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Unhealthy Diet in Children with Cancer: A Case-Reference Study

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Abstract

Objective

To explore the dietary intake of a children's cohort with cancer in comparison with an age-matched cohort of healthy children.

Methods

We enrolled children with a confirmed diagnosis of cancer (solid tumors, brain and blood malignancies) aged 1-18 years and age-matched children as controls. A 3-days standardized food record was collected by a dietician blinded to the diagnosis. Differences of consumptions of nutrients were compared by parametric and non-parametric tests, as appropriate. A multivariate discriminant analysis was used to identify the most effective nutrients to discriminate between the patients and controls.

Results

The diet of patients with solid tumors differed from that of the controls: they consumed a lower level of monounsaturated fats, a higher level of potential renal acid load and had a lower intake of vitamin E and B6. Children with blood malignancies showed greater differences with controls: they consumed lower quantities of calories, proteins, carbohydrates, monounsaturated fats, fibers and higher quantities of potential renal acid load and cholesterol. A multivariate analysis discriminated blood malignancy patients by controls, with 90% efficiency, by a lower intake of vitamin E, B6, saturated fats, starch and a higher intake of sodium and vitamin A.

Conclusions

This extensive analysis of nutrients showed imbalances from recommended dietary intake in children affected by cancer, with significantly less protective nutrients.

Keywords

Pediatric cancer, Pediatric nutrition; Cancer/Neoplastic; Vitamins and cancer; Second cancer prevention; Long-term cancer-correlated complications.

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Introduction

Over the past decades, progresses in the diagnosis and treatment of childhood cancer (5-year survival rate approaches 80%) have led to a rapidly growing cohort of survivors [1,2]. Earlier studies conducted by the Childhood Cancer Survivor Study have underlined that by 30 years from diagnosis, 18% of survivors will die because of the disease, 75% of survivors will develop a chronic health condition [3-11] (especially cardiovascular and metabolic complications), and almost 10% of survivors develop a second malignant neoplasm [12-15]. Studies have shown that approximately 1/3 of survivors are overweight [16]. A recent study found that cancer survivors required approximately 500 Kcal/day less than typical adult estimated energy needs, which may be an important factor contributing to obesity in this group [17]. The levels of physical activity in childhood cancer survivors are lower than recommended [18]. Nutrition status is very important at diagnosis because it can impact on cancer prognosis. The nutritional status of children of pediatric oncology units should be evaluated regularly to assure maintenance of adequate nutritional status and growth. However, the food habits of child cancer survivors are not well documented. The few existing studies that suggest a lack of adherence to current dietary guidelines [19,20], evaluate the adherence only for adult survivors of childhood cancer. A recent study examining the current health behavior practices among survivors indicated that most exhibited undesirable health behaviors, including failure to adhere to recommend guidelines for fruit, vegetable or calcium intake and exercise [21]. Nowadays, studies regarding adherence to current dietary guidelines in a pediatric cancer population are lacking. Therefore, a comprehensive assessment of the intake of key nutrients and food groups in pediatric patients is not possible. This assessment is essential for the development of an early targeted nutritional intervention in order to meet the specific nutritional needs of this high-risk population. The aim of this study is to explore the food consumption of a cohort of children affected by cancer in comparison with age-matched healthy children.

Patients and Methods

Patients

Inclusion criteria: aged 1-18 years and a confirmed diagnosis of cancer.

Exclusion criteria: associated metabolic diseases or genetic syndrome.

Controls

Inclusion criteria: Aged 1-18 years, consecutively recruited among children afferents to child health clinics at the hospital outpatient department of general pediatrics and family pediatricians or referred for minor surgery (cryptorchidism or circumcision, nevi, minor plastic surgery) at the inpatients department of pediatric general surgery.

Exclusion criteria: Associated metabolic diseases or genetic syndrome.

Sample Size

The sample size was estimated according to the following criteria: 30% detection in the difference of at-risk feeding between cases and

controls with 90% power, 1st -degree error of 0.05 and one case/one control. Based on these criteria, the estimated sample size was 64 for each cohort. We enrolled approximately 80 in each group to compensate for a 10% drop-out rate.

Food Consumption Questionnaire

At enrollment, information about the aim of the study was provided to the children's parents, and a written consent was collected from those who agreed to participate. The 3-days standardized food record was given and illustrated to the care giver in a neutral location away from the child by a professional dietician who was blinded to the diagnosis. The parents filled the food questionnaire for three consecutive days and they returned it later for cases. For controls, the food questionnaire was administered at admission for three days before any intervention. A specific questionnaire for the consumption of fruits and vegetables was also used. The data were analyzed by the WinFood software, Medimatica S.u.r.l. Colonella (TE), Italy.

Statistics

The variables were screened for distribution, and parametric or non-parametric methods were adopted as appropriate. The variables which showed a positive correlation with age (Pearson' r), were adjusted for age by a linear regression (Table 1). The differences between the means of the variables, adjusted for weight and age, were analyzed by Student's t-test. A multivariate discriminant analysis was used to identify the most efficient variables (nutrients) able to discriminate between the cases and controls. Wilk's Lambda was used to estimate the ability of each variable that was added to the model to discriminate between the two groups, ranging from 0=total distance to 1=total overlap. An F (variance ratio) test was used to evaluate the significance of the contribution of each variable to the model.

Results

From January to November 2017, 84 eligible cases were identified, of which 8 did not accept to participate (9.5%) and 76 were enrolled. The enrollees included patients with the following cancer types: 20 with leukemia (12 acute lymphoblastic leukemia and 8 acute myeloid leukemia), 17 with lymphoma (11 Hodgkin's lymphoma and 6 non-Hodgkin's lymphoma), 19 with brain malignancies and 20 with other solid tumors. In the same period ninety two children were eligible as controls, 12 did not accepted to be interviewed (13%); 80 controls were recruited. Fourteen were enrolled at the same children's hospital (among those admitted for minor health problems) and 66 at the family pediatrician's office. Controls were frequency matched to cases, since no baseline variables were significantly different among both groups. Patients and controls were similar for age, sex, anthropometric measures, and surgical intervention. We didn't find exclusion criteria among eligible patients and controls. Only two children had oral candidiasis and one mild nausea with vomiting during the days of recording dietary intake data. We grouped patients into the following categories: solid tumors (solid tumors and brain malignancies) and blood malignancies (leukemia and lymphoma cancers) (Table 2).

Macronutrients

No significant difference was observed for the mean consumption of energy (calories/kg of body weight), and carbohydrates (gr/kg of body weight) between all patients and controls. A lower intake of fats (gr/kg of body weight) was observed in patients vs. controls. The intake of unsaturated fats was also lower in patients vs. controls. In contrast, the intake of cholesterol (mg/calories) was higher in patients compared to controls. The consumption of vegetable proteins (gr/die) was also lower in patients; in particular, patients consumed less dietary fiber (gr/kg of body weight) than controls (Table 3) (Figure 1-6).

Salts, minerals and vitamins

The daily intake of sodium (mg/die) was higher in patients vs. controls; while the intake of potassium (mg/die) and magnesium (mg/die) was lower in patients vs. controls. Copper (mg/die) and selenium (μg/die) intake were higher in patients vs. controls. Unexpectedly, patients had a high intake of vitamin A (μg/die) vs. controls. Folic acid (μg/die), vitamin B6 (mg/die) and vitamin E (mg/die) were lower in patients vs. controls. The total polyphenols (mg/die) intake was lower in patients vs. controls (Table 3), (Figure 7 and 8).

