

# Preoperative evaluation of skeletal muscle mass in the risk assessment for the short-term outcome of elderly colorectal cancer patients undergoing colectomy

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Received January 25, 2018; Accepted March 28, 2018

DOI: 10.3892/mco.2018.1607

**Abstract.** The prevalence of colorectal cancer in the elderly population is increasing; therefore, surgical interventions with a risk of potential complications are more frequently performed. The aim of the present study was to elucidate whether sarcopenia has a clinical impact on short-term outcomes, such as morbidity and hospital stay after surgery, in elderly patients with colorectal cancer. A total of 82 elderly patients undergoing colectomy for colorectal cancer between January 2011 and December 2015 in our institute were included in the study, and skeletal muscle mass was measured as total psoas area at the level of the third lumbar vertebra (L3) using enhanced computed tomography scans. The patients were divided into two subgroups, namely those with and those without sarcopenia, based on median skeletal muscle mass in men and women, and the association with complications was analyzed. A total of 40 patients (48.8%) were diagnosed with sarcopenia. The patients with sarcopenia exhibited a significantly higher incidence of total complications (55 vs. 31.0%,  $P=0.028$ ) and longer hospital stay ( $25.9\pm 21.2$  vs.  $18.2\pm 8.5$  days,  $P=0.039$ ). The multivariate logistic analysis revealed that sarcopenia was an independent risk factor for postoperative surgical complications. The short-term outcomes, such as postoperative surgical complications and hospital stay, were affected by preoperative sarcopenia in elderly colorectal cancer patients. To improve the short-term outcomes of such patients, it is necessary to carefully plan the surgical procedure, perioperative care and the surgical strategy using preoperative sarcopenia assessment.

## Introduction

Colorectal cancer is the third most commonly diagnosed cancer in men and the second in women, with an estimated 1.4 million new cases and 693,900 deaths occurring in 2012 (1,2). Complete resection is crucial for the cure of colorectal cancer. However, the morbidity and mortality of radical colectomy are 20-30 and 1-2%, respectively (3-7).

The number of elderly patients with colorectal cancer is rapidly growing worldwide. With individuals aged  $\geq 80$  years representing the fastest growing subset of the population, the management of complex surgical issues is becoming increasingly more challenging (8). Elderly patients more often have co-morbidities and age-related physiological problems compared with non-elderly patients. Elderly patients are likely to exhibit a reduction in skeletal muscle mass and function with aging (9). Skeletal muscle is crucial to physical function, health and quality of life, while muscle mass and strength are clearly compromised in elderly patients (10).

It was recently demonstrated that preoperative sarcopenia is a risk factor for surgical complications (11,12). In addition, a number of previous studies have demonstrated that the development of postoperative complications increases the risk of disease recurrence in various types of malignancies (13-16). Therefore, it is important to predict the occurrence of complications prior to surgery and to determine the most appropriate perioperative care.

The aim of the present study was to elucidate whether sarcopenia has a clinical impact on short-term outcomes, such as morbidity and hospital stay after surgery, in elderly patients with colorectal cancer.

## Patients and methods

**Patients.** A total of 82 consecutive patients were selected from the database of the Department of Surgery of Kamishirane Hospital (Yokohama, Japan) according to the following criteria: i) Histologically-proven colorectal adenocarcinoma, ii) patients who underwent curative colectomy for colorectal cancer as a primary treatment between January 2011 and

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**Key words:** sarcopenia, colorectal cancer, complications

Table I. Patient demographic and clinicopathological characteristics.

Factors	All (n=82)	Sarcopenia (n=40)	No sarcopenia (n=42)	P-value
Sex, n (%)				0.837
Male	38 (46.3)	19 (47.5)	19 (45.2)	
Female	44 (53.7)	21 (52.5)	23 (54.8)	
Age (mean ± SD), years	86.1±4.9	86.4±4.8	85.6±5.0	0.444
BMI (mean ± SD), kg/m <sup>2</sup>	20.7±3.9	21.7±4.2	19.8±3.1	0.023 <sup>a</sup>
ASA grade, n (%)				0.621
I, II	33 (40.2)	15 (37.5)	18 (42.9)	
III, IV	49 (58.8)	25 (62.5)	24 (57.1)	
Comorbidities, n (%)				
Hypertension	42	21 (52.5)	21 (50.0)	0.821
Diabetes mellitus	16	7 (17.5)	9 (21.4)	0.654
Cerebrovascular disease	13	8 (20.0)	5 (11.9)	0.316
COPD	6	4 (10.0)	2 (4.8)	0.363
Tumor location, n (%)				0.665
Colon	72	34 (87.2)	38 (90.2)	
Rectum	9	5 (12.8)	4 (9.8)	
Pathological T factor, n (%)				0.097
T1, T2	13	4 (10.0)	9 (23.8)	
T3, T4	68	36 (90.0)	32 (76.2)	
Pathological N factor, n (%)				0.852
Negative	47	23 (57.5)	24 (59.5)	
Positive	34	17 (42.5)	17 (40.5)	
Pathological stage, n (%)				0.738
I/II	41	21 (52.5)	20 (48.8)	
III/IV	40	19 (47.5)	21 (51.2)	

<sup>a</sup>Statistically significant difference. BMI, body mass index; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; SD, standard deviation.

