG (12.9% *vs.* 8.3%, $p = 0.03$). Mean preoperative level of serum albumin were significantly lower in the SG than in the NSG (3.14 ± 0.51 *vs.* 3.25 ± 0.52, $p = 0.025$). Besides, the SG had higher rate of hypoalbuminemia (75.2% *vs.* 63.7%, $p = 0.003$) and anemia (90.8% *vs.* 75.8%, $p = 0.001$), compared with the NSG. The SG had more nutritional support before surgery than the NSG (7.5% *vs.* 2.5%, $p = 0.03$). There were no significant differences in family history, history of smoking, history of previous abdominal, and preoperative transfusion between the SG and the NSG (Table 1).

Operative characteristics

When analyzing the operation details, the rate of emergency operation was higher in the NSG than in the SG (14.6% *vs.* 6.8%, $p = 0.005$). The indication for surgery was not significantly different between the two groups, except that the peritonitis for surgery is higher in the NSG than the SG (15.3% *vs.* 8.0%, $p = 0.012$). More patients in the SG had stoma formation, compared with the NSG (18.7% *vs.* 13.4%, $p = 0.015$). The SG had longer mean operation time (170.9 ± 64.9 *vs.* 158.2 ± 61.3, $p = 0.034$). There were no significant differences in operative approach, type of anastomosis, and operative details between the SG and NSG (Table 2).

Postoperative outcomes

The SG tend to have longer postoperative length of hospital stay, compared with the NSG (14.8 ± 15.2 *vs.* 12.2 ± 11.4, $p = 0.05$). In terms of postoperative complication, there were no significant differences in total, infectious, intra-abdominal, and Clavien-Dindo classification grade ≥ III complications between the SG and NSG (Table 3). Nevertheless, on multivariable analysis, preoperative sarcopenia [NSG; relative risk (RR) = 0.532, 95%-confidence internal (CI): 0.283-0.998; $p = 0.049$] was a risk factor for total complication. Also, history of previous perianal surgery (RR = 2.607, 95%-CI: 1.336-5.089; $p = 0.005$), history of perianal fistula (No; RR = 0.449, 95%-CI: 0.228-0.885; $p = 0.021$), preoperative transfusion (yes; RR = 1.772, 95%-CI: 1.039-2.739; $p = 0.023$), BMI (under-weighted; RR = 1.711, 95%-CI: 1.024-2.86; $p = 0.004$), and operative approach (laparoscopy; RR = 0.327, 95%-CI: 0.153-0.699; $p = 0.004$) were risk factors for total complication (Table 4). On

recurrence-free survival (RFS) analyses, the 5-year clinical (SG, 43.7% ± 2.6% *vs.* NSG, 44.5% ± 4.1%, $p = 0.96$) and 5-year surgical RFS (SG, 92.2% ± 1.4% *vs.* NSG, 90.2% ± 2.5%, $p = 0.98$) were not significantly different between the SG and NSG (Figure 2).

Changes of sarcopenia and those effects on recurrence

In terms of the change of postoperative sarcopenia, 18 patients (4.4%) in the SG and 6 patients (3.8%) in the NSG did not perform CT follow-up, so the change could not be confirmed. Among the SG, 240 patients (58.2%) still showed sarcopenia (post-SG) and 154 patients (37.4%) recovered from sarcopenia (post-NSG) on postoperative follow-up CT. Of the NSG, 142 patients (90.4%) still non-sarcopenia (post-NSG) and only 4 patients (5.7%) changed to sarcopenia (post-SG) after bowel surgery (Figure 3). On RFS analyses, the 5-year clinical RFS was no significantly different between the post-SG and post-NSG (post-SG, 39.3% ± 3.2% *vs.* NSG, 46.7% ± 3.0%, $p = 0.24$), but the post-SG had significantly lower 5-year surgical RFS, compared with the post-NSG (88.7% ± 2.1% *vs.* 93.8% ± 1.5%, $p = 0.019$) (Figure 3). When subgroup analysis was performed on the change in sarcopenia within the each groups, of the preoperative SG, the 5-year surgical RFS rate of the post-SG was significantly lower than that of the post-NSG (89.1% ± 2.1% *vs.* 96.6% ± 1.5%, $p = 0.03$), but the 5-year clinical RFS was different between the two postoperative groups (39.9% ± 3.2% *vs.* 47.3% ± 4.2%, $p = 0.53$). On subgroup analysis, among the preoperative NSG, the 5-year clinical (22.2% ± 13.9% *vs.* 45.2% ± 4.3%, $p = 0.004$) and surgical RFS (77.8% ± 13.9% *vs.* 91.0% ± 2.5%, $p = 0.038$) in the post-SG was significantly lower than in the post-NSG (Figure 3).

