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Skeletal muscle mass is associated with severe dysphagia in cancer patients

Hidetaka Wakabayashi[1,2]*, Masato Matsushima[2], Rimiko Uwano[1], Naoko Watanabe[1], Hideyuki Oritsu[1] & Yoshitaka Shimizu[1]

[1]*Department of Rehabilitation Medicine, Yokohama City University Medical Center, 4-57 Urafune-chou, Minami ward, Yokohama 232-0024, Japan;* [2]*Division of Clinical Epidemiology, Jikei University School of Medicine, 3-25-8 Nishi-shinbashi, Minato ward, Tokyo 105-0003, Japan*

Abstract

Background The purpose of this study was to assess the association between skeletal muscle mass, activities of daily living (ADLs) and severe dysphagia in cancer patients.

Methods A nested case-control study was performed in 111 consecutive cancer patients with dysphagia who were prescribed speech therapy. Skeletal muscle mass comprising the cross-sectional area of the left and right psoas muscles was assessed via abdominal computed tomography at the third lumbar vertebral level. ADLs were evaluated by the Barthel Index. The severity of dysphagia was assessed by the Food Intake Level Scale and was characterized by non-oral feeding or oral food intake at discharge. Univariate and logistic regression analyses were applied to examine the associations between dysphagia, skeletal muscle index (SMI) and ADLs.

Results There were 86 men and 25 women (mean age, 70 years). The mean SMI was 5.68 ± 1.74 cm^2/m^2 in men and 4.43 ± 1.21 cm^2/m^2 in women. The median Barthel Index score was 20. Thirty-three patients were on non-oral feeding at discharge. The mean SMI did not differ significantly between non-oral feeding and oral food intake groups in *t*-test. The median Barthel Index score was lower in the non-oral feeding group in Mann–Whitney *U* test. Logistic regression analysis of the severity of dysphagia adjusted for age, sex, SMI, Barthel Index score, serum albumin, cancer type and stage, and vocal cord paralysis showed that SMI was associated independently with oral food intake at discharge. Barthel Index score showed a tendency to be associated with oral food intake.

Conclusions Skeletal muscle mass is associated with severe dysphagia in cancer patients. ADLs show a tendency to be associated with severe dysphagia in cancer patients.

Keywords Sarcopenia; Carcinoma; Sarcopenic dysphagia; Rehabilitation; Nutrition

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**Correspondence to: Hidetaka Wakabayashi, Yokohama City University Medical Center, Department of Rehabilitation Medicine, 4-57 Urafune-chou, Minami ward, Yokohama, Kanagawa 232-0024, Japan: Tel: +81-45-261-5656, Fax: +81-45-253-9955, E-mail: noventurenoglory@gmail.com*

Introduction

Dysphagia is common in cancer patients. Oropharyngeal dysphagia has been reported in 50.6% of head and neck cancer patients treated with surgery and radiotherapy or chemoradiotherapy.[1] Approximately one third of dysphagia patients with head and neck cancer have developed pneumonia requiring treatment with aspiration pneumonia-associated mortality documented in 20 to 65% of cases.[2] Progressive dysphagia, weight loss and heartburn unresponsive to medical treatment are common clinical presentations of patients with esophageal cancer.[3] Dysphagia management is important because dysphagia increases the risk of complications such as aspiration pneumonia, choking, dehydration, malnutrition and poorer quality of life following loss of the joy of eating.[4]

Cancer patients have a high prevalence of sarcopenia and cancer cachexia. Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength, associated with a risk of adverse outcomes such as physical disability, poor quality of life and death.[5] The prevalence of sarcopenia measured using the definition of the European Working Group on Sarcopenia in Older People

was 1–33% in geriatric settings.[6] In contrast, a systematic review[7] showed the prevalence of sarcopenia was reported to be 16.2–67% in patients with pancreatic ductal adenocarcinoma, and sarcopenic obesity was considered a poor prognostic factor. Among patients with bladder cancer, 68.8% were sarcopenic, with sarcopenia being independently associated with increased cancer-specific survival and all-cause mortality.[8] Cancer cachexia was defined as a multifactorial syndrome defined by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that could not be fully reversed by conventional nutritional support, leading ultimately to progressive functional impairment.[9] Cachexia is prevalent in 50–80% of cases with advanced cancer, with the mortality rate of patients with cancer and cachexia being 80%.[10] Because cachexia can cause disease-related sarcopenia, these two conditions are regarded as important current and future public health issues.

