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Original article

Muscle mass, quality, and strength; physical function and activity; and metabolic status in cachectic patients with head and neck cancer

Nao Ohmae [a], Sonoko Yasui-Yamada [a, *], Taiki Furumoto [b], Kyoko Wada [a], Haruka Hayashi [a], Midori Kitao [a], Ayaka Yamanaka [a], Miyu Kubo [a], Momoyo Matsuoka [c], Seiichiro Kamimura [c], Aki Shimada [c], Nori Sato [b], Yoshiaki Kitamura [c], Shinsuke Katoh [b], Noriaki Takeda [c], Yasuhiro Hamada [a]

[a] Department of Therapeutic Nutrition, Institute of Biomedical Sciences, Tokushima University Graduate School, 3-18-15, Tokushima 770-8503, Japan
[b] Department of Rehabilitation Medicine, Tokushima University Hospital, 2-50-1, Tokushima 770-8503, Japan
[c] Department of Otolaryngology, Institute of Biomedical Sciences, Tokushima University Graduate School, 3-18-15, Tokushima 770-8503, Japan

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SUMMARY

Background & aims: Cancer cachexia is commonly associated with poor prognosis in patients with head and neck cancer (HNC). However, its pathophysiology and treatment are not well established. The current study aimed to assess the muscle mass/quality/strength, physical function and activity, resting energy expenditure (REE), and respiratory quotient (RQ) in cachectic patients with HNC.
Methods: This prospective cross-sectional study analyzed 64 patients with HNC. Body composition was measured via direct segmental multifrequency bioelectrical impedance analysis, and muscle quality was assessed using echo intensity on ultrasonography images. Muscle strength was investigated utilizing handgrip strength and isometric knee extension force (IKEF). Physical function was evaluated using the 10-m walking speed test and the five times sit-to-stand (5-STS) test. Physical activity was examined using a wearable triaxial accelerometer. REE and RQ were measured via indirect calorimetry. These parameters were compared between the cachectic and noncachectic groups.
Results: In total, 23 (36%) patients were diagnosed with cachexia. The cachectic group had a significantly lower muscle mass than the noncachectic group. Nevertheless, there was no significant difference in terms of fat between the two groups. The cachectic group had a higher quadriceps echo intensity and a lower handgrip strength and IKEF than the noncachectic group. Moreover, they had a significantly slower normal and maximum walking speed and 5-STS speed. The number of steps, total activity time, and time of activity (<3 Mets) did not significantly differ between the two groups. The cachectic group had a shorter time of activity (≥3 Mets) than the noncachectic group. Furthermore, the cachectic group had a significantly higher REE/body weight and REE/fat free mass and a significantly lower RQ than the noncachectic group.
Conclusions: The cachectic group had a lower muscle mass/quality/strength and physical function and activity and a higher REE than the noncachectic group. Thus, REE and physical activity should be evaluated to determine energy requirements. The RQ was lower in the cachectic group than that in the noncachectic group, indicating changes in energy substrate. Further studies must be conducted to examine effective nutritional and exercise interventions for patients with cancer cachexia.

1. Introduction

Cancer cachexia is a multifactorial syndrome characterized by loss of skeletal muscle mass (with or without loss of fat mass) [1]. Cachexia is common in patients with head and neck cancer (HNC), with an incidence of 31%–42% [2,3]. Pretreatment cachexia is

* Corresponding author. Department of Therapeutic Nutrition, Institute of Biomedical Sciences, Tokushima University Graduate School, 3-18-15 Kuramoto-Cho, Tokushima 770-8503, Japan.
E-mail address: yamada.sonoko@tokushima-u.ac.jp (S. Yasui-Yamada).