Blood malignancies vs. solid tumors

While conducting the food questionnaire evaluations, we observed that the blood malignancy patients often reported very peculiar feeding patterns (for example they ate very often snacks and pizzas); hence, we analyzed the differences between the two groups of patients. As reported in (Table 4), significant differences were observed between the two groups of patients, namely: Higher energy, carbohydrate, starch, fats and fiber consumption in the solid tumor group vs. the blood malignancy group in contrast, the consumption of cholesterol and Vitamin A was lower in the solid tumor group than blood malignancy.

Differences in the Diet of Blood Malignancy or Solid Tumor Patients vs. the Controls' Diet

(Figure 9 and 10) shows the percentage of the differences between the mean consumption of controls and that of cases, computed as: (mean of nutrients consumed by controls - mean of nutrients consumed by patients)*100/ (mean of nutrients consumed by controls) [7-10]. As far as the macronutrients are concerned, it can be noted that children affected by solid tumors did not show major differences in their dietary intake compared to controls, with the exception of less monounsaturated fats and PRAL. However, children affected by blood malignancies showed large differences in most of the macronutrients, including fewer calories, proteins, carbohydrates,

Table 1: Regression for age.

Nutrients	B	F	p
Calories/kg of body weight	-0.715	160.91	<0.0001
Proteins (gr/kg of body weight)	-0.682	134.20	<0.0001
Carbohydrates (gr/kg of body weight)	-0.699	147.07	<0.0001
Fats (gr/kg of body weight)	-0.596	84.79	<0.0001
Starch (gr/kg of body weight)	-0.569	73.78	<0.0001
Fibers (gr/kg of body weight)	-0.612	92.45	<0.0001
Potential renal acid load (PRAL) (pr/die)	0.188	5.60	<0.019

Table 2: Baseline and clinical characteristics of the patients and controls.

Variable	Patients (76)	Controls (80)	p
Sex n (%) Male	47 (61.84)	35 (43.75)	ns
Age at entry, years* • 1-5 • 5-10 • 10-15 • >15	Mean 9.9 ± 5.1 15 (19.7) 17 (22.3) 25 (32.8) 19 (25.0)	Mean 8.6 ± 4.8 18 (22.5) 29 (36.2) 23 (28.7) 10 (12.5)	 ^ ns <ns
Weight (kg)*	40.1 ± 24.3	32.9±17.2	^ns
Height (cm)*	135 ± 0.3	129±0.27	^ns
BMI*	19.9 ± 5.8	18.2±3.31	^ns
Diagnosis, n % Treatment protocols stage and steroids use, n (%)	**Brain Malignancies, 19 (25)** Induction/Consolidation, 11 (58); Maintenance, 0; Rescue, 2 (10.5); Follow up, 5 (26.3); Steroid, 11 (58); **Solid Tumors, 20 (26.3)** Induction/Consolidation, 11 (55) Maintenance, 1 (5); Rescue, 1 (5); Follow up, 7 (35); Steroid, 14 (70); **Leukemia, 20 (26.3)** Induction/Consolidation, 16 (80); Maintenance,3 (15); Rescue, 0; Follow up,1 (5); Steroid, 17 (85); **Lymphoma, 17 (22.3)** Induction/Consolidation, 11 (65); Maintenance,1 (5); Rescue, 1 (5); Follow up, 4 (23.5); Steroid, 16 (94)		
Inpatients n (%) Outpatient's n (%)	38 (50) 38 (50)	14 (17.5) 66 (82.5)	<ns
Surgical intervention, n (%)	28(36.8)	14 (17.5)	<ns

Table 3: Macronutrients, micronutrients and Vitamins differences.

Nutrients	Patients, n=76	Controls, n=80	t	p
Calories/kg of body weight*	38.1 ± 17.7	43.0 ± 16.9	t=1.79	p=0.07
Fats (gr/kg of body weight)	1.3 ± 0.95	1.78 ± 1.15	t=2.78	p=0.006
Unsaturated fats (%)	1.3 ± 1.7	2.8 ± 2.1	t= 4.5	p<0.001
Cholesterol (mg/calories)	228.7 ± 179.5	146.4 ± 107.5	t=3.45	p<0.001
Proteins (gr/kg of body weight)*	1.6 ± 0.8	1.8 ± 0.7	t=1.78	p= 0.07
Vegetable proteins (gr/die)	3.5 ± 3.0	8.8 ± 5.5	t=7.5	p<0.001
Fibers (gr/kg of body weight)*	0.3 ± 0.2	0.39±0.16	t=3.89	p<0.001
Sodium (mg/die)	1,006.2 ± 741.1	762.0 ± 480.6	t=2.42	p<0.01
Potassium (mg/die)	1,234.6 ± 561.4	1,617.6 ± 718.8	t= 3.71	p<0.001
Magnesium (mg/die)	88.9 ± 44.8	110.5 ± 49.4	t=2.85	P<0.005
Copper (mg/die)	1.4 ± 1.2	0.9 ± 0.6	t=3.44	p<0.001
Selenium (µg/die)	40.7 ± 36.0	25.4 ±17.7	t=3.35	p<0.001
Vitamin E (mg/die)	4.0 ± 1.9	7.5 ± 4.7	t=6.18	p<0.001
Vitamin B6 (mg/die)	0.9 ± 0.5	1.1 ±0.5	t=2.29	p=0.023
Vitamin A (µg/die)	1831.8 ± 1501.6	1111.5 ±1246.5	t=3.05	p=0.003
Folic acid (µg/die)	131.1 ± 70.2	182.8 ± 118.3	t=3.34	p<0.001
Polyphenols(mg/die)	139.2 ± 151.3	287.7 ± 241.2	t=4.37	p<0.001

starch, fats and dietary fiber than controls. In addition, they showed excess total cholesterol, less monounsaturated fats, and excess PRAL consumption. As far as micronutrients are concerned, solid tumor patients showed a higher consumption of sodium and a less consumption of potassium, vitamin B6 and vitamin E. The blood malignancy patients consumed less potassium, calcium, magnesium, folic acid and vitamin E than solid tumor patients [9-10]. Unexpectedly, they consumed an excess of copper, selenium and vitamin A.

Factors affecting the observed differences between patients and controls

We evaluated the possible influences of factors, such as age of children at enrollment, diagnosis (solid tumors, brain malignancies, leukemia and lymphoma), stage of treatment (eg they were receiving chemotherapy, radiotherapy, in remission, relapse, receiving steroids, in preparation for a bone marrow transplant) on the observed differences. The patients seen as outpatients did not differ significantly from their peers admitted to the hospital, for both the solid tumor group and the blood malignancy group. Similarly, patients that underwent surgery did not show major differences compared to controls. Therapy also did not appear to influence the dietary choices of the patients (Table 5). The patients that received steroids did not develop a greater at-risk feeding habit in our cohort (Table 6).