The association between sarcopenia and dysphagia has been explored in the elderly[11,12] but not in cancer patients. Sarcopenic dysphagia is characterized by the loss of swallowing muscle mass and function associated with generalized loss of skeletal muscle mass and function.[4,13] Mid-upper arm circumference and calf circumference have been shown to correlate with dysphagia in hospitalized elderly individuals.[14,15] Decreased maximum voluntary tongue pressure against the palate and dysphagia has been attributed to sarcopenia or the causes of sarcopenia in the elderly.[16] Cachexia and dysphagia can cause severe alterations in nutrition in cancer patients that may lead to irreversible nutritional compromise and death.[17] However, the association between sarcopenia and severe dysphagia in cancer patients remains unknown.

Abdominal computed tomography (CT) is an accurate, practical approach to quantifying whole-body and regional skeletal muscle mass.[18] Abdominal CT is performed clinically for staging and diagnostic purposes in cancer patients. Cross-sectional imaging using CT is the preferred method for analysing muscle mass in patients with cancer.[9] However, no studies have reported the association between skeletal muscle mass assessed by abdominal CT and severe dysphagia. Further, while dysphagia has been associated with impaired activities of daily living (ADLs) in older adults,[19–23] the association between ADLs and severe dysphagia has not yet been evaluated in cancer patients. Therefore, the aim of the current study was to investigate the association between skeletal muscle mass assessed by abdominal CT, ADLs and severe dysphagia in cancer patients.

Materials and methods

A nested case-control study was performed in consecutive cancer patients with dysphagia who had been admitted to the Yokohama City University Medical Center, a tertiary-care acute general hospital, (mean length of stay, 13.8 days) and referred to the department of rehabilitation medicine between May 2010 and April 2014. Patients who needed speech therapy for dysphagia rehabilitation were referred to the Department of Rehabilitation Medicine by attending physicians. All patients were prescribed speech therapy for dysphagia rehabilitation one to three times a week at the bedside or gymnasium. Dysphagia rehabilitation by the physiatrists involved dysphagia assessment, direct exercises using food or drink and indirect exercises without the use of food or drink. Each session of speech therapy for dysphagia rehabilitation lasted between 20 min and 40 min. Some patients were also prescribed with physical therapy, which included range of motion exercises, resistance training, movement exercises, ambulation exercises and occupational therapy including functional occupational therapy, ADLs exercises and cognitive training five times a week.

Patients who had been diagnosed with cancer and prescribed speech therapy for dysphagia rehabilitation by physiatrists were included in the study. Patients who had not undergone an abdominal CT for cancer staging and diagnostic purposes during the period between 60 days before admission and 1 week after speech therapy was prescribed for dysphagia rehabilitation were excluded. The ethics committee of the Yokohama City University Medical Center approved the study. All participants provided informed consent prior to enrollment.

The severity of dysphagia was assessed by the Food Intake Level Scale[24] at discharge by a speech therapist. The Food Intake Level Scale is a 10-point observer-rating scale that measures the severity of dysphagia. Levels 1–3 relate to various degrees of non-oral feeding. Levels 4–6 pertain to various degrees of oral food intake and alternative nutrition. Levels 7–9 refer to various degrees of oral food intake alone, whereas Level 10 indicates normal oral food intake. The reliability and validity of the Food Intake Level Scale have been previously established.[24] We divided the study sample into cases and controls based on the severity of dysphagia at discharge. Patients who were on non-oral feeding (Levels 1–3) were designated as cases. Patients capable of oral food intake (Levels 4–10) were classified as controls because these levels did not properly reflect the severity of dysphagia in postoperative esophageal cancer patients. These patients frequently could not intake sufficient energy orally and needed alternative nutrition at discharge despite having mild or no dysphagia. In the 7-point ordinal Functional Oral Intake Scale, the corresponding categories characterizing the severity of dysphagia are represented by Level 1 (nothing by mouth) and Levels 2–7 (oral diet).[25]

We assessed skeletal muscle mass by measuring the cross-sectional area of the left and right psoas muscles via abdominal CT (Slice-O-Matic software v.5.0; Tomovision, Magog, Quebec, Canada) at the caudal end of the third lumbar vertebra.[26,27] Core muscle size measured as the total psoas area at

the third or fourth lumbar vertebra is a precise indicator of total skeletal muscle mass.[28] Simple psoas cross-sectional area measurement is a quick and easy method to assess sarcopenia.[29] Two physical therapists were trained to correctly identify and quantify the third lumbar vertebrae and psoas muscle. Muscles were quantified within a Hounsfield unit range of −29 to 150. Observers were blinded to the severity of dysphagia. The skeletal muscle index was calculated as total psoas muscle area divided by height squared. Because presarcopenia has been identified as an independent risk factor for the development of liver failure in Japanese cancer patients,[30] the cut-off value for this condition was defined as <5.67 cm^2/m^2 in men and <3.95 cm^2/m^2 in women.

