



Difficulty swallowing and food bolus obstruction in advanced cancer: association with the cachexia-related quality of life

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Background: Swallowing disorders including difficulty swallowing and food bolus obstruction, result in reduced dietary intake—a common occurrence that leads to cachexia in patients with advanced cancer. This study examined the effects of swallowing difficulty and food bolus obstruction on cachexia-related quality of life (QOL).

Methods: This study secondarily analyzed data from a self-reported questionnaire survey of adult patients with advanced cancer at 11 palliative care services. Difficulty swallowing and food bolus obstruction were measured using the 11-point Numeric Rating Scale (NRS), whereas dietary intake and cachexia-related QOL were assessed using the Ingesta-Verbal/Visual Analog Scale and the Functional Assessment of Anorexia/Cachexia Therapy Anorexia/Cachexia Subscale. A multiple logistic regression model was employed to determine the factors associated with varying degrees of difficulty swallowing and food bolus obstruction.

Results: Of the invited 495 patients, 378 agreed to participate (response rate 76.4%). After excluding participants with missing data, the data of 332 participants were analyzed; 26.5% had difficulty swallowing (NRS ≥ 1) and 28.3% had food bolus obstruction (NRS ≥ 1). Multivariate analysis revealed a substantial association between difficulty swallowing and food bolus obstruction and a decrease in cachexia-related QOL, regardless of performance status and the existence of cachexia. The coefficients for difficulty

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swallowing and food bolus obstruction were -6.34 [95% confidence interval (CI): -9.55 to -3.14 , $P < 0.001$] and -5.88 (95% CI: -8.68 to -3.09 , $P < 0.001$), respectively.

Conclusions: Cachexia-related QOL deteriorated as difficulty swallowing and food bolus obstruction worsened; thus, healthcare providers must diagnose and treat swallowing disorders in a timely manner to prevent progression of cachexia and improve cachexia-related QOL.

Keywords: Advanced cancer; swallowing disorders; dietary intake; quality of life (QOL)

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Introduction

Cancer cachexia is a multifactorial syndrome involving the constant loss of skeletal muscle mass with or without fat mass loss that cannot be completely reversed by usual nutritional care and can lead to progressive functional impairment (1,2). This phenomenon is a consequence of imbalances in protein and energy levels caused by a combination of reduced dietary consumption, hypo-anabolism, and hyper-catabolism due to systemic inflammation (1,2). The prevalence of cachexia among patients with late-stage cancer is 50–80%, with a mortality rate of approximately 20–30% (3). Nevertheless, a universal plan of action to combat cachexia in patients with cancer has not yet been established, despite its high incidence rate and adverse effects on the longevity and quality of life (QOL)

of cancer patients (4,5).

In systemic inflammation, pro-inflammatory cytokines act through changes in the central nervous system, particularly the hypothalamic-pituitary-adrenal axis and sympathetic nervous system (6). Thus, exposure to pro-inflammatory cytokines in the central nervous system evokes anorexia and reduced dietary intake in patients with advanced cancer, although increasing dietary intake is a principal component of cancer cachexia management (6). In addition, patients frequently suffer from nutritional impact symptoms, which reduce dietary intake and promote weight loss, including pain, nausea and vomiting, taste and smell disturbances, drowsiness, and depression, leading to impaired physical function and deteriorated QOL (6-10).

An observational study conducted in patients with various types of advanced cancer in palliative care settings demonstrated that oral issues result in nutritional impact symptoms that in turn influence the physical, social, and psychological well-being of patients; therefore, such oral issues must be assessed in the early stages to prevent an inability to eat or drink (11). The study also showed a strong relationship between mucositis, dry mouth, and swallowing disorders (11). Among oral issues, difficulty swallowing and food bolus obstruction directly cause reduced dietary intake; these are commonly observed symptoms that lead to cachexia in patients with advanced cancer (6-9). As some of these patients may benefit from oral care to mitigate nutritional impact symptoms and nutritional care to increase dietary intake, they must be provided with the opportunity to receive optimal care (12,13).

In previous studies that measured QOL of patients with difficulty swallowing and food bolus obstruction, Swallowing QOL questionnaire (SWAL-QOL) and the Swallowing Quality of Care questionnaire (SWAL-CARE), which measure overall QOL, were the tools used

Highlight box

Key findings

- Swallowing disorders were independently associated with cachexia-related QOL and dietary intake in patients with advanced cancer in palliative care settings.

