JOURNAL OF THE
ANUS, RECTUM AND COLON
dx.doi.org/10.23922/jarc.2021-057
http://journal-arc.jp

Original Research Article

Impact of Sarcopenia on Postoperative Complications in Obstructive Colorectal Cancer Patients Who Received Stenting as a Bridge to Curative Surgery

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Abstract

Objectives: Understanding the relationship between sarcopenia and malignancy is increasingly important since they inevitably affect the aging population. We investigated the clinical significance of sarcopenia in nonmetastatic obstructive colorectal cancer (OCRC) patients who were inserted self-expandable metallic stent and underwent curative surgery.

Methods: Plain cross-sectional CT images obtained before stenting were retrospectively analyzed in 92 patients. Muscle volume loss (myopenia) and decreased muscle quality (myosteatosis) were evaluated as skeletal muscle index (SMI) and intramuscular adipose tissue content (IMAC), respectively.

Results: This study included 54 men and 38 women, with a median age of 70.5 years. The median interval between SEMS placement and the surgery was 17 days (range, 5-47). There were 35 postoperative complications. The median postoperative hospital stay was 15.5 days (range, 8-77). Twenty-eight patients (41.3%) were classified as SMI-low, and 31 (34.1%) patients were classified as IMAC-high. In multivariate analysis, IMAC-high [hazard ratio (HR) = 7.68, 95% confidence interval (CI) 2.22-26.5, P = 0.001] and right-sided tumor (HR = 5.79, 95% CI 1.36-24.7, P = 0.018) were independent predictors of postoperative complications. IMAC-high (HR = 23.2, 95% CI 4.11-131, P < 0.001) and elevated modified Glasgow prognostic score (mGPS) (HR = 5.85, 95% CI 1.22-28.1, P = 0.027) were independent predictors of infectious complications. Relapse-free survival and overall survival were not significantly different regardless of the SMI or IMAC status.

Conclusions: IMAC was associated with postoperative complications and infectious complications. Myosteatosis might be a stronger predictor of postoperative complications than myopenia.

Keywords

cancer, colon, obstruction, sarcopenia, self-expandable metallic stent, complication

J Anus Rectum Colon 2022; 6(1): 40-51

Introduction

Sarcopenia is a progressive age-related condition of decreased muscle volume and function originally defined by Rosenberg in 1988[1]. Sarcopenia was not merely a functional decline, and it was associated with a risk of adverse events such as physical disability, poor quality of life, falls, and mortality[2-4]. As both sarcopenia and malignancy inevitably affect the aging population, it is increasingly important to understand their relationship. In oncology settings,

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Received: September 6, 2021, Accepted: October 29, 2021

sarcopenia was associated with short- and long-term outcomes. Sarcopenia was associated with increased postoperative complications, infectious complications, prolonged length of stay, and increased toxicity of chemotherapy[5-7]. It was also correlated with decreased overall survival (OS), cancer-specific survival (CSS), and relapse-free survival (RFS)[7]. CT-based assessment of muscle volume loss (myopenia) was the most common diagnostic method. Skeletal muscle index (SMI), presented as skeletal muscle areas at the third lumbar vertebrae (L3) normalized for stature, was one of the most frequently used parameters[5]. Another manifestation of sarcopenia is myosteatosis, which is an accumulation of fat deposits in the muscle. It was associated with decreased muscle quality[8,9] and might not be assessed by simple measurement of muscle mass. Intramuscular adipose tissue content (IMAC) was thought to represent the quality of the muscle and proposed as a new parameter of sarcopenia[10,11].

Colorectal cancer (CRC) is one of the world's most common malignancies. In 2020, over 1.9 million new cases were diagnosed, with nearly 935,000 patients dying from the disease, making it the second-leading cause of cancer mortality[12]. Intestinal obstruction is a frequent presenting sign of CRC with an incidence as high as 30%[13]. Obstructive colorectal cancer (OCRC) was responsible for 85% of colonic emergencies[14], often requiring multiple-stage surgery with a high morbidity and stoma rate. Intestinal decompression using self-expandable metallic colonic stent (SEMS) as "a bridge to surgery (BTS)" is now considered as an attractive treatment option[15].

Although CT-based myopenia was more prevalent in OCRC patients than in non-OCRC patients[16], little was known about the impact of sarcopenia, especially myosteatosis, on this particular population. In the present study, we investigated the clinical significance of sarcopenia represented as SMI (myopenia) and IMAC (myosteatosis) in nonmetastatic OCRC patients who were inserted SEMS and underwent curative surgery.

