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Original

Examination of fatty infiltration of skeletal muscles by CT value in the evaluation of sarcopenia during preoperative chemotherapy for esophageal cancery

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Abstract

Sarcopenia was associated with postoperative complications and poor prognosis in various cancers. We aimed to evaluate quantitative and qualitative changes by using computed tomography (CT) during preoperative chemotherapy. We retrospectively reviewed 60 patients who received preoperative chemotherapy, followed by esophagectomy. We assessed the change in muscle mass and CT value of the bilateral iliopsoas and erector spinae muscles before and after chemotherapy and examined how these changes affect the postoperative period. The area of iliopsoas muscles significantly decreased between before and after chemotherapy (1217.3 ± 417.5 vs. 1123.4 ± 354.6, $p < 0.001$). Meanwhile, there was no significant difference in the area of the erector spinae muscles. Although there was no significant difference in the CT value of iliopsoas muscles between before and after chemotherapy, the CT value of the erector spinae muscle significantly decreased (44.2 ± 11.6 vs. 42.5 ± 11.4, $p = 0.015$). Our results indicated that chemotherapy might have a different effect on different muscles. It was suggested that the assessment of sarcopenia requires not only the assessment of muscle mass but also the assessment of fatty infiltration. We developed a simple and quantitative method to evaluate sarcopenia during preoperative chemotherapy by assessing CT value.

Key words: *sarcopenia, computed tomography value, preoperative chemotherapy, esophageal cancer*

I. Introduction

Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass (SMM) and strength, and poses a risk of adverse outcomes, including physical disability, poor quality of life, and death [1]. Various factors can induce sarcopenia, such as age, endocrine decline, neurodegenerative diseases, disuse due to immobility, inadequate

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nutrition, and cancer cachexia [1]. Several studies have revealed that sarcopenia is associated with complications and poor prognosis for patients with esophageal cancer after surgery [2-4].

Currently, the standard treatment in Japan for advanced esophageal squamous cell carcinoma (ESCC) of clinical stages II and III in Japan is neoadjuvant chemotherapy (NAC) followed by surgery [5]. Although NAC improves long-term outcomes, adverse events associated with chemotherapy sometimes result in nutritional disorders or muscle weakness [6, 7]. Kamitani et al. evaluated the progression of sarcopenia using SMM during NAC for esophageal cancer and revealed that the loss of SMM negatively impacted long-term outcomes [8]. In contrast, Ozawa et al. reported that the progression of sarcopenia during preoperative treatment did not affect the prognosis, although pretherapeutic sarcopenia was correlated with worse disease-free survival [9]. The impact of sarcopenia progression during preoperative chemotherapy on survival is still a controversial subject [8-11]. In most previous reports, SMM was measured by computed tomography (CT) as the cross-sectional transverse area of skeletal muscle at the level of the third lumbar vertebra (L3) [8-11]. Furthermore, in the evaluation of sarcopenia, an assessment of muscle composition, such as fatty infiltration, was necessary [1]. Fatty infiltration is also associated with attenuation of skeletal muscle, but muscle weakness due to fatty infiltration cannot be assessed by CT measurement of muscle volume [12, 13]. As a result, an analysis of quantitative changes by measuring skeletal muscle only may be insufficient to accurately assess skeletal muscle changes. In this study, we aimed to evaluate not only the "quantity of muscle" changes by measuring SMM but also the "quality of muscle" changes by measuring fatty infiltration using CT value during preoperative chemotherapy for patients with ESCC, and examine how these changes affect the postoperative period.

II. Materials and Methods

1. Patients

We retrospectively reviewed 82 consecutive patients with advanced ESCC, who received preoperative chemotherapy, including induction chemotherapy, followed by Mckeown esophagectomy at the Department of Surgery, Iwate Medical University Hospital, between March 2011 and October 2020. Sixty patients were included in the analysis, excluding 22 patients whose non-enhanced CT images before and after chemotherapy were not obtained but who had enhanced CT images. The location of the tumor was defined according to the Japanese Classification of Esophageal Cancer, 11th edition [14]. Clinical stages were classified according to the Union for International Cancer Control classification (7th edition).