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Abbreviations

HNC	head and neck cancer
REE	resting energy expenditure
RQ	respiratory quotient
IKEF	isometric knee extension force
5-STS	five times sit-to-stand
EI	echo intensity
SMM	skeletal muscle mass
DSM-BIA	direct segmental multi-frequency bioelectrical impedance analysis
BW	body weight
R	resistance
Xc	reactance
ASM	appendicular skeletal muscle mass
BFM	body fat mass
PBF	percent body fat
ECW/TBW	extracellular water/total body water
BMI	body mass index
SMI	skeletal muscle mass index
PhA	Phase angle
RF	rectus femoris
VI	vastus intermedius
MT	muscle thickness
FT	fat thickness
IC	indirect calorimetry
CRP	C-reactive protein
IMAT	intramuscular adipose tissue

associated with poor prognosis such as more treatment toxicities, poorer responses to chemotherapy, decreased quality of life [4], and decreased survival [2]. However, the pathophysiology of cachexia is multifactorial, and the provision of effective nutritional and exercise interventions remains a challenge. Contrary cachexia in other types of cancer, cachexia in HNC has not been explored [3].

First, with regard to body composition, cachectic patients with HNC had a significantly lower muscle mass than noncachectic patients before treatment [3]. In recent years, in addition to muscle mass, muscle quality has been used to diagnose sarcopenia. It is assessed using highly sensitive imaging tools, such as magnetic resonance imaging and computed tomography scan, which can determine muscle fat infiltration, and muscle attenuation [5]. Moreover, echo intensity (EI) on ultrasound images is utilized to assess muscle quality since non-contractile tissues associated with myosteatosis present with hyperechogenicity [5,6]. Muscle quality assessment can help monitor treatment response in sarcopenia [5]. However, there are no previous reports on muscle quality in patients with cachexia.

Second, patients with cancer cachexia have a negative energy balance due to reduced food intake and/or abnormal metabolism [1,7]. Nevertheless, there is no enough evidence that strongly supports this notion. Patients with severe weight loss have a higher resting energy expenditure (REE) than those with a stable weight [8]. Meanwhile, another report showed no significant difference in REE with or without weight loss [9]. To the best of our knowledge, there is only one report comparing the REE of patients with and without cachexia according to the definition of Fearon et al. Results showed that patients with cachexia had a higher REE/lean body mass than those without [10]. Moreover, the respiratory quotient (RQ) of cachectic patients was lower than that of noncancer patients. In addition, patients with cachexia had a lower physical function than those without [10]. Based on these data, patients with cachexia might have a high REE and low energy consumption from physical activity. However, whether REE, RQ, and physical activity differ between cachectic and noncachectic patients with HNC remains unclear.

The current study aimed to assess the muscle mass/quality/strength, physical function and activity, REE, and RQ in cachectic patients with HNC and to provide information that can contribute to nutritional and rehabilitation therapy for cancer cachexia.

2. Material and methods

2.1. Patients

This was prospective cross-sectional study. Patients with newly diagnosed HNC admitted to the Department of Otolaryngology of Tokushima University Hospital from January 2015 to March 2021 were recruited in the research. Patients with pacemakers and metallic prostheses were excluded before informed consent because direct segmental multifrequency bioelectrical impedance analysis (DSM-BIA) is contraindicated or it is not possible to precisely measure their body composition in these patients. In total, 66 patients who provided a written informed consent were included. The accuracy of measuring skeletal muscle mass (SMM) via DSM-BIA was dependent on hydration status. Hence, two patients with evident edema were excluded. This study was approved by the ethical committee of the Tokushima University Hospital (2161-3).

2.2. Data collection

Data on age, height, sex, cancer site and stage, and serum chemistry parameters were collected from the electronic medical records of the patients.

2.3. Direct segmental multifrequency bioelectrical impedance analysis

Body weight (BW) was assessed with a scale to the nearest 0.1 kg (TANITA, Tokyo, Japan) while the participants were wearing light clothing without shoes. Body composition was evaluated via DSM-BIA using InBodyS10® (InBody Co., Ltd., Seoul, Korea). Measurement was performed prior to treatment. The patients fasted for at least 4 h prior to measurement, and they were evaluated while in supine position. InBodyS10® was used to measure impedance at six frequencies (1, 5, 50, 250, 500, and 1000 kHz) and reactance (Xc) at three frequencies (5, 50, and 250 kHz) each at five segments (right arm, left arm, trunk, right leg, and left leg) using an eight-point tactile electrode. Body composition such as SMM was calculated using a specific formula in the inner software based on height and 30 impedance measured at six frequencies. Inbody S10® automatically displays SMM, appendicular skeletal muscle mass (ASM), body fat mass (BFM), percent body fat (PBF), and extracellular water/total body water (ECW/TBW). Body mass index (BMI) was calculated as weight divided by height in meters squared (kg/m^2). Skeletal muscle mass index (SMI) was calculated as ASM divided by height in meters squared (kg/m^2). Resistance (R) was calculated mathematically based on impedance and Xc values using trigonometric functions. Phase angle (PhA) value at 50 kHz was calculated as PhA (degrees) = arctan (Xc/R) × (180/π).