Methods

We reviewed 92 consecutive nonmetastatic OCRC patients who were treated with SEMS as BTS at Sendai City Medical Center between 2013 and 2020. The patients had total or subtotal malignant colonic obstruction, as evidenced by the following symptoms and findings: (1) obstructive symptoms such as abdominal pain, fullness, vomiting, and constipation, (2) contrast-enhanced CT findings of colorectal tumor with dilation of proximal bowel, and (3) severe stricture or obstruction demonstrated by contrast enema and colonoscopy. Patients were excluded if there were signs of peritonitis, perforation, or other serious complications demanding urgent surgery. The research excluded patients with benign illness, distant metastases, a positive surgical margin, or invasion from a non-colonic malignancy. Chronic inflammation was not present in any of the patients, and patients were not taking steroids or other immunosuppressive agents. There was no neoadjuvant chemoradiation therapy given to any of the patients. The protocol for this retrospective research project was approved by the ethics committee of the institution with a waiver of informed consent (#2020-0060), and this study conforms to the provisions of the Declaration of Helsinki.

The ColoRectal Obstruction Scoring System (CROSS) was used to access the severity of the obstruction, which provides a point score depending on the patient's oral intake level: CROSS 0, requiring continuous decompression; CROSS 1, no oral intake; CROSS 2, liquid or enteral nutrient intake; CROSS 3, soft solids, low-residue, and full diet with symptoms of stricture; and CROSS 4, soft solids, low-residue, and full diet without symptoms of stricture[17]. Insertion of the SEMS was performed by endoscopists. A guidewire was introduced across the neoplastic stenosis under endoscopic and fluoroscopic guidance. Niti-S colonic stent (TaeWoong Medical, Gimpo-si, Korea) or HANAROSTENT (Boston Scientific, Tokyo, Japan) was deployed over the wire and through the scope without balloon dilatation. The colon proximal to the stenosis was evaluated by water-soluble contrast enema or colonoscopic examination.

All patients subsequently received curative surgical resection. The Clavien-Dindo (CD) classification[18] was used to classify postoperative complications, and the AJCC Cancer Stating Manual (7th edition)[19] was used for pathological tumor staging. Right-sided tumor was defined as colonic lesion proximal to the splenic flexure. Long-term outcomes were defined as RFS and OS. RFS was measured from the date of the surgery to the date of the disease recurrence, and OS was measured from the date of the surgery to the date of death of any cause.

SMI and IMAC were evaluated on plain cross-sectional CT images obtained before stenting using Synapse Vincent software (Fujifilm, Tokyo, Japan). SMI was evaluated on a CT image at the third lumbar vertebra (L3) using Hounsfield units (HU) thresholds of −29 to 150. The sum of skeletal muscle areas was normalized for stature (m^2) and reported as SMI (cm^2/m^2)[5]. IMAC was calculated as follows: IMAC = region of interest (ROI) of the multifidus muscle (HU)/ ROI of subcutaneous fat (HU). The multifidus muscles were traced at the level of the umbilicus, and the average of CT values (in HU) was calculated. CT value of the subcutaneous fat was calculated as an average of four circles traced on the subcutaneous fat area away from major vessels at the same level. In general, IMAC tended to be a negative value, and high IMAC was considered to represent poor muscle quality[10,11].

Blood samples were taken before surgery, and anemia was defined as hemoglobin <13 g/dl in men and <12 g/dl in

women[20]. The modified Glasgow prognostic score (mGPS) is a cumulative score composed of elevation of serum C-reactive protein (CRP) and decrease in serum albumin, representing inflammation and nutrition status of the patients. Patients who had both elevated serum CRP (>1.0 mg/dL) and hypoalbuminemia (<3.5 g/dL) were allocated mGPS of 2. Patients who had only elevated serum CRP but not hypoalbuminemia were allocated mGPS of 1. Patients who had neither or only hypoalbuminemia were allocated mGPS of 0[21].

Continuous variables were presented as median (range) or mean ± SD and were tested using the Mann-Whitney U test. Fisher's exact test was used to analyze categorical variables in a cross-table. Survival rate was determined according to the Kaplan-Meier method and was analyzed by the log-rank test. The gender-specific cutoff value was established using receiver operating characteristic (ROC) curve analysis using postoperative complications as an endpoint. The cutoff value was computed using the most prominent point on the ROC curve (Youden index = maximum [sensitivity − (1 − specificity)]), as well as the area under the ROC (AUROC) curve. Multivariate analysis was performed with logistic regression. Factors shown to have a *P*-value of < 0.1 in the univariate analyses were included in the multivariate analysis. For statistical analysis, EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) was used, which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). Differences with *P*-values < 0.05 were considered significant[22].

Results

During the study period, 92 OCRC cases received curative surgery. Table 1 summarizes the characteristics of patients. There were 54 men and 38 women, with a median age of 70.5 years (range, 37-93) and median follow-up time of 30 months (range, 1-98). The tumor was located in the left in 68 (73.9%) cases and right in 24 cases. Concerning the CROSS classification, 52 patients (56.5%) were CROSS 0, 7 patients (7.6%) were CROSS 1, 10 patients (10.9%) were CROSS 2, and 23 patients (25.0%) were CROSS 3.

