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Changes in nutritional status of children with cancer depending on clinical, demographic and social factors

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Abstract

Introduction: The aim of this study was to evaluate the nutritional status of children undergoing cancer treatment and to assess changes in their nutritional status depending on selected clinical, demographic, and social factors.

Material and methods: This was a single-center prospective cohort study of children aged 2 to 18 years who were diagnosed with cancer and received treatment between October 2019 and January 2022. The nutritional status of patients was evaluated before and after cancer treatment based on measurements of weight, body mass index (BMI), height, and arm anthropometry (MUAC, mid-upper arm circumference; TSFT, triceps skinfold thickness, and SCFT, subscapular skinfold thickness). Body composition (UMA, upper arm muscle area), arm fat index (AFI), and the sum of SCFT and TSFT (SFsum) were also assessed. Additionally, the nutritional status of patients at baseline was compared to that of a control group consisting of 30 healthy children. The obtained results were analyzed depending on selected demographic, clinical, and social factors.

Results: The study included 40 patients (median age 11.29 years [range 2.08–17.67]; male 67.5%). At baseline, malnutrition was reported in 5% and 7.5% of children based on weight and BMI respectively, and in 7.5% of patients based on MUAC. At follow-up, malnutrition increased by 17.5% based on body weight and BMI, and by 2.5% based on MUAC. UMA allowed the diagnosis of protein-energy malnutrition in 27.5% of patients. Moreover, low UMA was significantly more common in children with cancer than in controls. Overnutrition at follow-up was identified in a higher percentage of patients based on AFI and SFsum measurements than based on BMI (27.5%, 35%, and 10%, respectively). There were no differences in anthropometric measurements or body composition depending on the type of cancer, intensity of treatment, or place of residence. However, weight, BMI, MUAC, UMA, and SFsum were higher in males, suggesting the possible effect of sex. A higher prevalence of underweight determined by BMI was noted in patients whose parents had university education or were between the ages of 18 and 35.

Conclusions: Children with cancer show changes in the nutritional status compared to healthy children. Body composition can be used to identify these changes with greater accuracy than anthropometric measurements such as weight, height, BMI, and arm anthropometry. The risk of changes in nutritional status can be determined based on selected clinical, demographic, and social factors.

Keywords: children, cancer, nutritional status, body composition

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Introduction

Children with cancer may present with abnormalities in nutritional status that can be found at the time of diagnosis, or during and after cancer treatment [1–4]. Conditions that constitute high-risk factors for malnutrition (both undernutrition and overnutrition) in children with cancer include advanced solid tumors, central nervous system tumors, high-risk acute lymphoblastic leukemia, high-risk lymphoma, nasopharyngeal carcinoma, as well as multiple relapsed and high-risk leukemias [5]. Malnutrition can complicate cancer treatment and worsen the prognosis [6, 7]. It also increases the risk of metabolic disorders in survivors [8, 9].

Identifying children with cancer who are at higher risk of nutritional disorders such as undernutrition and overnutrition may aid decision-making on appropriate management, thus preventing complications. Therefore, it is important to determine risk factors for malnutrition and to identify pediatric patients with cancer who require close monitoring.

The aim of the present study was to evaluate the nutritional status of children receiving cancer treatment. Moreover, we aimed to assess changes in the nutritional status depending on selected clinical, demographic, and social factors.

Material and methods

Study design

This observational, prospective, single-center study was conducted in pediatric patients with newly diagnosed cancer who were hospitalized between October 2019 and January 2022 in the Pediatric Department of Hematology, Oncology and Transplantology at the University Hospital in Lublin, Poland. The study compared the nutritional status of children with cancer at diagnosis to that of a group of healthy children (the control group), and also showed changes in the nutritional status of children with cancer during treatment.The nutritional status of the patients was assessed at the baseline examination (before cancer treatment) and again at the follow-up examination (after treatment). The treatment endpoint in patients with hematological malignancies was evaluated before starting maintenance treatment, while in those with solid tumors it was evaluated upon completion of the first-line treatment protocol. Subsequently, changes in the nutritional status were assessed according to clinical (type of cancer, intensity of treatment), demographic (sex, age group), and social (age of parents, education of parents, place of residence) characteristics of the patients' families.

Study population

The study included consecutive pediatric patients aged 2 to 18 years with newly diagnosed cancer. Exclusion criteria were age under 2 years at diagnosis, relapsed or secondary malignancy, and hematopoietic stem cell transplantation. Patients received standard treatment according to the type and stage of cancer.

The control group included children who were not under specialized care for chronic diseases, were not taking any chronic medications, and who did not present with signs of active infection upon enrollment to the study. Controls were recruited from among the children of the investigators and those of their relatives and friends.

Demographic and clinical data including age, sex, type of cancer, and intensity of treatment were obtained from the hospital registry. Information on the social status (the age of the parent when the child was diagnosed with cancer, parents' educational status, place of residence) was obtained from parents using a dedicated questionnaire.

Nutritional assessment

The nutritional status of participants was assessed based on anthropometric measurements including body weight, height, body mass index (BMI), mid-upper arm circumference (MUAC), triceps skinfold thickness (TSFT), subscapular skinfold thickness (SCFT) and body composition including sum of SCFT and TSFT (SFsum), upper arm muscle area (UMA), and arm fat index (AFI). Anthropometric measurements were assessed both as raw values and were also interpreted according to age- and sex-adjusted growth charts to obtain percentile rankings. Local reference values were used for weight, height, BMI, and MUAC indices of healthy children and adolescents in Poland [10–13]. UMA, AFI, and SFsum were calculated according to the age- and sex-matched norms of Frisancho [14].

All measurements were taken by the same physician twice: at baseline and then at follow-up. Nutritional status assessment is described in detail in the Supplementary Material (S1).

Statistical analysis

Statistical analyses were performed at baseline and after treatment in participants for whom complete data was available at both timepoints (n = 40). Data was analyzed using descriptive statistics (mean [SD]; median, Q1–Q3, min–max, frequency and rate. Mann-Whitney, Kruskal-Wallis, Wilcoxon, and Fisher tests were used. A p-value of <0.05 was considered significant. All statistical analyses were performed using R version 4.1.1.