What is known and what is new?

- The correlations between difficulty swallowing and food bolus obstruction and the decrease in dietary intake and impaired QOL are yet to be determined in the context of advanced cancer patients undergoing palliative care.
- Cachexia-related QOL and dietary intake deteriorated as difficulty swallowing and food bolus obstruction worsened in patients with advanced cancer receiving palliative care.

What is the implication, and what should change now?

- Healthcare providers must diagnose and treat swallowing disorders, such as difficulty swallowing and food bolus obstruction, in a timely manner to prevent progression of cachexia and improve cachexia-related QOL.

(14-16). According to these studies, high quality of life was significantly associated with low levels of difficulty swallowing and food bolus obstruction. To the best of our knowledge, the relationship between difficulty swallowing and food bolus obstruction and decreased dietary intake and compromised QOL among advanced cancer patients receiving palliative care has not yet been clarified. Therefore, this study aimed to investigate the prevalence and severity of difficulty swallowing and food bolus obstruction and examine the effect of these symptoms on dietary intakes and cachexia-related QOL. We present this article in accordance with the STROBE reporting checklist (available at <https://apm.amegroups.com/article/view/10.21037/apm-22-1203/rc>).

Methods

This study comprises a sub-analysis of data obtained from a multicenter self-reported questionnaire-based study that aimed to develop measurement tools for the evaluation of eating-related distress in patients with advanced cancer. The methodology applied in that study has been described and published previously (17). In summary, this research was conducted at specialized palliative care facilities, including palliative care outpatient services, hospital palliative care teams, and palliative care units, spread across eleven hospitals in Japan, from July 2020 to July 2021. Patients recently referred to the participating palliative care institutions during the study period were consecutively recruited. Data were gathered from a predetermined number of patients based on the size and location of each institution. The eligibility criteria were as follows: (I) new referral to palliative care, (II) age ≥ 20 years, (III) diagnosis of locally advanced or metastatic cancer (including hematological neoplasms), (IV) awareness of the malignancy diagnosis, and (V) ability to respond to a self-reported questionnaire. This analysis excluded patients who: (I) were forbidden to eat by the primary physician for medical reasons and (II) had serious psychological distress that was recognized in an interview with the palliative care physician. Moreover, patients who refused to participate in the study were excluded.

The present study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and the ethical guidelines for medical and health research involving human subjects issued by the Ministry of Health, Labour and Welfare in Japan. The study was approved by the National Cancer Center Research Ethics Review Board (No. 2020-

070). Japanese law does not require individual informed consent from participants in a non-invasive observational trial such as this study; therefore, we used an opt-out method. If patients did not want to participate, we requested them to return the questionnaire, stating “no participation” on it. The completion and return of the questionnaire was regarded as consent to participate.

Measurement

Demographic and clinical characteristics

Demographic and clinical characteristics, including sex, age, primary site of cancer, Eastern Cooperative Oncology Group Performance Status (ECOG-PS) (18), and treatment history (pre-chemotherapy, chemotherapy, and previously untreated/treated) were obtained from the self-reported questionnaires. Anthropometric measurements, such as current body weight, previous body weight, and height, were self-reported by the patients and were used to determine the body mass index (BMI) and percentage of weight loss (%WL) over a span of 6 months. BMI was computed by dividing the current body weight (in kilograms) by the square of the height (in meters), while %WL was calculated using the following formula: $\%WL = [\text{current body weight (in kilograms)} - \text{previous body weight (in kilograms)}] / \text{previous body weight (in kilograms)} \times 100$.

Difficulty swallowing and food bolus obstruction

The patients were requested to evaluate their present difficulty swallowing and food bolus obstruction using an eleven-point Numerical Rating Scale (NRS) (9,10,19). The NRS scale scores ranged from 0 to 10, where 0 corresponded to no difficulty in swallowing and food bolus obstruction, and 10 was indicative of the most severe difficulty swallowing and food bolus obstruction; correspondingly, elevated scores denoted greater severity of the disturbances.