As for SEMS placement, the technical success which was defined as correct placement was 100%, and clinical success which was defined as resolution of occlusive symptoms was 98.9%. There were two stenting-related complications. One patient complained of mild abdominal pain after SEMS placement, and another patient with inadequate drainage required insertion of a transanal decompression tube for additional drainage. The postoperative course of the former patient was uneventful. The latter patient suffered from postoperative ileus which was resolved with conservative treatment.

The median interval between SEMS placement and the surgery was 17 days (range, 5-47). Laparoscopic surgery was performed in 40 (43.5%) cases, and conversion to open procedure was noted in 4 cases (10.0%) due to severe adhesion in 3 and the tumor with direct invasion to the bladder in 1. The remaining 52 cases (56.5%) were treated with open surgical approach. There was a gradual change in our management of OCRC cases, and the cases were divided according to the year of the operation (Table S1). When SEMS was introduced in our institution in 2013, all the OCRC cases were treated with open surgical approach. The number of cases treated with laparoscopic approach gradually increased as we developed expertise in laparoscopic surgery. In recent years, more patients were temporarily discharged after stenting and underwent preoperative evaluations on an outpatient basis. As a result, recent cases were more likely to undergo laparoscopic colectomy with a longer bridging interval at a statistically significant level. Moreover, in recent years, more patients with CROSS score of 3 were treated with SEMS, and the length of postoperative hospital stay became shorter. Lymphatic invasion was less frequent in recent cases.

A total of 82 patients (89.1%) underwent curative resection with primary anastomosis. Stoma was constructed in ten patients, including five diverting stomas. Blood transfusion was not administered during surgery. There were 35 (38.0%) postoperative complications with 7 major postoperative complications (CD grade III or greater), including 1 in-hospital death secondary to anastomotic leakage. Infectious complications were documented in 17 cases. The median postoperative hospital stay was 15.5 days (range, 8-77). Adjuvant chemotherapy was administered for 47 cases (51.1%).

Preoperative laboratory data were available in 86 cases. The median interval between blood sampling and surgery was 1 day (range, 1-21). Anemia was present in 63 (73.3%) cases.

The median value of SMI was significantly higher in men than in women (42.6 and 36.8, respectively; $P < 0.001$). ROC curve analysis showed the optimal cutoff values for SMI in men and women were 44.2 (AUROC = 0.63) and 31.2 (AUROC = 0.44), respectively. In the present study, 38 patients (41.3%) were classified as SMI-low. The median value of IMAC was significantly lower in men than in women (−0.34 and −0.13, respectively; $P < 0.001$). The cutoff values for IMAC in men and women were −0.30 (AUROC = 0.74) and 0.05 (AUROC = 0.61), respectively. There were 31 (34.1%) patients in the IMAC-high group. There was one patient whose CT image at umbilical level was not available and IMAC was not evaluated. At the L3 level, psoas muscles lie beside the vertebra and are surrounded by the kidney and major abdominal vessels. Thus, the contour of the psoas muscle was not distorted, and the accurate measurement of SMI was not interfered with by the distended bowel.

Table 1. Characteristics of the 92 Colorectal Cancer Cases.

Value		Value	
Age	70.5	Histological differentiation	
[min-max]	[37-93]	tub	90
Gender		por	2
Male	54	Lymphatic invasion	
Female	38	-	18
		+	74
BMI	21.6	Venous invasion	
[min-max]	[16.0-31.8]	-	29
ASA-PS		+	63
1	21	Harvested lymph node	
2	65	<12	7
3	6	≥12	85
Anemia [a]		CROSS before stent placement	
-	23	0	52
+	63	1	7
mGPS [a]		2	10
0	54	3	23
1	2		
2	30	Bridging interval (d)	17
Tumor site		[min-max]	[5-47]
left	68	Type of surgery	
right	24	Resection with primary anastomosis	82
		Resection with diverting stoma	5
ascending colon	6	Hartmann's procedure	5
transverse colon	18		
descending colon	17	Laparoscopic resection (conversion)	40 (4)
sigmoid colon	38	Postoperative complications [b]	
rectum	13	Grade I	16
Stage		Grade II	12
I	1	Grade III	3
II	47	Grade IV	3
III	44	Grade V	1
Depth of invasion (T stage)			
T2	1	Postoperative hospital stay (d)	15.5
T3	69	[min-max]	[8-77]
T4	22	Adjuvant chemotherapy	
Lymph node metastasis (N stage)		-	45
-	48	+	47
+	44		

[a] Data are unavailable in 6 cases

[b] Clavien-Dindo classification

ASA-PS American Society of Anesthesiologists-Physical Status

mGPS modified Glasgow Prognostic Score

CROSS ColoRectal Obstruction Scoring System

Table 2, 3 present the relationship between the SMI and IMAC status and clinicopathological parameters of the patients, respectively. The SMI-low status was significantly associated with male sex ($P < 0.001$), low BMI ($P = 0.031$), low CA19-9 level ($P = 0.033$), and postoperative complications ($P = 0.005$). Other clinicopathological factors and the length of postoperative hospital stay were comparable between the groups. IMAC-high status was significantly associated with age over 70 ($P = 0.004$), postoperative complications ($P < 0.001$), infectious complications ($P < 0.001$), longer postoperative hospital stay ($P = 0.003$), and not administering adjuvant chemotherapy ($P = 0.048$). In the present study, neither SMI nor IMAC status was associated with anastomotic leakage.