2.4. Diagnosis of cancer cachexia

Cachexia was assessed using the criteria by Fearon et al. [1], which were as follows: weight loss of >5% over the last 6 months; BMI of <20 kg/m^2 and any degree of weight loss (>2%); SMI derived via DSM-BIA, which is consistent with sarcopenia (men: <7.0 kg/m^2, women: <5.7 kg/m^2) and any degree of weight loss (>2%). The SMI cutoff values were based on the Asian Working Group for Sarcopenia 2019 guideline [11]. Patients who met at least one of the three criteria were diagnosed with cachexia.

2.5. Muscle strength

The handgrip strength of both hands was evaluated using a dynamometer (Takei Scientific Instruments, Niigata, Japan) while the patients were in the standing position. The assessments were repeated twice on each hand, and the maximum value was used. Isometric knee extension force (IKEF) was measured in the right leg using a hand-held dynamometer (μTas F-1, Anima, Tokyo, Japan). The patients repeated the test twice, and the maximum value was used in the analysis. The IKEF value was expressed relative to BW (% BW) [12].

2.6. Ultrasound measurement and physical functional assessments

Of 64 patients, 51 underwent ultrasonography. Images were obtained using a B-mode ultrasound imaging device (EUB-8500, Hitachi, Tokyo, Japan) with a linear-array probe. Ultrasound images were obtained at the midpoint of the right anterior thigh while in the supine position. A water-soluble permeable gel was applied to the skin surface of the thigh, and ultrasonic measurements were performed to prevent losing muscle shape without pressing the skin surface. EI was determined via an 8-bit gray-scale analysis, and the mean EI of the regions of interest in the rectus femoris (RF) muscle and vastus intermedius (VI) muscle was expressed as a value from 0 (black) to 255 (white). The muscle thickness (MT) of the quadriceps femoris muscle was defined as the sum of the muscle thickness of the RF and VI muscle. The fat thickness (FT) of the thigh front was evaluated as the distance between the fascia of the RF muscle and dermis. Physical function was assessed using the 10-m walking speed test and the five times sit-to-stand (5-STS) test. In the former, the patients were instructed to walk with normal or maximum levels of effort from the starting line toward the finish line. In the later, the patients were instructed to fold their arms in front of their chest and perform five standing and sitting motions as fast as possible, and the required time was recorded. All ultrasound measurements and physical functional tests were performed by a well-trained physical therapist.

2.7. Physical activity

The number of steps and activity time were used to measure physical activity. Of 64 patients, 57 wore a triaxial accelerometer (Active style PRO JHA-350IT; Omron, Kyoto, Japan) on the waist all day for 7 days between admission and treatment. The average value per day was applied in the analysis. The activity intensity was classified as low intensity (<3 Mets) and moderate-intensity (≥3 Mets) [13].

2.8. Indirect calorimetry

Of 64 patients, 30 underwent indirect calorimetry (IC) for the assessment of carbon dioxide production and oxygen consumption. REE and RQ were evaluated via IC using AE-310S (Minato Medical Science Co., Osaka, Japan). All patients were smoke-free prior to the measurement. IC was performed for 30 min in the morning after the patients fasted overnight with the last medication taken the previous night. None of the patients were taking any medications containing lactulose, which may increase CO_2 and may affect REE. Moreover, it was conducted while the patients were lying in the supine position. REE was calculated using the Weir's equation, which does not include urinary nitrogen, assuming a protein-energy ratio of 12.5% [14].

2.9. Statistical analysis

All statistical analyses were performed using JMP version 13.0 software (SAS Institute Inc., Cary, NC, the USA). Continuous variables without a normal distribution were presented as median and interquartile range. To compare patients with cachexia and those without, Wilcoxon rank-sum test and chi-square test were used to evaluate continuous and categorical variables, respectively. A p-value of <0.05 was considered statistically significant.