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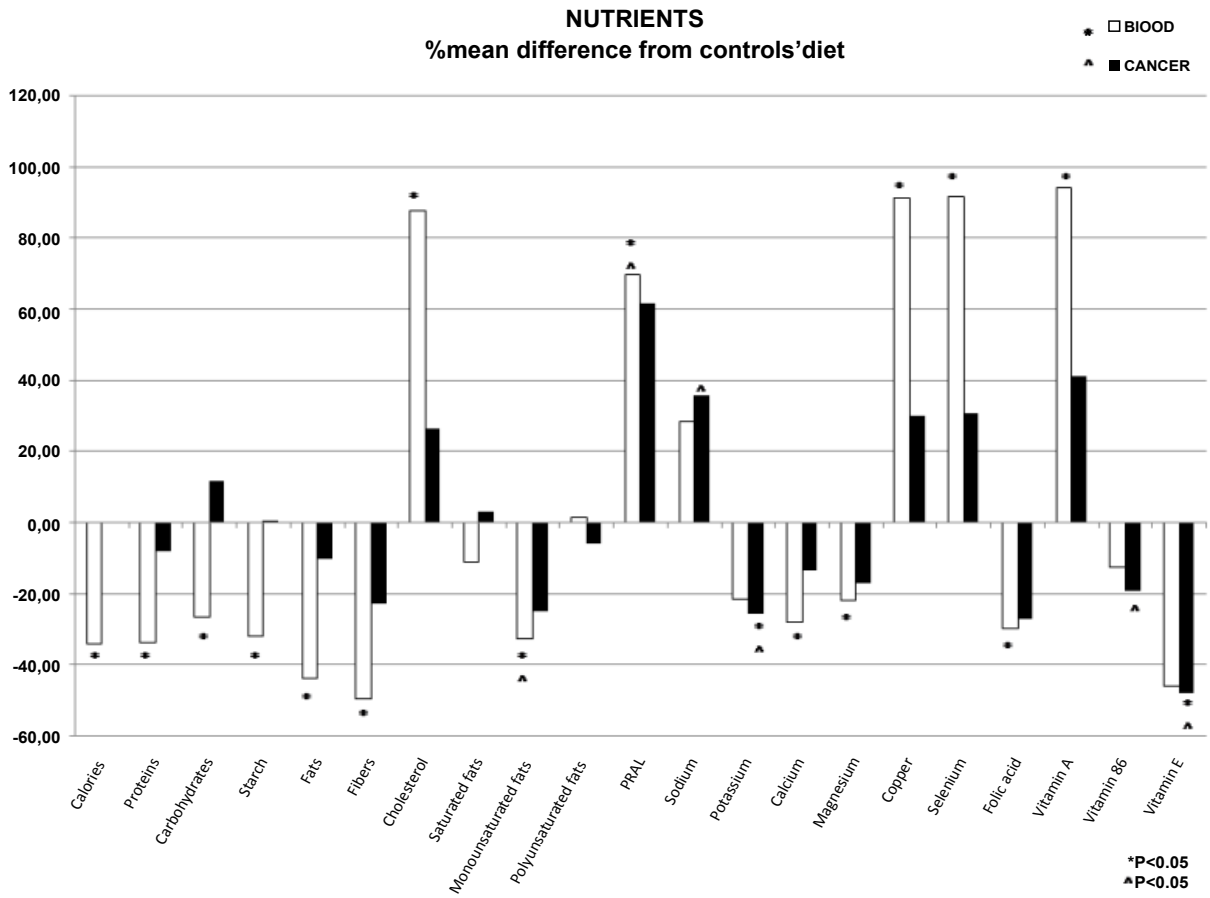

Figure 1: Percentage of the differences between the mean consumption of controls and that of cases. ^ indicates the significance ($p<0.05$) of differences between solid tumor and control.

˚ indicates the significance ($p<0.05$) of differences between blood malignancy and control.

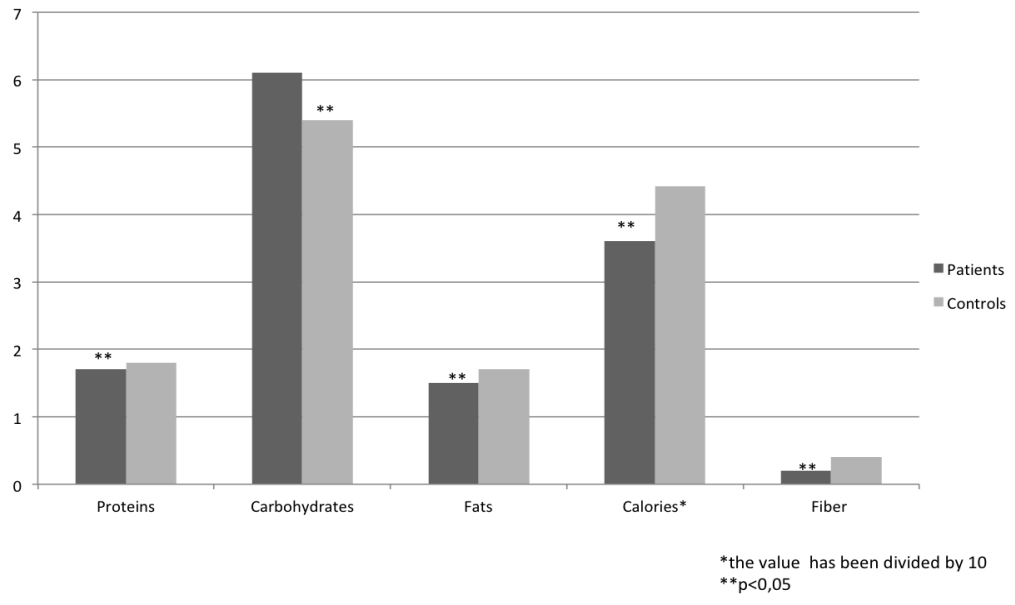

Figure 2: Differences (˚indicates significance $p<0.05$) in calories and macronutrients in patients *vs* controls.