Table 2. Association between the SMI Status and Clinicopathological Parameters in 92 Colorectal Cancer Cases.

Value	SMI		*P* value	Value	SMI		*P* value
	low	normal			low	normal	
Age				Histological differentiation			
<70	16	28	0.40	tub	38	52	0.51
≥70	22	26		por	0	2	
Gender				Lymphatic invasion			
Male	34	20	< 0.001	-	7	11	1.00
Female	4	34		+	31	43	
BMI				Venous invasion			
	21.1	22.2	0.031	-	10	19	0.50
	[16.0-28.3]	[17.0-31.8]		+	28	35	
ASA-PS				Harvested lymph node			
1	8	13	0.81	<12	4	3	0.44
2, 3	30	41		≥12	34	51	
Anemia [a]				CROSS before stent placement			
-	8	15	0.47	0	21	31	0.41
+	28	35		1	5	2	
mGPS [a]				2	4	6	
0	20	34	0.27	3	8	15	
1, 2	16	16		Interval between stenting and operation (d)			
CEA					17	17	0.67
<5	19	23	0.52		[5-46]	[5-47]	
≥5	18	31		Complication CD Grade ≥ I			
CA 19-9				-	17	40	0.005
<37	35	45	0.35	+	21	14	
≥37	3	9		Complication CD Grade ≥ III			
Tumor site				-	34	51	0.44
left	29	39	0.81	+	4	3	
right	9	15		Infectious complication			
Stage				-	28	47	0.17
I, II	23	25	0.21	+	10	7	
III	15	29		Anastomotic leak			
Depth of invasion (T stage)				-	36	52	1.00
T2, 3	30	40	0.63	+	2	2	
T4	8	14		Postoperative hospital stay (d)			
Lymph node metastasis (N stage)					17	15	0.10
-	23	25	0.21		[8-77]	[8-48]	
+	15	29		Adjuvant chemotherapy			
				-	19	26	1.00
				+	19	28	

[a] Data are unavailable in 6 cases

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CD Clavien-Dindo classification

Regarding postoperative complications, factors identified as significant predictors in univariate analyses were male sex (P = 0.019), anemia (P = 0.007), mGPS ≥ 1 (P = 0.032), right-sided tumor (P = 0.005), SMI-low (P = 0.005), and IMAC-high (P < 0.001). In multivariate analysis, IMAC-high [hazard ratio (HR) = 7.68, 95% confidence interval (CI) 2.22-26.50, P = 0.001] and right-sided tumor (HR = 5.79, 95% CI 1.36-24.70, P = 0.018) were independent predictors of postoperative complications (Table 4).

Regarding infectious complications, factors identified as significant predictors in univariate analyses were mGPS ≥ 1 (P = 0.025), right-sided tumor (P = 0.035), and IMAC-high (P < 0.001). In multivariate analysis, anemia (P = 0.070) and operative time ≥ 240 min (P = 0.071) were included in

Table 3. Association between the IMAC Status and Clinicopathological Parameters in 91 Colorectal Cancer Cases.

Value	IMAC		*P* value	Value	IMAC		*P* value
	normal	high			normal	high	
Age				Histological differentiation			
<70	35	8	0.004	tub	58	31	0.55
≥70	25	23		por	2	0	
Gender				Lymphatic invasion			
Male	32	22	0.12	-	12	6	1.00
Female	28	9		+	48	25	
BMI				Venous invasion			
	21.6	21.8	0.34	-	18	11	0.64
	[15.9-31.8]	[17.0-31.5]		+	42	20	
ASA-PS				Harvested lymph node			
1	17	3	0.06	<12	4	3	0.69
2, 3	43	28		≥12	56	28	
Anemia [a]				CROSS before stent placement			
-	18	5	0.13	0	36	15	0.34
+	37	25		1	5	2	
mGPS [a]				2	4	6	
0	34	19	1.00	3	15	8	
1, 2	21	11		Interval between stenting and operation (d)			
CEA					17	19	0.12
<5	30	11	0.19		[5-44]	[6-47]	
≥5	29	20		Complication CD Grade ≥ I			
CA 19-9				-	46	10	< 0.001
<37	53	26	0.53	+	14	21	
≥37	7	5		Complication CD Grade ≥ III			
Tumor site				-	57	27	0.22
left	47	20	0.21	+	3	4	
right	13	11		Infectious complication			
Stage				-	56	18	< 0.001
I, II	31	17	0.83	+	4	13	
III	29	14		Anastomotic leak			
Depth of invasion (T stage)				-	59	28	0.11
T2, 3	46	24	1.00	+	1	3	
T4	14	7		Postoperative hospital stay (d)			
Lymph node metastasis (N stage)					15	19	0.003
-	31	17	0.83		[8-74]	[8-77]	
+	29	14		Adjuvant chemotherapy			
				-	25	20	0.048
				+	35	11	