October 2016, iii) patients who did not experience weight loss prior to surgery and iv) patients who had undergone abdominal computed tomography (CT) imaging within 1 month prior to surgery.

**Assessment of skeletal muscle mass.** To assess skeletal muscle mass related to sarcopenia, which is defined as a decrease in muscle mass due to aging and/or other causes, the skeletal muscle area at the level of the third lumbar vertebra (L3) in a preoperative CT horizontal section [psoas muscle index (PMI), calculated as psoas muscle cross-sectional area (cm<sup>2</sup>)/height (m<sup>2</sup>)] was used to calculate the median of each man and woman as a cut-off value. Regarding the actual measurement of the skeletal muscle area, the outline of the large psoas muscle was traced as the region of interest in the CT image and the total area was calculated.

**Surgical procedure.** The type of the surgical approach was determined by each surgeon. In principle, laparoscopic-assisted surgery was performed by a 5-port method under general and epidural anesthesia (17). Functional end-to-end anastomosis was performed for right-sided colectomy, and the

double-stapling technique was performed for left-sided colectomy and anterior resection of the rectum. The number and position of intra-abdominal drainage tubes were determined by each surgeon. Pathological staging was performed according to the Union for International Cancer Control classification (18). The appropriate length of resection and the levels of lymph node dissection were determined by the 2010 Japanese Society for Cancer of the Colon and Rectum Guidelines (19,20).

**Perioperative care.** In principle, the patients received the same perioperative care. In brief, the patients were allowed to eat until midnight on the day prior to surgery and were required to drink the contents of two 500-ml bottles containing oral rehydration solution until 3 h prior to surgery. The nasogastric tube was removed on postoperative day (POD) 1. Oral intake was initiated on POD 2, beginning with water and an oral nutritional supplement. The patients began to eat solid food on POD 3, starting with rice gruel and soft food on POD 3 and advancing stepwise to regular food intake on POD 7. The patients were discharged when they had achieved adequate pain relief and soft food intake, had returned to their preoperative mobility level and had normal laboratory results.

Table II. Patient preoperative laboratory data.

Factors	All (n=82)	Sarcopenia (n=40)	No sarcopenia (n=42)	P-value
Hemoglobin (g/dl)	11.1±2.0	10.8±1.9	11.3±2.0	0.110
Total protein (g/dl)	6.2±0.7	6.2±0.9	6.3±0.6	0.602
Albumin (g/dl)	3.3±0.6	3.3±0.5	3.2±0.6	0.543
C-reactive protein (mg/dl)	0.32±0.24	0.41±0.15	0.23±0.20	0.090

Table III. Postoperative surgical complications according to the Clavien-Dindo classification.

Grade	Complications	No.
II	TIA	1
	SSI	9
	Ileus	2
	Pneumonia	3
	Colitis	2
	Urinary tract infection	3
	Renal failure	1
IIIa	Pleural effusion	1
	Intraperitoneal abscess	1
	Ileus	5
IIIb	Anastomotic leakage	2
	Gallbladder perforation	1
	Ileus	1
IVa	Anastomotic leakage	1
V	Pneumonia	2
	Heart failure	1

TIA, transient ischemic attack; SSI, surgical site infection.

**Evaluation of operative morbidity and mortality.** Surgical and non-surgical complications were assessed prospectively and were classified according to the Clavien-Dindo classification (21). Operative mortality was defined as postoperative death from any cause within 30 days after surgery or during the same hospital stay.

**Evaluations and statistical analyses.** Univariate and multivariate logistic regression analyses were performed to identify the risk factors for morbidity. Comparisons between the two groups were analyzed by the Chi-squared test. Linear regression models were fitted to the multivariate analysis. To select a model, backward elimination was used. All statistical tests were two-sided, and significance was set at  $P < 0.05$ . The SPSS software package (v11.0 J Win; SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. This study was approved by the Institutional Review Board of the Kamishirane Hospital.

