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Citation for final published version:

Koshimoto, Saori, Amano, Koji, Hopkinson, Jane B. , Okamura, Satomi, Sakaguchi, Tatsuma, Arakawa, Sayaka, Tokoro, Akihiro, Mori, Naoharu, Nozato, Junko, Iriyama, Tetsuji, Sato, Shingo and Takeuchi, Takashi 2025. Sex-related differences in eating-related distress experienced by patients with advanced cancer. *Supportive Care in Cancer* 33 (3) , 241. 10.1007/s00520-025-09302-2

Publishers page: <https://doi.org/10.1007/s00520-025-09302-2>

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Original Article

Sex-related differences in eating-related distress experienced by patients with advanced cancer

Running Title

Sex-related differences in eating-related distress

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Abstract

Background

Sex-related differences in eating-related distress (ERD) experienced by cancer patients have not previously been clarified.

Methods

We conducted a multicenter survey among advanced cancer patients referred to palliative care. Data on patient characteristics were collected from the electronic medical records, and data on measurement outcomes were obtained from a questionnaire. Patients were categorized into male and female groups. We measured ERD using the Questionnaire for Eating-Related Distress among Patients with advanced cancer (QERD-P). The QERD-P comprises 3 items in each of the 7 factors, for a total of 21 items, and each item is rated on a 7-point Likert scale. High scores indicate worse distress. Comparisons were calculated using the Mann–Whitney U test. To assess associations between sexes and ERD, multivariate logistic regression analysis was performed.

Results

A total of 192 patients were enrolled and divided into the male ($n = 92$) and female ($n = 100$) groups. The total score of the QERD-P was significantly higher in the male group ($p = 0.018$). The subtotal scores of “reasons why I cannot eat,” “insufficient information,” and “arguments with my family” were significantly higher in the male group ($p = 0.035$, 0.032 , and 0.003 , respectively). The male group had significantly higher risks for ERD associated with “arguments with my family” and “time with my family” (odds ratio [OR] 2.69, 95% confidence interval [CI] 1.38–5.24; OR 2.28, 95% CI 1.15–4.53).

Conclusions

Males had significantly worse ERD and were at higher risk of ERD in family relationships than females.

Keywords

cancer; cachexia; systemic inflammation; symptom; distress; quality of life

Abstract, 250 words; Text, 2471 words; Tables, 6; Figures, 1; References: 38

Introduction

A majority of patients with advanced-stage cancers are affected by cancer cachexia, a wasting disorder associated with appetite loss, reduced dietary intake, and weight loss. Systemic inflammation due to host-tumor interactions and cancer treatments contribute to the wasting process [1-7]. Cancer cachexia induces various physical and psychological symptoms in patients, which in turn generate various types of distress, experienced by both patients and their family caregivers. Eating-related distress (ERD) is one of the typical forms of distress observed among patients with cancer cachexia [8-15].

Qualitative studies have investigated the tensions that exist between cachectic patients with advanced cancer and their family caregivers over food, showing the anxiety and distress that surround eating issues [16, 17]. A nationwide survey regarding bereaved family members of patients who had died of cancer found family caregivers can experience high levels of ERD and need nutritional support when caring for patients [18]. A quantitative study revealed that both patients with advanced cancer with cachexia and their family caregivers had greater ERD than those without cachexia [19]. In addition to these studies, a mixed-methods study conducted on male patients with advanced cancer and their partners reported that partners were more concerned about the patients' weight loss than the patients were themselves and that partners expressed feelings of deep concern, frustration, and insufficiency in their loving and innovative efforts to prepare appealing food [20]. Furthermore, a qualitative study revealed the unmet support needs among family caregivers of patients with advanced cancer and eating problems. The study comprised 31 patients (i.e., 27 males and 4 females) and 31 family caregivers (i.e., 4 males and 27 females), showing that family caregivers required more knowledge about nutrition and how to best provide nutritional care [21]. The findings of these studies implied that the specific ERD experienced by male patients is due to the unique struggles of female caregivers and the role of nourishing patients [16-21].

Thus, previous studies have indicated the possibility of sex-related differences in ERD, but the elements of ERD that differ between the sexes and to what extent remain unclear. Recently, The Questionnaire for Eating-Related Distress among Patients with advanced cancer (QERD-P) has been developed to specifically measure ERD, based on findings obtained in previous studies [22]. Therefore, the present study aimed to investigate whether there were sex-related differences in ERD experienced by patients with advanced cancer referred to palliative care using the QERD-P and to determine any associations between sex and the ERD factors.