Results

Characteristics of study population

A total of 49 patients met the inclusion criteria for this study. During the study, one patient was excluded due to recurrence, one patient withdrew from the study, one patient moved to another treatment center, and six patients required longer treatment. Therefore, the final study sample

Table I. Baseline characteristics of study and control groups

Variable		Study group n = 40	Control group n = 30	*p*-value
Sex n [%]	Female	13 (32.5)	14 (46.7)	0.3386[a]
	Male	27 (67.5)	16 (53.3)	
Age, years	Mean (SD)	9.8 (4.93)	7.74 (4.3)	0.1228[b]
	Median (Q1–Q3)	11.29	6.5	
	Range	(5.25–13.27) 2.08–17.67	(4.65–9.96) 2.17–17.58	
Age group, years n [%]	Pre-school (2–5)	12 (30.0)	11 (36.7)	0.3387[a]
	School (6–12)	16 (40.0)	14 (46.7)	
	Adolescent (13–18)	12 (30.0)	5 (16.7)	
Place of residence n [%]	Rural	21 (52.5)	7 (23.3)	<0.001[a]
	Urban — city	8 (20.0)	22 (73.3)	
	Urban — town	11 (27.5)	1 (3.3)	
Education of parents n [%]	Elementary	6 (15.0)	1 (3.3)	<0.001[a]
	Secondary	11 (27.5)	0 (0.0)	
	University	23 (57.5)	29 (96.7)	
Age of parents, years n [%]	18–35	10 (25.0)	28 (93.3)	0.0015[a]
	36–45	19 (47.5)	2 (6.7)	
	≥46	11 (27.5)	0 (0.0)	

N — number; Q — quartile; SD — standard deviation

included 40 patients: 30 patients with hematological malignancies (15 with acute lymphoblastic leukemia, eight with Hodgkin's lymphoma, five with non-Hodgkin's lymphoma, and two with acute myeloid leukemia) and 10 patients with solid tumors (two with central nervous system tumor, two with Wilms tumor, three with soft tissue sarcoma, two with Ewing sarcoma, and one with germ cell tumor). Most patients with hematological malignancies received low and intermediate intensity treatment due to their low risk group classification (SR — standard risk; IR — intermediate risk), while most patients with solid tumours received high intensity treatment due to their high stage of disease (III and IV) (p = 0.246). The mean follow-up of patients with hematological malignancies was 38.89 ± 14.61 weeks, and of those with solid tumors was 45.44 ± 19.02 weeks. The baseline characteristics of the study and control groups are set out in Table I. Detailed clinical, demographic, and social characteristics of the study group are presented in the Supplementary Material (Tab. S1–S3).

Differences in anthropometric parameters were calculated using Fisher test ([a]) or Mann-Whitney test ([b]). A p-value <0.05 was considered significant.

Anthropometric measurements and body composition in study vs. control group

At baseline, there were no differences in anthropometric parameters or body composition between the study and control groups (see Tab. II). However, a comparison of the percentile values of these parameters revealed that low UMA was more common in patients with cancer compared to controls (27.5% vs. 3.3% respectively, p = 0.0137; see Fig. 1).

Anthropometric measurements and body composition in whole study group at baseline vs. follow-up

Analysis of the whole study group revealed no significant differences in anthropometric measurements and body composition at follow-up vs. baseline (see Tab. II). However, a comparison of the percentile values of these parameters at follow-up revealed that more children had undernutrition identified based on weight (p = 0.0514), BMI (p = 0.0690) and MUAC (p =1.000), while overnutrition was more common based on AFI (p = 0.4218) and SFsum (p = 0.6295) (see Fig. 1).

Anthropometric measurements and body composition in study group at baseline vs. during follow-up depending on demographic, clinical, and social factors

Demographic factors

An increase in weight (p = 0.0027), BMI (p = 0.0082), MUAC (p =0.0107), UMA (p = 0.0248), and SFsum (p = 0.002) was observed at follow-up vs. baseline only in boys (see Tab. III). On the other hand, analysis of percentile values indicated that girls had a higher prevalence of underweight

Table II. Anthropometric measurements and body composition in study group at baseline and follow-up vs. control group

Parameter	Study group n = 40		*p*-value[a] (study group: baseline vs. follow-up	Control group n = 30	*p*-value[b] (study group at baseline vs. control group)
	Baseline	Follow-up			
	37.84 (19.56)	38.43 (19.71)		29.76 (16.39)	
Weight, kg	32.2 (21.42–54.50)	34.95 (21.38–51.75)	0.2117	24.75 (17.85–32.75)	0.1287
	13.3–77	13.7–82.5		11–68	
	140.31 (29.16)	143.69 (26.94)		128.35 (27.41)	
Height, cm	145 (117.25–166)	150 (120–167)	<0.001	123 (109.25–138)	0.1014
	89–183	97–183		89–194	
	17.71 (3.42)	17.24 (3.65)		16.71 (2.4)	
BMI, kg/m^2	16.64 (15.43–19.6)	16.16 (14.8–18.72)	0.3681	16.36 (14.82–18.51)	0.2991
	13.55–27.94	12.22–28.89		12.89–22.32	
	21.41 (4.97)	22.02 (4.88)		20.25 (3.97)	
MUAC, cm	19.75 (17.38–25.5)	20.75 (18.38–25.12)	0.1134	19.75 (17–22.75)	0.4612
	14.5–32	15.5–32.5		14.5–29	
	27.46 (13.33)	28.66 (14)		23.92 (9.91)	
UMA, cm^2	23.29 (17.65–35.08)	23.88 (19.42–34.95)	0.1231	22.52 (16.61–28.17)	0.3454
	10.26–65.4	12.15–62.82		12.4–49.44	
	28.54 (7.26)	29.78 (6.95)		29.12 (6.33)	
AFI, %	28.39 (24.38–33.17)	28.95 (25.53–31.97)	0.5862	29.25 (25.65–33.37)	0.6139
	11.72–46.65	16.58–51.24		11.5–41.57	
	19.97 (9.31)	21.26 (7.58)		18.52 (6.16)	
SFsum, mm	16.06 (14–23)	19 (16.79–24)	0.2122	15.25 (14–23)	0.7301
	11.46–49.3	12–45		11–36	

Data presented as mean (SD), median (Q1–Q3), and min–max values. Differences in anthropometric parameters were calculated using Wilcoxon test ([a]) or Mann-Whitney test ([b]). A *p*-value <0.05 was considered significant.; AFI — arm fat index; BMI — body mass index; MUAC — mid-upper arm circumference; SCFT — subscapular skinfold thickness; SFsum — sum of subscapular and triceps skinfold thickness; TSFT — triceps skinfold thickness; UMA — upper arm muscle area

than boys as determined by weight ($p = 0.022$) and BMI ($p = 0.0322$) (see Tab. IV).

Analysis by age showed significant differences in height, with the highest growth rate noted in the group of preschool children, and the lowest in adolescents ($p < 0.001$) (see Tab. III).

Clinical factors

There were no significant differences in anthropometric measurements or body composition at follow-up vs. baseline depending either on the type of the tumor or the intensity of treatment (see Tab. III and IV).