3. Results

3.1. Characteristics of the patients

Table 1 presents the characteristics of the patients. Of 64 patients, 23 (36%) were diagnosed with cachexia. The cachectic group had a significantly lower height, BW, BMI, SMM, SMI, and PhA than the noncachectic group. However, there was no significant difference in terms of BFM and PBF between the two groups. The cachectic group had a significantly higher ECW/TBW than the noncachectic group. The cachectic group had a significantly lower serum albumin level and a significantly higher C-reactive protein (CRP) level than the noncachectic group.

3.2. Ultrasound measurement

Table 2 shows the variables measured via ultrasonography between patients with cachexia and those without. The cachectic group had a significantly lower quadriceps MT than the noncachectic group. Meanwhile, there was no significant difference in the thigh front FT between the two groups. The cachectic group had a significantly higher quadriceps EI than the noncachectic group.

3.3. Muscle strength and physical function and activity

Table 3 shows the muscle strength and physical function and activity of patients with cachexia and those without. The cachectic group had a lower handgrip strength and IKEF than the noncachectic group. Moreover, they had a significantly slower normal and maximum walking speed and 5-STS speed. The number of steps, total activity time, and time of activity (<3 Mets) did not significantly differ between the two groups. The cachectic group had a shorter time of activity (≥3 Mets) than the noncachectic group.

3.4. Indirect calorimetry

Table 4 shows the REE and RQ of patients with cachexia and those without. The cachectic group had a significantly higher REE/BW and REE/FFM than the noncachectic group. The cachectic group had a significantly lower RQ than the noncachectic group. Since 25 of the 30 patients (7 with cachexia and 18 with noncachexia) wore triaxial accelerometers, we performed additional analyses. The estimated total energy expenditure (REE + activity energy expenditure) was not significantly different between the cachectic and noncachectic groups (31.0 kcal/kg vs. 28.0 kcal/kg, $P = 0.123$).

Table 1
Characteristics of the patients.

	All patients (n = 64)	Cachectic group (n = 23)	Noncachectic group (n = 41)	P-value
Age (years)	67 (61–74)	69 (61–80)	67 (61–71)	0.226
Sex, n (%)				0.132
Male	51 (80)	16 (70)	35 (85)	
Female	13 (20)	7 (30)	6 (15)	
Cancer site, n (%)				0.573
Hypopharynx	16 (25)	5 (22)	11 (27)	
Oropharynx	13 (20)	6 (26)	7 (17)	
Larynx	12 (19)	3 (13)	9 (22)	
Nasopharynx	10 (16)	2 (9)	8 (20)	
Oral cavity	5 (8)	3 (13)	2 (5)	
Maxillary sinus	5 (8)	3 (13)	2 (5)	
Others	2 (3)	1 (4)	1 (2)	
Unknown primary	1 (2)	0 (0)	1 (2)	
Cancer stage, n (%)				0.183
I	2 (3)	0 (0)	2 (5)	
II	13 (20)	2 (9)	11 (27)	
III	14 (22)	6 (26)	8 (20)	
IV	33 (52)	15 (65)	18 (44)	
Unknown	2 (3)	0 (0)	2 (5)	
Height (cm)	165.6 (158.9–169.6)	159.3 (153.2–169.0)	166.7 (160.9–170.4)	**0.046**
BW (kg)	57.6 (48.5–66.2)	48.6 (46.2–57.9)	61.2 (52.5–69.8)	**<0.001**
BMI (kg/m^2)	21.2 (19.3–24.0)	19.8 (18.4–21.3)	22.0 (20.0–24.6)	**0.020**
SMM (kg)	22.4 (20.2–26.8)	20.3 (17.6–22.2)	25.5 (21.2–27.8)	**<0.001**
SMI (kg/m^2)	6.4 (5.9–7.2)	5.9 (5.2–6.4)	6.9 (6.2–7.7)	**<0.001**
BFM (kg)	13.8 (9.9–18.0)	12.8 (9.1–16.4)	14.2 (10.2–18.9)	0.341
PBF (%)	24.4 (19.7–29.6)	24.4 (19.5–30.9)	23.5 (19.7–28.0)	0.576
PhA (°)	4.91 (4.41–5.65)	4.47 (4.08–5.11)	5.30 (4.58–5.85)	**0.002**
ECW/TBW	0.392 (0.384–0.397)	0.395 (0.388–0.405)	0.390 (0.381–0.395)	**0.008**
Albumin level (g/dL)	3.7 (3.4–4.0)	3.4 (3.1–3.9)	3.8 (3.6–4.1)	**0.003**
CRP level (mg/dL)	0.4 (0.2–1.6)	1.6 (0.9–3.7)	0.3 (0.1–0.7)	**0.003**