Methods

Study design, setting, and patient population

This survey was performed using a self-reported questionnaire in hospital palliative care teams and palliative care units at 6 cancer institutes in Japan between November 2023 and June 2024. All patients who met the eligibility criteria were enrolled. The inclusion criteria were established as follows: patients who were 1) newly referred to palliative care, 2) aged ≥ 18 years, 3) diagnosed with locally advanced or metastatic cancer and hematologic neoplasms, 4) aware of the diagnosis of cancer, and 5) able to complete a self-reported questionnaire. However, patients who could not eat by mouth for medical reasons, those with emotional distress that was too severe (as determined in an interview with the palliative care physician), and those who refused to participate in this study were excluded.

Ethics approval and consent to participate

This study was conducted in accordance with the ethical standards outlined in the Helsinki Declaration and the ethical guidelines for medical and health research involving human subjects presented by the Ministry of Health, Labor, and Welfare in Japan [23]. This study received approval from the Institutional Review Board at Osaka University Hospital for all participating institutes (approval number 23226). Completion and return of the questionnaire was considered consent to participate in this study. Patients who were unwilling to participate in this study were asked to return the questionnaire marked with "no participation."

Measurements

Information on patient characteristics, such as sex, age, Eastern Cooperative Oncology Group (ECOG) performance status [24], and treatment status (i.e., pre-chemotherapy, chemotherapy, and never treated/previous treatment), was collected. Patients who decided to cease or not undergo cancer treatments were categorized as never treated/previous treatment. In addition, the most recent blood test results acquired within the week prior to answering the questionnaire were recorded.

Data on patient anthropometric measurements (i.e., height [m], current body weight [kg], and body weight 6 months ago [kg]) were also obtained. The body mass index (BMI) was calculated by dividing the body weight [kg] by the height [m] squared. The weight loss rate over 6 months was calculated using the following formula: $(\text{body weight 6 months ago [kg]} - \text{current body weight [kg]}) / \text{body weight 6 months ago [kg]} \times 100$. Patients with a 6-month weight loss rate $> 5\%$ or $\text{BMI} < 20 \text{ kg/m}^2 + 6\text{-month weight loss rate} > 2\%$ were diagnosed with cachexia, based on the international diagnostic criteria on cancer cachexia [2].

Participating patients' dietary intake was assessed using the Ingesta-Verbal/Visual Analog Scale (IVVAS), which is a 10-point scale. Higher scores indicate better dietary intake (0, nothing at all; 10, as usual). In medical oncology, a dietary intake score of 7 or less suggests that patients have a nutritional risk of weight loss [25, 26].

Nineteen nutrition impact symptoms (NISs) were evaluated using a numerical rating scale (NRS) ranging between 0 and 10 (0, no; 1–3, mild; 4–6, moderate; 7–9, severe; 10, unbearable) [27]. NISs are considered effective patient-centered outcome measurements, validated and supported by a systematic review and clinical recommendations edited by the American Society for Parenteral and Enteral Nutrition [28]. Having 4 or more NISs with a score of $\text{NRS} \geq 4/10$ was shown to be significantly associated with reduced food intake, as assessed using the IVVAS, ERD measured using the QERD-P, and depression diagnosed using the Patient Health Questionnaire-9 [29-33].

Participating patients' anxiety, depression, and distress were assessed using the Hospital Anxiety and Depression Scale (HADS)-Anxiety, HADS-Depression, Distress thermometer, and Impact thermometer [34-36]. Each of the seven questions included in the HADS-Anxiety and HADS-Depression is scored on a scale of 0 to 3, with the total score ranging from 0 to 21. A higher total score indicates greater anxiety and depression. A score of 8 to 10 is considered "suspicious" and a score of 11 or higher is considered "anxious and depressed" [34, 35]. The Distress thermometer and Impact thermometer range between 0 (not at all) and 10 (overwhelming) [36].

Patients' quality of life was evaluated using the European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30) [37].

ERD experienced by patients was measured using the QERD-P. The QERD-P long version contains 3 items in each of the 7 factors, for a total of 21 items, and each item is rated on a 7-point Likert scale. High scores indicate worse distress. The 7 factors related to ERD are (1) reduced dietary intake, (2) reasons why I cannot eat, (3) becoming weaker, (4) insufficient information, (5) arguments with my family, (6) change in appearance, and (7) time with my family. The QERD-P short version contains 7 representative items, one selected from each of the 7 factors. Each item is rated on a 7-point Likert scale, and high scores indicate worse distress [22].