2. Chemotherapy

For patients with advanced ESCC, preoperative chemotherapy included cisplatin/ fluorouracil (CF) and docetaxel/ cisplatin/ fluorouracil (DCF); standard DCF (sDCF), or biweekly DCF (bDCF). The details and selection criteria for each regimen were previously described [15, 16]. In brief, the CF regimen comprised of cisplatin (80 mg/m^2) on day 1 and 5-fluorouracil (5-FU, 800 mg/m^2) on days 1–5 [7, 15]. The standard DCF regimen consisted of docetaxel (60–70 mg/m^2) on day 1, cisplatin (80 mg/m^2) on day 1, and 5-FU (800 mg/m^2) on days 1–5 until October 2017; and docetaxel (70 mg/m^2) on day 1, cisplatin (70 mg/m^2)

on day 1, and 5-FU (750 mg/m^2) on days 1–5 from November 2017 [13]. The bDCF regimen consisted of docetaxel (30 mg/m^2) on day 1 and 15, cisplatin (80 mg/m^2) on day 1, and 5-FU (800 mg/m^2) on days 1–5 [16]. The regimens were repeated every 3 to 4 weeks. All patients underwent CT to evaluate the clinical response according to the Response Evaluation Criteria in Solid Tumors v. 1.1. Adverse events were assessed based on the Common Terminology Criteria for Adverse Events v. 4.0.

For nutritional therapy during chemotherapy, we calculated the optimal caloric intake for each patient. If the patients' oral intake was inadequate, it was supplemented with oral nutrition. An enteral diet was administered to patients with esophageal stenosis due to cancer via a nasal feeding tube until they could take food orally. Patients who were evaluated to have lower than their age-equivalent muscle strength were treated by a physiotherapist with exercise therapy during preoperative chemotherapy.

3. Surgical procedure

Radical esophagectomy via a right thoracotomy or thoracoscopy, including robot-assisted surgery, was performed as previously reported [17]. The reconstruction conduit was a gastric tube pulled through the posterior mediastinum or retrosternal route with cervical esophagogastrostomy [18]. Postoperative complications were defined as grade II or higher according to the Clavien–Dindo classification [19].

4. Imaging and analysis

All non-enhanced abdominal CT scans were performed using a 64-slice multi-detector CT scanner (Canon Aquilion 64, Canon Medical Systems, Otawara, Japan) with the following parameters: 3-mm section thickness and interval, 0.5 s rotation time, 120 kVp tube voltage, and an automatic tube current modulation program with images reconstructed using Adaptive Iterative Dose Reduction 3D (AIDR 3D: Canon Medical Systems). Then, the region of interest (ROI) for the bilateral iliopsoas and erector spinae muscles was manually drawn to the cross-sectional CT image at the L3 vertebral body level (Fig. 1). Coarse calcification and prominent artifacts were carefully avoided. Next, a 3D slicer (v. 4.10.2; open-source software) was used for manual segmentation by radiologists (A.T), and the extracted ROIs were analyzed using MATLAB (version R2020b, MathWorks). An open-source radiomics library (PyRadiomics; Harvard Medical School, Harvard, MA, USA) was used to extract the mean area and CT values of the bilateral iliopsoas and erector spinae muscles.

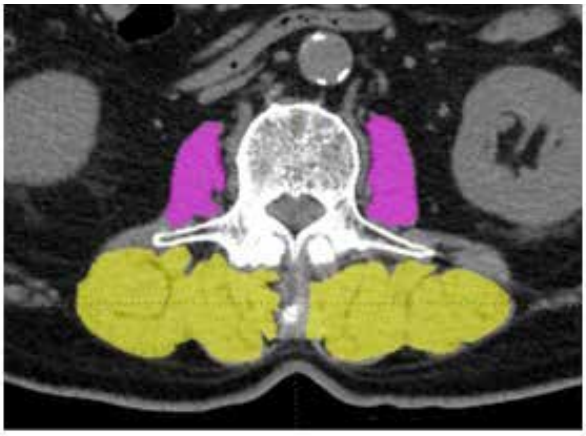

Fig. 1. The region of interest (ROI) for the bilateral iliopsoas and erector spinae muscles in the cross-sectional computed tomography (CT) image at the L3 vertebral body level. The area marked in pink shows iliopsoas muscles, while the area marked in yellow shows erector spinae muscles.