Dietary intake and cachexia-related QOL

The patients were instructed to assess their dietary intake using the Ingesta-Verbal/Visual Analog Scale (Ingesta-VVAS) (20), whereby higher scores signified improved dietary intake. Cachexia-related QOL was assessed using the Functional Assessment of Anorexia/Cachexia Therapy Anorexia Cachexia Subscale (FAACT ACS), which is a patient-reported outcome measure designed specifically to evaluate the distinct symptoms and concerns related to cachexia. The FAACT ACS consists of twelve items that

measure cachexia-related symptoms and concerns, yielding a score for each domain. Furthermore, the subscales derived from the twelve-item FAACT ACS, including the five-item anorexia symptoms and four-item anorexia concerns subscales, have been found to be useful for assessing these parameters in patients with lung cancer. These subscales have also been applied to evaluate the effects of cachexia treatment on patients with advanced cancer (21-24). The Japanese version of the FAACT ACS has been published by the developers (25).

Statistical analysis

The primary endpoints of this study were difficulty swallowing, food bolus obstruction, dietary intake, and FAACT ACS. Patients with missing data related to the primary endpoints were excluded from the analysis. Patient demographics and clinical characteristics are reported as number (%) for categorical variables and mean [standard deviation (SD)] for continuous variables. Cachexia was defined according to the international consensus criteria (1) as %WL over the previous six months $\geq 5\%$ or BMI $< 20 \text{ kg/m}^2 + \% \text{WL}$ over the previous six months $\geq 2\%$.

To explore the potential confounding variables such as sex, age, primary cancer site, ECOG PS, anticancer treatment status (pre-chemotherapy, chemotherapy, and never treated/previously treated), and cachexia (non-cachexia and cachexia) and examine their impact on difficulty swallowing (NRS ≥ 1) and food bolus obstruction (NRS ≥ 1), independent-samples *t*-tests and analysis of variance (ANOVAs) were used.

Difficulty swallowing and food bolus obstruction were categorized into three levels for analysis, as per previous research: NRS =0 was defined as none, NRS =1-3 as mild, and NRS ≥ 4 as moderate to severe (10). The relationships among difficulty swallowing (three groups), food bolus obstruction (three groups), dietary intake, twelve-item FAACT ACS score, five-item anorexia symptoms scores, and four-item anorexia concerns scores were investigated using independent-samples *t*-tests and ANOVA (24).

To identify factors associated with the levels of difficulty swallowing and food bolus obstruction, a multivariate model adjusted for sex, age (two groups: < 69 and ≥ 70 years), primary cancer site, ECOG PS (two groups: PS 0-2 and PS 3-4), treatment status (pre-chemotherapy, chemotherapy, and never treated/previously treated), and cachexia (non-cachexia and cachexia) was generated using multiple logistic regression. A robust linear model with crude estimation

was developed to assess the effects of dietary intake and FAACT ACS score on difficulty swallowing and food bolus obstruction. Significance was set at $P < 0.05$. SPSS version 28.0.1 (IBM Corp., Armonk, NY, USA) and EZR (Saitama Medical Center, Jichi Medical University) (26) were used for all analyses.

Results

Out of the 495 patients who were invited to participate in the study, 378 (76.4%) provided responses to the questionnaire, with no refusals. However, 46 patients were deemed ineligible for analysis because of missing data pertinent to the primary endpoints, ultimately resulting in a total of 332 patients.

The patient demographics and clinical characteristics

The patient demographics and clinical characteristics are presented in *Table 1*. In this study cohort, 51.5% of the patients were male, and the mean age was 61.6 ± 12.1 years. The primary cancer sites were located in the upper/lower gastrointestinal tract, liver/biliary system/pancreas, and lung in 13.9%, 17.2%, and 22.6% of the patients, respectively. The ECOG-PS scores were 0-2 and 3-4 for 71.9% and 26.8% of the patients, respectively. The proportion of patients who were receiving chemotherapy and those who were never treated or previously treated was 65.4% and 26.8%, respectively. Moreover, 46.7% of patients had cachexia.