Statistical analysis

We divided the patients into 2 groups based on their biological sex. We presented patient characteristics and anthropometric

measurements as proportions (%) for categorical variables and medians (interquartile range [IQR]) for continuous variables, where appropriate. We made comparisons between males and females using the Mann–Whitney U test or chi-squared test, where appropriate.

To examine the association of sexes with the ERD experienced by patients, a multivariate logistic regression analysis was performed. The ERD scores for a dependent variable were divided into two categories using their medians, because no appropriate cutoff values have been shown. A multivariate model was adjusted for the sex (female and male), age (< 65 and ≥ 65 years old), primary cancer site (lung, gastrointestinal, and others), ECOG PS (0 or 1, 2, and 3 or 4), and treatment status (non-chemotherapy and chemotherapy).

All results were considered to be significant if the p-value was less than 0.05. All analyses were performed using SPSS software version 22.0 (IBM, Tokyo).

Results

A total of 201 patients were eligible and recruited for this study, but 9 patients declined. Thus, 192 patients were initially included. However, 10 patients did not have essential values, such as scores of the QERD-P. Finally, a total of 182 patients were included in the main analysis (Figure 1).

Patient characteristics are summarized in Table 1. All participating patients were divided into the male (n = 92) and female (n = 100) groups. There were no significant differences between the two groups, except for the primary cancer site. Moreover, differences in dietary intake and NISs between the male and female groups are presented in Table 2. There were no significant differences between the two groups, except for abnormal smell and difficulty swallowing. Furthermore, differences in anxiety, depression, and distress between the male and female groups are described in Table 3. No significant differences were observed between the two groups, except for the proportion of patients with a HADS-Anxiety score of 11 or more. In addition, differences in EORTC QLQ-C30 between males and females are shown in Table 4. No significant differences were observed between the two groups, except for nausea and vomiting, included in the symptom scales.

Differences in ERD measured using the QERD-P between the male and female groups are described in Table 5. The total scores of the QERD-P long and short versions in the male group were significantly higher than those in the female group (85.0 and 76.0, $p = 0.018$; 27.0 and 25.0, $p = 0.018$). The subtotal scores of “reasons why I cannot eat,” “insufficient information,” and “arguments with my family” were significantly higher in the male group ($p = 0.035$, 0.032 , and 0.003 , respectively). The males had significantly worse ERD than the females in this population. Specifically, the male patients were more distressed than the female patients regarding the three factors.

Associations between sex and ERD assessed using the QERD-P are presented in Table 6. The male group had significantly higher risks for ERD regarding “arguments with my family” and “time with my family” (odds ratio [OR] 2.69, 95% confidence interval [CI] 1.38–5.24, $p = 0.004$; OR 2.28, 95% CI 1.15–4.53, $p = 0.019$, respectively) than the female group. The male patients were likely to have higher ERD concerning family relationships than the female patients in this population.

Discussion

This was the first study to investigate whether there were sex-related differences in ERD experienced by patients with advanced cancer referred to palliative care using the recently developed QERD-P. Furthermore, this study examined the associations between sex and the ERD factors. The results showed that male patients had significantly worse ERD than female patients and that male

patients were likely to have a higher risk of ERD regarding family relationships than female patients. In particular, the concerns about “arguments with my family” and “time with my family” were significantly associated with the males’ emotional distress related to eating problems. These findings are consistent with those reported in previous studies, showing that male patients felt pressure regarding meals from female caregivers who were responsible for nourishing them [20, 21]. Female family caregivers of male patients are likely to be more worried about patients’ dietary intake and weight loss than the patients themselves. Hence, female caregivers who have a nourishing role within the family frequently struggle to prepare appealing food for their male patients. Furthermore, female family caregivers usually want to know how to best provide nutritional care to their loved ones and regain their body weight. Male patients know that they need to eat more but they cannot, and they feel that they are being forced to eat by the female caregivers, who passionately struggle with the role of nourishing the patient. These feelings on both sides may lead to arguments among male patients and female family caregivers, and male patients may avoid eating with their family members to avoid such conflicts. This is thought to be an underlying issue behind the male patient’s distress [16-21]. In summary, when healthcare providers deliver palliative care to male patients with advanced cancer and their female caregivers, the emotional conflicts stemming from these family relationships need to be considered, and an explanation of these conflicts between male patients and their female caregivers should be provided by palliative care practitioners with the aim to prevent the situation from getting worse.

