

Association of dietary patterns with overweight risk and all-cause mortality in children with cancer

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BACKGROUND/OBJECTIVES: This study aimed to investigate the association of dietary patterns with overweight risk and all-cause mortality in pediatric cancer patients.

SUBJECTS/METHODS: Prospective cohort study was undertaken; 83 cancer patients admitted to the pediatric cancer ward at a university hospital in Seoul were included and followed for obesity and death over 24 months. Food consumption data were collected from patients using validated meal order sheets for breakfast, lunch, and dinner at the pediatric cancer ward over 3 days. Using principal component analysis, three dietary patterns were derived from 29 food groups.

RESULTS: Eighteen deaths occurred among the patient cohort during the follow-up period. The "spicy & fried meat and fish" dietary pattern was positively associated with overweight risk at both baseline [odds ratio (OR) = 4.396, 95% confidence interval (CI) = 1.111-17.385, *P* for trend = 0.023] and after 6 months (OR = 4.088, 95% CI = 1.122-14.896, *P* for trend = 0.025) as well as all-cause mortality (hazard ratios = 5.124, 95% CI = 1.080-24.320, *P* for trend = 0.042), when comparing the highest and lowest tertiles after adjusting for covariates. The "fish, egg, meat, and fruits & vegetables" dietary pattern was associated with lower overweight risk after 24 months (OR = 0.157, 95% CI = 0.046-0.982, *P* for trend = 0.084).

CONCLUSION: The results imply that dietary patterns might be associated with weight gain and premature death among pediatric cancer patients.

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INTRODUCTION

Continued technological advancements in cancer treatment have led to significant improvements in the prognostic outcomes and survival rates of many types of childhood malignancies [1]. According to data from Statistics Korea, the relative 5-year survival rates of pediatric cancer patients have increased from 41.2% (1993 to 1995) to 68.1% (2008 to 2012), with treatment rates reported to be as high as 80%. Despite this success, childhood cancer survivors face numerous long-term complications, including obesity, endocrine disorders (e.g., thyroid disease, disorders affecting regulation of pubertal growth), cardiac disease, osteonecrosis, pulmonary disorders, neurological and neurosensory disorders, and secondary cancers [2,3]. Over 60% of pediatric cancer survivors have been reported to suffer from one or more of these complications, depending on the diagnostic category and study population [4,5]. Consequently, long-term monitoring has become an important part of the overall healthcare strategy for pediatric cancer survivors.

Obesity is recognized as a major long-term complication affecting the health status and mortality of pediatric cancer patients, and long-term survivors of pediatric cancer are more likely to be obese than children of the same age and sex in the reference population [6]. Overweight or obesity has known to be associated with increased incidence of treatment-related mortality [7,8] and relapse risk [9] as well as reduction of overall quality of life of patients due to physical impairment and negative psychological impact [10]. However, the mechanism(s) contributing to obesity in pediatric cancer patients have not been clearly identified. Various factors such as hypothalamic-pituitary axis damage from cancer treatments, adverse effects of chemotherapy, growth hormone deficiencies, steroid use, biological characteristics at diagnosis, inactivity, and diet have been considered as potential causes of obesity in pediatric cancer patients [11]. Among them, diet is one of the main factors that can be modified through lifestyle interventions in order to prevent obesity and premature death in pediatric cancer patients.

Previous studies have reported that pediatric cancer patients

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are more likely to exhibit unhealthy dietary behaviors, including low intakes of fruits and vegetables [12-15] and whole grains [12,15] as well as high intake of energy from fat [12,15,16], sweets [12,15], sodium [12], and refined carbohydrates [15]. However, most studies have focused on the relationship between individual nutrients or foods and obesity among children with cancer. Until now, the association between overall diet quality and obesity or mortality has not yet been evaluated.

A dietary pattern approach can be useful for assessing associations between overall diet quality and health outcomes, as it takes into account the complex interactions between nutrients and other dietary components [17]. To the best of our knowledge, very few reported studies have focused on the association of dietary patterns with obesity and mortality in pediatric cancer patients. Therefore, we examined associations between dietary patterns and overweight risk and all-cause mortality using data from pediatric cancer patient cohorts.