Prevalence and factors associated with difficulty swallowing and food bolus obstruction

The incidence of difficulty swallowing, encompassing both difficulty swallowing and food bolus obstruction, is illustrated in *Table 2*. Of the patients undergoing palliative care for advanced cancer, 26.5% and 28.3% experienced difficulty swallowing (NRS ≥ 1) and food bolus obstruction (NRS ≥ 1), respectively. Male sex (difficulty swallowing, $P = 0.027$); age ≥ 70 years (difficulty swallowing, $P = 0.037$; and food bolus obstruction, $P = 0.049$); head and neck organs as the primary cancer site (difficulty swallowing, $P < 0.001$; food bolus obstruction, $P = 0.026$); ECOG-PS 3-4 (difficulty swallowing, $P = 0.019$; food bolus obstruction, $P = 0.01$); and ongoing or completed treatment (difficulty swallowing, $P = 0.017$; food bolus obstruction, $P = 0.007$) were associated with difficulty swallowing and food bolus obstruction (both

Table 1 Patient characteristics (n=332)

Characteristics	Value
Sex [n (%)]	
Male	171 (51.5)
Female	161 (48.5)
Age (mean ± standard deviation)	61.6±12.1
Age [n (%)]	
<69 years	239 (71.9)
≥70 years	93 (28.0)
Primary cancer site [n (%)]	
Upper and lower gastrointestinal tract	46 (13.9)
Liver, biliary system, and pancreas	57 (17.2)
Lungs	75 (22.6)
Breasts	25 (7.5)
Gynecology	19 (5.7)
Urology	18 (5.4)
Otolaryngology	12 (3.6)
Hematology	9 (2.7)
Others	66 (19.9)
ECOG performance status [n (%)]	
0–2	239 (71.9)
3–4	89 (26.8)
Treatment status [n (%)]	
Pre-chemotherapy	21 (6.3)
Chemotherapy	217 (65.4)
Never treated/previously treated	89 (26.8)
Cachexia [n (%)]	
Non-cachexia	156 (47.0)
Cachexia	155 (46.7)

The sums of some percentages were not 100% owing to missing values. ECOG, Eastern Cooperative Oncology Group.

NRS ≥1).

Association between swallowing disorders with dietary intake and cachexia-related QOL

The relationships between difficulty swallowing and food bolus obstruction with dietary intake, 12-item FAACT A/CS, 5-item anorexia symptoms, and 4-item anorexia

concerns are summarized in *Table 3*. Increased severity of difficulty swallowing and food bolus obstruction were significantly correlated with reduced dietary intake (as determined by the Ingesta-VVAS score) and poor QOL related to cachexia (evaluated using the twelve-item FAACT A/CS and five-item anorexia symptoms and four-item anorexia concerns subscales).

Multivariate analysis showed that difficulty swallowing and food bolus obstruction were significantly associated with reduced dietary intake independent of performance status and the presence of cachexia, with coefficients of -0.76 (95% CI: -1.48 to -0.054 , $P<0.034$) and -1.04 (95% CI: -1.91 to -0.16 , $P<0.019$) for difficulty swallowing and food bolus obstruction, respectively (*Tables 4, 5*).

Further, multivariate analysis revealed that difficulty swallowing and food bolus obstruction were significantly associated with lower 12-item FAACT A/CS score, independent of performance status and the presence of cachexia, with coefficients of -6.34 (95% CI: -9.55 to -3.14 , $P<0.001$) and -5.88 (95% CI: -8.68 to -3.09 , $P<0.001$) for difficulty swallowing and food bolus obstruction, respectively (*Tables 4, 5*).

Discussion

To the best of our knowledge, this is the first multicenter study to explore the relationships between swallowing disorders including difficulty swallowing and food bolus obstruction, with cachexia-related QOL and dietary intake in patients with advanced cancer in a palliative care setting. This study demonstrated that swallowing disorders were independently associated with cachexia-related QOL and dietary intake in patients with advanced cancer in palliative care settings.

We determined the prevalence and risk factors for swallowing disorders in patients in an advanced palliative care setting and confirmed that swallowing disorders are associated with reduced dietary intake and lower cachexia-related QOL. Difficulty swallowing and food bolus obstruction were observed in 26.5% and 28.3% of our participants, respectively. The frequency of difficulty swallowing is 5–54% across all stages of cancer (11,27–29). However, to the best of our knowledge, no study has assessed the frequency of food bolus obstruction in patients with cancer. In this study, the frequency of food bolus obstruction was significantly higher during and after chemotherapy. Furthermore, a previous study reported that difficulty swallowing was statistically associated with head

Table 2 Prevalence of swallowing disorders (difficulty swallowing, food bolus obstruction)

