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Applied nutritional investigation

An early moderate recommendation for energy intake based on nutritional status and clinical outcomes in patients with cancer: A retrospective study

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ABSTRACT

Objectives: We investigated the nutritional status and clinical outcomes of patients with cancer based on their energy intake after nutritional recommendations.
Methods: This study was a retrospective study. Body weight, nutritional status, dietary intake, and clinical outcomes were collected from medical records. We assessed the data according to energy intake: <50% of the recommended intake was insufficient energy intake (IEI group), 50% to 79% was moderate energy intake (MEI group), and ≥80% was adequate energy intake (AEI group).
Results: A total of 111 patients with cancer were enrolled in the present study. After nutritional recommendation, the number of subjects in the IEI and MEI groups were significantly decreased as patients shifted to the after-AEI group ($P < 0.01$). A significantly high proportion of patients had lower malnutrition universal screening tool and patient-generated subjective global assessment scores in the after-AEI group ($P < 0.01$). Subjects in the after-MEI and after-AEI groups showed slight gains in body weight ($P = 0.07$) and positively correlated with the energy ($\beta = 0.05$; $P = 0.07$) and protein intake ($\beta = 0.04$; $P = 0.01$). Significantly low proportions of patients with cancer died during hospitalization in the after-MEI and after-AEI groups, but significantly high proportions of patients with cancer in the after-MEI and after-AEI groups reached their ideal body weight ($P = 0.03$) compared with that in the after-IEI group.
Conclusions: Patients with cancer who comply with a moderate energy intake recommendation (50%–79%) within at least 28 d may limit body weight decrease and improve nutritional status and clinical outcomes.

Introduction

Cancer is the second leading cause of death worldwide [1] and has been the first leading cause of death in Taiwan for >35 y [2]. Patients with cancer usually suffer from undernutrition due to limited food intake and hypermetabolism [3]. According to a recent report from the Prevalence of Malnutrition in Oncology study, 51% of patients with cancer had nutritional impairment and 43% were at risk for undernutrition. In addition, 64% of patients with cancer suffered from body weight loss between 1 kg and 10 kg during the prior 6 mo [3]. Another study conducted by NutriCancer2012 found that the prevalence of undernutrition among patients with cancer was 39% and notably, patients and relatives may underestimate the rate of undernutrition [4]. Anorexia is a major reason for undernutrition in patients with cancer [5–7]. Cancer therapy may alter appetite signals and cause mouth ulcers, gastrointestinal obstruction, and diarrhea [6,7]. The European Society for Clinical Nutrition and Metabolism (ESPEN) expert group recommended that, in addition to early nutritional screening for patients with cancer in the course of medical care, increasing caloric intake may assist in decreasing patients' inflammation and hypermetabolic status and further improve clinical outcomes [5].

The ESPEN guidelines on nutrition in patients with cancer recommended that the energy intake should range between 25 and 30 kcal/

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Table 1
Characteristics and hematological parameters of patients with cancer at baseline

	IEI (n = 28)*	MEI (n = 47)†	AEI (n = 36)‡	*P* value
Men, n (%)	17 (60.7)	27 (57.4)	19 (52.8)	0.81
Age, y, means ± SD (medians)	55.7 ± 8.9 (57.0)	58.3 ± 10.8 (58.0)	58.8 ± 11.5 (58.0)	0.48
Body weight (kg)	45.3 ± 5.9 (44.4)	45.8 ± 6.1 (46.5)	44.9 ± 6.2 (45.0)	0.78
Body mass index (kg/m^2)	17.1 ± 1.5 (17.5)	17.1 ± 1.5 (17.5)	17.0 ± 2.0 (16.9)	0.86
ECOG-PS > 2 points, n (%)	3 (10.7)	4 (8.5)	0 (0.0)	0.16
Tube feeding, n (%)	0 (0.0)	10 (21.3)	7 (19.4)	0.03
Cancer type, (n (%)				
Head and neck	12 (42.9)	16 (34.0)	8 (22.2)	0.21
Esophagus	4 (14.3)	3 (6.4)	4 (11.1)	0.52
Lung	2 (7.1)	10 (21.3)	5 (13.9)	0.25
Breast	3 (10.7)	2 (4.3)	2 (5.6)	0.53
Gastric	1 (3.6)	5 (10.6)	5 (13.9)	0.38
Pancreatic	3 (10.)	4 (8.5)	4 (11.1)	0.91
Colorectal	1 (3.6)	2 (4.3)	5 (13.9)	0.17
Ovarian	0 (0.0)	1 (2.1)	0 (0.0)	0.50
Other	2 (7.1)	4 (8.5)	3 (8.3)	0.98
Cancer stages, n (%)				0.05
I	0 (0.0)	2 (4.3)	0 (0.0)	
II	1 (3.6)	4 (8.5)	11 (30.6)	
III	3 (10.7)	7 (14.9)	2 (5.6)	
IV	23 (82.1)	33 (70.2)	22 (61.1)	
V	1 (3.6)	1 (2.1)	1 (2.8)	
Cancer treatment				0.11
Chemotherapy	11 (39.3)	16 (34.0)	10 (27.8)	
Radiation therapy	0 (0.0)	0 (0.0)	1 (2.8)	
CCRT	9 (32.1)	11 (23.4)	9 (25.0)	
Surgery alone	1 (3.6)	2 (4.3)	0 (0.0)	
Chemotherapy + surgery	7 (25.0)	12 (25.5)	16 (44.4)	
Chemoradiotherapy + surgery	0 (0.0)	6 (12.8)	0 (0.0)	
Palliative care	0 (0.0)	0 (0.0)	0 (0.0)	
Hematology, means ± SD (medians)				
Hemoglobin (mmol/L)	6.3 ± 1.3 (6.1)*	6.1 ± 1.1 (6.2)*	6.8 ± 1.2 (6.9)	0.04
White blood cell (× 10^9/L)	8.3 ± 7.6 (6.4)	8.0 ± 5.2 (6.0)	6.6 ± 3.6 (6.1)	0.75
Albumin (g/L)	33.0 ± 5.0 (34.0)*	37.0 ± 8.0 (37.0)*	38.0 ± 2.0 (37.0)	0.03
BUN (mmol/L)	8.9 ± 7.7 (6.6)	6.6 ± 3.1 (6.1)	6.2 ± 2.4 (5.9)	0.53
Creatinine (μmol/L)	95.5 ± 65.4 (75.1)	75.1 ± 21.2 (76.0)	77.8 ± 22.1 (74.3)	0.89
GOT (IU/L)	33.9 ± 18.6 (28.5)	28.4 ± 14.1 (25.5)	34.6 ± 15.1 (28.0)	0.20
GPT (IU/L)	31.5 ± 31.6 (18.0)	20.9 ± 16.0 (16.0)	26.3 ± 18.8 (21.5)	0.21
hs-CRP (mg/L)	105.0 ± 90.0 (68.0)	86.0 ± 73.0 (58.0)	51.0 ± 56.0 (40.0)	0.21