Discussion

The current study showed the incidence of sarcopenia in patients with Crohn's disease requiring bowel surgery was around 72.4%. Although direct comparison seems difficult due to the heterogeneity in the definition of sarcopenia, the incidence in the current study seems to be quite high. Although there was no statistical difference in the duration of disease between the two groups, the age at diagnosis is younger in the SG. It can be presumed that sarcopenia may have occurred as the morbidity of the disease of prolonged. The incidence of perianal inflammation in patients with CD ranges from 25% to 80%[17]. The results of our study showed that the SG had more history of perianal fistula or perianal surgery,

which means that CD activity was not controlled, which may have led to sarcopenia. As a method of evaluating nutritional status, serum albumin, and hemoglobin values in addition to muscle volume can be measured. In this study significant hypoalbuminemia and anemia was observed in the SG. As in our study, preoperative serum albumin and hemoglobin levels were lower in the SG. It is thought that the difference between the two groups was due to the fact that interleukin-6, which is associated with activated Crohn's disease, blocks the synthesis of albumin or affects its degradation[18]. Although hemoglobin is not a direct marker of inflammation, but anemia is known to occur when chronic inflammation persists. As with this general idea, our study show that anemia was more common in the SG as a secondary effect of inflammation[19]. Sarcopenia and malnutrition in CD had a multifactorial etiology. Insufficient energy intake, malabsorption, enteric nutrient loss, and drug-related effects collectively influence each other to cause sarcopenia. Reduction of the general condition due to these various causes eventually lead to a decrease in the patient's performance and mobilization and that lead to atrophy of the muscle as well as a decrease in muscle development. In addition, there were reports that sarcopenia was associated with the severity of IBD[20], and there were results that it helped to make treatment decisions in IBD patients[21]. The decision on the timing of operation is an important factor in the operation of CD patients. Our study showed that emergency surgery was performed more frequently in the NSG due to peritonitis. Because the general condition was relatively good in the NSG, medical treatment was continued, and it is thought that emergency surgery was performed for peritonitis due to treatment failure of the medical treatment. In the SG, where the activity of CD was relatively poorly controlled, it can be assumed that bowel inflammation and bowel edema were more severe than in the NSG, and therefore the operation time and stoma formation rate were higher than those of the SG.

In general, it is expected that the nutritional status of the SG or the general condition of the patient will be poor. Zhang et al. compared the postoperative outcomes with and without sarcopenia in CD patients. They reported that the presence of sarcopenia in CD patients undergoing bowel resection is a factor that increases overall postoperative complications after surgery. Therefore the use of the SMI index together for sarcopenia with evaluation of nutritional status can be a cornerstone of the treatment process[22]. Nobuhide et al. reported that there were no differences in postoperative outcomes such as hospital day, incidence of Clavien-Dindo grade $\geq$ 2 complications, and in-hospital mortality among sarcopenia patients with panperitonitis[23]. According to our results, there was no difference in overall postoperative complications, and the postoperative length of hospital stay tended to be longer in the SG. According to a multivariable analysis of overall postoperative complications, history of perianal involvement, preoperative blood transfusion, preoperative sarcopenia, preoperative under-weighted, and open approach surgery were found to be influencing factors on overall postoperative outcomes after