BW, body weight; BMI, body mass index; SMM, skeletal muscle mass; SMI, skeletal muscle mass index; BFM, body fat mass; PBF, percent body fat; PhA, phase angle; ECW/TBW, extracellular water/total body water; CRP, C-reactive protein.
$p < 0.05$ are shown in bold.

Table 2
Comparison of variables measured by ultrasound images.

	All patients (n = 51)	Cachectic group (n = 20)	Noncachectic group (n = 31)	P-value
Quadriceps MT (cm)	2.34 (1.84–2.84)	1.91 (1.63–2.35)	2.64 (2.14–3.14)	**<0.001**
Thigh front FT (cm)	0.63 (0.50–0.87)	0.65 (0.50–0.77)	0.63 (0.51–0.91)	0.900
Quadriceps EI (pixel)	87.2 (76.7–102.2)	96.3 (85.6–104.6)	81.7 (69.1–97.6)	**0.023**

MT, muscle thickness; FT, fat thickness; EI, echo intensity.
$p < 0.05$ are shown in bold.

Table 3
Comparison of muscle strength and physical function and activity.

	Total number of patients (cachectic and noncachectic groups)	All patients	Cachectic group	Noncachectic group	P-value
Handgrip strength (kg)	63 (22, 41)	31.5 (25.5–37.0)	26.7 (22.0–32.2)	33.2 (28.1–39.2)	**0.002**
IKEF (%BW)	50 (19, 31)	53.1 (44.8–63.7)	44.5 (38.0–55.5)	58.2 (49.5–66.4)	**0.002**
Normal walking speed (m/s)	50 (20, 30)	1.15 (1.01–1.29)	1.04 (0.87–1.24)	1.21 (1.03–1.38)	**0.025**
Maximum walking speed (m/s)	47 (18, 29)	1.66 (1.42–1.91)	1.56 (1.20–1.69)	1.77 (1.54–1.94)	**0.021**
5-STS speed (s)	48 (18, 30)	8.2 (6.8–10.9)	10.0 (7.4–12.7)	8.1 (6.3–9.6)	**0.048**
Number of steps	57 (18, 39)	3100 (1629–4296)	2975 (869–3515)	3210 (1724–5332)	0.116
Activity time					
Total (min/day)	57 (18, 39)	829 (641–972)	828 (578–947)	829 (645–993)	0.764
<3 Mets (min/day)	57 (18, 39)	783 (619–903)	807 (567–935)	781 (619–902)	0.952
≥3 Mets (min/day)	57 (18, 39)	27 (15–44)	19 (11–30)	29 (18–46)	**0.046**

IKEF, isometric knee extension force; 5-STS, five times sit-to-stand.
$p < 0.05$ are shown in bold.

Table 4
Comparison of REE and RQ.

	All patients (n = 30)	Cachectic group (n = 10)	Noncachectic group (n = 20)	P-value
REE/BW (kcal/kg)	22.5 (21.2–24.3)	24.5 (23.1–25.1)	21.8 (20.0–23.0)	**0.002**
REE/FFM (kcal/kg)	29.6 (27.5–31.5)	31.2 (29.9–33.2)	28.2 (26.8–30.6)	**0.010**
RQ	0.88 (0.85–0.95)	0.85 (0.84–0.88)	0.90 (0.86–0.96)	**0.011**

REE, resting energy expenditure; RQ, respiratory quotient; BW, body weight; FFM, fat free mass.
$p < 0.05$ are shown in bold.