ADLs were evaluated by the Barthel Index[31] at the start of speech therapy for dysphagia rehabilitation. The Barthel Index consists of 10 items: (1) feeding, (2) moving from a wheelchair to bed and return, (3) grooming, (4) transferring to and from a toilet, (5) bathing, (6) walking on a level surface, (7) going up and down stairs, (8) dressing, (9) continence of bowels and (10) continence of bladder.

Cancer stage was based on the Union for International Cancer Control stage groupings (I, II, III and IV) based on the tumour, lymph node and metastasis (TNM) classification of malignant tumours,[32] with the exception of brain tumour (as the TNM classification does not apply to brain tumour). Body mass index (BMI), serum albumin, haemoglobin, C-reactive protein (CRP) and the modified Glasgow Prognostic Score (mGPS) were also assessed.[33] The mGPS is an inflammation-based prognostic score that is defined as follows: mGPS 0, CRP $\leq$1.0 mg/dL; mGPS 1, CRP $>$1.0 mg/dL; mGPS 2, CRP $>$1.0 mg/dL and serum albumin $<$3.5 g/dL. We divided the types of cancer into two groups: esophageal and pharyngeal cancer that directly cause organic dysphagia and other cancers. Vocal cord paralysis was assessed using a fibre-optic laryngoscope.

Statistical analyses were performed using IBM Statistical Package for the Social Sciences version 21 software (IBM Corporation, Armonk, NY, USA). Parametric data were reported as the mean ± standard deviation (SD), whereas non-parametric data were expressed as the median and 25–75 percentiles. The chi-squares test, *t*-test and Mann–Whitney *U* test were used to analyse the differences between the two groups stratified by non-oral feeding or oral food intake. The Pearson correlation test was performed to assess the coefficients of correlation between skeletal muscle index, BMI, serum albumin, haemoglobin and age. The Spearman rank correlation test was performed to examine the coefficients of correlation between the Barthel Index score, CRP and other variables. The *t*-test, Mann–Whitney *U* test, analysis of variance and Kruskal–Wallis test were applied to analyse the skeletal muscle index and Barthel Index score stratified by gender, cancer stage and mGPS. Dunn's test for multiple comparisons was also performed. Logistic regression analysis was used to examine whether the skeletal muscle index, and the Barthel Index score were associated independently with severe dysphagia following adjustment for covariates including age, gender, serum albumin, haemoglobin, cancer type and stage and vocal cord paralysis. A *P*-value $<$0.05 was considered statistically significant.

Results

During the research period, 127 cancer patients requiring speech therapy for dysphagia rehabilitation were referred to the department of rehabilitation medicine. Sixteen patients whose abdominal CT was not available during the period between 60 days before admission and 1 week after speech therapy was prescribed for dysphagia rehabilitation were excluded. The remaining 111 cancer patients, 86 men and 25 women (mean age ± SD, 70 ± 10 years) participated in this nested case-control study. Primary cancer types included esophageal (*n* = 55), lung (*n* = 13), gastric (*n* = 11), brain (*n* = 6), colon (*n* = 5), prostate (*n* = 5), hepatocellular (*n* = 2), thyroid (*n* = 2), pharyngeal (*n* = 2) and others (*n* = 10). Physical therapy and occupational therapy were performed in 101 patients and 16 patients, respectively.

Table 1 summarizes the measurements for skeletal muscle index, ADLs and severe dysphagia. Based on the Food Intake Level Scale, there were 33 cases (non-oral feeding; Level 1, *n* = 9; Level 2, *n* = 22; and Level 3, *n* = 2) and 78 controls (oral food intake: Level 4, *n* = 11; Level 6, *n* = 43; Level 7, *n* = 3; Level 8, *n* = 16; Level 9, *n* = 5) at discharge. The mean skeletal muscle index was 5.68 ± 1.74 cm^2/m^2 in men and 4.43 ± 1.21 cm^2/m^2 in women. The median Barthel Index score was 20 points.