[a] Data are unavailable in 6 cases

CD Clavien-Dindo classification

mGPS modified Glasgow Prognostic Score

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CROSS ColoRectal Obstruction Scoring System

the model. The result showed IMAC-high (HR = 23.20, 95% CI 4.11-131, $P < 0.001$) and mGPS ≥ 1 (HR = 5.85, 95% CI 1.22-28.1, $P = 0.027$) were independent predictors of postoperative infectious complications (Table 5).

Table 6 presents the details of the postoperative complications. Patients with right-sided disease were significantly more susceptible to postoperative ileus than those with left-sided disease ($P = 0.012$). Wound infection was more common in right-sided cases at a marginally significant level ($P = 0.049$).

The long-term outcomes were not significantly different regardless of the SMI or IMAC status (Figure 1). The difference of RFS and OS were nonsignificant according to SMI status ($P = 0.45$ and $P = 0.91$, respectively) nor IMAC

Table 4. Univariate and Multivariate Analysis of Postoperative Complications in 92 Obstructive Colorectal Cancer Patients.

Variable	Univariate analysis			Multivariate analysis		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Age (≥70)	2.02	0.85 - 4.77	0.11			
Gender (male)	2.99	1.19 - 7.50	0.019	3.04	0.75 - 12.40	0.12
BMI (≥22)	0.69	0.29 - 1.62	0.40			
ASA-PS (≥2)	1.73	0.60 - 4.97	0.31			
Anemia [a]	6.06	1.63 - 22.50	0.007	2.78	0.57 - 13.50	0.20
mGPS (≥1) [a]	2.69	1.09 - 6.67	0.032	2.54	0.74 - 8.75	0.14
Tumor site (right)	4.00	1.51 - 10.60	0.005	5.79	1.36 - 24.70	0.018
Depth of invasion (T4)	0.91	0.34 - 2.46	0.85			
Lymph node metastasis (N+)	0.60	0.26 - 1.41	0.24			
CROSS (0)	1.26	0.54 - 2.95	0.60			
Laparoscopic approach (no)	0.66	0.28 - 1.55	0.34			
Operative time (≥240 min.)	1.89	0.81 - 4.43	0.14			
Operation year (2017-20)	0.49	0.21 - 1.16	0.103			
SMI-low	3.53	1.46 - 8.53	0.005	1.68	0.46 - 6.14	0.44
IMAC-high	6.90	2.64 - 18.10	< 0.001	7.68	2.22 - 26.50	0.001

[a] Data are unavailable in 6 cases

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mGPS modified Glasgow Prognostic Score

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Table 5. Univariate and Multivariate Analysis of Infectious Complications in 92 Obstructive Colorectal Cancer Patients.

Variable	Univariate analysis			Multivariate analysis		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Age (≥70)	2.60	0.83 - 8.11	0.10			
Gender (male)	1.36	0.46 - 4.08	0.58			
BMI (≥22)	1.07	0.37 - 3.08	0.90			
ASA-PS (≥2)	2.54	0.53 - 12.20	0.24			
Anemia [a]	6.87	0.85 - 55.40	0.070	2.17	0.20 - 23.90	0.53
mGPS (≥1) [a]	3.64	1.17 - 11.30	0.025	5.85	1.22 - 28.10	0.027
Tumor site (right)	3.28	1.09 - 9.86	0.035	2.53	0.56 - 11.50	0.23
Depth of invasion (T4)	0.97	0.28 - 3.37	0.97			
Lymph node metastasis (N+)	0.72	0.25 - 2.09	0.54			
CROSS (0)	0.47	0.16 - 1.36	0.16			
Laparoscopic approach (no)	0.89	0.31 - 2.59	0.83			
Operative time (≥240 min.)	2.75	0.92 - 8.23	0.071	3.22	0.72 - 14.30	0.13
Operation year (2017-20)	0.63	0.22 - 1.80	0.39			
SMI-low	2.40	0.82 - 7.01	0.11			
IMAC-high	10.10	2.93 - 34.90	< 0.001	23.20	4.11 - 131.00	< 0.001

[a] Data are unavailable in 6 cases

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status ($P = 0.83$ and $P = 0.43$, respectively).

Discussion

Japan had the oldest population in the world, where peo-

Table 6. Postoperative Complications.