## Results

**Patients.** A total of 82 patients were selected for this study. The clinicopathological characteristics of the patients are

summarized in Table I. The median age of the study population was 85 years, 38 patients were male and 44 were female. Of the 82 patients, 31 received right-sided colectomy, 39 received left-sided colectomy, and 11 underwent rectal resection. The median duration of the surgery was 125 min (range, 62-287 min) and the median blood loss was 110 ml (range, 50-1,250 ml).

**Cut-off values for L3 skeletal muscle mass index (SMI).** The sex-specific cut-off values for L3 SMI associated with complications were 11.9 cm<sup>2</sup>/m<sup>2</sup> for men and 9.6 cm<sup>2</sup>/m<sup>2</sup> for women, obtained by means of optimum stratification. Using these cut-off values, 48.8% of the patients were found to be sarcopenic. Clinical associations in patients with or without sarcopenia are shown in Tables I and II. Patients with sarcopenia exhibited a higher BMI compared with those without sarcopenia ( $P = 0.023$ ).

**Surgical morbidity and mortality.** Postoperative complications were observed in 35 of the 189 patients (42.7%). Surgical-related mortality was reported in 3 cases in the present study. The details of the complications are presented in Table III. Ileus and surgical site infection were the most frequently diagnosed complications, followed by pneumonia and anastomotic leakage.

**Risk factors for surgical morbidity.** The risk factors for surgical morbidity were analyzed by univariate and multivariate analyses using the preoperative and perioperative factors. The results are summarized in Table IV. Among the various factors examined, sarcopenia ( $P = 0.027$ ) and intraoperative bleeding ( $P = 0.010$ ) were identified as statistically significant independent risk factors for overall morbidity.

## Discussion

The aim of the present study was to elucidate whether preoperative sarcopenia has a clinical impact on short-term outcomes, such as morbidity and hospital stay after surgery, in elderly patients with colorectal cancer. The major finding of the present study was that both short-term outcomes were affected by preoperative sarcopenia in elderly patients with colorectal cancer. A high degree of sarcopenia was an independent risk factor for postoperative complications and longer hospital stay. To improve the short-term outcomes of sarcopenic elderly patients with colorectal cancer, it is necessary to carefully plan the surgical procedure, perioperative care and surgical strategy.

First, regarding the association between preoperative sarcopenia and postoperative surgical complications, the

Table IV. Univariate and multivariate logistic regression analysis for postoperative surgical complications.

Factors	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Sarcopenia				
No	1.000		1.000	
Yes	2.726 (1.105-6.728)	0.030	3.508 (1.154-10.653)	0.027
Age, years				
<85	1.000			
≥85	0.741 (0.308-1.783)	0.503		
BMI, kg/m <sup>2</sup>				
<20	1.000			
≥20	1.837 (0.745-4.528)	0.187		
ASA grade				
I, II	1.000			
III, IV	2.396 (0.945-6.072)	0.066		
Cerebrovascular disorders				
No	1.000		1.000	
Yes	3.721 (1.040-13.310)	0.043 <sup>a</sup>	3.612 (0.741-17.607)	0.112
Diabetes mellitus				
No	1.000			
Yes	0.766 (0.249-2.353)	0.641		
COPD				
No	1.000			
Yes	2.903 (0.501-16.804)	0.235		
Operative time, min				
<120	1.000			
≥120	2.140 (0.825-5.552)	0.118		
Intraoperative bleeding, ml				
<100	1.000		1.000	
≥100	4.556 (1.713-12.118)	0.002 <sup>a</sup>	4.222 (1.416-12.592)	0.010 <sup>a</sup>

<sup>a</sup>Statistically significant difference. BMI, body mass index; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; OR, odds ratio; CI, confidence interval.

present study demonstrated that preoperative sarcopenia was an independent risk factor for surgical complications in elderly patients with colorectal cancer. Similar results have also been observed for other malignancies. For example, Margadant *et al* examined the prognostic value of muscle density as a predictor of postoperative complications in 373 elderly patients undergoing surgery for colorectal cancer (22). The Hounsfield Unit Average Calculation (HUAC or HU/mm<sup>2</sup>) of the psoas muscles at the level of the L3 was calculated on the scan. High and low muscle density groups were identified based on the lowest sex-specific HUAC quartile. The cut-off point for the lowest sex-specific quartile was ≤22.0 HU/mm<sup>2</sup> for men and ≤23.5 HU/mm<sup>2</sup> for women. A statistically significant association was observed between muscle density and a Clavien-Dindo score of ≥3 [odds ratio=1.84 (95% confidence interval: 1.11-3.06), P=0.019]. In addition, anastomotic leakage in patients with a primary anastomosis (n=287) occurred more frequently in patients with low muscle density (11.7 vs. 23.3%,