Age, Barthel Index score, cancer type, serum albumin and haemoglobin differed significantly between the non-oral feeding and oral food intake groups in univariate analysis (*Table* 1). The period between admission and prescription of speech therapy for dysphagia rehabilitation as well as the period between prescription of speech therapy for dysphagia rehabilitation and discharge were longer in the non-oral feeding group. In contrast, skeletal muscle index, presarcopenia, sex, cancer stage, vocal cord paralysis, BMI, CRP and mGPS did not differ significantly between non-oral feeding and oral food intake groups in univariate analysis.

The Pearson correlation test revealed significant correlations between skeletal muscle index and BMI (*Table* 2). In the Spearman rank correlation test, the Barthel Index score correlated significantly with serum albumin and haemoglobin but not with the skeletal muscle index. The mean skeletal muscle index was greater in men compared with women (*Table* 3). The Barthel Index score differed significantly between the mGPS 0, 1 and 2 subgroups. In the Dunn's test, the Barthel Index score differed significantly between mGPS 0 and mGPS 2.

Skeletal muscle index, Barthel Index score, age, gender, serum albumin, cancer type and stage and vocal cord paralysis

Table 1. Results of comparative tests for differences between subjects categorized by the severity of dysphagia[a]

	Total	Non-oral feeding	Oral food intake	*P*-value
Age, years	70 ± 10	73 ± 10	68 ± 10	0.013[b]
Sex, *n* (%)				0.778[c]
Male	86 (77%)	25 (76%)	61 (78%)	—
Female	25 (23%)	8 (24%)	17 (22%)	—
Cancer types				
Esophageal or pharyngeal	57 (51%)	11 (33%)	46 (59%)	0.013[c]
Others	54 (49%)	22 (67%)	32 (41%)	—
Cancer stage, *n* (%)				0.287[c]
1	20 (19%)	4 (13%)	16 (22%)	—
2	19 (18%)	5 (16%)	14 (19%)	—
3	39 (37%)	11 (34%)	28 (38%)	—
4	27 (26%)	12 (38%)	15 (21%)	—
Cancer treatment				<0.001[c]
Surgery	71 (64%)	13 (39%)	58 (74%)	—
Without surgery	40 (36%)	20 (61%)	20 (26%)	—
Psoas muscle area, cm^2	14.2 ± 5.1	12.7 ± 4.7	14.9 ± 5.1	0.038[b]
Male	15.5 ± 5.0	14.1 ± 4.7	16.1 ± 5.0	0.106[b]
Female	10.4 ± 3.0	9.1 ± 2.9	10.9 ± 3.0	0.185[b]
Skeletal muscle index, cm^2/m^2	5.40 ± 1.72	5.00 ± 1.73	5.56 ± 1.69	0.129[b]
Male	5.68 ± 1.74	5.23 ± 1.77	5.85 ± 1.72	0.161[b]
Female	4.43 ± 1.21	4.24 ± 1.46	4.51 ± 1.12	0.185[b]
Presarcopenia	52 (50%)	18 (60%)	34 (45%)	0.174[c]
Male	45 (55%)	16 (70%)	29 (49%)	0.095[c]
Female	7 (30%)	2 (29%)	5 (31%)	1.000[c]
Vocal cord paralysis	45 (43%)	7 (33%)	38 (52%)	0.130[c]
Barthel index	20 (0–65)	0 (0-30)	32 (5–74)	<0.001[d]
BMI	21.0 ± 3.6	20.1 ± 3.4	21.3 ± 3.7	0.154[b]
Albumin, g/dL	2.6 ± 0.6	2.4 ± 0.6	2.8 ± 0.6	0.003[b]
Haemoglobin, g/dL,	9.9 ± 1.6	9.4 ± 1.8	10.1 ± 1.6	0.031[b]
CRP, mg/dL	2.0 (1.0–4.5)	3.0 (1.2–5.6)	1.9 (0.8–4.3)	0.206[d]
mGPS, *n* (%)				0.323[c]
0	28 (26%)	21 (28%)	7 (23%)	—
1	4 (4%)	4 (5%)	0 (0%)	—
2	74 (70%)	50 (67%)	24 (77%)	—
Number of days from admission to speech therapy	18 (13–25)	20 (15–32.5)	17 (12–23)	0.033[d]
Number of days from speech therapy to discharge	31 (19–61)	55 (24.5–111.5)	30 (18–54)	0.011[d]

[a]Values represent the mean ± SD for age, psoas muscle area, BMI, albumin, and haemoglobin and the median (25th–75th percentiles) for the Barthel Index, CRP, and number of days from admission to speech therapy and from speech therapy to discharge.
[b]*t*-test.
[c]Chi-squared test.
[d]Mann–Whitney *U* test.
BMI, body mass index; CRP, C-reactive protein; mGPS, modified Glasgow Prognostic Score; SD, standard deviation.