Although sex-related differences were observed for some factors when measuring ERD using the QERD-P, no sex-related differences were observed in the total score for either the long or short versions. A narrative review reported that male patients with cancer generally have higher prevalence of cachexia, greater levels of weight loss or muscle wasting, and worse clinical outcomes compared with female patients with cancer [38]. The findings of this review support the findings of this study. However, few studies have investigated sex-related differences of clinical phenotypes in cancer cachexia as well as basic mechanisms underlying sex-related differences in cancer cachexia [38]. Considering that several items and factors can be used to assess differences in ERD between males and females, the QERD-P should be used according to the objectives of the given study.

This study has several strengths and limitations. Approximately 96% of all eligible patients were included, and data on approximately 95% of all participating patients were used in the main analysis. In addition, approximately 71% of all participants were receiving chemotherapy in multiple cancer institutes, suggesting that the findings of this study reflected the real situation of patients with advanced cancer undergoing cancer treatments. However, this study was only conducted among Japanese inpatients. Moreover, only data obtained at the time of the survey were analyzed, although the ERD experienced by patients may fluctuate during the clinical course. Furthermore, key information on living alone or with family caregivers was not collected in this study, and thus their influence on the results regarding their relationships with the participating patients was unknown. Nonetheless, the lack of data on family caregivers was not expected to be a major problem because male patients usually have female caregivers. In addition to these, differences between ethnic groups and by age groups, particularly younger generations, should also be considered. Further research is necessary to validate the present findings and clarify their relevance in clinical practice in different cultures and generations.

Conclusions

Among patients with advanced cancer referred to palliative care, males had significantly worse ERD and were at higher risk of ERD in family relationships than females. When palliative care practitioners involved in cancer care see a male patient, they must consider his ERD, specifically the distress derived from family relationships, to deliver beneficial care for this patient population.

Author contributions

Study concept and design: Koji Amano; collection and/or assembly of data: Saori Koshimoto, Koji Amano, Tatsuma Sakaguchi,

Sayaka Arakawa, Akihiro Tokoro, Junko Nozato, Tetsuji Iriyama, Shingo Sato, and Takashi Takeuchi; statistical analysis: Saori Koshimoto, Koji Amano, and Satomi Okamura; data analysis and interpretation: Saori Koshimoto, Koji Amano, and Jane Hopkinson; original draft preparation: Koji Amano; review and editing: Saori Koshimoto, Jane Hopkinson, Satomi Okamura, Tatsuma Sakaguchi, and Sayaka Arakawa; supervision: Akihiro Tokoro, Naoharu Mori, and Takashi Takeuchi. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

The authors declare no conflicts of interest.

Funding

The present study was supported by JSPS KAKENHI Grant Number 23K10970 (S.K.) and Project Mirai Cancer Research Grants (K.A.).

Institutional review board statement

This study received approval from the Institutional Review Board at Osaka University Hospital for all participating institutes (approval number 23226).

Informed consent statement

This study was conducted in accordance with the ethical standards outlined in the Helsinki Declaration and the ethical guidelines for medical and health research involving human subjects presented by the Ministry of Health, Labor, and Welfare in Japan [23]. Completion and return of the questionnaire was considered consent to participate in this study. Patients who were unwilling to participate in this study were asked to return the questionnaire marked “no participation.”

Data availability statement

The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

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Table 1. Patient characteristics			
	Male (n = 92)	Female (n = 100)	p-value
Age in years	69.0 (58.0, 76.0)	62.0 (51.3, 74.0)	0.051
Primary cancer site			
Upper and lower gastrointestinal tracts	15 (16.3)	9 (9.0)	< 0.001
Liver, biliary system, and pancreas	17 (18.5)	16 (16.0)	
Lung	26 (28.3)	14 (14.0)	
Breast	0 (0.0)	12 (12.0)	
Gynecologic	0 (0.0)	23 (23.0)	
Urological	13 (14.1)	1 (1.0)	
Head and neck	7 (7.6)	3 (3.0)	
Hematological	5 (5.4)	8 (8.0)	
Others	9 (9.8)	14 (14.0)	
ECOG PS			
0	1 (1.1)	1 (1.0)	0.165
1	19 (20.7)	18 (18.0)	
2	35 (38.0)	32 (32.0)	
3	29 (31.5)	46 (46.0)	
4	8 (8.7)	3 (3.0)	
Treatment status			
Pre-chemotherapy	14 (15.2)	10 (10.0)	0.498
Chemotherapy	62 (67.4)	74 (74.0)	
Never treated/previous treatment	16 (17.4)	16 (16.0)	
Albumin (g/dL)	3.3 (2.6, 3.7)	3.2 (2.8, 3.7)	0.886
C-reactive protein (mg/dL)	3.55 (0.68, 8.00)	2.02 (0.29, 7.29)	0.361
Body mass index (kg/m ²)	21.1 (19.2, 24.0)	20.5 (17.6, 24.3)	0.199
Weight loss rate over 6 months (%)	6.7 (2.4, 12.7)	6.2 (0.8, 11.8)	0.489
Cachexia/refractory cachexia, yes	61 (66.3)	62 (62.0)	0.551
Pleural effusion, ascites, or edema affecting weight, yes	20 (21.7)	22 (22.0)	1.000
Values represent n (%) or medians (interquartile range). ECOG PS, Eastern Cooperative Oncology Group Performance Status.			