Social factors

The place of residence had no impact on changes in anthropometric measurements. However, the level of parental education was associated with percentile BMI values: children whose parents had a higher level of education more often had underweight during treatment than children of parents with a lower level of education ($p = 0.0462$) (see Tab. V). Finally, the age of parents was associated with changes in percentile BMI values: children of younger parents (18–35 years) more often were underweight during treatment than were children of older parents (>35) ($p = 0.0108$) (see Tab. V).

Discussion

In our study, we investigated clinical, demographic, and social factors that might affect changes in the nutritional status of children with cancer. Participants were characterized according to cancer type (75% of patients had hematological malignancies, of whom 50% were diagnosed with acute lymphoblastic leukemia), intensity of treatment (55% of patients received low/intermediate-intensity treatment), sex (the male-to-female ratio was 2.07:1), age (40%

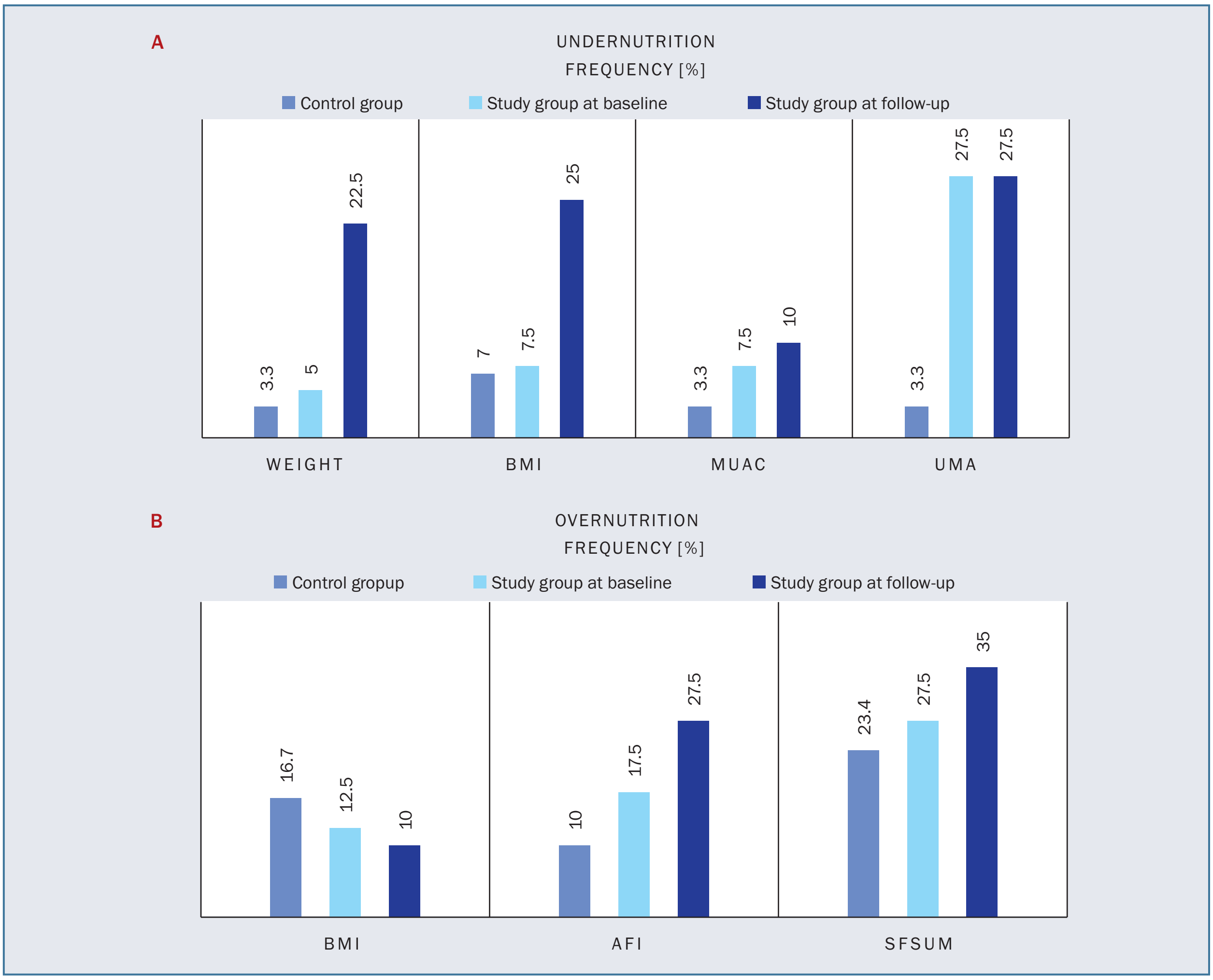

Figure 1. Nutritional status of patients determined by percentile distributions [%]: **A** — undernutrition; **B** — overnutrition; BMI — body mass index; MUAC — mid-upper arm circumference; SFsum — sum of subscapular and triceps skinfold thickness; UMA — upper arm muscle area

of school children vs. 30% of pre-school children and adolescents), place of residence (52.5% of children from rural areas), educational level of parents (57.2% of parents with higher education), and age of parents (47.5% of parents aged 36–45). The clinical and demographic characteristics of the study population are similar to the epidemiology of childhood cancer. The most common types of childhood cancer are hematological malignancies (leukemias and lymphomas), with higher incidence rates in boys (male-to--female ratio has been reported to range from 1:1 to 1:4 in the age group of 0–19 years) [15].

Current recommendations indicate that the proper assessment of the nutrition status in patients with cancer solely on the basis of weight and BMI may not be sufficient, because these parameters can be influenced by tumor mass, hydration status, as well as ascites and edema that are often present in cancer patients [5, 16, 17]. Therefore, in our study, apart from the standard parameters for the anthropometric assessment of the nutritional status (such as weight, height, BMI), we used the recommended methods based on arm anthropometry as well as lean body mass (MUAC, UMA) and body fat mass assessment (AFI, SFsum).

A comparison of anthropometric and body composition measurements revealed that the mean weight of patients with cancer was higher than that in healthy children (37.84 kg vs. 29.76 kg). In clinical practice, nutritional status is assessed using age- and sex-specific percentile rankings [10, 11]. This method was also used in our study. In patients with cancer, weight and BMI percentile ranking indicated malnutrition in 5% and 7.5% of cases, respectively, while MUAC indicated malnutrition in 7.5% of cases. The additional assessment of UMA reflecting lean body mass allowed us to identify protein-energy malnutrition in 27.5% of cases. Moreover, UMA deficiency was significantly more common in patients with cancer than in controls.