P=0.016). It was concluded that low muscle density is associated with major postoperative complications in older patients who undergo surgery for colorectal cancer. Moreover, Boer *et al* investigated the role of low skeletal muscle mass (sarcopenia) as prognostic factor for postoperative complications and survival in 91 patients with resectable colon cancer (23). In that study, skeletal muscle mass was measured as total psoas area and total abdominal muscle area at three anatomical levels on the preoperative CT scan. The study included 91 patients with a mean age of 71.2±9.7 years. Sarcopenia was found to be an independent risk factor for one or more complications. Taken together, the results of previous studies and the results of the present study indicate that preoperative sarcopenia may have a clinical impact on postoperative surgical complications in elderly patients with colorectal cancer. Further investigation should focus on the exact mechanism underlying the association between preoperative sarcopenia and the development of postoperative complications.

Second, in the present study, the hospital stay was significantly longer in patients with preoperative sarcopenia compared with those without preoperative sarcopenia ( $P=0.039$ ). Previous studies reported a similar trend. For example, Lieffers *et al* evaluated whether sarcopenia predicts primary colorectal cancer resection outcomes in stage II-IV patients ( $n=234$ ) (24). In that study, sarcopenia was assessed using preoperative CT images. Overall, 38.9% of the patients were found to be sarcopenic. The length of hospital stay was longer for sarcopenic patients ( $15.9\pm 14.2$  vs.  $12.3\pm 9.8$  days,  $P=0.038$ ), particularly for those aged  $>65$  years ( $20.2\pm 16.9$  vs.  $13.1\pm 8.3$  days,  $P=0.008$ ). In addition, Malietzis *et al* investigated the role of particular body composition profiles as prognostic markers for patients with colorectal cancer undergoing curative resection (25). Lumbar SMI, visceral adipose tissue surface area and mean muscle attenuation were calculated by analysis of CT images in their study, and the presence of myosteatosis was found to be associated with prolonged primary hospital stay ( $P=0.034$ ). These findings require confirmation by future prospective studies to determine the potential additional use of health services, such as home care, as well as the impact on quality of life and costs associated with sarcopenia.

There were certain differences when comparing the present with previous studies. First, the definition of elderly patients was different. We herein defined elderly patients as those aged  $\geq 80$  years, while elderly patients were defined as those aged  $\geq 70$  or  $\geq 75$  years in previous studies. Second, the definition and severity of the postoperative surgical complications were different. Complications of grade 2-5 according to the Clavien-Dindo classification that occurred during hospitalization and/or within 30 days after surgery were retrospectively determined from the patients' records in the present study, while complications of grade  $\geq 3$  according to the Clavien-Dindo classification were taken into consideration in previous studies. Third, the perioperative care, which affects the hospital stay after surgery and the frequency of postoperative complications, was different. The perioperative care was standardized and the same fast-track program was applied to all patients after surgery in the present study, while the perioperative care was not standardized in previous studies.

There were also certain limitations to the present study. First, this was a retrospective single-center study with a small sample size, and our findings may be due to chance alone. Second, the cut-off points for sarcopenia should be determined within each specific patient population and BMI category (obese, overweight, normoweight or underweight). In the present study, sarcopenia was defined based on the results of the previous studies. However, the cut-off value may depend on the patients' backgrounds. Thus, an appropriate cut-off value should be determined in other validation studies in other populations. A significantly larger sample would be required to undertake a cut-off point analysis. Third, there was a selection bias in the elderly patients in this series. Surgeons often avoid performing colectomy in elderly patients, as the procedure itself has a 1% mortality and 20-30% morbidity risk. Thus, the fact that elderly patients in this study received colectomy may itself be a potential source of bias.

In conclusion, the short-term outcomes were adversely affected by preoperative sarcopenia in elderly patients with colorectal cancer. Our results indicated preoperative

sarcopenia as an independent risk factor for postoperative complications and hospital stay. To improve the short-term outcomes of elderly sarcopenic patients with colorectal cancer, it is necessary to carefully plan the surgical procedure, perioperative care and surgical strategy.

#### Acknowledgements

Not applicable.

#### Funding

No funding was received.

#### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### Authors' contributions

HT and TA designed the study, performed the majority of the experiments and wrote the manuscript. HT and TA analyzed the patient's data. KI, HF, SS, TS, HM, TO, NY, YR and MM helped analyze patients' skeletal muscle mass data.

#### Ethics approval and consent to participate

This study was approved by the Institutional Review Board of the Kamishirane Hospital.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare that they have no competing interests.

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