Characteristics	Difficulty swallowing (NRS ≥ 1)				Food bolus obstruction (NRS ≥ 1)			
	N	%	95% CI	P	N	%	95% CI	P
Total (n=332)	88	26.5	0.22–0.31		94	28.3	0.23–0.33	
Sex				0.027				0.082
Male (n=171)	54	31.6	0.25–0.39		57	33.3	0.26–0.40	
Female (n=161)	34	21.1	0.15–0.27		37	23.0	0.16–0.29	
Age				0.037				0.049
<69 years (n=239)	50	20.9	0.16–0.26		55	23.0	0.18–0.28	
≥ 70 years (n=93)	38	40.9	0.31–0.51		39	41.9	0.32–0.52	
Primary cancer site				<0.001				0.026
Upper and lower gastrointestinal tract (n=46)	13	28.3	0.15–0.41		14	30.4	0.17–0.44	
Liver, biliary system, and pancreas (n=57)	12	21.1	0.10–0.32		12	21.1	0.10–0.32	
Lungs (n=75)	27	36.0	0.25–0.47		29	38.7	0.28–0.50	
Breast (n=25)	5	20.0	0.04–0.36		5	20.0	0.04–0.36	
Gynecology (n=19)	2	10.5	–0.03 to 0.24		3	15.8	–0.01 to 0.32	
Urology (n=18)	1	5.6	–0.05 to 0.16		2	11.1	–0.03 to 0.26	
Otolaryngology (n=12)	7	58.3	0.30–0.86		7	58.3	0.30–0.86	
Hematology (n=9)	0	0	0		2	22.2	–0.05 to 0.49	
Others (n=66)	21	31.8	0.21–0.43		20	30.3	0.19–0.41	
ECOG performance status				0.019				0.010
0–2 (n=239)	57	23.8	0.18–0.29		60	25.1	0.20–0.31	
3–4 (n=89)	30	33.7	0.24–0.44		33	37.1	0.27–0.47	
Treatment status				0.017				0.007
Pre-chemotherapy (n=21)	1	4.8	–0.04 to 0.14		2	9.5	–0.03 to 0.22	
Chemotherapy (n=217)	56	25.8	0.20–0.32		59	27.2	0.21–0.33	
Never treated/previously treated (n=89)	30	33.7	0.24–0.44		32	36.0	0.26–0.46	
Cachexia				0.071				0.27
Non-cachexia (n=156)	34	21.8	0.15–0.28		38	24.4	0.18–0.31	
Cachexia (n=155)	48	31.0	0.24–0.38		48	31.0	0.24–0.38	

NRS, Numerical Rating Scale; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group.

Table 3 Relationships between swallowing disorders and dietary intake

Swallowing disorders	Dietary intake (VAS)		12-item FAACT ACS		5-item anorexia symptoms		4-item anorexia concerns	
	Mean ± SD [95% CI]	P	Mean ± SD [95% CI]	P	Mean ± SD [95% CI]	P	Mean ± SD [95% CI]	P
Difficulty swallowing		0.006		<0.001		<0.001		0.008
None (NRS: 0) n=244	6.2±2.6 [5.8–6.5]		32±7.6 [31–33]		13±4.2 [13–14]		10±2.9 [10–10]	
Mild (NRS: 1–3) n=29	5.2±2.4 [4.6–5.9]		29±8.4 [27–31]		11±5.1 [10–13]		9.5±3.0 [8.7–10]	
Moderate-to-severe (NRS: ≥4) n=52	4.9±2.6 [3.9–5.9]		25±9.5 [21–28]		9.8±4.8 [8.0–11]		8.7±3.6 [7.3–10]	
Food bolus obstruction		<0.001		<0.001		<0.001		0.013
None (NRS: 0) n=238	6.2±2.6 [5.9–6.6]		32±7.8 [31–33]		14±4.3 [13–14]		10±3.0 [10–10]	
Mild (NRS: 1–3) n=54	5.3±2.2 [4.7–5.9]		29±7.5 [27–31]		11±4.3 [10–12]		9.5±2.9 [8.7–10]	
Moderate-to-severe (NRS: ≥4) n=40	4.6±2.7 [3.7–5.5]		25±8.6 [22–28]		9.9±4.8 [8.3–11]		9.0±3.4 [7.9–10]	

VAS, Visual Analogue Scale; FAACT ACS, Functional Assessment of Anorexia/Cachexia Therapy Anorexia Cachexia Subscale; SD, standard deviation; CI, confidence interval; NRS, Numerical Rating Scale.