Table 2. Differences in dietary intake and nutrition impact symptoms between males and females			
	Male (n = 92)	Female (n = 100)	p-value
Dietary intake			
Dietary intake score	5.0 (3.0, 7.0)	4.8 (2.0, 5.8)	0.155
Proportion of patients with a dietary intake score of 7 or less	78 (84.8)	85 (85.0)	0.841
Symptoms that interfere with patients' ability to ingest or digest nutrients			
Oral pain	0.0 (0.0, 0.0)	0.0 (0.0, 2.0)	0.119
Lack of appetite	5.0 (1.0, 7.0)	5.0 (2.0, 8.0)	0.342
Early satiety	5.0 (2.0, 7.0)	5.0 (2.0, 8.0)	0.172
Nausea	1.0 (0.0, 3.0)	1.0 (0.0, 5.0)	0.148
Vomiting	0.0 (0.0, 1.0)	0.0 (0.0, 2.0)	0.309
Constipation	4.5 (1.0, 7.0)	3.0 (0.0, 7.0)	0.453
Diarrhea	1.0 (0.0, 3.0)	0.0 (0.0, 3.0)	0.978
Abnormal taste	1.0 (0.0, 5.0)	0.0 (0.0, 3.8)	0.076
Abnormal smell	0.0 (0.0, 2.0)	0.0 (0.0, 1.0)	0.004
Dry mouth	2.0 (0.0, 5.0)	2.0 (0.0, 5.0)	0.917
Dental problems	0.0 (0.0, 2.0)	0.0 (0.0, 2.8)	0.917
Difficulty swallowing	0.0 (0.0, 3.0)	0.0 (0.0, 1.0)	0.028
Food bolus obstruction	0.0 (0.0, 3.0)	0.0 (0.0, 2.8)	0.161
Symptoms that compromise patients' desire to eat and take nutrients			
Fatigue	3.0 (2.0, 6.0)	4.0 (2.0, 6.0)	0.537
Drowsiness	3.0 (1.0, 5.0)	4.0 (1.0, 6.0)	0.381
Anxiety	3.0 (1.0, 5.0)	3.0 (1.0, 5.0)	0.941
Feeling sad	3.0 (1.0, 5.0)	3.0 (1.0, 5.0)	0.638
Symptoms that indirectly compromise patients' food and nutrient intake			
Pain other than oral pain	2.0 (0.0–7.0)	4.0 (0.0–7.0)	0.086
Shortness of breath	2.0 (0.0–5.0)	1.0 (0.0–3.0)	0.193
Number of nutrition impact symptoms with a score of 4 or more	6.0 (2.0–9.0)	6.0 (3.0–8.0)	0.809
Values represent n (%) or medians (interquartile range). Dietary intake was assessed using the Ingesta-Verbal/Visual Analog Scale (10-point scale). High scores indicate better dietary intake. Symptoms were rated between 0 and 10. High scores indicate worse symptoms.			

Table 3. Differences in anxiety, depression, and distress between males and females			
	Male	Female	p-value
Hospital anxiety and depression scale-Anxiety	(n = 85)	(n = 85)	
Anxiety	7.0 (5.0, 10.0)	8.0 (5.0, 11.0)	0.150
Proportion of patients with an Anxiety score of 8 or more	38 (44.7)	51 (60.0)	0.065
Proportion of patients with an Anxiety score of 11 or more	14 (16.5)	26 (30.6)	0.046
Hospital anxiety and depression scale-Depression	(n = 83)	(n = 83)	
Depression	9.0 (6.0, 12.0)	9.0 (5.0, 12.0)	0.608
Proportion of patients with a Depression score of 8 or more	57 (68.7)	52 (62.7)	0.513
Proportion of patients with a Depression score of 11 or more	27 (32.5)	33 (39.8)	0.419
Distress and impact thermometer	(n = 84)	(n = 89)	
Distress thermometer	6.0 (3.3, 8.0)	7.0 (5.0, 8.0)	0.116
Proportion of patients with a Distress thermometer score of 4 or more	63 (75.0)	74 (83.1)	0.422
Impact thermometer	5.0 (3.0, 8.0)	5.0 (3.0, 8.0)	0.963
Proportion of patients with an Impact thermometer score of 3 or more	67 (79.8)	72 (80.9)	1.000
Values represent n (%) or medians (interquartile range). Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (4-point scale). High scores indicate worse anxiety and depression. Emotional distress and its interference with daily life were rated between 0 and 10 using the Distress and Impact Thermometer. High scores indicate worse distress and impact.			