SUBJECTS AND METHODS

Participants

Of 130 children admitted to the pediatric cancer ward between October 28, 2013 and January 31, 2014, 83 who were diagnosed with cancer in accordance with the International Classification of Childhood Cancer (Third Edition) were selected as study subjects. Thirty-five patients prescribed to receive a low microbial diet for less than 3 consecutive days were excluded. Six patients lacking anthropometric data at diagnosis due to transfer from other hospitals as well as six patients hospitalized for peripheral blood stem cell transplantation were excluded. Information on general characteristics and disease status of subjects, including gender, age, age at diagnosis, diagnosis of cancer, steroid treatment, duration of disease, and absolute neutrophil counts (ANCs), was obtained through the electronic medical chart. In instances where patients were hospitalized more than once during the study period, data from the first hospitalization were used. All procedures were approved by the Catholic Medical Center Institutional Review Board (No. KC15RISI0145).

Medical examination and death ascertainment

Height and weight were measured by trained nursing staffs following standard procedures in order to assess overweight status at admission and follow-ups: after 6 months and 24 months. According to the recommendations from the Nutrition Committee of the Children's Oncology Group, a patient was defined as being overweight if the percentage of ideal body weight (PIBW) was $\geq 110\%$ [18]. Immunocompromised patients were defined as those with ANCs < 500 , in accordance with the American Cancer Society (2010). Deaths were confirmed by a review of medical records up to January 31, 2016.

Analysis of dietary patterns

Dietary patterns were analyzed using data from the meal order sheets for breakfast, lunch, and dinner at the pediatric cancer ward. The meals available on the order form consisted of both Korean and Western type food items, with menu rotations in 10-day cycles. Each patient could select a maximum

of six food items every day for breakfast (of 23, 26.1%), lunch (of 19, 31.6%), and dinner (of 16, 37.5%). We collected data on all food items ordered over a 3-day period. The validity of food selection frequency from the meal order forms was examined by comparison with food intake using the 3-day 24-hour recall data. The mean of Pearson correlation coefficients between the two methods was 0.42, ranging from 0.00 (cookies) to 0.91 (other grains).

For dietary pattern analysis, 220 food items consumed by the subjects were categorized into 29 groups, based on the food groups and items defined by Shin *et al.* [19] and the Korean National Health and Nutrition Examination Survey (KNHANES). Foods that could not be consumed on a low microbial diet (e.g., carbonated drinks, hamburgers, chocolate, ice cream, gum, candy, seeds and nuts, sandwiches, and simple sugars) were excluded as nobody selected. Foods that tended to be preferred by patients during chemotherapy, such as fried meat, processed meat, potatoes, and seasoned spicy meat, etc. [20,21], were divided into greater detail to reflect their dietary characteristics. In addition, the "grains" and "chicken" that children eat frequently were divided into "white rice" and "other grains" as well as "fried chicken", "seasoned spicy chicken", and "chicken", respectively.

Statistical analysis

All analyses were performed using Statistical Package for the Social Sciences for Windows Version 12.0, 2004, (SPSS Inc., Chicago, IL, USA). Statistical significance was defined by a *P*-value below 0.05. Comparisons between variables were conducted using linear regression analyses and the Mantel-Haenszel chi-square test. All statistical tests were two-sided.

To derive dietary patterns, principal component analysis was performed, and three distinct dietary patterns were identified through varimax rotation. The number of factors was selected from eigenvalues > 1.25 with identification of a break point in the scree plots [22]. Foods or food groups with an absolute factor loading > 0.30 are presented in Table 1. Participants were divided into three groups based on the tertile of each dietary pattern score, with the lowest tertile defined as the reference category. Relationships between dietary patterns and overweight were analyzed using logistic regression analysis, adjusted for covariates. The final model (Model 2) was controlled for sociodemographic characteristics such as age (years, continuous) and gender (men, women), and treatment effects such as diagnostic categories [Acute lymphoblastic leukemia (ALL), Peripheral blood stem cell transplantation (PBSCT), and Others] and duration of disease (day, continuous). The results were presented as odds ratios (OR) with 95% confidence intervals (CI). The Cox proportional hazard model was used to examine the association between dietary pattern and all-cause mortality, adjusted for age at diagnosis (years, continuous), gender (men, women), diagnostic categories (ALL, PBSCT, and Others), and duration of disease (day, continuous), and the results are presented as hazard ratios (HR) with 95% CI. In the survival analysis, age at diagnosis was used as a confounding variable instead of age. To test for linear trends across tertiles of dietary pattern scores, we created a continuous variable using the median value of each tertile of total dietary pattern scores.