5. Outcome measures

Patients' clinical data were collected from the hospital database. Factors including age, sex, body mass index (BMI), TNM classification,

Table 1. Patients' characteristics

Characteristic	n = 60
Age (year)[§] (range)	64.3 ± 9.4 (33–79)
Sex (male/female)	48/12
BMI (kg/m^2) [§]	22.4 ± 3.8
ASA-PS (0/1/2/3)	54/6/0/0
Tumor location[#] (Ut/Mt/Lt/Ae)	8/33/17/2
Clinical T stage [b] (T1/T2/T3/T4a/T4b)	3/13/38/5/1
Clinical N stage [b] (0/1/2/3)	8/35/15/2
Clinical M stage [b] (0/1)	59/1
Clinical stage [b] (I/IIA/IIB/IIIA/IIIB/IIIC/IV)	6/2/8/25/12/6/1
Preoperative chemotherapy (CF/sDCF/bDCF)	10/18/32
Courses of chemotherapy (1/2/3/ ≧ 4)	8/21/23/8
Comorbidities	
Heart disease	33
Pulmonary disease	7
Diabetes mellitus	11
Cerebrovascular disease	2
Sarcopenia	
Before chemotherapy	53
After chemotherapy	54
Surgical procedure	
(Right thoracotomy/thoracoscopic/robotic)	4/45/11
Lymph node dissection (Two field/three field)	19/41

[§] Mean ± standard deviation.
[#] According to the Japanese Classification of Esophageal Cancer, 11th edition (Ut, upper thoracic esophagus; Mt, middle thoracic esophagus; Lt, lower thoracic esophagus; Ae, abdominal esophagus).
[b] According to the Union for International Cancer Control classification, 7th edition.
ASA-PS, American Society of Anesthesiologists performance states; BMI, Body Mass Index; CF, cisplatin and 5-fluorouracil; sDCF, standard docetaxel, cisplatin, and 5-fluorouracil; bDCF, biweekly docetaxel, cisplatin, and 5-fluorouracil.

comorbidities, American Society of Anesthetists-physical status (ASA-PS), therapeutic effect of chemotherapy, duration of postoperative hospital stay, postoperative complications, and overall survival (OS) were evaluated. The bilateral iliopsoas muscles were measured before and after chemotherapy, and the psoas muscles index (PMI) was calculated using the following formula; L3 iliopsoas area (cm^2) / height^2 (m^2). A PMI of 6.36 cm^2/m^2 for men and 3.92 cm^2/m^2 or less for women was defined as sarcopenia [20]. Nutritional index changes were calculated based on blood test results before and after chemotherapy; albumin-globulin ratio (AGR), platelet lymphocyte ratio (PLR), and prognostic nutrient index (PNI) [21–23].

6. Statistical analyses

All statistical analyses were performed using SAS statistical analysis software, JMP 14.2 (Aa Institute Inc., Cary, NC, USA). Changes in skeletal muscle area and CT values before and after chemotherapy were compared using the Wilcoxon's signed-rank test. Then, the differences in patient characteristics and outcomes between the two groups were estimated using the x^2 test, Student's

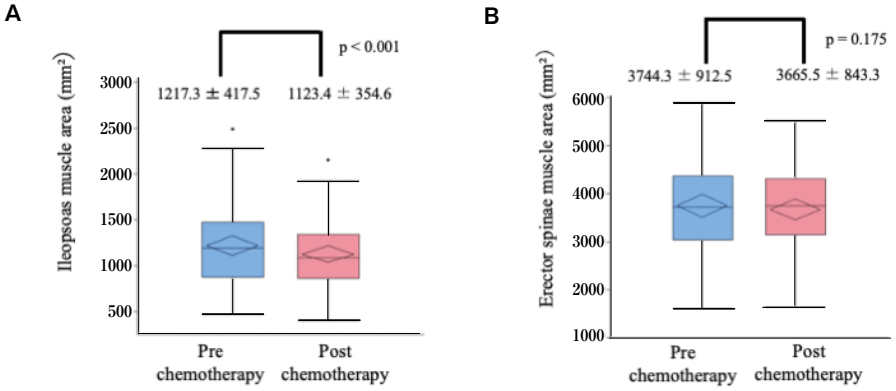

Fig. 2. Iliopsoas muscle and erector spinae muscles area before and after preoperative chemotherapy.
(A) Iliopsoas muscle area. (B) Erector spinae muscles area.