There is very little literature on the nutritional status in children with cancer compared to a control group. In a Korean study, Yang et al. [18] assessed the nutritional

Table III. Changes in anthropometric and body composition parameters from baseline to follow-up according to clinical, demographic, and social factors

Parameter	Weight, kg	Height, cm	BMI, kg/m²	MUAC, cm	UMA, cm²	AFI, %	SFsum, mm
Hematological malignancies	0.56 ± 6.03 (−15 to 10.5) 1.45 (−1.75 to 4.55)	3.47 ± 3.49 (0 to 10) 2.75 (0 to 7.5)	−0.52 ± 2.37 (−7.15 to 2.93) −0.21 (−1.65 to 0.65)	0.71 ± 2.4 (−5.5 to 5) 0.5 (−0.5 to 2.5)	1.65 ± 5.49 (−11.7 to 11.48) 1.37 (−1.49 to 4.26)	0.62 ± 7.53 (−11.75 to 20.16) −0.38 (−3.87 to 4.33)	1.39 ± 7.68 (−16 to 22) 1.75 (−1.7 to 6)
Solid tumors	0.67 ± 3.73 (−5.1 to 7) 0.4 (−1.85 to 3.57)	3.1 ± 2.88 (0 to 8) 3 (0.25 to 5)	−0.35 ± 1.76 (−3.12 to 2.30) 0.13 (−1.7 to 0.93)	0.3 ± 2.42 (−2.5 to 6) 0.25 (−0.88 to 0.88)	−0.14 ± 4.71 (−9.55 to 8.17) −0.46 (−1.52 to 1.75)	3.1 ± 7.76 (−7.36 to 19.55) 3.45 (−1.82 to 6.97)	1.01 ± 5.54 (−8 to 12.54) −0.25 (−1.88 to 3.43)
Low/intermediate intensity treatment	0.15 ± 5.62 (−15 to 10.5) 0.85 (−0.98 to 2.15)	3.32 ±3.45 (0 to 10) 2.75 (0 to 5.75)	−0.69 ± 2.37 (−7.15 to 2.54) −0.4 (−1.65 to 0.33)	0.33 ± 2.4 (−5.5 to 4.5) 0.25 (−0.05 to 1.5)	0.46 ± 5.7 (−11.7 to 9.71) 1.21 (−0.79 to 3.74)	0.5 ± 7.39 (−10.35 to 20.16) −1.22 (−3.87 to 4.29)	1.45 ± 7.35 (−16 to 22) 1.33 (−1.7 to 4)
High intensity treatment	1.12 ±5.47 (−10.4 to 9.2) 2.8 (−2.35 to 5.03)	3.44 ± 3.25 (0 to 8.5) 2.5 (0.25 to 5.75)	−0.21 ± 2.04 (−4.21 to 2.93) 0.25 (−1.94 to 0.98)	0.94 ± 2.39 (−2.5 to 6) 0.5 (−0.88 to 2.5)	2.11 ± 4.79 (−3.29 to 11.48) 0.41 (−1.68 to 4.53)	2.15 ±7.9 (−11.75 to 19.55) 1.71 (−2.87 to 6.99)	1.1 ± 7.09 (−13 to 12.54) 0.75 (−1.88 to 6)
Female sex	(−3.2 ± 6.02 (−15 to 6.7) −2.4 (−6.3 to 1.1)	2.35 ± 3.01 (0 to 10) 2 (0 to 3)	−1.83 ± 2.52 (−7.15 to 2.43) −1.76 (−2.44 to −0.24)	−0.92 ± 2.26 (−5.5 to 2.5) −0.5 (−2.5 to 0.5)	−1.5 ± 6.15 (−11.7 to 8.8) −1.69 (−3.29 to 2)	−2.06 ± 4.63 (−7.99 to 4.71) −3.24 (−6.12 to 1.11)	−3.09 ± 5.37 (−16 to 4) 4 (−0.25 to 7.2)
Male sex	2.41 ± 4.26 (−10.4 to 10.5)* 2.4 (0.25 to 5.2)*	3.87 ± 3.4 (0 to 9) 3.5 (0.5 to 8)	0.17 ± 1.75 (−4.21 to 2.93)* 0.28 (−0.83 to 1)*	1.34 ± 2.1 (−2.5 to 6)* 1 (−0.25 to 2.5)*	2.52 ± 4.38 (−6.62 to 11.48)* 1.46 (−0.27 to 4.46)*	2.83 ± 8.24 (−11.75 to 20.16) 0.79 (−1.92 to 7.44)	3.4 ± 7 (−13 to 22)* 4 (−0.25 to 7.2)*
Pre-school age	0.94 ± 1.67 (−2.2 to 3.2) 0.9 (0.15 to 2.25)	6.38± 3.28 (0 to 10)* 8 (5.75 to 8.12)*	−0.93 ± 1.12 (−3.12 to 0.34) −0.83 (−1.47 to 0.03)	0.56 ± 1.54 (−2.5 to 2.5) 0.5 (−0.5 to 1.75)	1.04 ± 3.24 (−6.62 to 4.33) 1.37 (0.62 to 3.59)	−0.34 ± 8.02 (−10.35 to 20.16) −1.27 (−5.54 to 1.56)	1.38 ± 4.56 (−8 to 7.51) 1.33 (−1.12 to 5.25)
School age	−0.66 ± 6.68 (−15 to 7) 1.45 (−3.1 to 4.17)	3.19 ± 2.56 (0 to 8.5)* 3 (1.75 to 4.25)*	−0.86 ± 2.78 (−7.15 to 2.47) 0.21 (−1.94 to 0.81)	0.19 ± 2.76 (−5.5 to 6) 0.25 (−0.62 to 1.5)	0.94 ± 5.97 (−11.7 to 11.48) 0.41 (−1.26 to 4.62)	0.91 ± 8.84 (−11.75 to 19.55) −1.75 (−5.17 to 7.79)	−0.81 ± 8.38 (−16 to 12.54) −0.75 (−5.97 to 4.5)
Adolescent age	1.88 ± 6.28 (−6.8 to 10.5) 2.35 (−3.07 to 7.03)	0.62 ± 1.11 (0 to 3.5)* 0 (0 to 1)*	0.49 ± 2.01 (−2.44 to 2.93) 0.64 (−1.1 to 2.46)	1.21 ± 2.6 (−2.5 to 5) 0.75 (−1 to 3.62)	1.71 ± 6.34 (−9.55 to 9.71) 0.98 (−2.71 to 8.2)	3.27 ± 4.99 (−4.03 to 14.52) 3.4 (0.53 to 5.17)	4.01 ± 7.05 (−4.5 to 22) 2.92 (−0.87 to 6.35)

→

Table III (cont.). Changes in anthropometric and body composition parameters from baseline to follow-up according to clinical, demographic, and social factors