surgery. It has been reported that anal involvement of CD has a more aggressive disease course and requires more intensive treatment[24]. Our results also showed that perianal involvement increased the incidence of postoperative complications. This result is probably due to the involvement of the anus with disease progression. The results of previous studies on the association between perioperative blood transfusion and adverse postoperative outcomes are controversial. The results of our study showed a high risk for overall postoperative complications, which is considered to be an increased inflammatory response or immunosuppression response by transfused red cells[25]. Recently, even in emergency surgery, there were reported that laparoscopic surgery has advantages in postoperative pain, hospital day, and recovery compared to open surgery. laparoscopic surgery may cause less tissue damage, inflammation, and immune dysfunction than open surgery[26]. Although inexperienced surgeons may prefer open surgery due to insufficient bowel preparation and fragile inflammatory tissue, it is advantageous to try laparoscopy if possible. In addition to surgery, recent studies have shown that muscle mass is considered an important factor in anti-TNF therapy, one of the main treatments for CD patients. It is possible that the muscle affects the anti-TNF storage and anti-inflammatory action, and it is thought that it will affect the determination of the appropriate therapeutic dose of medication[27, 28]. In our study, there was no difference according to medication in SG and NSG, and additional studies are needed to investigate the effect of postoperative complications depending on medication and sarcopenia.

Holt et al. reported that visceral adiposity but not sarcopenia could predict endoscopic recurrence after surgery with Crohn's disease[29]. When analyzing the presence or absence of sarcopenia after surgery, there was a difference only in 5-year surgical RFS, and it is thought that recovery of the patient's nutritional status after surgery could be used as one predictor of disease control. We analyzed that there would be differences in surgical and clinical RFS according to changes in muscle index compared to pre-operative conditions after surgery, and this difference could be used as a major predictor for recovery after surgery. In subgroup analysis, preoperative SG and NSG were re-evaluated for sarcopenia at 6 months after surgery. Regardless of the muscle volume condition before surgery, if sarcopenia persists due to postoperative complication or no improvement in nutritional status at 6 months after surgery, the rate of disease recurrence was high, and escalation of medical treatment in CD can be considered as an indicator. Persistent sarcopenia is one of the several other host factors in CD patients, and is expected as a new indicator to evaluate the severity of the disease and the responsiveness of treatment.

Our study has several limitations. First, as a retrospective study after surgery, selection bias may occur, but the bias was reduced by including all patients who had undergone surgery for CD for a specific

period without artificial exclusion. Second, our study was conducted only in a single medical center, and there may be limitation in diversity and surgical treatment methods. However, it is a center that has experience in CD and is standardized for surgical and medical treatment. The operation was also performed by a surgeon with experience in CD.

Conclusion

More than 70% of patients with CD disease just before surgery had sarcopenia. Sarcopenia was one of risk factors for overall postoperative complication and the sustained sarcopenia after bowel resection might be affected on RFS. If sarcopenia persists after surgery, aggressive treatment may be considered

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Table 1 Demographics of the sarcopenia group and the non-sarcopenia group