and neck cancer (11), while another study suggested that swallowing disorders were frequently observed not only in patients with head and neck cancer but also in patients with other types of cancer (29). In this study, swallowing disorders were also frequently found in patients with cancer of lung (difficulty swallowing, 36%; food bolus obstruction, 38.7%), liver, biliary system, pancreas (difficulty swallowing, 21.1%; food bolus obstruction, 21.1%), and breast (difficulty swallowing, 20.0%; food bolus obstruction, 20.0%). These results indicate that swallowing disorders are a common symptom of cancer, regardless of the primary site of origin. This study also indicated that patients with advanced cancer, particularly older male patients with head and neck cancer and worse ECOG-PS, were likely to have difficulty swallowing and food bolus obstruction, both during and after treatment. This finding is consistent with those of previous studies (29–31). Therefore, healthcare providers must consider the possibility of swallowing disorders when providing care to this vulnerable patient population.

Most importantly, cachexia-related QOL and dietary intake deteriorated with the worsening of difficulty swallowing and food bolus obstruction. Difficulty swallowing was associated with a dysphagia-specific health-related QOL impairment (30). In this study, besides the performance status and cachexia, difficulty swallowing and food bolus obstruction were independently associated with cachexia-related QOL. Furthermore, difficulty swallowing and food bolus obstruction negatively affected QOL related to cachexia symptoms and concerns. Ingenuity in food form and enhanced rehabilitation should be considered to improve difficulty swallowing and food bolus obstruction in these patients. However, although there is limited availability of treatment in palliative care settings (31), difficulty swallowing and food bolus obstruction must be diagnosed and treated carefully with fiberoptic endoscopic or videofluoroscopic examination of swallowing to improve cachexia-related QOL, independent of the performance status and cachexia.

Table 4 Difficulty swallowing: multivariate analysis (dietary intake; FAACT ACS, 12 items)

Characteristics	Dietary intake			FAACT ACS, 12 items		
	Coefficient	95% CI	P	Coefficient	95% CI	P
Difficulty swallowing						
None (NRS: 0)	Ref.			Ref.		
Mild (NRS: 1–3)	–0.76	–1.48 to –0.054	0.034	–3.34	–5.62 to –1.07	0.004
Moderate-to-severe (NRS: ≥4)	–0.45	–1.46 to 0.55	0.37	–6.34	–9.55 to –3.14	<0.001
Sex						
Male (n=178)	Ref.			Ref.		
Female (n=165)	0.052	–0.53 to 0.63	0.86	–0.24	–2.10 to 1.61	0.79
Age						
<69 years	Ref.			Ref.		
≥70 years	0.39	–0.23 to 1.03	0.21	1.22	–0.79 to 3.23	0.23
Primary cancer site						
Upper and lower gastrointestinal tract	Ref.			Ref.		
Liver, biliary system, and pancreas	–0.094	–0.92 to 0.90	0.98	–2.08	–4.99 to 0.82	0.15
Lungs	0.68	–0.19 to 1.55	0.12	–0.32	–3.10 to 2.46	0.82
Breast	0.093	–1.11 to 1.30	0.87	0.93	–2.90 to 4.78	0.63
Gynecology	0.88	–0.43 to 2.19	0.19	–0.65	–4.86 to 2.77	0.75
Urology	0.56	–0.84 to 1.97	0.43	–1.71	–6.19 to 3.28	0.45
Otolaryngology	0.058	–1.51 to 1.63	0.94	2.09	–2.91 to 7.10	0.41
Hematology	1.61	–0.074 to 3.29	0.06	5.02	–0.34 to 10.3	0.066
Others	0.82	–0.081 to 1.72	0.074	0.66	–2.21 to 3.54	0.64
ECOG performance status						
0–2	Ref.	–		–		
3–4	–2.33	–2.94 to –1.71	<0.001	–5.45	–7.41 to –3.49	<0.001
Treatment status						
Pre-chemotherapy	Ref.			Ref.		
Chemotherapy	0.021	–1.11 to 1.06	0.97	2.78	–0.85 to 6.41	0.13
Never treated/previous treatment	–0.19	–1.41 to 1.00	0.74	1.51	–2.32 to 5.34	0.43
Cachexia						
Non-cachexia	Ref.			Ref.		
Cachexia	–1.13	–1.66 to –0.59	<0.001	–2.46	–4.17 to –0.75	0.0049

FAACT ACS, Functional Assessment of Anorexia/Cachexia Therapy Anorexia Cachexia Subscale; ECOG, Eastern Cooperative Oncology Group; NRS, Numerical Rating Scale; CI, confidence interval; Ref., reference group.