Parameter	Weight, kg	Height, cm	BMI, kg/m²	MUAC, cm	UMA, cm²	AFI, %	SFsum, mm
Place of residence rural	0.79 ± 5.96 (−12.6 to 10.5) 0.3 (−2.2 to 5.4)	3.36 ± 3.21 (0 to 9) 3 (0 to 6)	−0.54 ± 2.36 (−5.76 to 2.65) −0.17 (−2.44 to 0.99)	0.65 ± 2.33 (−4 to 4.5) 0.5 (−0.8 to 2.5)	1.73 ± 5.23 (−8.79 to 11.48) 1.01 (−1.65 to 4.59)	1.21 ± 8.36 (−11.75 to 20.16) −1.78 (−4.03 to 6.53)	1.38 ± 8.23 (−13 to 22) 0 (−2 to 7)
Place of residence urban to city	0.27 ± 7.4 (−15 to 8) 1.4 (−0.83 to 4.67)	4.69 ± 3.1 (0 to 8) 4.5 (2.38 to 8)	−0.68 ± 3.15 (−7.15 to 2.93) −0.27 (−1.83 to 1.15)	0.69 ± 3.73 (−5.5 to 6) 0.75 (−1 to 2.38)	−0.04 ± 7.46 (−11.7 to 9.28) 1.3 (−3.23 to 3.54)	3.32 ± 9.17 (−10.35 to 19.55) 4.22 (−1.57 to 7.36)	1.23 ± 8.61 (−16 to 12.54) 2.51 (−2.28 to 6.35)
Place of residence urban to town	0.43 ± 2.93 (−6.3 to 3.9) 1.2 (−0.75 to 2.1)	2.45 ± 3.64 (0 to 10) 0 (0 to 4)	−0.21 ± 0.93 (−2.13 to 1.01) 0.24 (−0.72 to 0.31)	0.45 ± 1.23 (−1 to 2.5) 0.5 (−0.5 to 1)	1.11 ± 3.78 (−4.48 to 8.8) 1.04 (−1.28 to 3.1)	−0.22 ± 4.36 (−7.99 to 6.01) 0.53 (−1.37 to 1.71)	1.18 ± 3.42 (−5.3 to 6) 1.5 (−1 to 4.04)
Education of parents elementary	−2.38 ± 6.43 (−10.4 to 9.2) −2.9 (−4.68 to −2.25)	2.0 ± 2.76 (0 to 6) 0.5 (0 to 4)	−1.64 ± 2.39 (−4.21 to 2.65) −2.14 (−2.96 to −1.1)	−0.83 ± 2.36 (−2.5 to 3.5) −1.75 (−2.5 to −0.25)	−1.54 ± 6.11 (−9.55 to 9.12) to 2.75 (−3.25 to −0.6)	0.7 ± 7.06 (−8.52 to 7.72) 2.91 (−5.24 to 6.07)	−2.69 ± 6.04 (−11 to 6) −1.33 (−6.5 to −0.54)
Education of parents secondary	1.65 ± 6.72 (−15 to 10.5) 2.6 (−0.25 to 4.7)	3.5 ± 1.5 (1 to 6) 3.5 (2.5 to 4.5)	−0.18 ± 2.76 (−7.15 to 2.93) 0.76 (−1.32 to 1)	0.7 ± 2.86 (−5.5 to 5) 0.5 (−0.65 to 2)	1.31 ± 6.64 (−11.7 to 11.48) 2.33 (−1.39 to 4.31)	2.75 ± 9.51 (−11.75 to 20.16) 2.32 (4.12 to 7.56)	1.7 ± 10.32 (−16 to 22) 4.07 (−1.88 to 6.5)
Education of parents university	0.85 ± 4.55 (−12.6 to 7) 1.2 (0.1 to 3.1)	3.67 ± 4.02 (0 to 10) 2 (0 to 8)	−0.31 ± 1.87 (−5.76 to 2.47) 0 (−1.16 to 0.45)	0.93 ± 2.1 (−4 to 6) 0.5 (−0.5 to 2.5)	1.87 ± 4.35 (−8.79 to 9.71) 1.28 (−0.46 to 4.18)	0.66 ± 6.9 (−10.35 to 19.55) −0.71 (−2.7 to 3.8)	2.14 ± 5.34 (−8 to 12.54) 1.67 (−1.25 to 5)
Age of parents 18 to 35	−0.84 ± 4.43 (−12.6 to 2.4) 0.25 (−0.6 to 1.58)	5.5 ± 3.27 (0 to 10)* 5.5 (3.25 to 8)*	−1.44 ± 1.74 (−5.76 to 0.34) −1.29 (−1.67 to −0.3)	−0.13 ± 1.76 (−4 to 2.5) −0.25 (−0.73 to 0.88)	−0.54 ± 4.18 (−8.79 to 3.82) 0.51 (−1.37 to 2.14)	0.27 ± 7.81 (−7.56 to 20.16) −1.8 (−3.09 to −0.47)	0.14 ± 4.15 (−8 to 7) −0.5 (−1.7 to 1.93)
Age of parents 36 to 45	1.28 ± 5.84 (−15 to 10.5) 2 (−2.05 to 5.2)	3.82 ± 3.28 (0 to 8.5)* 3.5 (0.5 to 7)*	−0.33 ± 2.37 (−7.15 to 2.65) 0.11 (−1.39 to 0.86)	0.74 ± 2.75 (−5.5 to 6) 0.5 (−0.75 to 2.5)	1.25 ± 6.13 (−11.7 to 11.48) 1.14 (−2.12 to 4.52)	2.46 ± 8.79 (−11.75 to 19.55) 1.11 (−3.42 to 7.85)	1.75 ± 9.08 (−16 to 22) 1 (−2.56 to 6.76)
Age of parents ≥46	0.67 ± 6.01 (−10.4 to 8) 1.8 (−2.75 to 4.95)	0.68 ± 1.01 (0 to 2.5)* 0 (0 to 1.5)*	0.14 ± 2.21 (−4.21 to 2.93) 0.66 (−0.99 to 1.46)	1.05 ± 2.23 (−2.5 to 5) 1 (−0.25 to 2)	2.71 ± 4.57 (−2.58 to 9.71) 2 (−1.04 to 6.24)	0.01 ± 4.89 (−8.52 to 7.15) 0.53 (−3.64 to 4.1)	1.54 ± 5.76 (−11 to 10) 3 (−0.75 to 4.04)

Data presented as mean ± SD (minimum/maximum), median (Q1 to Q3); *Significant differences (*p* to values are provided in text). Differences in anthropometric parameters were calculated using Mann to Whitney test (for type of cancer, treatment intensity, and sex) or Kruskal-Wallis test (for age, place of residence, and level of education).; AFI — arm fat index; BMI — body mass index; MUAC — mid-upper arm circumference; SFsum — sum of subscapular and triceps skinfold thickness; UMA — upper arm muscle area

Table IV. Distribution of percentile values at baseline and follow-up according to clinical and demographic factors