AEI, adequate energy intake; BUN, blood urea nitrogen; CCRT, concurrent chemoradiotherapy; ECOG-PS, Eastern Cooperative Oncology Group performance status; GOT, glutamic-oxaloacetic transaminase; GPT, glutamate-pyruvate transaminase; Hs-CRP, high-sensitivity C-reactive protein; IEI, insufficient energy intake; MEI, moderate energy intake; SD, standard deviation.
*Less than 50% of the recommend energy intake.
†Fifty percent to 79% of the recommend energy intake.
‡Equal to or more than 80% of the recommend energy intake.

kg/d and protein intake >1 g/kg/d (if possible, up to 1.5 g/kg/d) [8]. Adequate protein intake in patients with cancer can maintain their muscle mass, reserve muscle, and increase tolerance and treatment efficacy during cancer therapy [9]. Increasing appetite to meet the recommendation of energy or protein intake is the main mission of dietitians; however, patients with cancer often suffer from anorexia. In this study, we investigated the nutritional status and clinical outcomes in patients with cancer according to their energy or protein intake after nutritional recommendations by dietitians to understand whether patients with cancer can meet these recommendations.

Methods

Study design and participants

This study was designed as a retrospective study and approved by the institutional review board of the Chung Shan Medical University Hospital in Taiwan (CSMUH No: CS2-19094). We collected medical records from August 1, 2018 to July 31, 2019 from the Department of Oncology at the Chung Shan Medical University Hospital, which is a medical center in the central region of Taiwan.

Patients with cancer were diagnosed at the time of admission and completed nutritional status screening with the malnutrition universal screening tool (MUST). Patients with cancer who had MUST scores ≥2 points and were receiving enteral nutrition were recruited into the study. Patients under parenteral nutrition therapy, albumin or blood transfusion therapy, or those with hospital stays <2 d were excluded.

Data collection and nutritional recommendation

Demographic data, such as sex, age, use of tube feeding, type of cancer, cancer stage, and Eastern Cooperative Oncology Group performance score, were obtained from the medical records. Patients with cancer were stratified into 3 groups according to their energy intake at the time of admission. Energy intake was defined as follows: <50% of the recommended intake was classified as insufficient energy intake (IEI group), 50% to 79% of the recommended intake as moderate energy intake (MEI group), and ≥80% of the recommended intake as adequate energy intake (AEI group). We used 24-h recall as a dietary assessment for patients with cancer to examine whether the patients reached the energy or protein recommendation at baseline and after recommendation.

The nutritional recommendation protocol was as follows: Registered dietitians visited patients with cancer at the time of admission (baseline) to provide recommendations on energy (25–30 kcal/kg/d) and protein (1.0–1.5 g/kg/d) intake based on ESPEN guidelines for patients with cancer [8]. We collected data on energy and protein intake, body weight, nutritional status scoring (MUST and patient-generated subjective global assessment [PG-SGA]) [10], and hematology (serum albumin and high sensitivity C-reactive protein [hs-CRP] levels at baseline and 1 mo [28 d] after nutritional recommendations). Clinical outcomes, such as

complications, death during hospitalization, and length of hospital stay, were collected from the medical records after recommendation.