Table 2. Results of the Pearson correlation and Spearman rank correlation tests[a]

	Barthel index	BMI	Albumin	Haemoglobin	CRP	Age
Skeletal muscle index	0.021	0.508*	0.038	0.086	0.009	−0.127
Barthel index	—	−0.021	0.326*	0.246*	−0.113	−0.145
BMI	—	—	0.137	0.190	0.024	−0.253*
Albumin	—	—	—	0.684*	−0.465*	−0.246*
Haemoglobin	—	—	—	—	−0.331*	−0.008
CRP	—	—	—	—	—	0.057

*Statistically significant at $P < 0.05$.
[a]Values represent the Spearman rank correlation coefficients for the Barthel Index and CRP and the Pearson correlation coefficients for BMI, albumin, haemoglobin, and age.
BMI, body mass index; CRP, C-reactive protein.

were included in the logistic regression analysis of severe dysphagia. There was no multicollinearity between these variables. Forced entry logistic regression analysis showed that the skeletal muscle index (odds ratio [OR] 1.829; 95% confidence interval [CI] 1.107–3.022; $P = 0.018$) was associated independently with oral food intake at discharge ($R^2 = 0.185$, $P < 0.001$; Hosmer–Lemeshow test, $P = 0.081$) (*Table* 4). The Barthel Index score (OR 1.019; 95% CI 0.997–1.042; $P = 0.098$) showed a tendency of being associated independently with oral food intake at discharge.

Table 3. Results of comparative tests for differences in skeletal muscle index and Barthel Index score in subjects categorized by sex, cancer stage, and modified Glasgow Prognostic Score

	Skeletal muscle index[a]	*P*-value	Barthel index[b]	*P*-value
Sex		<0.001[c]	—	0.891[d]
Male	5.68 ± 1.74	—	20 (0–60)	—
Female	4.43 ± 1.21	—	10 (0–86)	—
Cancer stage		0.441[e]		0.786[f]
1	5.58 ± 1.57	—	20 (0–86)	—
2	4.91 ± 1.58	—	10 (0–65)	—
3	5.64 ± 1.78	—	29.5 (0–72)	—
4	5.29 ± 1.67	—	7.5 (0–49)	—
mGPS		0.655[e]		0.048[f]
0	5.17 ± 1.81	—	45 (0–92.5)	—
1	5.53 ± 1.71	—	57 (31–72.5)	—
2	5.25 ± 2.29	—	10 (0–52.5)	—
Multiple comparison test mGPS and Barthel index				
0 vs. 1	—	—	—	0.495
0 vs. 2	—	—	—	0.043
1 vs. 2	—	—	—	0.103

[a]Values represent the mean ± standard deviation.
[b]Values represent the median (25th–75th percentiles).
[c]*t*-test.
[d]Mann–Whitney *U* test.
[e]Analysis of variance.
[f]Kruskal–Wallis test.
mGPS, modified Glasgow Prognostic Score.

Table 4. Forced entry logistic regression analysis

	OR[a]	95% CI[b]		*P*-value
Age	1.378	0.194	9.777	0.749
Sex	1.033	0.949	1.126	0.451
Skeletal muscle index	1.829	1.107	3.022	0.018
Barthel index	1.019	0.997	1.042	0.098
Albumin	1.759	0.443	6.987	0.422
Cancer stage 1	2.935	0.366	23.513	0.311
Cancer stage 2	2.653	0.390	18.051	0.319
Cancer stage 3	3.035	0.360	25.590	0.307
Cancer types	2.043	0.386	10.820	0.401
Vocal cord paralysis	1.572	0.403	6.129	0.515
Constant	<0.001	—	—	0.072

[a]OR, adjusted odds ratio.
[b]CI, confidence interval.

Discussion

This study addressed two issues concerning the associations among skeletal muscle mass, ADLs and the severity of dysphagia in cancer patients. Firstly, the skeletal muscle index was associated independently with severe dysphagia after adjustment for the Barthel Index score, age, gender, serum albumin, haemoglobin, cancer type and stage and vocal cord paralysis. Secondly, the Barthel Index score tended to be associated independently with severe dysphagia in cancer patients.