Parameter		Type of cancer				Intensity of treatment				Sex				Age					
		Hematological malignances n = 30		Solid tumors n = 10		Low- / /intermediate- -intensity treatment n = 22		High-intensity treatment n = 18		Female n = 13		Male n = 27		Pre-school age n = 12		School age n = 16		Adolescent age n = 12	
		B	F	B	F	B	F	B	F	B	F	B	F	B	F	B	F	B	F
Weight	Underweight and at risk for underweight	1 (3.3)	7 (23.3)	1 (10.0)	2 (20.0)	0 (0.0)	4 (18.2)	2 (11.1)	5 (27.8)	0 (0.0)*	6 (46.2)*	2 (7.4)	3 (11.1)	0 (0.0)	1 (8.3)	1 (6.2)	4 (25.0)	1 (8.3)	4 (33.3)
	Overweight and obese	4 (13.3)	3 (10.0)	1 (10.0)	1 (10.0)	2 (9.1)	2 (9.1)	3 (16.7)	2 (11.1)	2 (15.4)	1 (7.7)	3 (11.1)	3 (11.1)	1 (8.3)	0 (0.0)	4 (25.0)	4 (25.0)	0 (0.0)	0 (0.0)
Height	Deficiency and low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Above the normal and high	5 (16.7)	5 (16.7)	4 (40.0)	1 (10.0)	4 (18.2)	2 (9.1)	5 (27.8)	4 (22.2)	5 (38.5)	3 (23.1)	4 (14.8)	3 (11.1)	3 (25.0)	1 (8.3)	3 (18.8)	3 (18.8)	3 (25.0)	2 (16.7)
BMI	Underweight	1 (3.3)	7 (23.3)	2 (20.0)	3 (30.0)	0 (0.0)	5 (22.7)	3 (16.7)	5 (27.8)	1 (7.7)*	7 (53.8)*	2 (7.4)	3 (11.1)	0 (0.0)	2 (16.7)	1 (6.2)	5 (31.2)	2 (16.7)	3 (25.0)
	Overweight and obesity	4 (13.4)	3 (10.0)	1 (10.0)	1 (10.0)	2 (9.1)	2 (9.1)	3 (16.7)	2 (11.2)	3 (23.1)	1 (7.7)	2 (7.4)	3 (11.1)	1 (8.3)	1 (8.3)	4 (25.0)	3 (18.8)	0 (0.0)	0 (0.0)
MUAC	Very low and low	2 (6.7)	2 (6.7)	1 (10.0)	2 (20.0)	0 (0.0)	2 (9.1)	3 (16.7)	2 (11.1)	0 (0.0)	3 (23.1)	3 (11.1)	1 (3.7)	1 (8.3)	1 (8.3)	1 (6.2)	2 (12.5)	1 (8.3)	1 (8.3)
	Above average and excess	5 (16.7)	6 (20.0)	1 (10.0)	1 (10.0)	3 (13.6)	4 (18.2)	3 (16.7)	3 (16.7)	2 (15.4)	1 (7.7)	4 (14.8)	6 (22.2)	2 (16.7)	3 (25.0)	3 (18.8)	3 (18.8)	1 (8.3)	1 (8.3)
UMA	Low muscle and below average	7 (23.3)	7 (23.3)	4 (40.0)	4 (40.0)	5 (22.7)	4 (18.2)	6 (33.3)	7 (38.9)	4 (30.8)	4 (30.8)	7 (25.9)	7 (25.9)	3 (25.0)	3 (25.0)	5 (31.2)	5 (31.2)	3 (25.0)	3 (25.0)
	Above average and high muscle	5 (16.6)	6 (20.0)	2 (20.0)	1 (10.0)	4 (18.2)	3 (13.6)	3 (16.7)	4 (22.2)	4 (30.8)	1 (7.7)	3 (11.1)	6 (22.2)	1 (8.3)	2 (16.7)	4 (25.0)	5 (31.2)	2 (16.7)	0 (0.0)

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Table IV (cont.). Distribution of percentile values at baseline and follow-up according to clinical and demographic factors

Parameter		Type of cancer				Intensity of treatment				Sex				Age					
		Hematological malignances n = 30		Solid tumors n = 10		Low-/intermediate-intensity treatment n = 22		High-intensity treatment n = 18		Female n = 13		Male n = 27		Pre-school age n = 12		School age n = 16		Adolescent age n = 12	
		B	F	B	F	B	F	B	F	B	F	B	F	B	F	B	F	B	F
AFI	Lean and below average	3 (10.0)	2 (6.7)	2 (20.0)	1 (10.0)	1 (4.5)	1 (4.5)	4 (22.2)	2 (11.1)	2 (15.4)	2 (15.4)	3 (11.1)	1 (3.7)	1 (8.3)	1 (8.3)	1 (6.2)	0 (0.0)	3 (25.0)	2 (16.7)
	Above average and excess fat	7 (23.4)	9 (30.0)	0 (0.00)	2 (20.0)	5 (22.7)	6 (27.3)	2 (11.2)	5 (27.8)	2 (15.4)	0 (0.0)	5 (18.5)	11 (40.7)	2 (16.7)	3 (25.0)	4 (25.0)	5 (31.2)	1 (8.3)	3 (25.0)
SFsum	Lean and below average	0 (0.0)	1 (3.3)	1 (10.0)	1 (10.0)	0 (0.0)	0 (0.0)	1 (5.6)	2 (11.1)	1 (7.7)	2 (15.4)	1 (7.7)	2 (15.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)	2 (16.7)
	Above average and excess fat	9 (30.0)	13 (43.4)	2 (20.0)	1 (10.0)	8 (36.4)	9 (40.9)	3 (16.7)	5 (27.8)	3 (23.1)	1 (7.7)	3 (11.1)	1 (7.7)	4 (33.3)	6 (50.0)	6 (37.6)	6 (37.6)	1 (8.3)	2 (16.7)

Data presented as n [%]; *Significant differences (p-values are provided in text). Differences in anthropometric parameters were calculated using Fisher test; AFI — arm fat index; B — baseline; BMI — body mass index; F — follow up; MUAC — mid-upper arm circumference; SCFT — subscapular skinfold thickness; SFsum — sum of subscapular and triceps skinfold thickness; TSFT — triceps skinfold thickness; UMA — upper arm muscle area

status of children with cancer based on weight, height, and BMI. Similarly to our study, no significant differences were noted between patients with cancer and healthy controls.

In our study, the incidence of malnutrition before treatment was lower in patients with hematological malignancies than in patients with solid tumors. Our results are in line with the available literature that reports an incidence of malnutrition of 5–10% for leukemias and 0–30% for solid tumors [19].