Value	Grade[a] ≥ III	Grade[a] ≥ I	right [n=24]	left [n=68]	*P* value
Postoperative complications	7	35	15 (63)	20 (29)	0.007
Anastomotic leakage	4	4	2 (8)	2 (3)	0.28
Ileus	1	12	7 (29)	5 (7)	0.012
Intraabdominal abscess	1	1		1 (1)	1
Arterial thorombus	1	1		1 (1)	1
Wound infection		9	5 (21)	4 (6)	0.049
Pneumonia		3	1 (4)	2 (3)	1
Lymphorrhea		2		2 (3)	1
Diarrhea		1		1 (1)	1
Wound bleeding		1		1 (1)	1
Urinary retention		1		1 (1)	1

[a] Clavien-Dindo classification

Data are expressed as n (%)

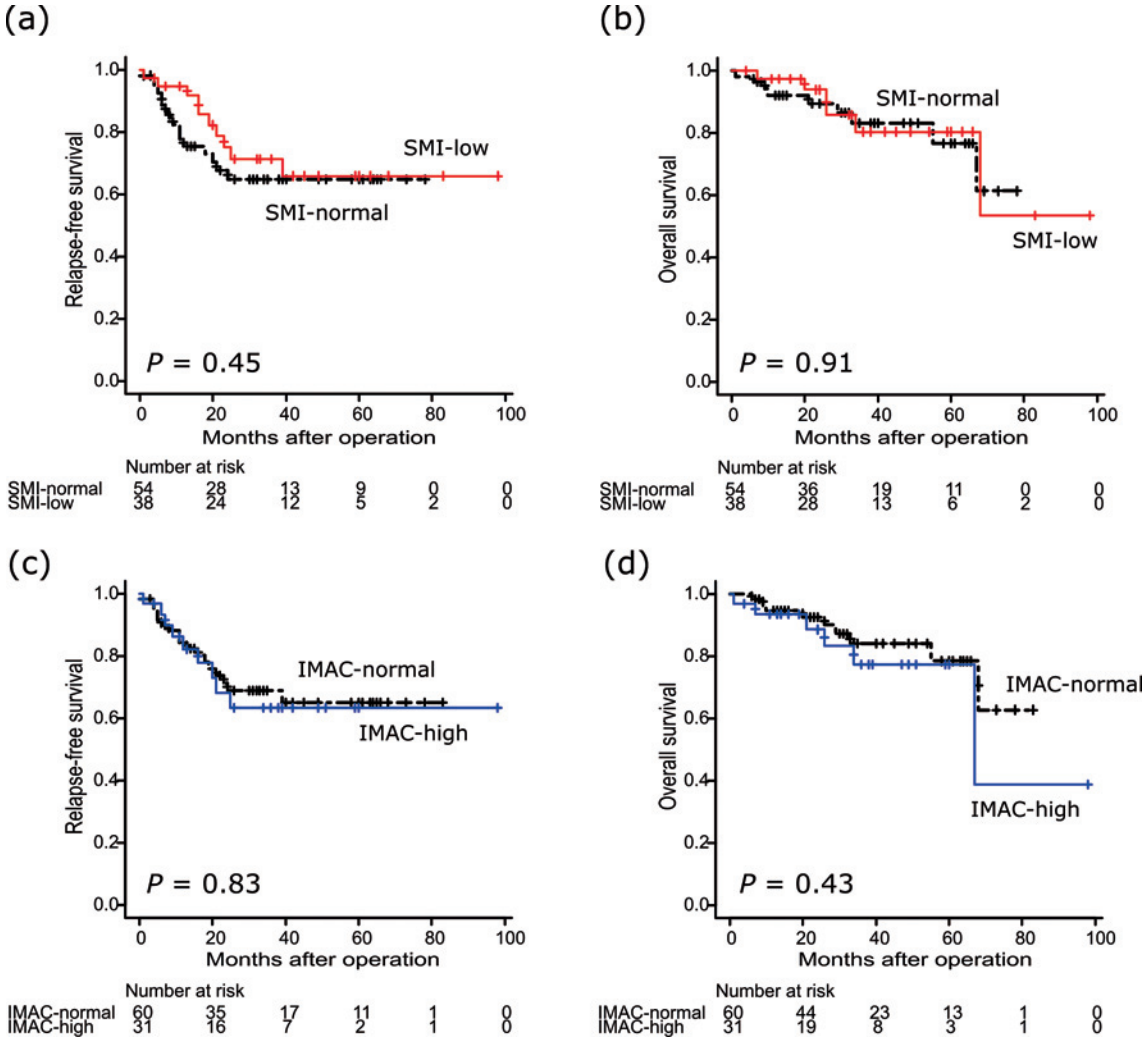

Figure 1. Survival curves of obstructive colorectal cancer patients who received stenting as a bridge to curative surgery. The differences of relapse-free survival and overall survival were nonsignificant according to SMI status (a and b, respectively) or IMAC status (c and d, respectively).