The skeletal muscle index was associated independently with severe dysphagia after adjustment for the Barthel Index score, age, gender, serum albumin, haemoglobin, cancer type and stage, and vocal cord paralysis. One cause of dysphagia in cancer patients is loss of the swallowing muscles accompanying generalized skeletal muscle loss. Using ultrasonography, Tamura *et al.*[34] evaluated the thickness of the central part of the tongue, a swallowing muscle, in the elderly and showed that age and mid-arm muscle area, which reflects generalized skeletal muscle, were independently associated with tongue thickness. This finding indicates that loss of both generalized skeletal and swallowing muscles can occur simultaneously. Using CT in healthy older adults, Feng *et al.*[35] assessed the geniohyoid muscle, another swallowing muscle, and found that the cross-sectional area of this muscle was significantly smaller in male aspirators compared with non-aspirators. This finding suggests that loss of swallowing muscle may be a component of aspiration. On the other hand, generalized skeletal muscle loss may also result from poor dietary intake and malnutrition caused by severe dysphagia. Improved nutrition can ameliorate both skeletal muscle mass and dysphagia.

The Barthel Index score showed a tendency to be associated independently with severe dysphagia after adjustment for skeletal muscle index, age, gender, serum albumin, haemoglobin, cancer type and stage, and vocal cord paralysis. Cancer is a common causative disease in patients with hospital-associated deconditioning.[36,37] Hospital-associated deconditioning is characterized by functional decline that occurs during acute hospitalization because of illness or injury or both and is unrelated to a specific neurological or orthopaedic insult or both.[38] A longer period between admission and prescription of speech therapy for rehabilitation of dysphagia in the non-oral feeding group may be due to a deterioration in general condition that may affect this association. In our previous cohort study,[36,37] 88–91% of patients with hospital-associated deconditioning were malnourished. Malnutrition can cause dysphagia[39,40] and has been associated with dysphagia and head lifting strength

which reflects the strength of the suprahyoid muscles.[41] Malnutrition and nutrition-related sarcopenia may account for the association between ADLs and dysphagia. In fact, dysphagia has been associated with nutritional status and ADLs in elderly individuals requiring long-term care.[23] Improvement of ADLs may affect the severity of dysphagia.

Elderly with low skeletal muscle mass, poor physical performance and a diagnosis of sarcopenia have been reported by both the European Working Group on Sarcopenia in Older People[5] and the Asian Working Group for Sarcopenia.[42] Subjects in the present study had a median Barthel Index score of 20 points, suggesting that many were unable to independently walk on a level surface at a speed exceeding the usual gait of 0.8 m/s, which is indicative of poor physical performance. Therefore, the association between skeletal muscle mass, ADLs and dysphagia may signify an existing relationship between generalized skeletal muscle sarcopenia and dysphagia in cancer patients. For individuals with sarcopenia and disability, including rehabilitation nutrition as part of a combined programme for both rehabilitation and nutritional care management may improve sarcopenia and sarcopenic dysphagia.[8]

This study had several limitations. Firstly, diagnostic testing for sarcopenia was not performed as grip strength and usual gait speed was not assessed during the study. Many patients could not walk independently as shown by the median Barthel Index score of 20 points. Secondly, nutritional status and cachexia were not evaluated by validated methods such as the mini nutritional assessment short form[43–45] or criteria established by an international consensus on cancer cachexia.[9] Instead of cancer cachexia, we assessed the mGPS using an inflammation-based prognostic score. Thirdly, cancer types were analysed by esophageal and pharyngeal cancer, which directly cause organic dysphagia and other cancer in the study because of the small numbers of patients with each cancer diagnosis. Strict inclusion criteria setup and sample size calculation should be performed in future research. Further studies investigating skeletal muscle mass, ADLs and dysphagia should evaluate sarcopenia, malnutrition and cachexia in patients with specific types of cancer.

In conclusion, skeletal muscle mass is associated with severe dysphagia in cancer patients. ADLs show a tendency to be associated with severe dysphagia in cancer patients. Cancer patients with dysphagia should be assessed for sarcopenia.

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All authors of this manuscript have complied with the guidelines of ethical authorship and publishing as stated in the *Journal of Cachexia, Sarcopenia and Muscle* 2010; 1:7–8 (von Haehling S, Morley J. E., Coats A. J., and Anker S. D.). The ethics committee of the Yokohama City University Medical Center approved the study. This study has been performed in accordance with the ethical standards established in the 1964 Declaration of Helsinki and later amendments.

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Conflict of interest

None declared.

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