UNIVERSIDADE FEDERAL DE UBERLÂNDIA
RESIDÊNCIA MULTIPROFISSIONAL EM SAÚDE
ATENÇÃO EM SAÚDE DA CRIANÇA

Débora Santana Alves

ESTADO NUTRICIONAL E DÉFICIT DE CRESCIMENTO EM CRIANÇAS E ADOLESCENTES COM CÂNCER EM DIFERENTES MOMENTOS DO TRATAMENTO

Uberlândia-MG
2020

Débora Santana Alves

ESTADO NUTRICIONAL E DÉFICIT DE CRESCIMENTO EM CRIANÇAS E ADOLESCENTES COM CÂNCER EM DIFERENTES MOMENTOS DO TRATAMENTO

Trabalho de Conclusão de Residência apresentado a Comissão de Residência Uni e Multiprofissional, da Universidade Federal de Uberlândia, como requisito para obtenção do título de pós-graduada.

Orientadora: Profª. Drª. Geórgia das Graças Pena

Uberlândia-MG

2020

NUTRITIONAL STATUS AND DEFICIT ON GROWTH IN CHILDREN AND ADOLESCENTS WITH CANCER AT DIFFERENT MOMENTS OF TREATMENT

Débora Santana Alves[1], Dayane Tonaco Assunção[2], Nayara Cristina da Silva[3], Cássia Maria Oliveira[4], Anna Beatriz Costa Neves do Amaral[5], Geórgia das Graças Pena[6*]

[1] Dietitian, Resident in Child Health, Federal University of Uberlandia, Brazil. deborasantanaalves21@gmail.com

[2] Dietitian, School of Medicine; Nutrition Course, Federal University of Uberlândia, Brazil. dtonaco@gmail.com,georgia@ufu.br

[3] Graduate Program in Health Sciences, Federal University of Uberlandia, Brazil. nayara.cristina.silva@outlook.com

[4] Dietitian. Food and Nutrition Service of Hospital of the Federal University of Uberlandia, Brazil. cassia.oliveira@ufu.br

[5] Medical Oncopediatrics of the Oncology Department of the Clinical Hospital of the Federal University of Uberlândia, Brazil. beatriz_amaral@hotmail.com

***Corresponding author:**

[6] Geórgia das Graças Pena, Graduate Program in Health Sciences, Federal University of Uberlandia, Uberlandia, Minas Gerais, Brazil. Address: Av. Pará, 1720, bloco 2U. Campus Umuarama +55 34 3225-8584, Zip Code 38.405-320 Uberlândia – MG, Email: georgia@ufu.br

DEFICIT ON GROWTH IN CHILDREN AND ADOLESCENTS WITH CANCER

The authors declare no potential conflicts of interest.

Words: 2836

Chart: 4

Childhood cancer is a rare disease, but with a high mortality rate. This is a period of development and growth requires a large amount of calories and protein, which is increased in cancer patients due to illness and treatment. In addition, children and adolescents with cancer have a reduced food intake which has an impact on nutritional status, and which can be irreversible in this age group, compromising the weight and the expected growth. To our knowledge, this is one of the few studies that stratify patients according to their age and it is also the first study to assess the growth deficit in the most robust way, which may be more noticeable the impact of moment of treatment. Therefore, it is important to professionals evaluate to weight gain and height in each consultation, looking for the best health strategies to prevent nutritional deficit in these patients.

Background and objectives: Malnutrition is common in children and adolescents undergoing cancer treatment and can contribute to a worse prognosis. Despite this concern, there are few studies investigating the impact of the cancer treatment at different moments on nutritional status. So, the aim of this study was to evaluate the association of moments on nutritional status in children and adolescents with cancer. **Methods:** a retrospective study was performed from January 2013 to December 2015, including data from all clinical records of children and adolescents with cancer under 18 years old undergoing oncology treatment in a public university hospital of tertiary level, that is a regional reference for cancer treatment. Clinical, nutritional support and anthropometric data were collected in four moments of treatment: diagnosis (T0), 3 months (T1), 6 months (T2) and 1 year (T3) after cancer diagnosis. In addition, nutritional indicators were also evaluated. Generalized Estimating Equation models were performed to determine the association of moments of treatment on nutritional status. **Results: The** sample was composed of 73 patients included in this study, of 73 patients, 54.8%(40) were male. The frequency of malnutrition was high at all times ranged from 13.0%(7) to 18.6%(11) and all indicators decreased in T1, modest recovery in T2 and recovered more strongly in T3 ($p < 0.001$). Growth was also impacted during treatment in patients 0 to 5 years old and over 10 years, being an important impairment for proper development. The greatest impact was in patients under 2 years in the first three months of treatment. **Conclusions:** The moment was associated with decreased percentiles in development indicators, especially at T1 and T2. Despite the weight recovery in T3, there were still deficits in growth.