RESULTS

Dietary patterns of subjects

Factor analysis revealed three distinct dietary patterns: “fish, egg, meat, and fruits & vegetables”, “white rice and fried chicken”, and “spicy & fried meat and fish” based on the factor loadings (Table 1). The three dietary patterns explained 27.4% of the variance in total food intake (11.7%, 8.7%, and 7.1%, respectively). The “fish, egg, meat, and fruits & vegetables” pattern featured high consumption of fish, eggs, fruits & vegetables, meat, tofu, seasoned spicy fish, and other grains. The “white rice and fried chicken” pattern was highly correlated with white rice, fried chicken, soy sauce & soybean pastes, and chicken. The “spicy & fried meat and fish” pattern showed a high loading for seasoned spicy chicken, fried tofu, seasoned spicy fish, fried fish, and fried meat.

Baseline characteristics of subjects according to the dietary patterns

The baseline characteristics of the study participants are shown in Table 2. The mean age was 7.6 years, and the percentage of boys was 61.4%. The disease with the highest

number of cases was ALL (n = 46, 55.4%), followed by other pediatric cancers (n = 25, 30.1%) and PBSCT (n = 12, 14.5%). In all, 35 children (42.2%) were receiving steroid treatment at the study baseline. The percentage of children that were overweight at the study baseline was 26.5% (n = 22). The number of patients in whom PIBW had increased from the time of diagnosis to the study baseline was 51 (61.4%).

Children with high scores for the “fish, egg, meat, and fruits & vegetables” pattern were less likely to be overweight at diagnosis ($P = 0.025$). Higher scores for the “white rice and fried chicken” pattern were observed in boys ($P = 0.042$), younger children ($P = 0.002$), and those with a shorter duration of disease ($P = 0.038$). Children with high scores for the “spicy & fried meat and fish” pattern were more likely to be overweight at diagnosis ($P = 0.017$) and baseline ($P = 0.041$) as well as have normal ANCs ($P = 0.017$).

Association between dietary pattern and overweight

The OR and 95% CI of overweight according to the tertile of each dietary pattern are presented in Table 3. Children in the highest tertile of the “spicy & fried meat and fish (T3)”

Table 1. Factor loading matrix¹⁾ for the three dietary patterns²⁾

	Fish, egg, meat and fruits & vegetables	White rice and fried chicken	Spicy & fried meat and fish	
Bread	-.790			
Fish	.600			
Eggs	.591			
Milk	-.541			
Fruits and vegetables	.475			
Meat	.460		-.325	
Noodles and wheat flour	-.330			
Tofu	.326			
Processed meat	-.318			
French fries	-.316			
Sauce and seasoning	-.301			
Kimchi				
Seasoned spicy meat				
Seaweed				
White rice		.862		
Other grains	.317	-.801		
Fried chicken		.570		
Soy sauce and soybean pastes		.326		
Pizza				
Porridge				
Seasoned spicy chicken			.588	
Fried tofu			.514	
Seasoned spicy fish	.322		.502	
Fried fish			.488	
Cereal		-.337	-.480	
Chicken		.334	-.366	
Fried meat			.350	
Potatoes and pumpkin			-.322	
Cookies				
Percentage of variability	11.645	8.706	7.075	Σ27.4

¹⁾ The correlation among the food groups and each factor (dietary patterns). For simplicity, factor loading values less than 0.30 are not listed in the matrix.

²⁾ Three dietary patterns were derived by principal component analysis after entering the 29 food groups into the FACTOR PROCEDURE.