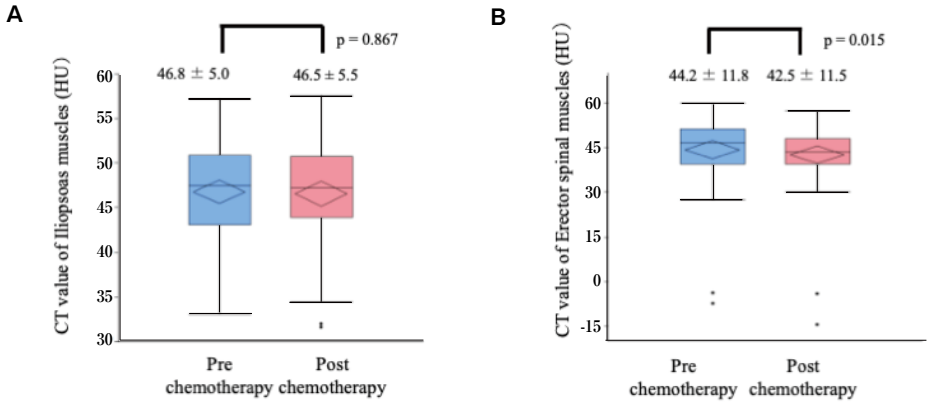

Fig. 3. Computed tomography (CT) value of iliopsoas and erector spinae muscles before and after preoperative chemotherapy.
(A) CT value of iliopsoas muscles. (B) CT value of erector spinae muscles.

T-test, Wilcoxon's rank test. Also, $p < 0.05$ was considered statistically significant. The correlation coefficient was assessed using correlation analysis. OS data were analyzed using the Kaplan–Meier method, and the statistical significance of survival was analyzed using the log-rank test.

III. Results

1. Patient characteristics

Table 1 presents the clinical characteristics of the patients. The patients' average age was 64.3 years, and 48 patients (80%) were male. Fifty-three patients (88.3%) before chemotherapy and 54 patients (90%) after chemotherapy had sarcopenia, with most patients presenting with sarcopenia before surgery. The chemotherapy regimens were CF (10 patients), sDCF (18 patients), and bDCF (32 patients). The average courses of chemotherapy were 1.9 for CF, 2.3 for sDCF, and 2.9 for bDCF.

2. Changes in iliopsoas and erector spinae muscle areas

Figure 2 depicts the changes in iliopsoas and erector spinae muscle areas during preoperative chemotherapy. The area of the iliopsoas muscles

Table 2. Analysis of factors associated with iliopsoas muscle loss

	LL group (n = 30)	SL group (n = 30)	p-value
Age (year)[§] (range)	64.1 ± 10.6	64.5 ± 8.5	0.872
Sex (male/female)	4/26	8/22	0.197
BMI (kg/m^2) [§]	22.4 ± 4.4	22.4 ± 3.1	0.977
ASA-PS (0/1/2/3)	27/3/0/0	27/3/0/0	1.000
Tumor location [#] (Ut/Mt/Lt/Ae)	2/20/8/0	6/13/9/2	0.136
Clinical T stage [♭] (T1/T2/T3/T4a/T4b)	1/4/21/3/1	2/9/17/2/0	0.423
Clinical N stage [♭] (0/1/2/3)	3/18/8/1/	5/17/7/1	0.898
Clinical stage [♭] (I/IIA/IIB/IIIA/IIIB/IIIC/IV)	1/2/3/13/7/4/0	5/0/5/12/5/2/1	0.302
Preoperative chemotherapy (CF/sDCF/bDCF)	3/11/16	7/7/16	0.288
Clinical response (CR/PR/SD/PD)	0/22/8/0	0/15/14/1	0.138
C–D classification of postoperative complications [†]			
(Grade I/II/IIIa/IIIb)	4/8/2/0	3/8/1/1	0.525
Length of hospital stay (day) [§]	20.5 ± 9.4	16.0 ± 5.7	0.030*
Δ AGR [§]	9.1 ± 17.9	11.1 ± 15.2	0.647
Δ PLR [§]	7.2 ± 33.3	7.8 ± 44.2	0.952
Δ PNI [§]	− 7.0 ± 12.1	− 3.9 ± 11.6	0.314
Adverse events associated with chemotherapy			
Hematologic toxicity (grades 3 and 4) (yes/no)			
Neutropenia	21/9	19/11	0.584
Febrile neutropenia	3/27	4/26	0.687
Anemia	3/27	1/29	0.301
Thrombocytopenia	2/28	1/29	0.554
Non-hematologic toxicity (grades 3 and 4) (yes/no)	4/26	1/29	0.161
Nausea/vomiting			
Diarrhea	8/22	2/28	0.038*
Stomatitis	4/26	6/24	0.488
Anorexia	3/27	2/28	0.640