Variables	Sarcopenia (n = 412)	Non-sarcopenia (n = 157)	*p*
Age at operation, years	31.2 ± 9.4	32.6 ± 9.8	*0.12*
Age at diagnosis, years	25.3 ± 9.3	27.5 ± 10.4	***0.02***
Sex, female/male	75 (18.2)/ 337 (81.8)	97 (61.8)/ 60 (38.2)	***0.001***
Duration of disease, months	75.1 ± 62.6	66.8 ± 58.4	*0.14*
Follow-up duration, months	88.8 ± 36.1	88.9 ± 34.0	*0.97*
BMI at operation, kg/m^2	17.55 ± 2.52	20.46 ± 3.32	***0.001***
Classification of BMI			***0.001***
underweighted	272 (66.0)	55 (35.0)	
normal range	137 (33.3)	84 (53.5)	
overweighted	3 (0.7)	18 (11.5)	
Family history of CD			*0.99*
Yes	14 (3.4)	5 (3.2)	
No	398 (96.6)	152 (96.8)	
History of smoking			*0.28*
None	261 (63.3)	107 (68.2)	
Ex-smoker	104 (25.2)	39 (24.8)	
Current smoker	47 (11.4)	11 (7.0)	
History of previous abdominal surgery			*0.8*
Yes	130 (31.6)	51 (32.5)	
No	282 (68.4)	106 (67.5)	
History of previous perianal surgery			***0.013***
Yes	184 (44.8)	51 (33.1)	
No	227 (55.2)	105 (66.9)	
History of perianal fistula			***0.001***
Yes	232 (56.3)	63 (40.1)	
No	180 (43.7)	94 (59.9)	
Montreal classification age, years			***0.03***
≤ 16 (A1)	53 (12.9)	13 (8.3)	
> 16, ≤ 40 (A2)	329 (79.9)	123 (78.3)	
> 40 (A3)	30 (7.3)	21 (13.4)	
Montreal classification behavior			*0.84*
Non-stricturing, non-penetrating (B1)	20 (4.9)	6 (3.8)	
Stricturing (B2)	145 (35.2)	54 (34.4)	
Penetrating (B3)	247 (60.0)	97 (61.8)	
Montreal classification location			*0.19*
Ileum (L1)	143 (34.7)	65 (44.4)	
Colon (L2)	35 (8.5)	8 (5.1)	
Ileocolon (L3)	234 (56.8)	84 (53.5)	

Preoperative level of serum albumin			***0.003***
hypoalbuminemia (< 3.5mg/dL)	314 (76.2)	100 (63.7)	
normal range	98 (23.8)	57 (36.3)	
Preoperative level of hemoglobulin			***0.001***
anemia (woman < 12 mg/dL, man < 14 mg/dL)	374 (90.8)	119 (75.8)	
normal range	38 (9.2)	38 (13.4)	
Preoperative transfusion			*0.26*
Yes	183 (44.4)	61 (38.9)	
No	229 (55.6)	96 (61.1)	
Preoperative nutritional support			***0.03***
Yes	31 (7.5)	4 (2.5)	
No	381 (92.5)	153 (97.5)	

Results reported as mean ± SD or no. (%) of patients.

Table 2. Operative details of the sarcopenia group and the non-sarcopenia group

Variables	Sarcopenia (n = 412)	Non-sarcopenia (n = 157)	*p*
Operative approach			*0.36*
Open	352 (85.4)	129 (82.2)	
Laparoscopy	60 (14.6)	28 (17.8)	
Emergency operation	28 (6.8)	23 (14.6)	***0.005***
Indication for surgery			
Abscess at the time of surgery	99 (24.0)	34 (21.7)	*0.58*
Obstruction at the time of surgery	130 (31.6)	46 (29.3)	*0.69*
Fistula at the time of surgery	125 (30.3)	47 (29.9)	*0.99*
Peritonitis at the time of surgery	33 (8.0)	24 (15.3)	***0.012***
Others	25 (6.1)	6 (3.8)	*0.14*
Methods of anastomosis			***0.015***
Hand-sewn	16 (3.9)	0 (0)	
Stapled	319 (77.4)	136 (86.6)	
Stoma formation without anastomosis	77 (18.7)	21 (13.4)	
Types of anastomosis			*0.73*
End-to-end	21 (6.3)	6 (4.4)	
End-to-side	30 (9.0)	13 (9.6)	
Side-to-side	284 (84.8)	117 (68.0)	
Operation time, min	170.9 ± 64.9	158.2 ± 61.3	***0.034***
Operative details			*0.39*
Small bowel surgery (SBS) only	101 (24.5)	48 (30.6)	
ICR with or without SBS	122 (29.6)	52 (33.1)	
RHC with or without SBS	102 (24.8)	37 (23.6)	
TC with or without SBS	41 (10.0)	11 (7.0)	
TPC with or without SBS	23 (5.6)	6 (3.8)	
LHC, AR, or LAR with or without SBS	13 (3.1)	1 (0.6)	
APR or Hartmann's procedure	10 (2.5)	2 (1.3)	

Results reported as no. (%) of patients.