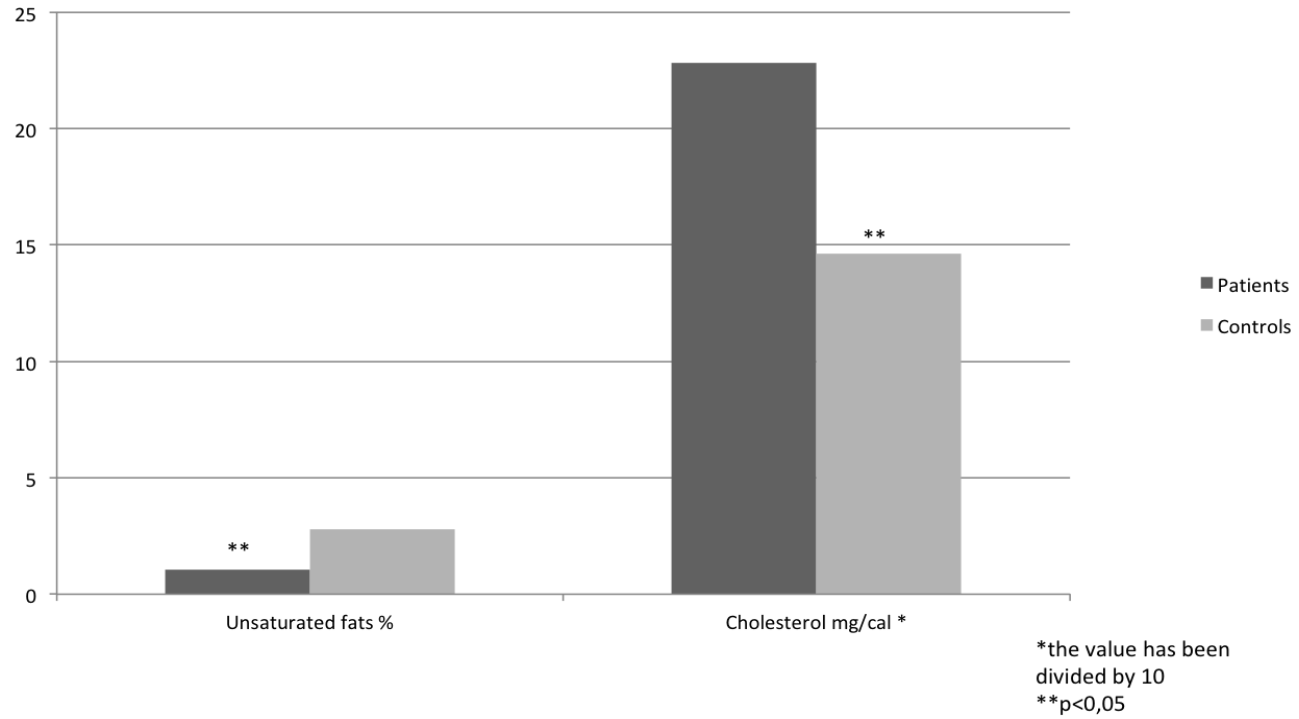

Figure 3 Differences (*indicates significance p<0.05) in fats in patients *vs* controls.

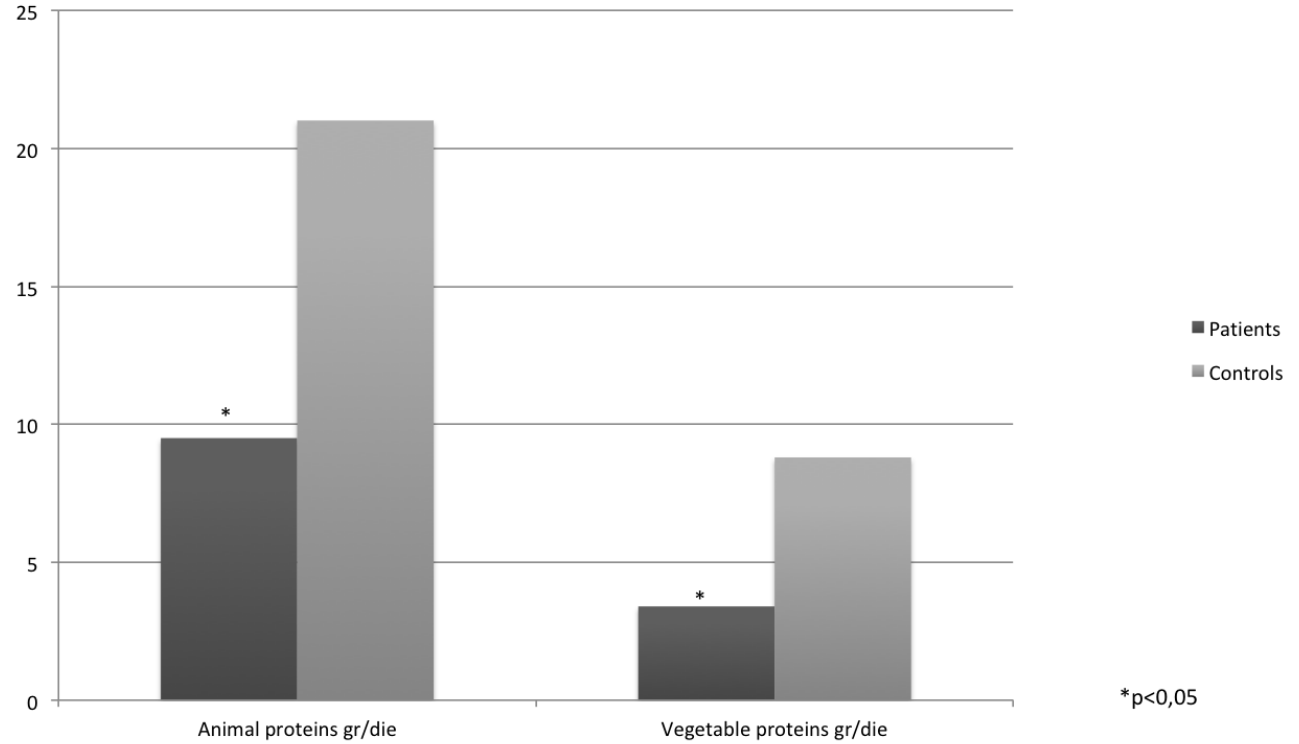

Figure 4: Differences (*indicates significance p<0.05) in proteins in patients *vs* controls.

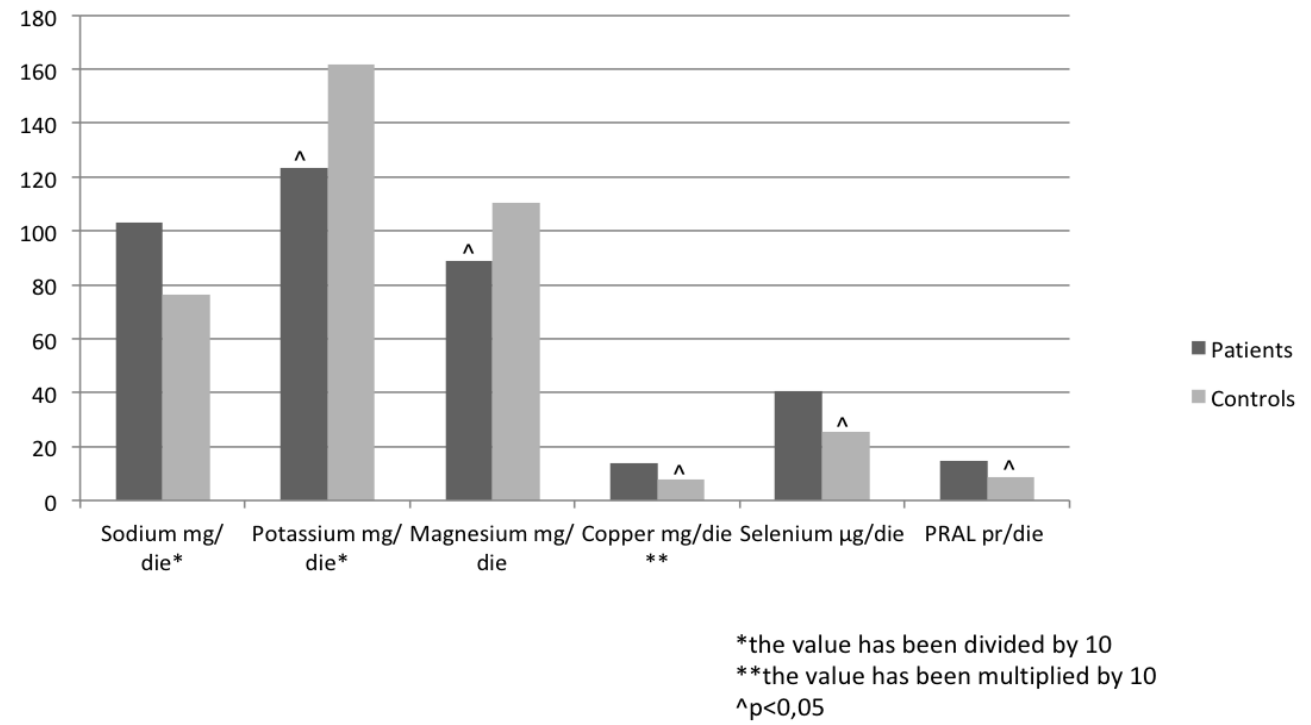

Figure 5: Differences (^indicates significance p<0.05) in salts and minerals in patients *vs* controls.