In our population, the incidence of malnutrition after treatment increased based on weight and BMI, while no significant changes were noted for MUAC and UMA. On the other hand, overnutrition after treatment was diagnosed more often based on fat assessment (SFsum and AFI) than based on BMI. In patients with solid tumors, we noted a lower increase in UMA and a higher percentage of patients with low muscle and fat mass (AFI) after treatment, while patients with hematological malignancies showed an increase in the incidence of overnutrition (based on AFI and SFsum assessment). Our findings are in line with the literature reporting a higher incidence of malnutrition in patients with solid tumors as well as overweight and obesity in hematological malignancies with concomitant protein-energetic undernutrition [5, 8, 19–24]. In a Scottish study on the nutritional status in patients with cancer, Iniesta et al. [25] concluded that arm anthropometry is a better reflection of malnutrution than BMI, because it indicates abnormalities suggesting a worsening nutritional status (especially in the first three months of treatment) and then overnutrition. Our results are in line with these findings, while no or only small changes in UMA or MUAC during treatment are likely due to the fact that the time from baseline to follow-up was too short to reveal any quantitative changes in lean body mass assessed by these parameters.

Available studies indicate that the greatest changes in the nutritional status occur in the first months of treatment [18, 25–27]. Yoruk et al. [27] assessed changes in the nutritional status during the treatment of children with cancer. They observed a significant improvement in the nutritional status during a 6-month treatment, despite an initial deterioration irrespective of the type of cancer and the risk of malnutrition. In our study, there were no significant changes in the nutritional status during the mean follow-up of 9.32 months. Moreover, no significant changes in anthropometric or body composition parameters were noted depending on the clinical characteristics of cancer.

However, our study showed that the demographic and social characteristics of patients and their families affected the direction of changes in individual anthropometric parameters. According to the literature, factors that can shape nutritional behaviors of children, and thus their nutritional status, include sex, age of the patient and their parents, place of residence, and educational level of parents [28]. In our study, sex was shown to influence the

Table V. Distribution of percentile values according to social factors

Parameter		Place of residence						Education of parents						Age of parents					
		Rural n = 21		Urban – city n = 8		Urban – town n = 11		Elementary n = 6		Secondary n =11		University n = 23		18–35 n = 10		36–45 n = 19		≥46 n = 11	
		B	F	B	F	B	F	B	F	B	F	B	F	B	F	B	F	B	F
Weight	Underweight and at risk for underweight	1 (4.8)	5 (23.8)	1 (12.5)	2 (25.0)	0 (0.0)	2 (18.2)	1 (16.7)	1 (16.7)	1 (9.1)	3 (27.3)	0 (0.0)	5 (21.7)	0 (0.0)	3 (30.0)	1 (5.3)	2 (10.5)	1 (9.1)	4 (36.4)
	Overweight and obesity	4 (19.0)	2 (9.5)	0 (0.0)	1 (12.5)	1 (9.1)	1 (9.1)	2 (33.3)	0 (0.0)	1 (9.1)	1 (9.1)	2 (8.7)	3 (13.0)	0 (0.0)	0 (0.0)	4 (21.1)	4 (21.1)	1 (9.1)	0 (0.0)
Height	Deficiency and low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Above the norm and high	5 (23.8)	3 (14.3)	2 (25.0)	1 (12.5)	3 (27.3)	3 (27.3)	2 (33.3)	0 (0.0)	1 (9.1)	1 (9.1)	6 (26.1)	5 (21.7)	1 (10.0)	0 (0.0)	6 (31.6)	4 (21.1)	2 (18.2)	2 (18.2)
BMI	Underweight	1 (4.8)	6 (28.6)	1 (12.5)	1 (12.5)	1 (9.1)	3 (27.3)	1 (16.7)	1 (16.7)	1 (9.1)	3 (27.3)	1 (4.3)*	6 (26.1)*	0 (0.0)*	5 (50.0)*	1 (5.3)	2 (10.5)	2 (18.2)	3 (27.3)
	Overweight and obesity	3 (14.3)	2 (9.6)	1 (12.5)	1 (12.5)	1 (9.1)	1 (9.1)	2 (33.3)	0 (0.0)	2 (18.2)	1 (9.1)	1 (4.3)	3 (13.0)	0 (0.0)	1 (10.0)	4 (21.0)	3 (15.8)	1 (9.1)	0 (0.0)
MUAC	Very low and low	1 (4.8)	2 (9.5)	1 (12.5)	0 (0.0)	1 (9.1)	2 (18.2)	1 (16.7)	1 (16.7)	1 (9.1)	1 (9.1)	1 (4.3)	2 (8.7)	0 (0.0)	2 (20.0)	2 (10.5)	1 (5.3)	1 (9.1)	1 (9.1)
	Above average and excess	4 (19.0)	4 (19.0)	0 (0.0)	1 (12.5)	2 (18.2)	2 (18.2)	2 (33.4)	0 (0.0)	1 (9.1)	3 (27.3)	3 (13.0)	4 (17.4)	0 (0.0)	2 (20.0)	5 (26.3)	5 (26.3)	1 (9.1)	1 (9.1)
UMA	Low muscle and below average	4 (19.0)	6 (26.6)	4 (50.0)	3 (37.5)	3 (27.3)	2 (18.2)	1 (16.7)	1 (16.7)	4 (36.4)	5 (45.5)	6(26.1)	5 (21.7)	3 (30.0)	5 (50.0)	3 (15.8)	3 (15.8)	5 (45.5)	3 (27.3)
	Above average and high muscle	3 (14.3)	5 (23.8)	2 (25.0)	1 (12.5)	2 (18.2)	1 (9.1)	3 (50.0)	1 (16.7)	2 (18.2)	1 (9.1)	2 (8.7)	5 (21.7)	0 (0.0)	1 (10.0)	6 (31.6)	5 (26.3)	1 (9.1)	1 (9.1)

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Table V (cont.). Distribution of percentile values according to social factors

Parameter		Place of residence						Education of parents						Age of parents					
		Rural n = 21		Urban – city n = 8		Urban – town n = 11		Elementary n = 6		Secondary n = 11		University n = 23		18–35 n = 10		36–45 n = 19		≥46 n = 11	
		B	F	B	F	B	F	B	F	B	F	B	F	B	F	B	F	B	F
AFI	Lean and below average	1 (4.8)	1 (4.8)	1 (12.5)	1 (12.5)	3 (27.3)	1 (9.1)	2 (33.3)	0 (0.0)	1 (9.1)	0 (0.0)	2 (8.7)	3 (13.0)	1 (10.0)	0 (0.0)	3 (15.8)	1 (5.3)	1 (9.1)	2 (18.2)
	Above average and excess fat	2 (9.5)	6 (28.6)	2 (25.0)	3 (37.5)	3 (27.3)	2 (18.2)	0 (0.0)	1 (16.7)	2 (18.2)	3 (27.3)	5 (21.7)	7 (30.4)	1 (10.0)	2 (20.0)	4 (21.0)	6 (31.6)	2 (18.2)	3 (27.3)
SFsum	Lean and below average	0 (0.0)	1 (4.8)	0 (0.0)	0 (0.0)	1 (9.1)	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	2 (8.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (9.1)	2 (18.2)
	Above average and excess fat	6 (28.6)	8 (38.1)	2 (25.0)	2 (25.0)	3 (27.3)	4 (36.4)	2 (33.3)	1 (16.7)	4 (36.4)	4 (36.4)	5 (21.7)	9 (39.1)	3 (30.0)	3 (30.0)	6 (31.6)	8 (42.1)	2 (18.2)	3 (27.3)