[§] Mean ± standard deviation.
[#] According to the Japanese Classification of Esophageal Cancer, 11th edition (Ut, upper thoracic esophagus; Mt, middle thoracic esophagus; Lt, lower thoracic esophagus; Ae, abdominal esophagus).
[♭] According to the Union for International Cancer Control classification, 7th edition.
[†] Clavien–Dindo classification.
*$p < 0.05$.
Δ AGR, Change in albumin-globulin ratio; Δ PLR, Change in platelet lymphocyte ratio; Δ PNI, Change in prognostic nutrition index; ASA-PS, American Society of Anesthesiologists performance states; CR, Complete response; PD, Progression disease; PR, Partial response; SD, Stable disease.
LL group, large loss of muscle mass group; SL group, small loss of muscle mass group.

significantly decreased between before and after chemotherapy (1217.3 ± 417.5 vs. 1123.4 ± 354.6, $p < 0.001$, Fig. 2A). However, there was no significant difference in the area of the erector spinae muscles between before and after chemotherapy (3744.3 ± 912.5 vs. 3665.5 ± 843.3, $p = 0.175$, Fig. 2B). Figure 3 shows the CT values of the iliopsoas and erector spinae muscle areas during preoperative chemotherapy. Although there was no significant difference in the CT value of the iliopsoas muscles between before and after chemotherapy (46.8 ± 5.0 vs. 46.5 ± 5.5, $p = 0.867$, Fig. 3A), the CT value of the erector spinae muscles significantly decreased between before and after chemotherapy (44.2 ± 11.6 vs. 42.5 ± 11.4,

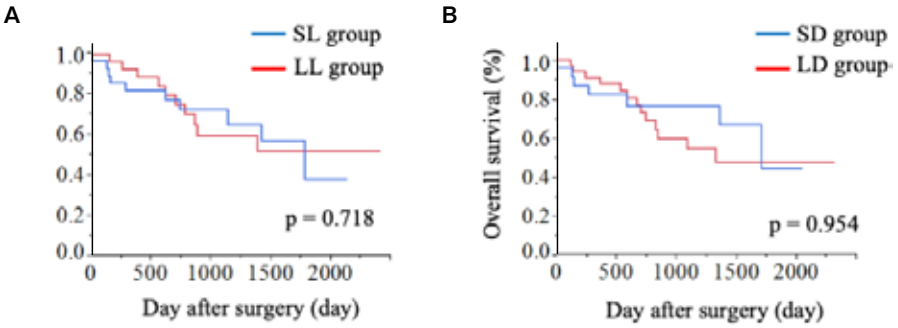

Fig. 4. Overall survival (OS) rates
(A) OS in large loss of muscle mass group (LL group) and small loss of muscle mass group (SL group). (B) OS in a large decrease of computed tomography (CT) value group (LD group) and small decrease group (SD group).

p = 0.015, Fig. 3B). There was no correlation between changes in skeletal muscle area and changes in CT values (r = 0.320).