ple over 65 accounted for 28.2% of the total population in 2019[23]. Sarcopenia is increasingly drawing attention since it was associated with short- and long-term outcomes of various medical conditions[2-4]. Sarcopenia is classified into two types: (1) primary sarcopenia, which is caused solely by aging, and (2) secondary sarcopenia, which is triggered by physical inactivity or underlying chronic conditions including inflammatory disease, malnutrition, and cancer[2]. In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP) proposed defining criteria[2]. However, the body compositions of Asian people are quite different from that of Westerners, and the criteria may not directly be applicable to the population. Therefore, in 2014, the Asian Working Group for Sarcopenia (AWGS) developed a diagnostic algorithm for the Asian population[3]. For the diagnosis of sarcopenia, measurements of muscle strength, physical performance, and muscle mass were recommended, and handgrip strength, gait speed, and muscle mass measurement were the variables included in the AWGS diagnostic algorithm[3].

In studies of patients with malignancy, which were mostly retrospective, CT-based muscle mass measurement was usually employed since CT was almost always performed for preoperative evaluation. Muscle tissue at the lumbar level was strongly correlated with whole body tissue[24], and good interobserver variability was demonstrated[25]. There are several methods to measure muscle volume with a variety of cutoff values, and the diagnosis of myopenia was not fully standardized. SMI was a widely used parameter, and it was demonstrated to correlate with short- and long-term outcomes of a variety of malignancies[5,6]. Deterioration of skeletal muscle quality is another factor contributing to the progression of sarcopenia, which might not be associated with the reduction of muscle volume. Decreased quality of the skeletal mass was characterized by an increase in intramuscular adipose tissue, which could be evaluated by HU value in CT images, and IMAC was proposed as an indicator of the muscle quality[8-11].

In the current study, we examined the relationship between CT-based muscle mass measurement and short- and long-term outcomes in nonmetastatic OCRC patients who had SEMS inserted and underwent curative surgery. We then found that SMI and IMAC were significantly associated with postoperative complications in univariate analyses. Multivariate analysis revealed IMAC-high status was an independent predictor of postoperative complications. Previous studies showed that sarcopenia defined as CT-based muscle loss was associated with postoperative complications in nonobstructive CRC[5]. Other than SMI, total psoas index (TPI) and total psoas area (TPA) were used as a diagnostic method, and the prevalence of sarcopenia ranged from 15% to 80%[5]. The result of the present study was in line with previous studies, and SMI-low status was associated with postoperative complications in OCRC patients, albeit only in univariate analysis. Compared to myopenia, fewer studies investigated the relationship between myosteatosis and postoperative complications in CRC patients, and assessment of myosteatosis was also not fully standardized. Some studies measured the HU value of the muscles at the L3 level, namely, skeletal muscle density (SMD), and demonstrated that the SMD was associated with postoperative complications[26]. Others measured psoas density[27] or Hounsfield unit average calculation (HUAC), which was an average HU of the psoas muscles corrected for psoas muscle area[28]. In the present study, we employed IMAC since it might have potential theoretical advantages. In IMAC, to offset the difference among scanning systems and conditions, HU value for multifidus muscles was normalized by HU value of subcutaneous fat[10,11]. IMAC was associated with postoperative complications in patients with gastric[29], pancreatic[30], and hepatocellular carcinoma (HCC)[11], and patients underwent hepatectomy for CRC metastases[31]. To the best of our knowledge, this was the first study to demonstrate that IMAC-high status was significantly associated with postoperative complications and infectious complications in OCRC patients.

Ileus and wound infection were frequent postoperative complications in the present study. They were mostly CD Grade I or II, but the clinical importance was apparent as they certainly hamper normal postoperative course. In fact, IMAC-high status was significantly associated with prolonged postoperative hospital stay. IMAC, but not SMI, was the independent predictor of postoperative complications in multivariate analysis. Some of the previous studies also demonstrated the superior predictive value of myosteatosis over myopenia[28,32,33], implying that myosteatosis might be a stronger predictor of postoperative complications than myopenia, although further researches are warranted.

IMAC-high status was associated with increased infectious complications, and its predictive ability was higher than that of mGPS, which was predictive of infectious complications after colorectal surgery in previous reports[34,35]. Previous studies demonstrated that IMAC was associated with infectious complications in patients with CRC[36] and those who underwent hepatectomy for HCC[33]. Myosteatosis defined by psoas density was associated with infectious complications in CRC patients[27]. Although not demonstrated in the present study, myopenia was also associated with infectious complications in CRC[16,36]. Impaired immunonutrition status and sarcopenia were significantly associated[37,38]. The systemic inflammatory response represented by neutrophil-to-lymphocyte ratio (NLR) was significantly associated with myopenia and myosteatosis[38]. Increased adipose tissue was associated with increased secretion of pro-inflammatory adipokines, such as leptin, TNF-α, interleukin (IL)-1, and IL-6[39,40]. Decreased muscle tissue

reduced the production of heat shock proteins (HSPs) and glutamine, which could impair the immune system[41]. These findings could partly explain the susceptibility of sarcopenic patients to postoperative complications, including infectious complications.