Statistical analysis

SigmaPlot software (version 12.0, Systat, San Jose, CA) was used for all data analyses. Descriptive statistics are presented as the means ± standard deviation (medians) or percentages in the present study. Shapiro-Wilk tests were used to examine the normality of the distribution. A 1-way analysis of variance or Kruskal-Wallis test was used to examine the differences in demographic data, energy and protein intake, nutritional status, changes in body weight, and clinical outcomes of patients with cancer among the 3 groups, and post hoc tests were used to assess statistically significant differences among the groups. A paired *t* test or Wilcoxon signed-rank tests were used to compare differences within groups before and after the recommendation. The differences in categorical variables were compared using χ^2 or Fisher's exact tests. McNemar's tests were used to compare the difference in the proportions of subjects in the 3 groups before and after the recommendation. Simple and multiple linear regressions were used to examine the correlations between the energy-protein intake recommendations and changes in body weight in patients with cancer after the recommendation and additionally adjusted for cancer type and treatment. A $P < 0.05$ was set for statistical significance.

We also performed post hoc tests to examine the statistical power of the sample size for nutritional status (PG-SGA) and changes in body weight after the recommendation. The detailed descriptions were as follows: Minimum detectable difference in the mean of nutritional status (PG-SGA) was 1.2 points, an expected standard deviation of residuals was 0.2, the number of groups was 3, the minimum group size (after-IEI) was 11, alpha = 0.05, and the analysis of variance power was 1.0. The Pearson correlation coefficient for changes in body weight and recommendations of protein intake was 0.25; sample size was 111, alpha = 0.05, and the correlation power was 0.8.

Results

Patient characteristics

A total of 111 patients with cancer were enrolled in the present study. The demographic and hematological data of the patients stratified by energy intake are shown in Table 1. Fifty-seven percent of patients were male and the mean age was 58 y. The median body mass index was 17 to 17.5 kg/m^2 in these populations. The MEI group had a significantly higher proportion of patients undergoing tube feeding therapy than the other groups ($P = 0.03$). There was no significant difference in cancer type among the 3 groups. With regard to the hematologic data, patients in the AEI group had significantly higher levels of hemoglobin ($P = 0.04$) and albumin ($P = 0.03$) than those in the IEI and MEI groups. The mean values for hs-CRP were high (>3 mg/L) in these patients with cancer; however, there was no significant difference in the level of hs-CRP among the 3 groups at baseline.

Nutrition status after recommendation

Table 2 shows the energy and protein intake and nutritional status of patients with cancer after the recommendation. Patients in the AEI group had a significantly higher energy and protein intake than those in the MEI and IEI groups at baseline and after the recommendation ($P < 0.01$). After the recommendation, the percentages of patients with adequate recommended energy and

Table 2
Energy and protein intake and nutritional status of patients with cancer after recommendation

	Baseline				After recommendation			
	IEI (n = 28)*	MEI (n = 47)†	AEI (n = 36)‡	*P* value§	IEI (n = 28)	MEI (n = 47)	AEI (n = 36)	*P* value§
Energy intake, kcal/d, means ± SD (medians)	277.1 ± 267.1 (300.0)	1174.6 ± 180.2 (1200.0)*	1526.7 ± 238.6 (1500.0)†	< 0.01	1019.3 ± 473.3 (1150.0)‖	1417.3 ± 379.9 (1410.0)*,‖	1576.6 ± 219.9 (1500.0)†,‖	< 0.01
Energy intake, kcal/kg/d, means ± SD (medians)	6.1 ± 5.9 (6.9)	25.8 ± 3.6 (25.5)*	34.3 ± 5.0 (33.6)†	< 0.01	23.0 ± 10.9 (25.3),‖	31.3 ± 8.2 (30.0)*,‖	35.6 ± 5.4 (34.3)†,‖	< 0.01
Recommendations of energy intake, %,means ± SD (medians)	15.8 ± 14.9 (17.7)	66.8 ± 8.1 (66.7)*	92.1 ± 9.0 (90.0)†	< 0.01	59.8 ± 27.8 (67.7)‖	80.4 ± 19.8 (77.8)*,‖	95.3 ± 9.0 (93.8)†,‖	< 0.01
Protein intake, g/kg/d, means ± SD (medians)	0.22 ± 0.24 (0.22)	0.87 ± 0.25 (0.92)*	1.27 ± 0.31 (1.21)†	< 0.01	0.89 ± 0.49 (0.90)‖	1.17 ± 0.44 (1.14)*,‖	1.36 ± 0.33 (1.35)†,‖	< 0.01
MUST, score, means ± SD (medians)	3.3 ± 1.1 (3.0)	2.1 ± 0.4 (2.0)*	2.0 ± 0.0 (2.0)*	< 0.01	2.4 ± 0.7 (2.5)‖	2.1 ± 0.5 (2.0)*	1.9 ± 0.5 (2.0)*	< 0.01
PG-SGA, score, means ± SD (medians)	8.5 ± 2.1 (8.5)	6.9 ± 2.2 (7.0)*	4.6 ± 1.5 (5.0)†	< 0.01	6.4 ± 2.1 (5.5)‖	5.8 ± 1.6 (5.0)‖	4.4 ± 1.3 (5.0)*	< 0.01

AEI, adequate energy intake; IEI, insufficient energy intake; MEI, moderate energy intake; MUST, malnutrition universal screening tool; PG-SGA, patient-generated subjective global assessment; SD, standard deviation
*Less than 50% of the recommend energy intake.
†Fifty percent to 79% of the recommend energy intake.
‡Equal or more than 80% of the recommend energy intake.
§The values were compared among the 3 groups.
‖Compared within the groups after recommendation, $P < .05$.