Table 3. Operative outcomes of the sarcopenia group and the non-sarcopenia group

Variables	Sarcopenia (n = 412)	Non-sarcopenia (n = 157)	*p*
Postoperative length of hospital stay, day	14.8 ± 15.2	12.2 ± 11.4	***0.05***
Total postoperative complication, yes	117 (28.4)	40 (25.5)	*0.53*
Infectious complication, yes	90 (21.8)	29 (18.5)	*0.42*
Intra-abdominal complication, yes	47 (11.4)	17 (10.8)	0.99
Clavien-Dindo Classification grade ≥ III complications	54 (13.1)	24 (15.3)	0.5
5-year clinical recurrence-free survival, %	43.7 ± 2.6	44.5 ± 4.1	0.96
5-year surgical recurrence-free survival, %	92.2 ± 1.4	90.2 ± 2.5	*0.98*

Table 4. Multivariable analysis for the overall postoperative complication

Variables	Univariable	Multivariable		
	p-value	Exp (B)	95% CI	*p-value*
Sex	*0.014*			*0.051*
History of previous abdominal surgery				*0.91*
History of previous perianal surgery				***0.005***
No		1		
Yes		2.607	1.336–5.089	
History of perianal fistula	*0.3*			***0.021***
Yes		1		
No		0.449	0.228–0.885	
Montreal classification, age	*0.87*			*0.61*
Montreal classification, behavior	*0.007*			*0.2*
Montreal classification, location	*0.006*			*0.31*
Preoperative hypoalbuminemia	*0.75*			*0.22*
Preoperative anemia	*0.41*			*0.34*
Preoperative nutritional support	*0.13*			*0.09*
Preoperative blood transfusion	***0.001***			***0.023***
No		1		
Yes		1.772	1.039–2.739	
Preopearative sarcopenia	*0.53*			***0.049***
Yes		1		
No		0.532	0.283–0.998	
BMI	*0.64*			***0.04***
Normal or over-weighted		1		
Under-weighted		1.711	1.024–2.86	
Smoking	*0.55*			*0.77*
Emergency operation	*0.14*			*0.29*
Operative approach	***0.001***			***0.004***
Open		1		
Laparoscopy		0.327	0.153–0.699	
Method of anastomosis	***0.034***			*0.061*
Types of anastomosis	*0.07*			*0.26*