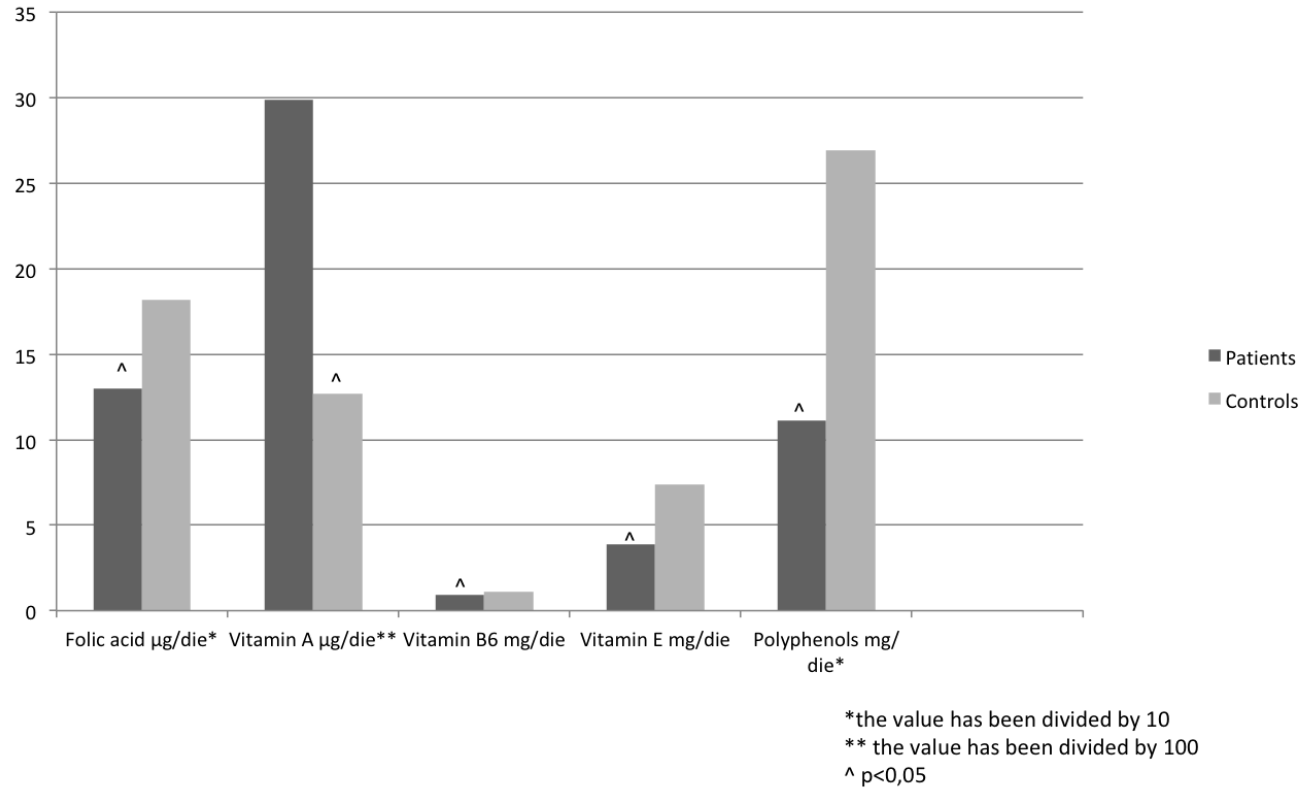

Figure 6: Differences (^indicates significance p<0.05) in vitamins and polyphenols in patients *vs* Controls.

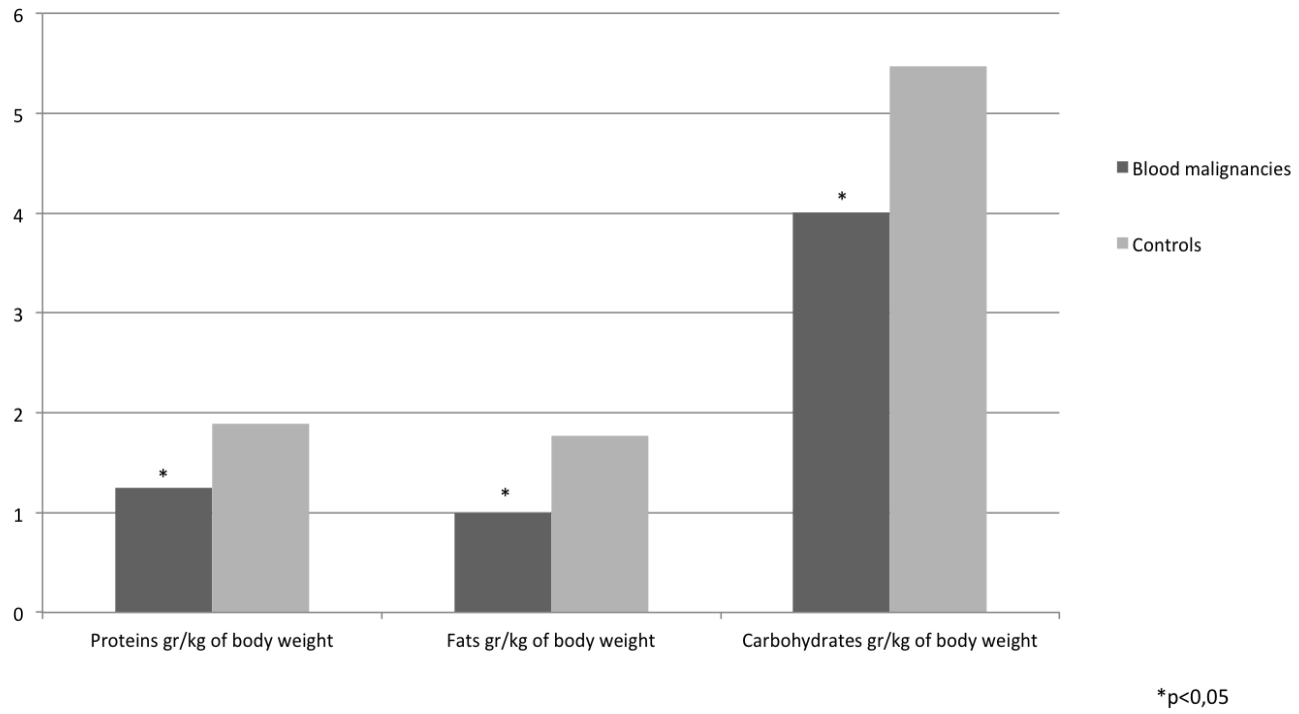

Figure 7: Differences (˚indicates significance p<0.05) in macronutrients in blood malignancies *vs* controls.