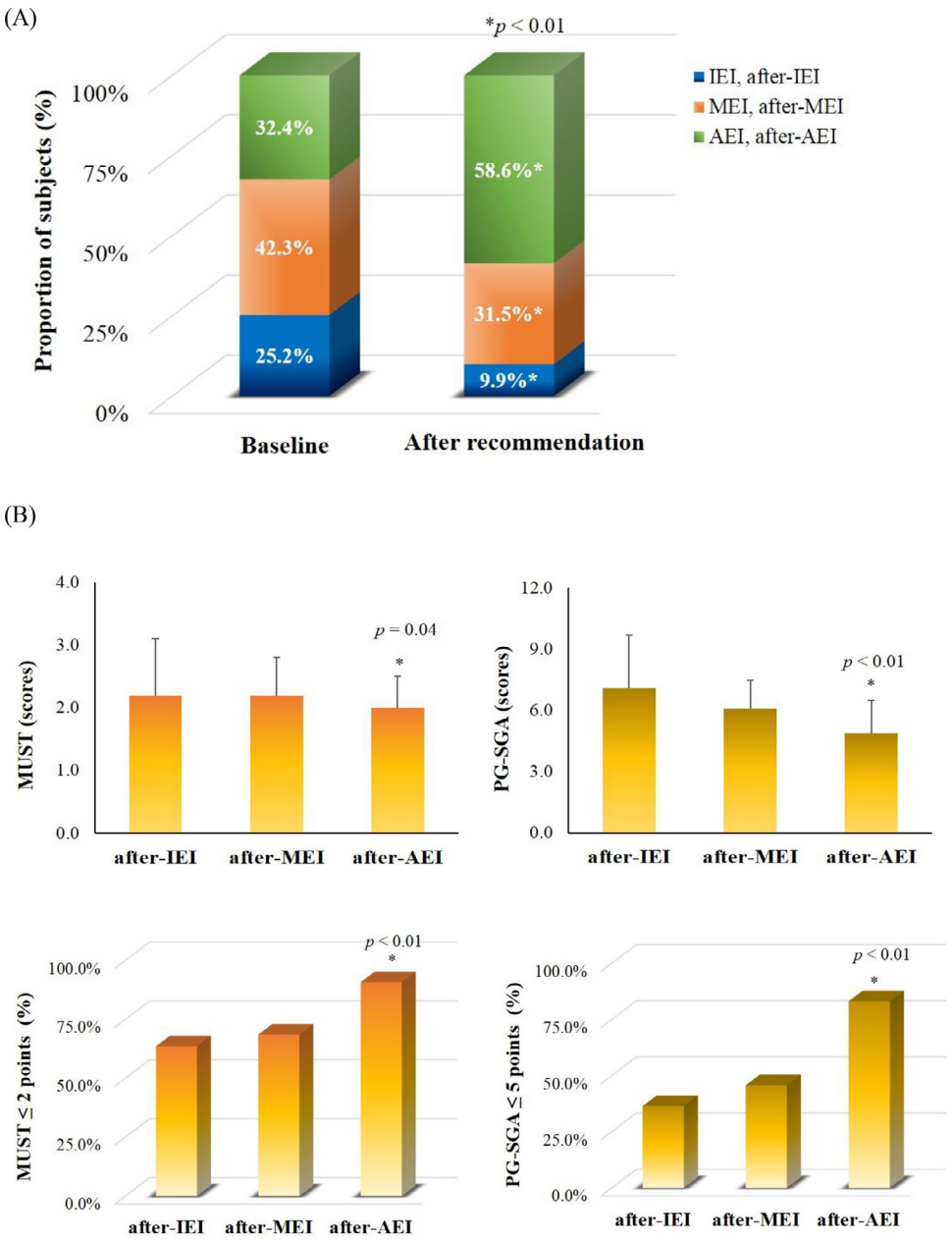

Fig. 1. Proportion of patients and nutritional scoring after recommendation; (A) changes in proportion of patients after recommendation; and (B) nutritional scoring after recommendation. After-IEI, patients with IEI (<50%) after recommendation (n = 11); after-MEI, patients with MEI (50%–79%) after recommendation (n = 35); after-AEI, patients with AEI intake (≥80%) after recommendation (n = 65). AEI, adequate energy intake; IEI, insufficient energy intake; MEI, moderate energy intake; MUST, malnutrition universal screening tool; PG-SGA, patient-generated subjective global assessment.

protein intakes were increased significantly ($P < 0.05$). With regard to nutritional status, patients in the MEI or AEI group had significantly lower MUST and PG-SGA scores than those in the IEI group ($P < 0.05$). Notably, the scores for the MUST and PG-SGA were increased in the IEI group after the recommendation ($P < 0.01$).