CI, confidence interval; BMI, body mass index

Figure 1. Study progress flow chart

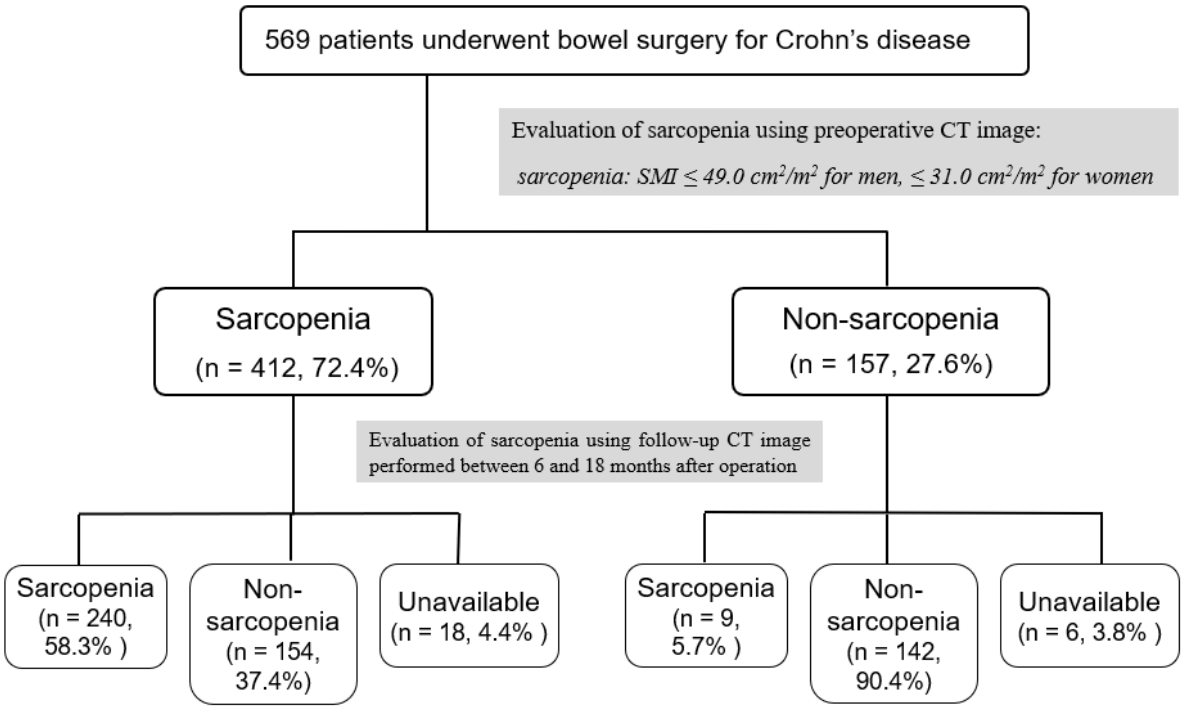


Figure 2. Clinical(a,c) and surgical(b,d) recurrence-free survivals in terms of the sarcopenia or the non-sarcopenia according to the pre- and post -operative period