Previous studies with CRC patients demonstrated conflicting results regarding sarcopenia and long-term outcomes; however, meta-analysis revealed sarcopenia defined by CT-based myopenia was significantly associated with OS, RFS, and CSS[7]. Another meta-analysis showed CT-based myosteatosis was significantly associated with poor OS[26]. Increased postoperative complications and decreased treatment tolerability to chemotherapy could be possible explanations[5,6]. However, two studies involving more than 400 CRC patients failed to demonstrate significant differences in OS and RFS between sarcopenic and non-sarcopenic patients[42,43]. Regarding the OCRC, CT-based myopenia was significantly associated with obstruction[16]. Lee et al. showed that SMI-low status was significantly associated with poor OS and RFS, whereas the status was not associated with postoperative complications in 214 OCRC patients[44]. In their study, SEMS were inserted in 117 (54.7%), stoma was created in 41 (19.2%), transfusion was administered to 107 (50.0%), and emergency surgery was performed in 15 cases (7.0%). In the present study, our cohort consisted only of OCRC cases who were inserted SEMS as a BTS, and neither SMI nor IMAC was associated with RFS and OS. The difference in the patients' characteristics and treatment strategy might explain the discrepancy from the results of previous studies. Further studies with a larger sample size were warranted.

There were several potential countermeasures to improve sarcopenia, i.e., pharmacological, nutritional, and exercise-based measures[45]. Yamamoto et al. conducted a prospective interventional study for 22 sarcopenic patients who underwent gastrectomy for gastric cancer[46]. With a median duration of 16 days, the program with exercise and nutritional support significantly improved total calorie and protein intakes as well as handgrip strength. Moreover, no patients in the intervention group developed severe complications of CD grade III or greater. On the other hand, a randomized controlled trial (RCT) demonstrated that exercise intervention did not result in statistically significant differences regarding postoperative complications[47]. Another RCT of a 4-week preoperative multimodal program, including exercise, nutritional, and psychological intervention, did not demonstrate reduction of postoperative complications and postoperative hospital stay[48]. Whether improving sarcopenia could improve short- and long-term outcomes remains unknown. Future prospective study is warranted in search of interventions to improve sarcopenia, which might result in decreased complications and improved survival. Currently, an international multicenter, prospective RCT to evaluate the multimodal prehabilitation program is underway[49].

Besides IMAC-high status, right-sided tumor was an independent predictor of postoperative complications, and ileus and wound infection were frequent complications observed in the right-sided cases. A significant association between right-sided tumor and postoperative complications was demonstrated in previous studies[50,51]. Campana et al. demonstrated that right laparoscopic colectomy was independently associated with CD grade ≥ I postoperative complications, whereas major complications (CD grade ≥ IIIb) were similar compared to left laparoscopic colectomy. Right colectomy had a fourfold higher risk of ileus than left colectomy[50]. Massoomi et al. showed that right colectomy had significantly more postoperative complications, urinary tract infection, pneumonia, and ileus than left colectomy[51]. Postoperative ileus is an important cause of prolonged hospitalization after colorectal surgery, and ileocolic anastomosis was significantly associated with ileus[52]. Our results were in line with previous findings. Surgeons have to be knowledgeable about the significant relationship between right-sided tumor and postoperative complications, especially ileus.

Several limitations must be acknowledged in the present study. CT was performed only before stenting, and SMI and IMAC values after stenting were not available. This study was retrospective in nature with a small sample size in a single institution. The patients consisted only of Japanese patients. The 30-month median follow-up period was rather short to draw firm conclusions on long-term oncological outcomes. The patients were nonmetastatic OCRC cases who were treated with SEMS and received curative surgery. They were a unique subset of CRC patients, and the results might not be readily generalizable to another patient population.

In summary, the result of the present study demonstrated that the IMAC-high status (myosteatosis) was an independent predictor of postoperative complications and infectious complications in nonmetastatic OCRC patients who were inserted SEMS as a BTS. Future studies on sarcopenia and malignancy should focus more on myosteatosis, especially IMAC. As sarcopenia and malignancy were expected to increase in aging countries, understanding their relationship and developing effective interventional strategies to improve sarcopenia are warranted.

Conflicts of Interest

There are no conflicts of interest.

Author Contributions

All listed authors participated meaningfully and met the four authorship criteria recommended by ICMJE. They have reviewed and approved the final manuscript.

Approval by Institutional Review Board (IRB)

The protocol for this research project was approved by the ethics committee of the Sendai City Medical Center (# 2020-0060), and the study conforms to the provisions of the Declaration of Helsinki.

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Supplementary Files

Table S1.

Please find supplementary file(s);
http://dx.doi.org/10.23922/jarc.2021-057