Figure 1A shows the proportions of patients with cancer after the recommendation. After the recommendation, the numbers of patients in the IEI and MEI groups at baseline significantly decreased as patients shifted to the after-AEI group ($P < 0.01$). We further assessed the nutritional status after the recommendation (Fig. 1B). The MUST ($P = 0.04$) and PG-SGA ($P < 0.01$) scores were significantly lower in the after-AEI group than in the after-IEI and after-MEI groups. Overall, 64%, 69%, and 91% of patients with cancer had lower MUST scores (≤2 points) in the after-IEI, after-MEI, and after-AEI groups, respectively (Fig. 1B; $P < 0.01$), and 36%, 46%, and 83% of patients with cancer had lower PG-SGA scores (≤5 points) in the after-IEI, after-MEI, and after-AEI groups, respectively (Fig. 1B; $P < 0.01$).

Body weight after recommendation

Figure 2 shows the changes in body weight after the recommendation. Patients in the after-MEI and after-AEI groups gained nominally significant body weight (Fig. 2A; $P = 0.07$). Notably, 46%, 31%, and 28% of patients with cancer demonstrated individual weight loss in the after-IEI, after-MEI, and after-AEI groups, respectively (Fig. 2B; $P = 0.10$). We further assessed the body weight and proportions of patients reaching ideal body weight after the recommendation