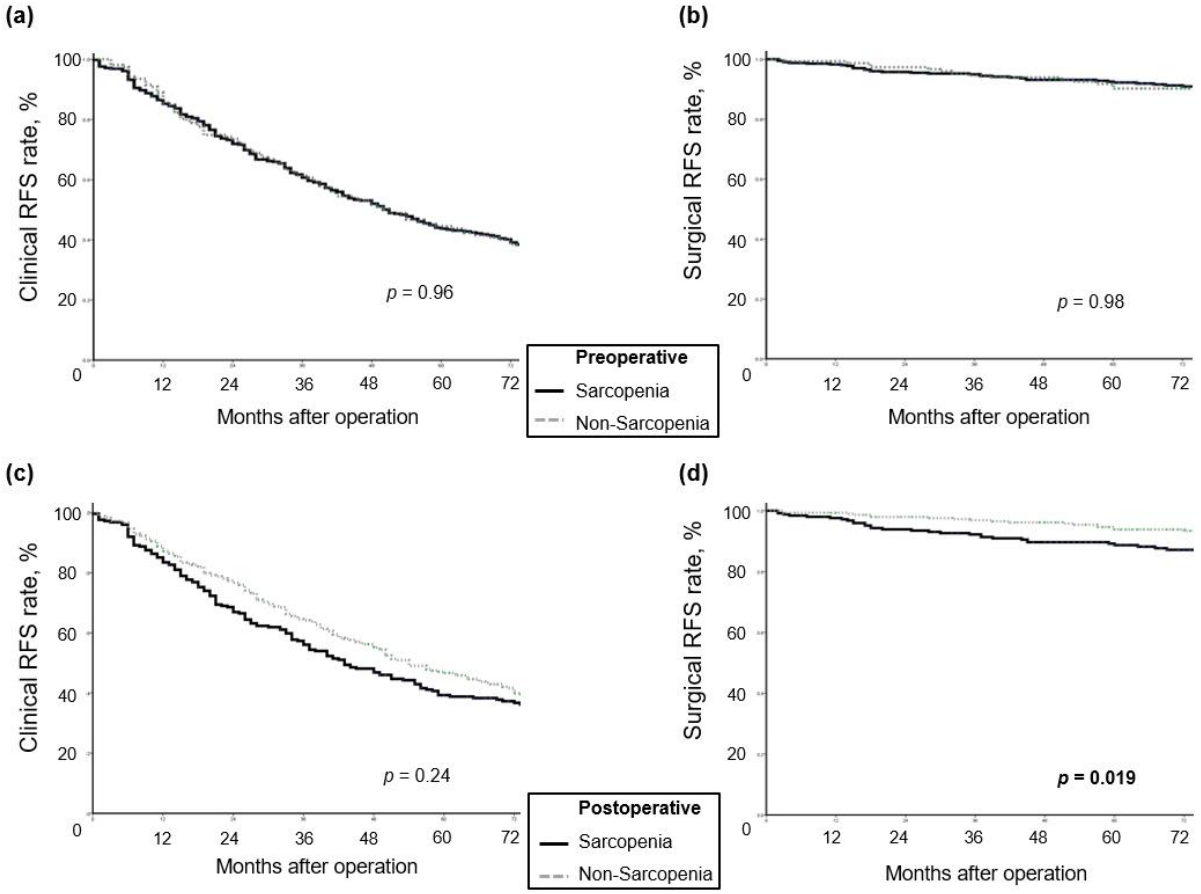
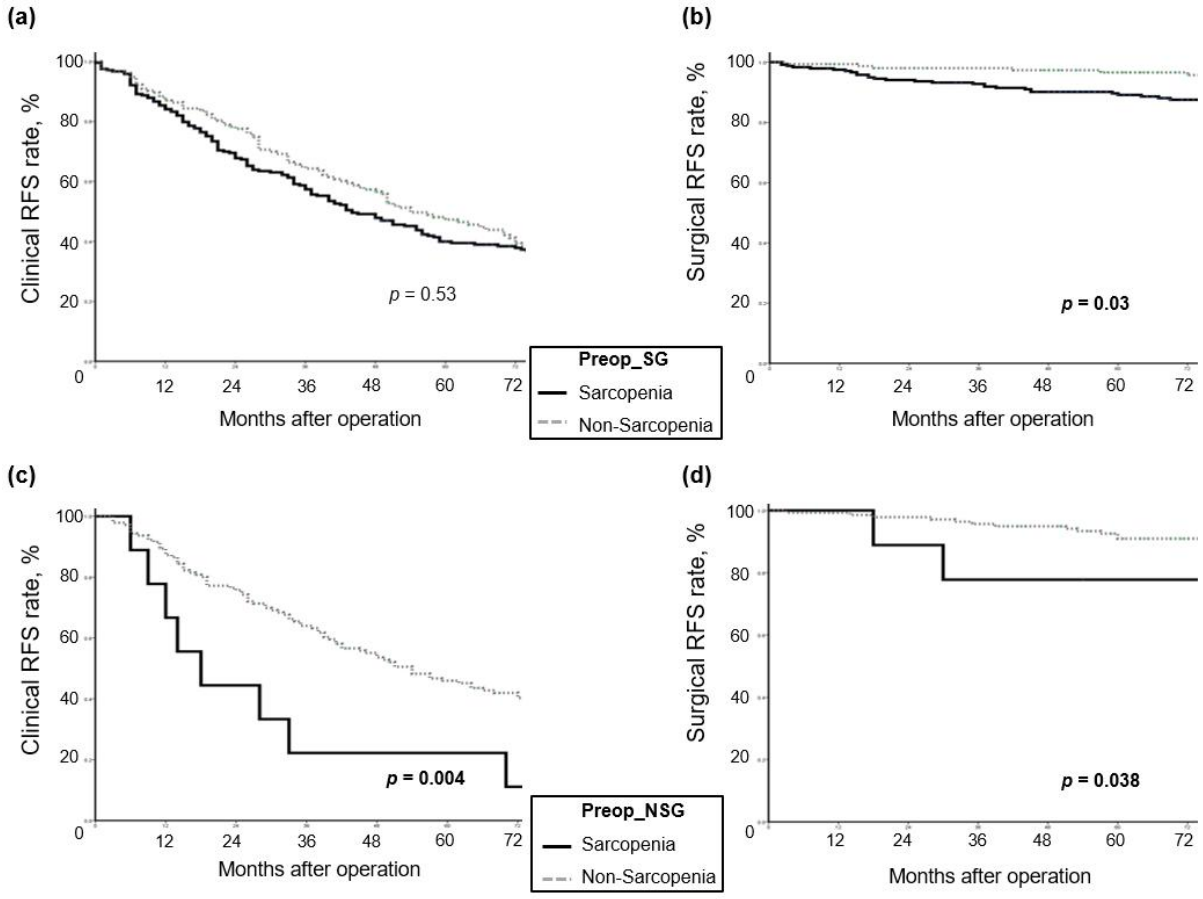