Table 2. Subjects' baseline characteristics by tertiles of dietary pattern scores

	Total	Fish, egg, meat and fruits & vegetables			White rice and fried chicken			Spicy & fried meat and fish			P-value	
		T1 ¹⁾	T2	T3	T1	T2	T3	T1	T2	T3		
Gender, male, n (%)	51 (61.4)	15 (55.6)	16 (57.1)	20 (71.4)	0.227	12 (44.4)	19 (67.9)	20 (71.4)	13 (48.1)	18 (64.3)	20 (71.4)	0.079
Age, yrs, n (%)					0.259							0.991
1	5 (6.0)	2 (7.4)	3 (10.7)	0 (0)		1 (3.7)	2 (7.1)	2 (7.1)	0 (0)	3 (10.7)	2 (7.1)	
2-4	27 (32.5)	10 (37.0)	8 (28.6)	9 (32.1)		3 (11.1)	10 (35.7)	14 (50.0)	9 (33.3)	11 (39.3)	7 (25.0)	
5-9	21 (25.3)	7 (25.9)	6 (21.4)	8 (28.6)		7 (25.9)	9 (32.1)	5 (17.9)	8 (29.6)	6 (21.4)	7 (25.0)	
≥ 10	30 (36.1)	8 (29.6)	11 (39.3)	11 (39.3)		16 (59.3)	7 (25.0)	7 (25.0)	10 (37.0)	8 (28.6)	12 (42.9)	
Age at diagnosis, yrs	7.0 ± 5.0	6.7 ± 5.5	7.1 ± 5.1	7.1 ± 4.5	0.957	8.8 ± 4.8	6.4 ± 4.9	5.8 ± 4.9	7.5 ± 5.4	5.6 ± 4.1	7.9 ± 5.4	0.198
Duration of disease, day	290.4 ± 330.9	297.2 ± 342.9	294.7 ± 277.9	279.5 ± 376.8	0.978	422.3 ± 460.9	215.0 ± 225.2	238.6 ± 226.3	292.7 ± 393.2	317.5 ± 245.5	261.1 ± 349.0	0.819
Diagnostic categories, n (%)					0.522							0.522
ALL	46 (55.4)	18 (66.7)	12 (42.9)	16 (57.1)		14 (51.9)	17 (60.7)	15 (53.6)	16 (59.3)	17 (60.7)	13 (46.4)	
PBSCT	12 (14.5)	3 (11.1)	5 (17.9)	4 (14.3)		7 (25.9)	2 (7.1)	3 (10.7)	2 (7.4)	5 (17.9)	5 (17.9)	
Others ³⁾	25 (30.1)	6 (22.2)	11 (39.3)	8 (28.6)		6 (22.2)	9 (32.1)	10 (35.7)	9 (33.3)	6 (21.4)	10 (35.7)	
Steroids treatment, n (%)	35 (42.2)	11 (40.7)	12 (42.9)	12 (42.9)	0.875	13 (48.1)	12 (42.9)	10 (35.7)	14 (51.9)	13 (46.4)	8 (28.6)	0.081
ANC < 500 (mm ³), n (%)	17 (20.5)	7 (25.9)	6 (21.4)	4 (14.3)	0.287	6 (22.2)	8 (28.6)	3 (10.7)	9 (33.3)	6 (21.4)	2 (7.1)	0.017
Overweight at diagnosis, n (%)	21 (25.3)	12 (44.4)	4 (14.3)	5 (17.9)	0.025	9 (33.3)	9 (32.1)	3 (10.7)	5 (18.5)	3 (10.7)	13 (46.4)	0.017
Overweight at baseline, n (%)	22 (26.5)	6 (22.2)	12 (42.9)	4 (14.3)	0.492	7 (25.9)	8 (28.6)	7 (25.0)	4 (14.8)	7 (25.0)	11 (39.3)	0.041
PIBW gain ⁴⁾ , n (%)	51 (61.4)	15 (55.6)	18 (64.3)	18 (64.3)	0.511	15 (55.6)	17 (60.7)	19 (67.9)	15 (55.6)	19 (67.9)	17 (60.7)	0.703

ALL, acute lymphoblastic leukemia; PBSCT, peripheral blood stem cell transplantation; ANC, absolute neutrophil count; PIBW, percentage of ideal body weight; T, tertile.

Data are presented as n (%) or mean ± standard deviations.

¹⁾ Tertiles of dietary pattern scores.

²⁾ P for trend was calculated from a linear regression analysis for continuous variables and Mantel-Haenszel χ^2 for categorical variables.

³⁾ Others: acute myeloblastic leukemia, neuroblastoma, aplastic anemia, Wilms tumor, relapsed lymphoma, sarcoma, osteosarcoma, etc.