Table 4. Differences in EORTC QLQ-C30 between males and females			
	Male (n = 80)	Female (n = 83)	p-value
Functional scales			
Physical functioning	50.0 (33.3, 78.3)	46.7 (33.3, 73.3)	0.889
Role functioning	33.3 (0.0, 66.7)	33.3 (0.0, 66.7)	0.654
Emotional functioning	66.7 (50.0, 83.3)	66.7 (50.0, 83.3)	0.753
Cognitive functioning	58.3 (33.3, 66.7)	66.7 (33.3, 83.3)	0.628
Social functioning	66.7 (33.3, 83.3)	50.0 (33.3, 66.7)	0.436
Symptom scales			
Fatigue	77.8 (55.6, 88.9)	77.8 (44.4, 88.9)	0.628
Nausea and vomiting	8.3 (0.0, 29.2)	16.7 (0.0, 50.0)	0.008
Pain	83.3 (33.3, 100.0)	83.3 (33.3, 100.0)	0.786
Dyspnea	33.3 (33.3, 100.0)	33.3 (0.0, 66.7)	0.103
Sleep disturbance	66.7 (33.3, 100.0)	66.7 (33.3, 100.0)	0.912
Appetite loss	66.7 (33.3, 100.0)	66.7 (33.3, 100.0)	0.805
Constipation	33.3 (33.3, 66.7)	33.3 (0.0, 66.7)	0.875
Diarrhea	33.3 (0.0, 33.3)	0.0 (0.0, 33.3)	0.885
Global health status	25.0 (16.7, 41.7)	25.0 (16.7, 50.0)	0.536
Financial difficulties	33.3 (0.0, 66.7)	33.3 (0.0, 66.7)	0.760
Values represent the median (interquartile range). QOL was assessed using the EORTC QLQ-C30. High scores indicate higher QOL in Functional scales and Global health status or worse symptoms and difficulties in Symptom scales and Financial difficulties. QOL, quality of life; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire.			

Table 5. Differences in eating-related distress between males and females			
	Male (n = 89)	Female (n = 93)	p-value
Factor 1: Reduced dietary intake			
It is distressing that I cannot eat even though I want to eat more.	5.0 (3.0, 6.0)	5.0 (3.0, 6.0)	0.523
It is distressing that I cannot enjoy eating.	5.0 (3.3, 6.0)	5.0 (3.0, 6.0)	0.572
It is distressing that I get full quickly and cannot eat enough.	5.0 (3.0, 6.0)	4.0 (3.0, 6.0)	0.638
Subtotal score	15.0 (9.0, 18.0)	15.0 (9.0, 18.0)	0.764
Factor 2: Reasons why I cannot eat			
I do not understand the reason why I cannot eat.	3.0 (2.0, 6.0)	3.0 (1.8, 4.0)	0.051
I do not understand the reason why I do not have an appetite.	3.0 (2.0, 5.5)	3.0 (1.0, 4.0)	0.021
I do not understand the reason why I cannot eat enough.	4.0 (2.0, 5.5)	3.0 (1.0, 4.0)	0.030
Subtotal score	10.0 (6.0, 16.0)	9.0 (4.0, 12.0)	0.035
Factor 3: Becoming weaker			
I am concerned that I will become weaker if I cannot eat.	6.0 (3.0, 6.0)	5.0 (4.0, 6.0)	0.646
I am concerned that I will lose muscle strength if I cannot eat.	6.0 (4.0, 6.0)	5.0 (4.5, 6.0)	0.658
I am concerned that I will lose weight if I cannot eat.	6.0 (3.0, 6.0)	5.0 (4.0, 6.0)	0.209
Subtotal score	17.0 (12.0, 18.0)	15.0 (12.0, 18.0)	0.388
Factor 4: Insufficient information			
I have insufficient information about which nutrients I should prioritize.	5.0 (3.3, 6.0)	4.0 (3.0, 5.0)	0.055
I have insufficient information about which nutrients I should avoid.	5.0 (3.0, 5.0)	4.0 (3.0, 5.0)	0.046
I have insufficient information about which nutritional supplements I should take.	5.0 (3.0, 5.0)	4.0 (2.0, 5.0)	0.033
Subtotal score	15.0 (9.0, 17.0)	12.0 (8.0, 15.0)	0.032
Factor 5: Arguments with my family			
I have arguments with my family about food.	2.0 (1.0, 4.0)	1.0 (1.0, 3.0)	0.003
I am troubled that my family seems to try to force me to eat.	2.0 (1.0, 4.0)	1.0 (1.0, 3.0)	0.022
I get frustrated with my family over food.	2.0 (1.0, 4.0)	1.0 (1.0, 3.0)	0.010
Subtotal score	6.0 (3.0, 11.0)	4.0 (3.0, 9.0)	0.003