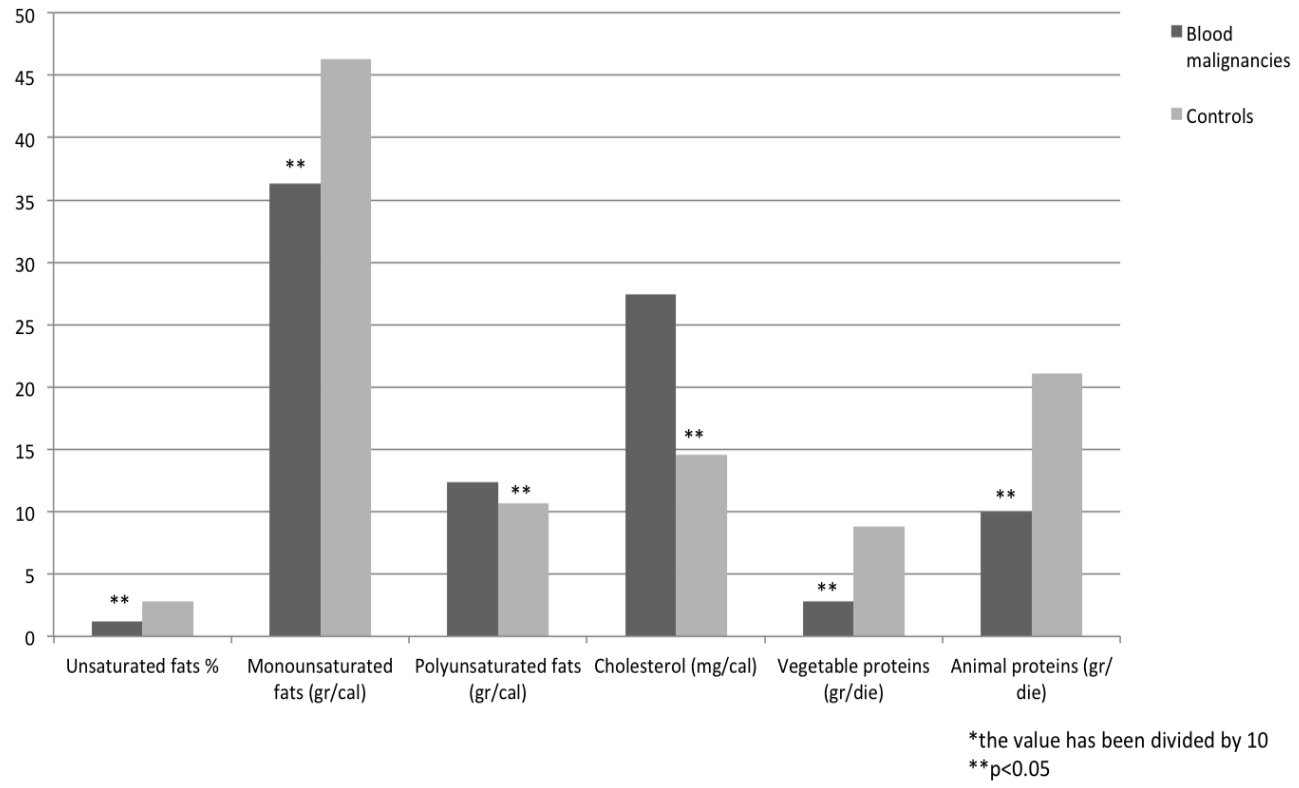

Figure 8: Differences (˚indicates significance p<0.05) in fats and proteins in blood malignancies *vs* controls.

Table 4: Subgroup differences in macronutrients and Vitamin A.

Nutrients	Solid tumor, n=39	Blood malignancy, n=37	Control, n=80	t	p
Calories/kg of body weight*	43.4 ± 16.1	32.4 ± 17.9	43.0 ± 16.9	t=-2.80	p<0.006
Carbohydrates (gr/kg of body weight) *	5.6 ± 2.1	4.2 ± 2.3	5.6 ± 2.2	t=-2.71	p<0.008
Starch (gr/kg of body weight)*	3.2 ± 0.9	2.6 ± 1.1	3.2 ± 1.0	t=-2.70	p<0.009
Fats (gr/kg of body weight)*	1.6 ± 0.6	1.2 ± 0.7	1.6 ± 0.6	t=-2.86	p<0.005
Cholesterol (mg/cal)	185.1 ± 116.8	274.6 ± 220.2	146.4 ± 107.5	t= 3.45	p<0.001
Fibers (gr/kg of body weight)*	0.4 ± 0.1	0.3 ± 0.2	0.4 ± 0.2	t=-2.72	p<0.008
Vitamin A (µg/die)	2,248.0 ± 2410.1	3,780.6 ± 3855.7	1111.5 ± 1246.5	t=3.05	p=0.003
*Adjusted for age					

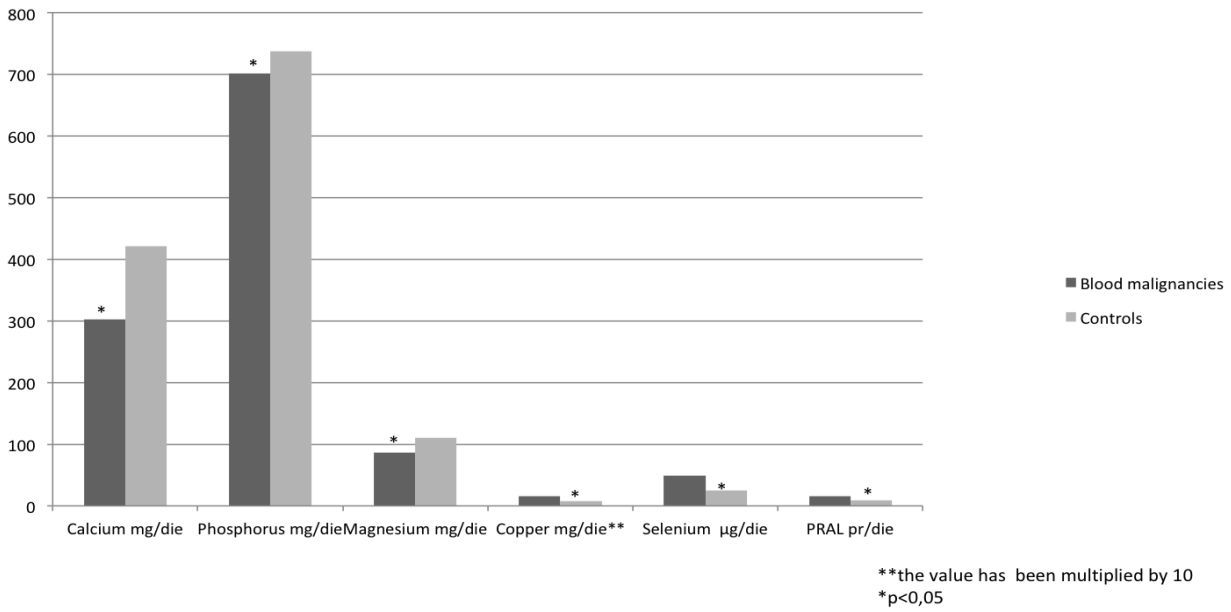

Figure 9: Differences (*indicates significance p<0.05) in salts and minerals in blood malignancies *vs* controls.