3. Factors associated with loss of iliopsoas muscles

We examined the factors associated with decreasing iliopsoas muscle area during preoperative chemotherapy. Based on changes in the iliopsoas muscle area before and after chemotherapy, as measured by a median value of change, patients were divided into two groups: the large loss of muscle mass group (LL group) and the small loss of muscle mass group (SL group) (Table 2). There were no significant differences in age, gender, BMI, tumor localization, clinical stage, chemotherapy regimens, or performance status between the two groups. Postoperative hospital stay was significantly prolonged in the LL group compared with the SL group (20.5 ± 9.4 vs. 16.0 ± 5.7, p = 0.030). There were no significant differences in the nutritional index, including AGR, PLR, and PNI, between the two groups. In terms of grade 3 or higher adverse events during chemotherapy, the frequency of diarrhea was significantly higher in the LL group than in the SL group (26.7% vs. 6.7%, p = 0.038). However, there was no significant difference in OS between the two groups (Fig. 4A).

4. Factors associated with a decrease in CT value of erector spinae muscles

Next, we examined the factors associated with a decrease in the CT value of erector spinae muscles during chemotherapy. Based on changes in the CT value of erector spinae muscles before and after chemotherapy, as measured by a median value of change, patients were divided into two groups: the large decrease in CT value group (LD group) and the small decrease group (SD group) (Table 3). Pre-treatment BMI was significantly lower in the LD group compared with the SD group (21.3 ± 3.1 vs. 23.6 ± 4.0, p = 0.002), but there were no significant differences in other patient characteristics between the two groups. There were no differences in the efficacy of chemotherapy, postoperative complications, or postoperative hospital stay between the two groups. Furthermore, there were no significant differences in the nutritional index and adverse events during chemotherapy between the two groups. There was no significant difference in OS between the two groups (Fig. 4B).

Table 3. Analysis of factors associated with a change in the CT value of erector spinae muscles

	LD group (n = 30)	SD group (n = 30)	p-value
Age (year)[§] (range)	63.4 ± 10.7	65.2 ± 8.2	0.469
Sex (male/female)	25/5	23/7	0.519
BMI (kg/m^2) [§]	21.5 ± 3.2	23.4 ± 4.1	0.050*
ASA-PS (0/1/2/3)	27/3/0/0	27/3/0/0	1.000
Tumor location [#] (Ut/Mt/Lt/Ae)	6/12/10/2	2/21/7/0	0.072
Clinical T stage [♭] (T1/T2/T3/T4a/T4b)	1/7/19/2/1	2/6/19/3/0	0.807
Clinical N stage [♭] (0/1/2/3)	4/18/7/1	4/17/8/1	0.992
Clinical stage [♭] (I/IIA/IIB/IIIA/IIIB/IIIC/IV)			
Preoperative chemotherapy (CF/sDCF/bDCF)	3/1/3/14/5/3/1	3/1/5/11/7/3/0	0.901
Clinical response (CR/PR/SD/PD)	4/8/18	6/10/14	0.571
C–D classification of postoperative complications [†] (Grade I/II/IIIa/IIIb)	0/19/11/0	0/18/11/1	0.598
Length of hospital stay (day) [§]	4/10/0/1	3/6/1/1	0.636
Δ AGR [§]	18.3 ± 6.4	18.1 ± 9.5	0.937
Δ PLR [§]	8.1 ± 16.0	12.0 ± 17.0	0.372
Δ PNI [§]	6.3 ± 35.5	8.7 ± 42.5	0.815
Adverse events associated with chemotherapy	− 7.6 ± 11.2	− 3.4 ± 12.3	0.172
Hematologic toxicity (grades 3 and 4) (yes/no)			
Neutropenia	19/11	21/9	0.584
Febrile neutropenia	3/27	4/26	0.688
Anemia	3/27	1/29	0.301
Thrombocytopenia	2/28	1/29	0.554
Non-hematologic toxicity (grades 3 and 4) (yes/no)			
Nausea/vomiting	2/28	3/27	0.640
Diarrhea	5/25	5/25	1.000
Stomatitis	6/24	6/24	1.000
Anorexia	3/27	2/28	0.640

[§] Mean ± standard deviation.
[#] According to the Japanese Classification of Esophageal Cancer, 11th edition (Ut, upper thoracic esophagus; Mt, middle thoracic esophagus; Lt, lower thoracic esophagus; Ae, abdominal esophagus).
[♭] According to the Union for International Cancer Control classification, 7th edition.
[†] Clavien–Dindo classification.
*$p < 0.05$.
Δ AGR, Change in albumin-globulin ratio; Δ PLR, Change in platelet lymphocyte ratio; Δ PNI, Change in prognostic nutrition index; ASA-PS, American Society of Anesthesiologists performance states; CR, Complete response; PD, Progression disease; PR, Partial response; SD, Stable disease.
LD group, large decrease in CT value group; SD group, small decrease in CT value group.