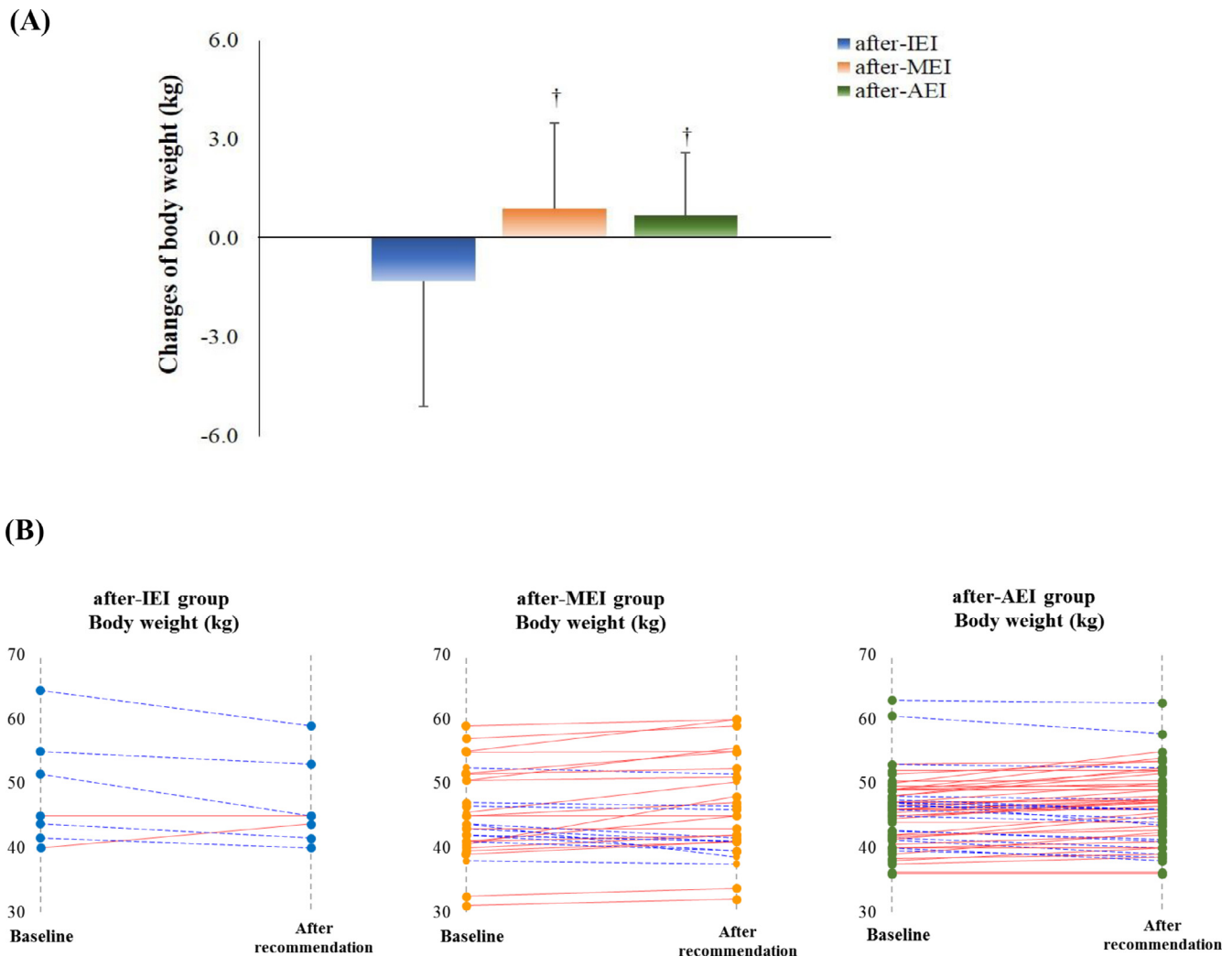

Fig. 2. Changes in body weight after recommendation; (A) mean changes in body weight after recommendation; and (B) changes in individual body weight after recommendation. After-IEI, patients with IEI (<50%) after recommendation (n = 11); after-MEI, patients with MEI (50%–79%) after recommendation (n = 35); after-AEI, patients with AEI (≥80%) after recommendation (n = 65). Blue dotted line is weight loss; red solid line is weight gain. † $P = 0.07$. AEI, adequate energy intake; IEI, insufficient energy intake; MEI, moderate energy intake.

according to patients with different cancer types (Fig. 3). Among the patients, patients with head and neck cancer had the most significant increase in body weight (Fig. 3A; 46.5 ± 5.2 kg to 47.3 ± 5.5 kg; $P = 0.02$), and the proportions of patients reaching ideal body weight significantly increased among patients with head and neck cancer (Fig. 3B; 77%–78%; $P = 0.04$) after the energy recommendation.

Moreover, we examined the correlations between energy and protein intake recommendations with changes in body weight after the recommendation (Fig. 4). The results showed that the changes in body weight were positively correlated with the energy (Fig. 4; $\beta = 0.05$; $P = 0.07$) and protein (Fig 4; $\beta = 0.04$; $P = 0.01$) intake recommendations. After adjusting for cancer type and treatment, there was still a significant positive correlation between changes of body weight and recommendations for energy ($\beta = 0.04$; $P = 0.08$) or protein ($\beta = 0.04$; $P = 0.02$) intake.

Clinical outcomes after recommendation

Table 3 shows the clinical outcomes of patients with cancer after the recommendation. A significantly lower proportion of patients died during hospitalization in the after-MEI and after-AEI groups than in the after-IEI group ($P < 0.01$). Moreover, a higher proportion of patients reached their ideal body weight in the after-MEI and after-AEI groups (20% and 40%, respectively) than in the after-IEI group ($P = 0.03$).

Discussion

Patients with cancer are well known to have a high prevalence of undernutrition [3–5]. In the present study, we found that a recommendation for 50% to 79% of energy intake can help patients with cancer at a high risk of undernutrition improve their nutritional status and lower mortality during hospitalization. In clinical sites, we often find that patients with cancer complain about having a poor appetite, and 25% of patients with cancer have an extremely low calorie intake (median caloric intake: 300 kcal) at the time of the first admitted visit. After a nutritional recommendation, both the energy intake (Fig. 1A) and body weight (Fig. 2) were increased and at the same time, high MUST or PG-SGA scores were decreased significantly (Table 2) in these patients with a MEI recommendation (50%–79%). In addition, when patients complied with recommendations to increase energy or protein intake by up to 50% (MEI group), they showed an increase in