Factor 6: Change in appearance			
It is hard for me to accept how much my appearance has changed.	4.0 (2.0, 5.0)	3.0 (1.0, 4.8)	0.004
It is hard for me to be seen by others as so skinny.	4.0 (2.0, 5.0)	3.0 (1.0, 5.0)	0.111
It is hard to see myself as so skinny.	4.0 (1.3, 5.0)	3.0 (1.0, 5.0)	0.506
Subtotal score	12.0 (6.0, 15.0)	9.0 (3.0, 13.0)	0.073
Factor 7: Time with my family			
I spend less time talking with my family because I do not eat with them.	4.0 (2.0, 5.0)	3.0 (1.0, 4.0)	0.021
I spend less time enjoying with my family during meals.	4.0 (2.0, 6.0)	4.0 (1.0, 6.0)	0.398
I spend less time in daily life with my family because I cannot eat.	4.0 (2.0, 5.0)	2.0 (1.0, 4.0)	0.029
Subtotal score	12.0 (6.0, 15.0)	10.0 (5.0, 13.0)	0.064
Total score of the long version	85.0 (64.0, 100.0)	76.0 (62.0, 87.0)	0.018
Total score of the short version	27.0 (20.0, 35.0)	25.0 (20.0, 30.0)	0.018
Values represent the median (interquartile range). Eating-related distress was assessed using the Questionnaire for Eating-Related Distress among Patients with advanced cancer (7-point scale). Boldfaced items indicate those belonging to the short version. High scores indicate worse distress.			

Table 6. Associations between sex and eating-related distress assessed using the QERD-P

Independent variables	Adjusted odds ratio	95% confidence interval	p-value
Factor 1: Reduced dietary intake (n =182)			
Sex (ref = female)			
Male	1.18	0.62, 2.28	0.615
Age (ref = < 65 years old)			
≥ 65 years old	0.52	0.27, 0.99	0.048
Primary cancer site (ref = lung)			
Gastrointestinal	4.48	1.80, 11.20	0.001
Others	2.40	1.02, 5.66	0.045
ECOG PS (ref = 0 or 1)			
2	1.26	0.53, 3.02	0.602
3 or 4	1.25	0.53, 2.92	0.610
Treatment status (ref = non-chemotherapy)			
Chemotherapy	1.43	0.71, 2.89	0.323
Factor 2: Reasons why I cannot eat (n =180)			
Sex (ref = female)			
Male	1.33	0.67, 2.64	0.413
Age (ref = < 65 years old)			
≥ 65 years old	1.63	0.83, 3.22	0.158
Primary cancer site (ref = lung)			
Gastrointestinal	0.61	0.24, 1.58	0.307
Others	0.83	0.34, 2.06	0.687
ECOG PS (ref = 0 or 1)			
2	0.65	0.27, 1.57	0.340
3 or 4	2.10	0.86, 5.10	0.102
Treatment status (ref = non-chemotherapy)			
Chemotherapy	1.91	0.91, 3.98	0.087
Factor 3: Becoming weaker (n =182)			
Sex (ref = female)			
Male	0.56	0.21, 1.51	0.251
Age (ref = < 65 years old)			
≥ 65 years old	1.79	0.69, 4.68	0.233
Primary cancer site (ref = lung)			
Gastrointestinal	1.94	0.53, 7.10	0.315
Others	1.29	0.41, 4.13	0.664
ECOG PS (ref = 0 or 1)			
2	0.53	0.13, 2.24	0.389
3 or 4	0.56	0.13, 2.34	0.427
Treatment status (ref = non-chemotherapy)			
Chemotherapy	1.49	0.55, 4.05	0.431