Figure 3. Clinical(a,c) and surgical(b,d) recurrence-free survivals in terms of the change of sarcopenia status according to the preoperative sarcopenia or non-sarcopenia



Abstract

Background

Crohn's disease (CD) is chronic, progressive, and inflammatory condition on any sites of the alimentary tract and is well known to be associated with malnutrition. Patients with CD will require abdominal surgery in 80% of their lifetime. Sarcopenia is an indicator of poor nutrition status. This study evaluated the effects of preoperative sarcopenia on postoperative outcomes including complication and recurrence.

Method

This single-center, retrospective study included patients who underwent abdominal surgery for CD between January 2006 and December 2016. This study analyzed the data using abdominal computed tomography (CT) images at the inferior endplate level of the 3rd lumbar vertebra taken within 1 month before surgery. The skeletal muscle index (SMI) was calculated as total abdominal muscle area (TAMA) / height^2 and sarcopenia was defined SMI of $\leq$ 49.0 cm^2/m^2 for men and $\leq$ 31.0 cm^2/m^2 for women using Korean specific cutoff value. The BMI was calculated as weight (kg)/height^2 (m^2). A BMI above 25 was considered obesity and a BMI below 18.5 was considered underweight.

Results.

Of the 569 patients enrolled, 412 patients (72.4%) had preoperative sarcopenia (sarcopenia group, SG) and 157 patients (27.6%) were within the normal range (non-sarcopenia group, NSG). There was a significantly younger in the SG at diagnosis (SG: 25.3 ± 9.3 *vs.* NSG: 27.5 ± 10.4, $p = 0.02$) than in the NSG (25.3 ± 9.3 *vs.* 27.5 ± 10.4, $p = 0.02$), and had higher rate of male patients (81.8% *vs.* 38.2%, $p = 0.001$), was lower mean BMI (17.55 ± 2.52 *vs.* 20.46 ± 3.32, $p = 0.001$), compared with the NSG. The NSG was related to emergency operation (14.6% *vs.* 6.8%, $p = 0.005$), and peritonitis (15.3% *vs.* 8.0%, $p = 0.012$), compared with the SG. The SG tend to have longer postoperative length of hospital stay, compared with the NSG (14.8 ± 15.2 *vs.* 12.2 ± 11.4, $p = 0.05$). On multivariable analysis, preoperative sarcopenia [NSG; relative risk (RR) = 0.532, 95%-confidence internal (CI): 0.283-0.998; $p = 0.049$] was a risk factor for total complication. Checking the change of postoperative sarcopenia using the followed-up CT, 240 patients (58.2%) of the SG still showed sarcopenia (post-SG) and 154 patients

(37.4%) recovered from sarcopenia (post-NSG). Of the NSG, 142 patients (90.4%) still non-sarcopenia (post-NSG) and only 4 patients (5.7%) changed to sarcopenia (post-SG) after bowel surgery. On RFS analyses, the 5-year clinical RFS was not significantly different between the post-SG and post-NSG (post-SG, 39.3% ± 3.2% *vs.* NSG, 46.7% ± 3.0%, $p = 0.24$), but the post-SG had significantly lower 5-year surgical RFS, compared with the post-NSG (88.7% ± 2.1% *vs.* 93.8% ± 1.5%, $p = 0.019$).

Conclusion

More than 70% of patients with CD disease just before surgery had sarcopenia. Sarcopenia was one of risk factors for overall postoperative complication and the sustained sarcopenia after bowel resection might be affected on RFS.