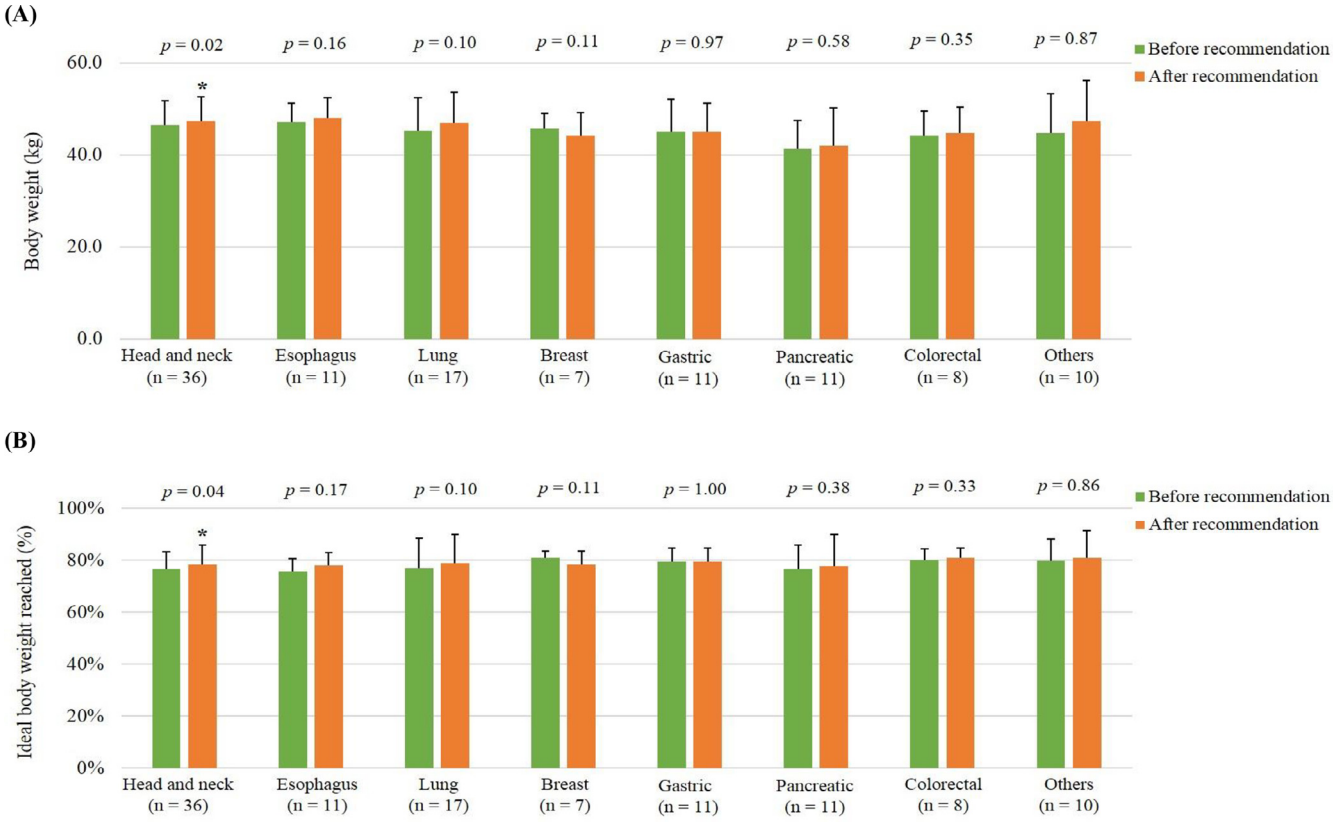

Fig. 3. Body weight (A) and proportion of patients reaching ideal body weight (B) after recommendation according to cancer type. $^{*}P < 0.05$.

body weight of 2.5% (+1.5 kg) after the recommendation (Fig. 3). Yang et al. indicated that nutrition counseling with energy requirements in oncology inpatients during admission may effectively ameliorate low energy intake and body weight loss, particularly in patients with head and neck cancer [11]. Our research also notes this phenomenon. Among the patients with cancer, there was a significant increase in body weight in patients with head and neck cancer, and the proportion of patients reaching ideal body weight significantly increased among patients with head and neck cancer (Fig. 3).

Cancer type and treatment may also have an impact on nutritional status, but there were no significant differences in cancer treatment and energy recommendation at baseline (Table 1). We further examined nutritional status according to cancer therapy and found that nutritional status after recommendation was not significantly different among the cancer therapies (data not shown; MUST: $P = 0.66$; PG-SGA: $P = 0.19$). Thus, nutritional status improvement in patients with cancer may result from the energy and protein recommendation. In addition, there was a high percentage of nasogastric tube feeding in patients with cancer who received a MEI recommendation in the present study (Table 1). Progressive wasting happens in patients with cancer because, in addition to diminished dietary intake, tumors cause metabolic alterations resulting in high energy expenditure. A slight increase in energy intake in patients with cancer may assist with decreasing body weight variation and increase survival rates [12]. Artificial nutrition support may achieve the goal of the energy intake

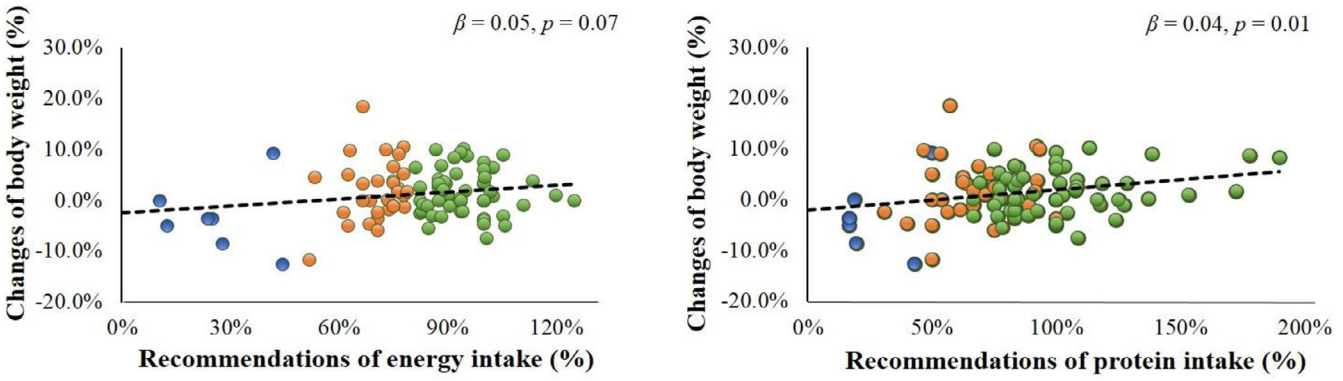

Fig. 4. Correlations between energy and protein intake recommendations with changes in body weight after recommendation. Blue dots: After-IEI, patients with IEI (<50%) after recommendation. Orange dots: After-MEI, patients with MEI (50%–79%) after recommendation. Green dots: After-AEI, patients with AEI (≥80%) after recommendation. AEI, adequate energy intake; IEI, insufficient energy intake; MEI, moderate energy intake.