Factor 4: Insufficient information (n =181)			
Sex (ref = female)			
Male	1.69	0.70, 4.06	0.241
Age (ref = < 65 years old)			
≥ 65 years old	1.61	0.68, 3.85	0.281
Primary cancer site (ref = lung)			
Gastrointestinal	1.11	0.32, 3.81	0.870
Others	1.03	0.32, 3.30	0.967
ECOG PS (ref = 0 or 1)			
2	1.20	0.35, 4.19	0.772
3 or 4	0.66	0.21, 2.07	0.476
Treatment status (ref = non-chemotherapy)			
Chemotherapy	2.12	0.87, 5.15	0.096
Factor 5: Arguments with my family (n =181)			
Sex (ref = female)			
Male	2.69	1.38, 5.24	0.004
Age (ref = < 65 years old)			
≥ 65 years old	0.93	0.48, 1.79	0.821
Primary cancer site (ref = lung)			
Gastrointestinal	1.64	0.67, 4.03	0.283
Others	1.47	0.61, 3.51	0.390
ECOG PS (ref = 0 or 1)			
2	0.57	0.24, 1.38	0.214
3 or 4	0.69	0.30, 1.60	0.387
Treatment status (ref = non-chemotherapy)			
Chemotherapy	1.05	0.51, 2.15	0.898
Factor 6: Change in appearance (n =182)			
Sex (ref = female)			
Male	1.69	0.85, 3.38	0.134
Age (ref = < 65 years old)			
≥ 65 years old	1.47	0.74, 2.90	0.270
Primary cancer site (ref = lung)			
Gastrointestinal	2.64	0.99, 7.06	0.053
Others	0.88	0.38, 2.07	0.773
ECOG PS (ref = 0 or 1)			
2	1.18	0.48, 2.89	0.718
3 or 4	1.52	0.62, 3.68	0.359
Treatment status (ref = non-chemotherapy)			
Chemotherapy	1.25	0.59, 2.63	0.558
Factor 7: Time with my family (n =180)			
Sex (ref = female)			
Male	2.28	1.15, 4.53	0.019

Age (ref = < 65 years old)			
≥ 65 years old	0.75	0.38, 1.47	0.397
Primary cancer site (ref = lung)			
Gastrointestinal	1.76	0.72, 4.32	0.219
Others	2.17	0.91, 5.17	0.079
ECOG PS (ref = 0 or 1)			
2	1.52	0.63, 3.70	0.353
3 or 4	1.64	0.69, 3.89	0.262
Treatment status (ref = non-chemotherapy)			
Chemotherapy	0.77	0.36, 1.62	0.484
Long version (n = 181)			
Sex (ref = female)			
Male	1.58	0.83, 3.00	0.165
Age (ref = < 65 years old)			
≥ 65 years old	0.81	0.42, 1.54	0.517
Primary cancer site (ref = lung)			
Gastrointestinal	1.58	0.65, 3.82	0.314
Others	0.81	0.35, 1.87	0.622
ECOG PS (ref = 0 or 1)			
2	0.70	0.29, 1.68	0.426
3 or 4	0.94	0.40, 2.17	0.875
Treatment status (ref = non-chemotherapy)			
Chemotherapy	0.96	0.48, 1.91	0.897
Short version (n = 181)			
Sex (ref = female)			
Male	1.82	0.95, 3.49	0.070
Age (ref = < 65 years old)			
≥ 65 years old	0.83	0.43, 1.59	0.572
Primary cancer site (ref = lung)			
Gastrointestinal	1.72	0.70, 4.19	0.237
Others	1.03	0.45, 2.37	0.948
ECOG PS (ref = 0 or 1)			
2	0.89	0.37, 2.11	0.783
3 or 4	1.45	0.62, 3.37	0.389
Treatment status (ref = non-chemotherapy)			
Chemotherapy	1.11	0.55, 2.23	0.770
Sex (female and male), age (< 65 and ≥ 65 years old), primary cancer site (lung, gastrointestinal, and others), ECOG PS (0 or 1, 2, and 3 or 4), and treatment status (non-chemotherapy and chemotherapy) were included in the multivariate analysis. QERD-P, Questionnaire for Eating-Related Distress among Patients with advanced cancer; ECOG PS, Eastern Cooperative Oncology Group Performance Status.			

Figure 1. Flow diagram of patient participation in the study.