4. Discussion

The current study investigated the prevalence of cachexia and compared the muscle mass/quality/strength, physical function and activity, REE, and RQ between cachectic and noncachectic patients with HNC. Approximately 36% of patients had cachexia. The cachectic group had lower muscle mass/quality/strength and physical function than the noncachectic group. Moreover, they had a higher REE and a lower RQ and moderate-intensity activity.

The prevalence rate of cachexia in patients with HNC at the start of treatment was similar between the current and previous studies (36% vs 31% [2] and 42% [3]). The DSM-BIA and ultrasound imaging results did not differ in terms of fat mass between patients with cachexia and those without. However, patients with cachexia had a lower muscle mass than those without. The PhA was lower in patients with cachexia than in those without. PhA obtained by BIA provides information on hydration status and body cell mass and cell integrity without algorithm-inherent errors or requiring assumptions such as constant tissue hydration [15]. The guideline from the European Working Group on Sarcopenia in Older People (2018) stated that “muscle quality has been assessed by BIA-derived phase angle measurement” [5]. Indeed, reports of healthy subjects by other investigators [16,17] and of patients with head and neck cancer by the current authors [18] have demonstrated that PhA correlates with EI. These findings suggest that PhA might reflect muscle quality. Present study showed that patients with cachexia had a higher EI, which is an indicator of intramuscular adipose tissue (IMAT) [5,6,19,20], than those without cachexia. A high preoperative IMAT content was a worse prognostic factor of overall survival and recurrence-free survival in patients who underwent hepatectomy for hepatocellular carcinoma [21]. Although the mechanism of IMAT accumulation is not completely understood, it is believed to be correlated with aging [22,23], physical inactivity, and sarcopenia [24]. In this study, patients with cachexia had a lower muscle mass and strength (i.e., sarcopenia) and a lower moderate-intensity activity, which might have led to a higher IMAT content. To summarize the DSM-BIA and ultrasound results, in addition to the fact that patients with cachexia had reduced muscle mass [2,3], we obtained novel findings showing that these patients also had a low muscle quality. Resistance training can decrease intramuscular fat and increase muscle mass [25,26]. In elderly hospitalized patients, decreased IMAT content in the quadriceps muscle was associated with recovery of activities of daily living rather than increased muscle mass [27]. In older adults with sarcopenia or dynapenia, combined bodyweight resistance exercise and protein and vitamin D supplementation for 12 weeks improved muscle quality and strength [28]. Further studies should be conducted to improve muscle mass/quality/strength in patients with cachexia.

Based on the walking and 5-STS speeds, patients with cachexia had impaired physical function at the start of treatment. In terms of physical activity, the cachectic group had a lower number of steps than the noncachectic group. However, the results did not significantly differ. The cachectic group had a lower moderate-intensity activity than the noncachectic group. Decreased moderate-intensity activity time may lead to loss of muscle mass.

Patients with cachexia had a higher REE than those without. Previous studies have reported that patients with esophageal cancer with weight loss had a higher REE than those without [29]. In addition, patients with pancreatic cancer with an acute phase protein response (CRP level of ≥10 mg/L) had a higher REE than those without (CRP level of <10 mg/L) [30]. Based on our study, cachexia was associated with weight loss and high CRP levels. Hence, these reports partly support our results. Patients with cachexia may have a high REE but normal total energy expenditure due to decreased physical activity [31]. In fact, based on the evaluation using a wearable device, the estimated total energy expenditure (REE + activity energy expenditure) was not significantly different between the cachectic and noncachectic groups in our study (31.0 kcal/kg vs. 28.0 kcal/kg, P = 0.123). However, because these results were obtained from a small sample size of only 25 patients, they must be revalidated with a larger sample size, and it is important to assess both REE and activity energy expenditure.