⁴⁾ PIBW gain from the diagnostic point.

Table 3. Odds ratios (95% CI) for overweight risk according to the tertiles (T) of dietary pattern scores at baselines and follow-ups

Food choice pattern	T	At baseline (n = 83/22 ¹⁾)		6 months (n = 77/26)		24 months (n = 64/26)	
		OR (95% CI)	P for trend	OR (95% CI)	P for trend	OR (95% CI)	P for trend
Fish, egg, meat and fruits & vegetables							
Model 1 ²⁾	T1	1	0.107	1	0.326	1	0.110
	T2	0.200 (0.054, 0.747)*		0.345 (0.101, 1.173)		0.349 (0.095, 1.286)	
	T3	0.330 (0.100, 1.083)		0.575 (0.184, 1.800)		0.297 (0.081, 1.093)	
Model 2 ³⁾	T1	1	0.102	1	0.266	1	0.084
	T2	0.199 (0.051, 0.733)*		0.381 (0.106, 1.364)		0.353 (0.085, 1.470)	
	T3	0.314 (0.093, 1.059)		0.515 (0.156, 1.697)		0.157 (0.046, 0.982)*	
White rice and fried chicken							
Model 1	T1	1	0.419	1	0.702	1	0.655
	T2	0.876 (0.256, 2.998)		0.522 (0.147, 1.849)		2.321 (0.598, 9.008)	
	T3	0.890 (0.257, 3.083)		0.976 (0.301, 3.162)		1.263 (0.337, 4.740)	
Model 2	T1	1	0.448	1	0.576	1	0.997
	T2	0.962 (0.248, 3.737)		0.430 (0.099, 1.858)		1.881 (0.359, 9.854)	
	T3	0.978 (0.247, 3.877)		0.799 (0.204, 3.126)		1.106 (0.224, 5.453)	
Spicy & fried meat and fish							
Model 1	T1	1	0.038	1	0.036	1	0.474
	T2	2.086 (0.520, 8.371)		1.591 (0.455, 5.564)		1.062 (0.312, 3.622)	
	T3	3.747 (1.011, 13.884)*		3.852 (1.129, 13.142)*		1.077 (0.286, 4.052)	
Model 2	T1	1	0.023	1	0.025	1	0.549
	T2	2.246 (0.537, 9.399)		1.526 (0.405, 5.756)		0.866 (0.219, 3.431)	
	T3	4.396 (1.111, 17.385)*		4.088 (1.122, 14.896)*		0.960 (0.233, 3.962)	

OR, odds ratio; CI, confidence interval; T, tertile.

¹⁾ n = total patients/overweight patients²⁾ Model 1 adjusted for age (years, continuous).³⁾ Model 2 adjusted for age (years, continuous), gender (men, women), diagnostic categories (acute lymphoblastic leukemia, peripheral blood stem cell transplantation, and others), and duration of disease (day, continuous).* $P < 0.05$ **Table 4.** Hazard ratios (HR) and 95% confidence intervals (95% CIs) for all-cause mortality by tertiles (T) of dietary pattern scores

Dietary pattern/Tertiles	T1	T2	T3	P for trend
Fish, egg, meat and fruits & vegetables				
Crude	1	0.913 (0.294, 2.830)	0.903 (0.291, 2.801)	0.883
Adjusted ¹⁾		0.568 (0.176, 1.834)	0.601 (0.177, 2.036)	0.372
White rice and fried chicken				
Crude	1	1.123 (0.377, 3.342)	0.741 (0.226, 2.430)	0.724
Adjusted		1.352 (0.346, 5.277)	0.685 (0.170, 2.763)	0.598
Spicy & fried meat and fish				
Crude	1	3.044 (0.614, 15.081)	5.965 (1.306, 27.251)	0.015
Adjusted		3.178 (0.554, 18.243)	5.124 (1.080, 24.320)	0.042

¹⁾ Cox proportional hazards regression model adjusted for age at diagnosis (years, continuous), gender (men, women), diagnostic categories (acute lymphoblastic leukemia, peripheral blood stem cell transplantation, and Others), and duration of disease (day, continuous).

pattern score were more likely to be overweight at both baseline (OR = 4.396, 95% CI = 1.111-17.385, P for trend = 0.023) and after 6 months (OR = 4.088, 95% CI = 1.122-14.896, P for trend = 0.025), as compared to the lowest tertile of the pattern score, after adjusting for age, gender, diagnostic categories, and duration of disease. Children in the highest tertile of the "fish, egg, meat, and fruits & vegetables (T3)" pattern score showed lower risk of overweight at 24 months (OR = 0.157, 95% CI = 0.046-0.982, P for trend = 0.084), as compared to the lowest tertile of the pattern score, after adjusting for covariates. The "white rice and fried chicken" pattern, however, did not show

any association with overweight in pediatric cancer patients.