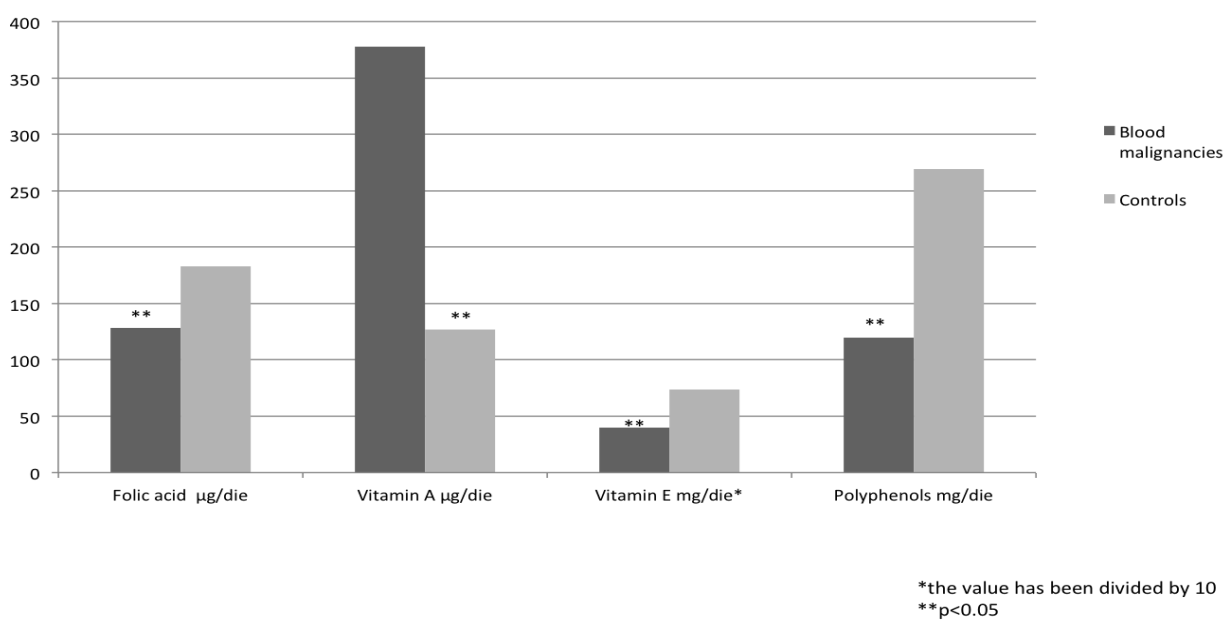

Figure 10: Differences (*indicates significance p<0.05) in vitamins and polyphenols in blood malignancies and controls.

Multivariate Analysis

Because solid tumor patients did not show major differences in their diet compared to healthy controls, we focused on the diet of blood malignancy patients to explore the relationship between the variables. Since the consumption of each nutrient is not independent from the other nutrients, by a multivariate approach, we attempted to identify the variables that contributed most to differentiating the diet of children affected by blood malignancies from that of controls. A multivariate discriminant model was adopted to estimate, using Wilk's Lambda (ranging from 0=complete division between groups to 1=complete overlap), the best variable to discriminate the feeding profile of blood malignancies versus healthy children. (Tables 7 and 8) shows the results of the discriminant analysis. At each step, the variable (nutrients) that is 'more different' between the blood malignancy vs. control group is entered. After the first entry, the second 'more different' variable is entered, according to its contribution to the model and after the first variable is considered. Therefore, at each step, the multivariate model is derived. Vitamin E intake, which was lower in patients, is the most potent discriminating variable, followed by the intake of sodium (higher in patients), saturated fats and starch (lower in patients), vitamin A (higher in patients) and vitamin B6 (lower in patients). The prediction of group membership obtained by the discriminant equation versus the actual membership of each individual provides an estimate of the efficiency of the model to discriminate between the groups. It is clear that approximately 90% of controls are correctly classified as controls, while approximately 79% of patients are also correctly classified. In particular, this model, which shows a very efficient separation of blood malignancies from controls, should not be used to predict the allocation of each individual by their food consumption. Rather, it should be used to explore, among the several significant differences observed between

Table 5: Status at enrollment.

Nutrients	Follow up, n=17	Therapy, n=59	t	p
Calories/kg of body weight	32.4 ± 21.2	38.1 ± 25.6	t=-0.92	p=0.36
Proteins(gr/kg of body weight)	1.2 ± 1.1	1.6 ± 1.1	t= -1.07	p= 0.29
Carbohydrates (gr/kg of body weight)	4.4 ± 2.8	5.3 ± 3.7	t=-0.95	p=0.34
Starch (gr/kg of body weight)	2.9 ± 1.7	2.8 ± 1.8	t= -0.26	p=0.79
Oligosaccharides (gr/kg of body weight)	1.1 ± 0.8	1.4 ± 1.2	t =-1.24	p =0.32
Fibers(gr/kg of body weight)	0.27 ± 0.2	0.3 ± 0.2	t=-0.35	p=0.72
Fats (gr/kg of body weight)	1.2 ± 1.0	1.3 ± 0.9	t= -0.54	p=0.59
Cholesterol (mg/cal)	174.1 ± 81.5	243.2 ±195.5	t=-2.13	p=0.03
Saturated fats (gr/cal)	9.7 ± 2.8	10.3 ± 4.2	t= -0.71	p= 0.47
Monounsaturated fats (gr/cal)	14.3 ± 5.1	12.9 ± 4.6	t=1.01	p=0.47
Polyunsaturated fats (gr/cal)	3.9 ± 1.1	3.9 ±1.2	t= -0.08	p=0.93
Vitamin A (µg/die)	2,524.0 ±1549,4	1,596.2 ± 1425.6	t= 2.11	p=0.04
Vitamin E (mg/die)	4.5 ±1.7	3.8 ± 1.9	t =1.34	p =0.19
Folic acid (µg/die)	152.1 ± 59.6	125.4 ± 72.1	t=1.52	p=0.13

Table 6: Steroids at enrollment.

Nutrients	YES	NO	t	p
Calories/kg of body weight	34.5 ± 24.0	44.1 ± 25.9	t=-1.42	p=0.16
Proteins (gr/kg of body weight)	1.4 ± 1.2	1.7 ± 1.0	t=-0.78	p=0.44
Carbohydrates (gr/kg of body weight)	4.7 ± 3.4	6.1 ± 3.9	t=-1.36	p=0.18
Starch (gr/kg of body weight)	2.7 ± 1.8	3.1 ± 1.7	t=-0.96	p=0.34
Oligosaccharides (gr/kg of body weight)	1.3 ± 1.2	1.5 ± 0.8	t=-1.01	p=0.31
Fibers (gr/kg of body weight)	0.3 ± 0.2	0.3 ± 0.2	t=-0.89	p=0.37
Fats (gr/kg of body weight)	1.2 ± 0.9	1.6 ± 1.0	t=-1.58	p=0.12
Cholesterol (mg/cal)	239.6 ± 194.7	196.1 ± 121.4	t=1.14	p=0.25
Saturated fats (gr/cal)	10.0 ± 4.0	10.6 ± 3.6	t=-0.59	p=0.55
Monounsaturated fats (gr/cal)	13.1 ± 5.0	13.4 ± 3.7	t=-0.24	p=0.81
Polyunsaturated fats (gr/cal)	3.9 ± 1.2	4.0 ± 1.1	t=-1.33	p=0.89
Vitamin A (µg/die)	1,927.1 ± 1942.8	2,469.4 ± 1517.8	t=1.26	p=0.21
Vitamin E (mg/die)	4.1 ± 1.9	4.0 ± 2.0	t=0.12	p=0.26
Folic acid (µg/die)	140.1 ± 72.7	113.2 ± 61.5	t=0.93	p=0.36

Table 7: Stepwise multivariate discriminant analyses. Efficiency of the model to discriminate between blood malignancies and controls.