Table 3
Clinical outcomes of patients with cancer after recommendation

	After IEI (n = 11)*	After MEI (n = 35)†	After AEI (n = 65)‡	*P* value
Length of hospital stay, d, means ± SD (medians)	14.7 ± 18.5 (6.0)	8.4 ± 10.2 (5.0)	7.9 ± 7.4 (5.0)	0.32
Complications during hospitalization, n (%)	1 (9.1)	2 (5.7)	2 (3.1)	0.62
Died during hospitalization, n (%)	4 (36.4)	3 (8.6)	0 (0.0)	< 0.01
Reach ideal body weight, n (%)	1 (9.1)	7 (20.0)	26 (40.0)	0.03

AEI, adequate energy intake; IEI, insufficient energy intake; MEI, moderate energy intake; SD, standard deviation.
*Less than 50% of the recommend energy intake.
†Fifty percent to 79% of the recommend energy intake.
‡Equal or more than 80% of the recommend energy intake.

recommendation [13]; thus, we suggest that if patients with cancer could achieve a moderate increase in caloric intake as early as possible (50%–79% of the recommended energy intake), body weight loss may be limited and nutritional status could be improved. If patients are suffering from anorexia, calories can be delivered through artificial nutrition support, such as nasogastric tube feeding, as soon as possible to lower the risk of undernutrition.

Metabolic alterations in cancer include a chronic systemic inflammatory response [14]. High inflammation status is associated with cancer risk and mortality [15,16]. In this study, hyperinflammation status in patients with cancer was not surprising (Table 1); however, the percentage of patients with a high inflammation status (hs-CRP > 40 mg/L) was decreased slightly among patients with cancer and a moderate or adequate recommendation of energy intake (data not shown; 27%, 17%, and 11% in after-IEI, after-MEI, and after-AEI groups, respectively; P = 0.30). Not only was a reduction in inflammation observed after the recommendation, but the proportion of patients with hypoalbuminemia (serum albumin < 30 g/L) was also decreased when patients complied with a moderate or adequate energy intake recommendation (data not shown; 36%, 6%, and 2% in the after-IEI, after-MEI, and after-AEI groups, respectively; P < 0.01).

Recently, a large randomized clinical trial was conducted in Switzerland, and the investigators suggested that individualized nutrition support in medical inpatients with nutritional risk showed a benefit for clinical outcomes, including survival, compared with the control treatment [17]. Our study also observed similar results. The proportion of patients who died during hospitalization was significantly decreased among patients who complied with a MEI recommendation. Although not reaching statistical significance, the proportion of complications during hospitalization was also decreased when patients complied with a MEI recommendation (Table 3). In this study, we excluded patients receiving total parenteral nutrition and those who suffered from serious disease to avoid an influence of disease severity on the current mortality results. Because patients with cancer are at a high risk of undernutrition and hyperinflammation, we suggest that dietitians encourage patients with cancer to meet at least 50% of the recommendation for energy intake within 28 d in clinical practice. This range of recommended energy intake may also inspire patients to feel confident in achieving the goal and may further improve the quality of life and efficacy of therapy. In the present study, we used the formulas according to the ESPEN guidelines [8] to assess patient caloric needs (energy range, 25–30 kcal/kg/d). Although indirect calorimetry may be more precise than these formulas, using indirect calorimetry for inpatients with cancer in clinical practice is not easy. Thus, we support that the strength of energy recommendations based on formulas is strong for patients with cancer [8].

Most patients with cancer experience weight loss during the cancer progression. The combined and early use of supplemental energy and protein, as well as the modulation of the inflammatory response, has been shown to benefit nutritional status and clinical outcomes [18]. Recently, some scholars have proposed that ghrelin [19-21] and microbiota [22,23] supplementation could be considered to increase appetite in patients with cancer. Ghrelin is a 28 amino-acid orexigenic gut hormone that stimulates food intake under conditions of anorexia, undernutrition, and cancer cachexia clinically [20,21]. A prospective, randomized, placebo-controlled phase 2 study by Hiura et al. demonstrated that the short-term administration of exogenous ghrelin may stimulate food intake and appetite in patients with esophageal cancer with fewer adverse events during chemotherapy [19].

Additionally, the microbiota plays a crucial role in regulating appetite by modulating intestinal satiety, which is controlled by the neuropeptidergic circuitry in the hypothalamus [22,23]. A recent randomized, double-blind, placebo-controlled trial successfully applied microbiota to enhance the immune response of patients with nasopharyngeal carcinoma [24]. Thus, we suggest that, in addition to encouraging patients with cancer to drink calories or eat often to obtain energy and promote weight gain, further studies could incorporate novel biotherapeutic strategies to improve appetite in patients with cancer during treatment. Furthermore, long-term observations of nutritional recommendations for patients with cancer is needed in the future.

Conclusions

For patients with cancer at a high risk of undernutrition, dietitians should promptly manage and target energy and protein intake to improve patients' nutritional conditions and clinical outcomes. Based on the results of the present study, we suggest that patients with cancer comply with a MEI recommendation (50%–79%) within 28 d to limit body weight decrease and improve nutritional status and clinical outcomes.

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