Association between dietary pattern and all-cause mortality

During the study period, 18 patients died while one patient was transferred to another facility. After adjusting for potential confounders, pediatric cancer patients in the highest tertile of the "spicy & fried meat and fish (T3)" pattern score showed increased risk of all-cause mortality (HR = 5.124, 95% CI = 1.080-24.320, P for trend = 0.042), as compared to the lowest tertile of the pattern score. No associations were observed between the other patterns and mortality (Table 4).

DISCUSSION

We identified three distinct dietary patterns among pediatric cancer patients. The “spicy & fried meat and fish” dietary pattern was positively associated with overweight risk and all-cause mortality, whereas the “fish, egg, meat, and fruits & vegetables” dietary pattern was associated with decreased overweight risk.

In the present study, the three identified dietary patterns explained 27.4% of the total variance in food intake, which is similar to a previous study (28.4%) by Shin *et al.* [19] on four types of dietary patterns (“traditional Korean,” “fast food,” “milk and cereals,” and “snacks”) consisting of similar food items and groups as the present study. Since total variance can differ according to the number of food items/dietary patterns, direct comparisons between studies are difficult [23,24]. However, most studies have used a threshold eigenvalue of 1.0 in order to identify two to three dietary patterns that explain 21.7-30.5% of the total variance [19,25,26]. When these dietary patterns were compared with previous results from the same country, the “fish, egg, meat, and fruits & vegetables” pattern exhibited a balanced dietary composition centered on rice and kimchi with fish, legumes, and seaweed [19]. Although most previous studies conducted in Korea have reported a “traditional Korean” dietary pattern, high consumption of rice and kimchi as the major dietary group for adolescents [27-29] as well as adults [30], our analysis showed that the “fish, egg, meat, and fruits & vegetables” pattern explained the highest in the variance of the total food intake. This may be due to the influence of parents, who are more concerned about their children’s health. A review of healthy children found that the family strongly influences childhood eating practices [31], however, these issues have not yet been examined among childhood cancer survivors. Therefore, further research is needed, specifically with regard to the effect of mothers on the dietary patterns of Korean pediatric cancer patients.

As studies analyzing dietary patterns in pediatric cancer patients are rare, it is difficult to compare these findings with previously published results. In the present study, the “spicy & fried meat and fish” dietary pattern was shown to be similar to Western style diets characterized by high intakes of energy-dense and fat-rich foods such as red and processed meat, high-fat dairy products, and snacks [32,33]. The Western dietary pattern in both adults and children is known to be positively associated with being overweight. A recent systematic review suggested that dietary patterns high in energy-dense, high-fat, and low-fiber foods predispose young healthy individuals becoming overweight and obese in later life [34]. Regarding children with cancer, several studies reported that long-term survivors of childhood cancer do not adhere to cancer prevention guidelines, as they consume more sweets and fat as well as less fiber than dietary recommendations [12,13,15,16]. Although data are scarce and inconsistent regarding the impact of spicy foods on obesity, a recent population-based epidemiological study in China suggested that spicy food intake is a potential risk factor for obesity, especially for central obesity in men [35]. Sun *et al.* speculated that spicy foods increase the palatability of meals and consequently may increase carbohydrate intake. Additionally, hot pepper consumption has been shown to increase the desire

to eat sweet foods, which reduce the sensation of heat and relieve pain on the tongue. Therefore, consumption of spicy foods may contribute to obesity. Further studies are needed to identify whether or not there is a causal mechanism between spicy food consumption and obesity.