Step	Nutrients	Wilks Lambda	F	P
1	Vitamin E	0.873	14.921	p<0.001
2	Sodium	0.732	18.661	p<0.001
3	Saturated fats	0.692	14.952	p<0.001
4	Starch	0.656	13.091	p<0.001
5	Vitamin A	0.609	12.697	p<0.001
6	Vitamin B6	0.574	12.119	p<0.001

Table 8: Classification of Groups.

Classifications			
Original Groups	**Predicted Group**		**Total**
	Blood malignancy	Controls	
Blood malignancy	22 (78.6)	6 (21.4)	28
Controls	8 (10.3)	70 (89.7)	78
86.8% of individuals are correctly classified.			

these two groups, which macro or micronutrient differentiates the diet of the patients from that of controls. It is clear that in cancer patients, there is a deficiency of vitamin E and B6, while vitamin A is consumed more by patients than by controls. The amount of sodium, saturated fats and starch is notably in excess in the diet of the cancer patients. In particular, the selection of the variables that were able to distinguish the diet of the blood malignancy cases from that of controls provided a reliable picture of the observations of the daily life of these patients. All caregivers observed an excessive consumption of salted snacks, sweets, and soft drinks as soon as the child entered into the diagnosis and treatment process (Tables 7 and 8).

Discussion

Cancer is a major cause of death in children worldwide, and the recorded incidence tends to increase with time. At the same time, 5-year survival rates improved considerably over the last decades after the implementation of intensive treatments, particularly in developed countries [1,22]. It is documented that second malignant neoplasms are a late-effect of cancer therapy and the primary cause of non-relapse-related late mortality after childhood cancer [6,10,13-15,23]. Diet is reported to be associated with the etiology of many cancers, and antioxidant-rich foods are believed to be protective factors [24-28]. Epidemiological and experimental evidence demonstrates that only a small proportion of cancers are inherited; nutrition, physical activity, and body composition can play an important role on genetic modification. Essentially this is good news. It means that a healthy lifestyle may stop cancer before it starts, can module cancer's recurrence and the onset of second tumors [29]. Unfortunately, many cancer survivors do not adhere to a healthy diet. In a study conducted to evaluate the dietary intake of adult's cancer survivors it was observed that none of the study participants reported complete adherence to the recommended dietary guidelines [30]. Although half of the participants in this study achieved the minimum daily targets of consuming 5 portions of fruit and vegetables and ≤30% of energy in the form of fats in their diet, most participants reported an intake of sodium and added sugars that considerably exceeded recommendations, together with a minor consumption of the recommended quantities of whole grains [30]. Malnutrition is a major concern in pediatric cancer [31-33]. A recent study showed that undernourished and over nourished patients had the lowest health-related quality of life of all cancer patients [34]. However, dietary recommendations are not very popular among parents. Even if malnutrition in pediatric cancer is a known aspect [33,35-41], its ascertainment and management remain variable [36,42-44], with malnourishment going unrecognized in many children and, consequently, untreated [45]. A recent systematic review of 46 studies shows that there is not sufficient evidence to accurately determine the prevalence of malnutrition in pediatric cancer worldwide [46]. The majority of studies evaluated malnutrition in acute lymphoblastic leukemia patients only, and data regarding malnutrition in both solid and brain tumor patients are limited. In our study, we observed significant differences in macronutrients, micronutrients, and vitamins between the blood malignancy and control group, while solid tumor children differentiated minimally from controls. The blood malignancy patients consumed low quantities of calories/kg of body weight, proteins, carbohydrates, monounsaturated fats, dietary fiber and high quantities of PRAL. They had a generally unhealthy diet. Both groups exhibited no frank evidence of malnutrition (body weight and body mass index were in the appropriate range for sex and age). A higher intake of sodium and a lower consumption of potassium were recorded in patients *vs*. control. In particular, blood malignancy children consumed higher quantities of commercially available chips and other salted snacks; they also consumed a lower amount of calcium and magnesium and a higher level of copper and selenium. The high levels of selenium can be related to the high intake of pizza and packaged chicken. The high levels of copper are probably attributable to the daily chocolate intake of these patients. The patients group has a lower intake of calcium, consistent with reports in the literature for adult survivors of childhood cancer [47]. In our cases, we observed a high consumption of vitamin A, which was exceptionally high in the blood malignancy group. By analyzing the details of the feeding report for this group of patients, we observed an excess consumption of pasta and pizza with tomato and soft drinks, which are likely sources of excess vitamin A. The cancer group consumed less food containing vitamin E and vitamin B6. The blood malignancy group also demonstrated a lower consumption of folic acid. Most of the controls were recruited in outpatient (83%), while half of the patients are outpatients: hence the 3-days food record reports more often in controls than in patients the diet received at home. This is actually the main result of our study: when children are admitted to hospital, their diet is likely to become less healthy. But why blood malignancies patients have a quite un-protective diet, also compared to children with solid tumors, is matter of concern: they share the same kitchen and are offered the same food in the hospital. Various nutritional strategies to assist in the maintenance or recovery of an optimal nutritional status of children and adolescents during treatment have been proposed [48]. It is crucial for health professionals and families to provide incentives for children to consume natural foods, such as fruits and vegetables during treatment. Highly palatable and foods rich in sugar, fats, sodium and other additives should be consumed moderately. Validating health effects of foods and food components represents the new target of nutrition research together with understanding the mechanisms through which dietary factors could prevent disease. A lot of effort is still needed to understand how the caloric intake, frequency and timing of the meal, modifications of individual nutrients, microbiome and nutritional history, interact with each other in modulating the key mechanisms that maintain the function of cells, tissues, and organs throughout life. The strengths of this study is based on the following features: the accurate collection of feeding habits by a 3-days controlled food record, shared with families and hospital staff, the availability of hospital-based matched controls and the extensive analysis of nutrients. The limitations of this study are the relatively small sample size, the cross-sectional design, with no follow up. But this was the available resources in our setting.

Conclusion

The results of this study provide a solid basis to develop a preventive and curative dietary intervention at the start of the diagnostic process of malignancies. The discovery of a malignancy in a child is likely to disrupt the familial feeding habits and drive these children toward an unhealthy diet. For this reason, an early dietary intervention should not be considered optional at the time of the severe involvement of the child and family, since the benefits of maintaining a healthy 'Mediterranean' style diet largely outweigh the burden of the dietary intervention.

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