Only few reports have assessed the RQ of patients with cancer. The current study had a novel finding that patients with cachexia had a lower RQ than those without. Previous reports have shown that the group following a 4-day high-protein diet (provided 30%, 40%, and 30% of energy from protein, carbohydrate, and fat, respectively) had a lower RQ than group following an adequate protein diet (provided 10%, 60%, and 30% of energy from protein, carbohydrate, and fat, respectively; RQ: 0.84 ± 0.02 vs. 0.88 ± 0.03, P < 0.001) [32]. Other reports have shown that a negative energy balance increased lipid oxidation and was associated with lower RQ [33]. In this study, to examine the possible influence of nutritional intake on RQ, we compared nutritional intake from postadmission to IC measurement for the 30 patients in whom RQ was measured. We found no significant difference in energy intake between the cachectic and noncachectic groups (34.9 [30.9–42.6] kcal/kg vs. 31.2 [25.4–33.1] kcal/kg, P = 0.050), and because both groups were not in a negative energy balance, it is unlikely that the difference in energy intake affected the RQ values. The energy from carbohydrate (62.0% vs. 64.0%, P = 0.155) and fat (22.4% vs. 22.5%, P = 0.859) was not significantly different between the two groups. Although the energy from protein was significantly higher in the cachectic group than in the noncachectic group (15.5% vs. 14.0%, P = 0.005), the difference was minimal. Since the aforementioned study compared a high-protein diet (30%) with an adequate protein diet (10%), the difference in protein-to-energy ratio in this study would not have affected RQ. These findings suggest that the lower RQ in the cachectic group was due to metabolic changes in this group, rather than differences in nutrient intake. Altered glucose metabolism and excessive mobilization of lipids are common in patients with cancer [34]. Cancer cells use carbohydrates as a primary energy source [35,36]. Patients with cancer had increased lipid oxidation and utilization of exogenous lipids, and these mechanisms were more evident in patients with weight loss [37]. Thus, fat intake should be increased to further prevent weight loss or to increase BW. The European Society for Clinical Nutrition and Metabolism guidelines recommend the replacement of carbohydrates with lipids as a source of energy in patients with cancer who presented with insulin resistance [38]. Another guideline suggested that lipid utilization is effective and may cover a major part of REE in patients with cancer who experiencing weight loss. Meanwhile, carbohydrate utilization is impaired in the presence of systemic inflammation and insulin resistance [31]. Taken together with our finding, changes in energy substrate must be considered in the nutritional management of patients with cancer cachexia.

The strength of this study is that it initially confirmed that cachectic patients with HNC had reduced muscle quality, increased REE, and decreased RQ. However, it also had some limitations. First, it was performed at a single institution, and the sample size was relatively small. Hence, our findings might not be generalizable to all patients with HNC. Second, several data were missing due to lack of patient consent, and this could have affected the research results. Third, factors (whether in menstrual period or not, whether after urination or defecation) were not fully complied with, which could have affected the BIA results. Forth, the study was cross-sectional in nature; thus, the longitudinal association between cachexia and other measured variables was not evaluated.

5. Conclusion

The cachectic group had a lower muscle mass/quality/strength and physical function than the noncachectic group. Moreover, they had a higher REE but a lower physical activity. Hence, REE and physical activity should be evaluated to determine energy requirements. The RQ was lower in the cachectic group than that in the noncachectic group, suggesting that the energy substrate might have changed. Further studies with larger sample sizes must be conducted to validate our results, and intervention trials should be performed to examine effective nutritional and exercise interventions for patients with cancer cachexia.

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Author contributions

Nao Ohmae: Data curation, formal analysis, investigation, visualization, and writing-original draft.

Sonoko Yasui-Yamada: Conceptualization, data curation, formal analysis, funding acquisition, investigation, project administration, supervision, visualization, and writing-original draft.

Taiki Furumoto: Data curation and investigation.

Kyoko Wada: Data curation and investigation.

Haruka Hayashi: Data curation and investigation.

Midori Kitao: Data curation and investigation.

Ayaka Yamanaka: Data curation and investigation.

Miyu Kubo: Data curation and investigation.

Momoyo Matsuoka: Investigation and resources.

Seiichiro Kamimura: Investigation and resources.

Aki Shimada: Investigation and resources.

Nori Sato: Data curation and investigation.

Yoshiaki Kitamura: Resources and writing - review & editing.

Shinsuke Katoh: Writing - review & editing.

Noriaki Takeda: Resources and writing - review & editing.

Yasuhiro Hamada: Writing - review & editing.

Declarations of competing interest

The authors declare no conflict of interest.

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