In our study, the “fish, egg, meat, and fruits & vegetables” dietary pattern was associated with lower overweight risk at the end of the study, in agreement with previous studies [36]. The “fish, egg, meat, and fruits & vegetables” dietary pattern, which is characterized by high intakes of fruits, vegetables, fish, and tofu, is similar to the Mediterranean diet. It is well known that the Mediterranean dietary pattern is inversely associated with risk of obesity [22]. In a study on 117 adult survivors of ALL, Tonorezos *et al.* [37] noted that the Mediterranean dietary pattern was associated with low body mass index, low visceral fat, low subcutaneous fat, and a small waist size.

In the present study, the proportion of patients whose PIBW increased was 59.4%, and the proportion of patients who were overweight increased from 26.5% at baseline to 40.6% at the end of the study. Although the percentage (26.5%) of patients that were overweight at baseline was relatively low compared to other studies reporting percentages of 38.2% [38] and 40% [39], the percentage (40.6%) of overweight patients at the end of the study was similar to those in other studies. It should be noted, however, that the percentage of overweight patients can vary according to the study group due to varying definitions of obesity and the population used. For example, in 1,291 Korean adolescents from the data of the 2005 KNHANES, 13.5% and 8.2% of 10 to 19-year-olds were overweight and obese, respectively [27], and 17.4% of 12 to 19-year-olds in the 2004 US National Health and Nutrition Examination Survey were obese [40]. Moreover, most previous studies have reported that significant weight gain often occurs in children with cancer between diagnosis and the end of treatment [13,39,41,42]. We also observed that among those patients who were overweight at baseline, 62% ($n = 10$) remained overweight by the end of the study. To prevent obesity, early lifestyle interventions targeting weight control at the point of diagnosis are needed for pediatric cancer patients.

In recent years, there has been growing evidence that dietary factors after cancer diagnosis are related to mortality, especially for adult colorectal, breast, and prostate cancer patients [43-46]. However, the influence of dietary intake on mortality in survivors of childhood cancer is largely unknown. Adult colon cancer survivors in the highest quintile of a Western dietary pattern score after diagnosis showed a 2.3-fold increase in risk of all-cause mortality, as compared to patients in the lowest quintile ($HR = 2.32$, 95% $CI = 1.36-3.96$, P for trend < 0.001) [43]. Similarly, Western dietary patterns have been reported to be positively associated with all-cause mortality in adult prostate cancer patients [45]. In this regard, the positive association between the “spicy & fried meat and fish” dietary pattern and mortality in our study is consistent with previous studies. Conversely, we observed no association between the “fish, egg, meat, and fruits & vegetables” dietary pattern and all-cause mortality, unlike previous study results. In a meta-analysis of 16 prospective cohort studies on the non-cancer population, higher consumption of fruits and vegetables, similar to the “fish, egg, meat, and fruits

& vegetables" dietary pattern in our study, was significantly associated with lower risk of all-cause mortality [47]. A separate meta-analysis of 117 cohort studies enrolling adult cancer survivors confirmed these findings by showing that higher intake of vegetables and fish was inversely associated with overall mortality [48]. Taken together, our findings could be used to guide dietary interventions aimed at improving long-term health outcomes among childhood cancer survivors.

This study is significant in that it is the first to examine the association between dietary factors of obesity and all-cause mortality through a dietary pattern analysis of pediatric cancer patients. However, there are several limitations. First, dietary patterns identified with food intake in the hospital may not accurately represent children's usual dietary intakes. Second, we analyzed dietary patterns by the food choice pattern, not actual food intake. Therefore, the results need to be confirmed using adequately quantified dietary intakes. Third, we did not analyze relative risk of mortality according to the interaction between dietary pattern and obesity. Finally, our sample size may not be sufficient to assess the association of dietary pattern with obesity and mortality. However, this study is the first cohort study to reveal associations between specific dietary patterns and overweight risk and all-cause mortality in pediatric cancer patients. Our results convey important messages for the clinical care of pediatric cancer patients in relation to obesity prevention.

In summary, the "spicy & fried meat and fish" dietary pattern was positively associated with overweight risk and all-cause mortality, whereas the "fish, egg, meat, and fruits & vegetables" dietary pattern was associated with lower overweight risk in pediatric cancer patients. Additional comprehensive studies are needed to fully elucidate the associations between dietary pattern as well as overweight risk and premature death in children with cancer.

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CONFLICT OF INTEREST

The authors declare no potential conflicts of interests.

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