Data presented as n [%]; [a]Significant differences (*p*-values are given in text). Differences in anthropometric parameters were calculated using Fisher test; AFI — arm fat index; B — baseline; BMI — body mass index; F — follow up; MUAC — mid-upper arm circumference; SCFT — subscapular skinfold thickness; SFsum — sum of subscapular and triceps skinfold thickness; TSFT — triceps skinfold thickness; UMA — upper arm muscle area

nutritional status of children with cancer. In children, differences in body composition can be seen during puberty. Boys acquire more muscle mass, especially in the upper body, while girls show an increase in fat tissue [29–30]. In our study, the median age of the girls fell during puberty (n = 6, 46.2% teenagers). Boys were younger than girls (n = 11, 40.7% school age). Boys showed a significantly higher increase in body mass, BMI, MUAC, UMA, AFI, and SFsum. After treatment, a higher percentage of boys showed greater muscle mass (MUAC, UMA) and fat mass (AFI, BMI) compared to girls, but the differences were not significant. Unlike boys, girls more often had malnutrition (low weight, BMI) after treatment. Moreover, the highest rates of excessive fat tissue (AFI, SF sum) after treatment were observed in the group of teenagers. We did not identify any other study that has reported that male sex is a protective factor against malnutrition. It is possible that the mean age of girls and boys influenced our results, but this hypothesis requires further research.

The age of children was significantly associated with the growth rate, with the highest rates in pre-school children and the lowest in teenagers (>13 years). We also found that children of parents aged over 46 had the least height gain, and children of younger parents (18–35) had the most height gain. The median height in the study group was higher than in the control group (145 cm vs. 123 cm) and was significantly higher after treatment than at baseline (150 cm vs. 145 cm). Few prospective studies have assessed the growth rate in patients with cancer. In a review paper, Iniesta et al. indicated that of the 13 studies that analyzed growth, only five included changes in growth after treatment. One of these studies showed normal growth compared to national norms, and four studies showed higher growth, although the mean growth rate was lower than the average. These studies assessed mainly children with acute lymphoblastic leukemia, and they usually showed normal growth on diagnosis. However, a significant reduction in the growth rate was shown during treatment and this was maintained until treatment completion [17].

Growth abnormalities are one of the late complications of cancer treatment. The results of a study assessing the health of Polish children and adolescents after cancer treatment showed high rates of short stature. Of the 1,761 participants whose health status was assessed five years after treatment completion, obesity or short stature alone (21.4%) and a variety of endocrine problems (short stature, obesity, thyroid dysfunction, and gonadal toxicity) were present in 323 patients (118 females, 15.0%; 205 males, 21.0%) [9]. Our findings add to the current literature on growth in childhood cancer, but they are not sufficient to determine whether the absence of growth abnormalities would be maintained in a longer-term follow-up after treatment.

Although in our study the place of residence did not have a significant effect on the nutritional status, we noted that an increase in muscle mass after treatment was the highest in children from rural areas. These patients most often showed UMA measurements indicating muscle mass that was above the norm and high.

Higher educational level of the parents was significantly associated with low BMI. However, these patients showed improvement in muscle mass and fat tissue mass after treatment; therefore, this observation should be treated with caution.

Younger age of the parents influenced low BMI, as confirmed by a smaller increase in body mass, MUAC, and UMA, and an increase in the percentage of children with low values of these parameters.

This was a prospective study involving pediatric patients with cancer. Few such studies have been conducted, although this is an important issue in the context of improving the nutritional status of children with cancer. In addition to the most common clinical factors, we assessed the demographic and social factors of patients' families that can lead to poor nutritional status (malnutrition, excess weight and obesity). Assessment of body composition was performed using low-cost and simple methods, but Frisancho centiles were required for interpretation, as more recent methods are not available. It is therefore necessary to update the norms for arm anthropometry measurements.

There were some other limitations to this study. One was the small sample size, which may have affected the statistical significance of the results. Another limitation was the problem of selecting a control group that reflected all the demographic and social factors of the study group. As a result, it was not possible to observe changes in the nutritional status of healthy children over the course of the study. In addition, the study group included patients with hematological malignancies who were at low risk of malnutrition but at high risk of overnutrition, and patients with solid tumors who were at high risk of malnutrition. A more narrowly selected group of patients would facilitate a more reliable determination of the impact of the analyzed factors, especially clinical factors such as the treatment used, and the occurrence of malnutrition and overnutrition in patients. Due to time constraints, the number of patients in our study was not sufficient to analyze the data on a larger scale. However, we believe that our study will inspire other researchers.

Conclusions

Our study highlights the importance of supportive care for children with cancer. Children with cancer have changes in nutritional status compared to healthy children. Body composition can be used to identify these changes with greater accuracy than anthropometric measurements, such as weight, height, BMI, and arm anthropometry. The monitoring of protein-energy and fat nutrition helps identify cancer patients with undernutrition and overnutrition. The risk of changes in nutritional status can be determined based on selected clinical, demographic, and social factors. Female patients have a higher risk of malnutrition, and therefore should receive special nutritional support. Education on nutrition in cancer should be provided to parents, particularly in the 18 to 35 age group. Further studies are needed to identify patients at risk of undernutrition, which will help improve the management of these patients during and after treatment.

Article information and declarations

Data availability statement

Data is provided within the manuscript or supplementary information files.

Ethics statement

This study was performed in line with the Declaration of Helsinki and was approved by the Ethics Committee of the Medical University of Lublin (26 Sept. 2019/No KE-0254/278/2019). Informed consent was obtained from all parents of children included in the study.

Authors' contributions

All authors contributed to study conception and design. Material preparation, data collection and analysis were performed by AM. First draft of manuscript was written by AM, and all authors commented on previous versions of manuscript. KD supervised study. All authors read and approved the final manuscript.

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Conflict of interest

The authors declare no conflict of interest.

Supplementary material

The Supplementary Material for this article can be found online at **Journal's website**.

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