IV. Discussion

The loss of muscle strength was associated with a decrease in not only SMM but also the fat content of muscles [12, 13]. The change in intramuscular fat infiltration was evaluated by CT values, and the decrease in SMM was evaluated by comparing skeletal muscle area. There was a significant decrease in iliopsoas muscle mass during preoperative chemotherapy, but no significant fatty infiltration change was observed in the iliopsoas muscle (Fig. 2). Conversely, there was no significant decrease in the volume of the erector spinae muscles, but there was a significant decrease in CT values during preoperative chemotherapy (Fig. 3). There was no correlation between changes in

the skeletal muscle area of the iliopsoas muscles and changes in CT values of the erector spinae muscles, indicating that chemotherapy might have a different effect on each muscle. Skeletal muscle fibers are classified as slow-twitch fiber (type I) and fast-twitch fibers (type IIa, IIx, and IIb) [24]. Type I fibers are more sensitive to inactivity, microgravity, and denervation-induced atrophy, whereas type II fibers are more vulnerable to cancer cachexia, diabetes, chronic heart failure, and aging [24]. The erector spinae muscles are skeletal muscles with predominantly type I fibers [25]. However, the iliopsoas muscles mainly consist of types I and IIa muscle fibers [26]. Muscle wasting could occur through multiple distinct signaling pathways with differential sensitivity between muscle fiber subtypes [24]. Differences in skeletal muscle composition may result in various chemotherapy effects on each muscle.

The frequency of diarrhea during chemotherapy was significantly higher in the LL group than in the SL group in this study (Table 2). This result suggested that iliopsoas muscle loss might be associated with chemotherapy-induced diarrhea. Several studies have also reported that sarcopenia is associated with toxicity during chemotherapy [27, 28]. Prado et al. reported that diarrhea and stomatitis were observed more among sarcopenic patients in their study of breast cancer patients with capecitabine treatment [28]. Sarcopenia was a significant predictor of toxicity in their study [28]. Conversely, intestinal mucosa damage and dehydration due to diarrhea might have caused the iliopsoas muscle loss. Further study is needed to determine the causal relationship between sarcopenia and toxicity including diarrhea.

The muscle attenuation and fatty infiltration in erector spinae muscles directly affects functional ability and increase the risk of injury in older patients because these are crucial for trunk stability [12]. The mechanism by which fatty infiltration of erector spinae muscles affects patients undergoing chemotherapy and surgery is unclear. In this study, there was no correlation between fatty infiltration, adverse events of chemotherapy, and postoperative complications, although patients in the LD group had a lower BMI before treatment compared with the SD group (Table 3). Patients with a lower BMI may be more susceptible to fatty infiltration of erector spinae muscles during chemotherapy. In a study of intramuscular adipose tissue of quadriceps femoris using enhanced echo intensity, Fukumoto et al. reported that fatty infiltration was not associated with BMI [29]. Moreover, the mechanism of chemotherapy-induced fatty infiltration of erector spinae muscles remains unexplored, necessitating further research.

CT is a very common imaging technique, and it is the first-line cross-sectional imaging technique for evaluating several acute and chronic diseases associated with aging, such as fractures, frailty, cancer, and cardiometabolic syndromes. Therefore, CT is increasingly being used to quantify skeletal muscle weakness in the diagnosis of sarcopenia [30]. CT criteria used to diagnose sarcopenia are also quite diverse. The most commonly used technique is to evaluate all skeletal muscles in axial slices at the L3 vertebral level [8-11, 31]. Furthermore, CT-derived muscle attenuation is increasingly being assessed as an indicator of muscle fat mass [30]. Overall, muscle attenuation on CT is due to muscle atrophy (i.e., fatty infiltration of

muscle) [13]. Currently, muscle weakness on CT is considered a poor prognostic factor in patients with cancer and others [32].