Table 5 Food bolus obstruction: multivariate analysis (dietary intake; FAACT ACS, 12 items)

Characteristics	Dietary intake			FAACT ACS, 12 items		
	Coefficient	95% CI	P	Coefficient	95% CI	P
Food bolus obstruction						
None (NRS: 0)	Ref.			Ref.		
Mild (NRS: 1-3)	-0.89	-1.62 to -0.15	0.017	-3.73	-6.08 to -1.38	0.0019
Moderate-to-severe (NRS: ≥4)	-1.04	-1.91 to -0.16	0.019	-5.88	-8.68 to -3.09	<0.001
Sex						
Male	Ref.			Ref.		
Female	-0.0021	-0.57 to 0.57	0.99	-0.22	-2.07 to 1.61	0.80
Age						
<69 years	Ref.			Ref.		
≥70 years	0.44	-0.18 to 1.06	0.16	1.49	-0.50 to 3.50	0.14
Primary cancer site						
Upper and lower gastrointestinal tract	Ref.			Ref.		
Liver, biliary system, and pancreas	-0.026	-0.93 to 0.88	0.95	-2.06	-4.97 to 0.85	0.16
Lungs	0.72	-0.14 to 1.59	0.10	-0.25	-3.03 to 2.51	0.85
Breast	0.085	-1.11 to 1.28	0.88	0.63	-3.19 to 4.46	0.74
Gynecology	0.92	-0.38 to 2.23	0.16	-0.49	-4.68 to 3.70	0.81
Urology	0.47	-0.92 to 1.87	0.50	-1.93	-6.40 to 2.54	0.39
Otolaryngology	0.23	-1.33 to 1.79	0.76	1.96	-3.03 to 6.97	0.43
Hematology	1.75	0.089 to 3.41	0.039	6.04	0.72 to 11.36	0.026
Others	0.81	-0.88 to 1.71	0.076	0.50	-2.37 to 3.38	0.72
ECOG performance status						
0-2	Ref.	-		-		
3-4	-2.23	-2.84 to -1.63	<0.001	-5.36	-7.31 to -3.42	<0.001
Treatment status						
Pre-chemotherapy	Ref.			Ref.		
Chemotherapy	0.034	-1.09 to 1.16	0.95	2.68	-0.92 to 6.29	0.14
Never treated/previously treated	-0.16	-1.35 to 1.03	0.79	1.49	-2.31 to 5.30	0.44
Cachexia						
Non-cachexia	Ref.			Ref.		
Cachexia	-1.15	-1.68 to -0.61	<0.001	-2.64	-4.34 to -0.94	0.0023

FAACT ACS, Functional Assessment of Anorexia/Cachexia Therapy Anorexia Cachexia Subscale; ECOG, Eastern Cooperative Oncology Group; NRS, Numerical Rating Scale; CI, confidence interval; Ref., reference group.

The current investigation has several strengths, such as the high response rate to the questionnaire survey, a multicentric design, and use of validated measurement tools. Nevertheless, there are certain limitations to this study. Firstly, since this was a cross-sectional analysis of the questionnaire survey, the causal relationship of each factor with swallowing disorders could not be established. Second, as data of non-responding patients were not obtained, a comparison between responding and non-responding patients was not possible. Finally, as patients who were forbidden to eat by the primary physician for medical reasons were excluded, the findings of this study might underestimate the proportion and magnitude of difficulty swallowing and food bolus obstruction.

Conclusions

Cachexia-related QOL and dietary intake deteriorated as difficulty swallowing and food bolus obstruction worsened in patients with advanced cancer receiving palliative care. Thus, healthcare providers must diagnose and treat swallowing disorders, such as difficulty swallowing and food bolus obstruction, in a timely manner to prevent progression of cachexia and improve cachexia-related QOL.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The present study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and the ethical guidelines for medical and health research involving human subjects issued by the Ministry of Health, Labour and Welfare in Japan. The study was approved by the National Cancer Center Research Ethics Review Board (No. 2020-070). Japanese law does not require individual informed consent from participants in a non-invasive observational trial such as this study; therefore, we used an opt-out method. If patients did not want to participate, we requested them to return the questionnaire, stating “no participation” on it. The completion and return of the questionnaire was regarded as consent to participate.

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