We evaluated sarcopenia during preoperative chemotherapy for patients with ESCC using a new method to assess fatty infiltration using CT. We discovered that the erector spinae and iliopsoas muscles may show different changes as sarcopenia progresses. Recently, there have been reports of the development of fully automated algorithms using deep learning to segment the abdomen from CT and quantify body composition [33]. These techniques could facilitate the quantification of body composition. Quantitative muscle imaging will be a major paradigm shift in medicine once initial promising results are corroborated and imaging studies are standardized, measurements are automated, cutoffs are established, and effective treatments are identified.

In this study, the decreasing in area of iliopsoas muscles or the decrease in CT value of the erector spinae muscles were not associated with operative complications in patients with ESCC. Patients with iliopsoas muscle loss or fatty infiltration of erector spinae muscles may not have increased postoperative complications due to appropriate perioperative management, such as rehabilitation and nutritional therapy [34]. Furthermore, the progression of sarcopenia during preoperative chemotherapy did not affect OS in this study. Ozawa et al. revealed no significant difference in disease-free survival rate in sarcopenia patients during preoperative treatment [9]. The researcher considered that the progression of sarcopenia during neoadjuvant therapy might have masked the actual sarcopenic influence in patients because it may be difficult to observe the sarcopenia progression in patients who had already presented sarcopenia in the pretherapeutic period. In our study, most patients (88.3%) had been diagnosed with sarcopenia before preoperative chemotherapy (Table 1).

The main influences on sarcopenia are exercise and nutrition therapy. In this study, physical therapists considered patient intervention for exercise therapy appropriate. Patients with consequent loss of muscle mass might not have received adequate loading. However, it was sometimes difficult to follow a predetermined program for exercise therapy during chemotherapy because the intervention must consider symptoms, such as nausea, vomiting, and anorexia. There was no significant difference in changes in nutritional indices between the two groups compared with the degree of reduction in iliopsoas muscle mass and CT values of the erector spinae muscles. Nutritional assessment was performed for each patient, and we believe that nutritional support was appropriately managed.

There are several limitations to this study. First, there were differences between the regimen and course of preoperative chemotherapy. Induction chemotherapy was started for patients with T4 cancer, and some patients did not have a predefined chemotherapy course. The intensity and course of chemotherapy might affect the degree of sarcopenia. Next, only the iliopsoas and erector spinae muscles were evaluated in this study. The effects of chemotherapy on other skeletal muscles were not examined, necessitating further studies. Finally, the observation period was short for survival analysis. This was a retrospective cohort study with a small study population in a single center. To confirm the long-term

outcomes, a well-designed large-scale prospective study is required.

We evaluated sarcopenia during preoperative chemotherapy for patients with ESCC assessing fatty infiltration using CT. Our findings revealed that preoperative chemotherapy for ESCC affects the iliopsoas and erector spinae muscles differently. The effect of chemotherapy on fatty infiltration of muscle needs further investigation in a larger patient population. Our results suggested that the assessment of sarcopenia requires not only the assessment of muscle mass but also the assessment of fatty infiltration at the same time, and our developed method is a useful with simple and quantitative method.

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CT 値を用いた 骨格筋の脂肪浸潤解析による 食道癌術前化学療法中のサルコペニアの評価

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要旨

食道癌患者の術前化学療法中のサルコペニアの進行を評価するため，骨格筋の量および質の変化を解析した．対象は食道癌に対して化学療法を施行後に食道亜全摘術を施行した 60 名．初診時と術前の単純 CT から第 3 腰椎レベルの腸腰筋および脊柱起立筋の骨格筋肉量，CT 値の変化を測定し，それらに影響を及ぼした因子を検討した．化学療法前後で腸腰筋面積は 1217.3 ± 417.5 から 1123.4 ± 354.6 へと有意に低下した ($p < 0.001$)．化学療法前後で脊柱起立筋の CT 値は 44.20 ± 11.80 から 42.54 ± 11.50 へと有意に低下した ($p = 0.015$)．腸腰筋の減少には下痢が関与している可能性が示唆された．化学療法は，骨格筋ごとに異なる影響を与えていた可能性が示唆された．サルコペニアの評価には骨格筋量の変化だけではなく質的変化も評価することが有用である．