Keywords: malnutrition, nutritional status, neoplasms, growth, child.

1. INTRODUCTION

Cancer is a leading cause of death in children and adolescents worldwide, with 12,500 new cases estimated of cancer for each year of the 2018-2019 biennium (1). The most common type of childhood cancer is leukemia, being most common in the age group of 2 to 5 years. The second most common type of malignant neoplasm is central nervous system tumors, which occur mainly between 10 and 15 years. Chemotherapy, radiotherapy, surgery and bone marrow transplantation are some types of treatment for this disease (2,3). The tumor and the type of treatment may contribute to malnutrition, the latter being able to cause gastrointestinal disturbances, food inappetence and mucositis, reducing food intake (4,5). As soon, malnutrition in children and adolescents undergoing cancer treatment remains a recurring complication that may lead to a worse prognosis of the disease.

The nutritional status of these patients is compromised, presenting continuous loss of muscle mass, causing progressive functional impairment, weight loss and growth deficit. The impact on growth is very important and may be irreversible and negatively influencing the expected height and may contribute to overweight and obesity. In addition, malnutrition can also affect treatment, decrease survival, increase the chances of infection and impair wound healing. Therefore, it is important to ensure adequate nutritional status for a good prognosis and development of these patients during treatment (5–8).

Until now, studies have assessed nutritional status during a given period of treatment (9,10) and few studies investigating throughout (11–13). These studies didn't use longitudinal analysis strategies. In addition, these studies not stratifying by age and associating nutritional status with time. We hypothesized that moment and type of treatment impact negatively on nutritional indicators impairing child development. Therefore, the aim of the present study was to evaluate the association of moment with nutritional indicators at four different moments during treatment.

2. METHODS

A retrospective study was conducted including data (from January/2013 to December/2015) of all clinical records (n=78) of children and adolescents cancer patients under 18 years old of a reference service of oncology sector in a public university hospital of tertiary level, which is a regional reference, where patients are referred for cancer treatment. Three clinical records were excluded because they were incomplete or with insufficient information and two participants with Down syndrome were excluded due to the need for evaluation in specific growth curves, besides presenting muscular hypotonia and changes in thyroid gland metabolism, demonstrating a tendency to overweight (14). Therefore, the final sample was composed by 73 clinical records. This study was approved by the Research Ethics (CAAE 79961417.0.0000.5152).

Data collect

Demographic, clinical and nutrition data were collected such as: sex, birth, diagnosis and consultant dates, cancer's diagnosis, cancer treatment scheme (chemotherapy, radiation therapy and bone marrow transplantation), surgery (for tumor extraction), type of nutritional therapy (oral, enteral and oral supplementation) and anthropometric evaluation. Four moments of the treatment were considered: the day of diagnosis (T0), three months (T1), six months (T2) and one year (T3) after cancer diagnosis. The cancer diagnoses were categorized into hematologic malignancies and solid tumors.

Weight-for-Age (WFA), Weight-for-Height (WFH), Body Mass Index (BMI)-for-age and Height-for-Age (HFA) were analyzed in percentiles in children 0 to 5 years old by Anthro® and more than 5 years old by AnthroPlus® (WHO, version 3.3.3 and 1.0.4, respectively). Percentile < 0.1 were classified as underweight. The following classifications for to appoint nutritional status were used: "shortness" for short stature for age and "underweight" for low weight for age, according to WHO (15).

Up to two years of age, the weight for age was considered for nutritional classification and over two years for BMI for age. Depending of the age, the anthropometric variables change. Children from 0 to 5 years old we used WFA, WFH, BMI and HFA indicators, from 5 to 10 years old we used the WFA, BMI and HFA and

in adolescents over 10 years old only use the BMI and HFA, as recommended by WHO (16).

Sample size and achieved power

The post hoc test was performed to estimate the observation power considering the difference between two dependent means tests, two-tailed, error of 0.05, sample size of 73, resulting in a power of 0.98. This analysis used G* Power software, version 3.1.

Statistical analysis

Firstly, the Kolmogorov-Smirnov normality test was performed. Descriptive statistics were used to describe clinical and anthropometric data, and expressed as percentage or median and interquartile range (IQ25-75%). Depending of the age, the anthropometric variables change. Children from 0 to 5 years old we used WFA, WFH, BMI and HFA indicators, from 5 to 10 years old we used the WFA, BMI and HFA and in adolescents over 10 years old only use the BMI and HFA, as recommended by WHO (16). Differences between the percentiles at the four moments of the study were estimated by Friedman's non-parametric test and the Bonferroni post hoc test. In order to observe the association between the moments and type of treatment (main exposures) on nutritional indicators (outcomes) the Generalized Estimation Equation (GEE) was performed by age groups. GEE is a method that consider the association between different observations in the same individual in longitudinal studies, performing a better evaluation of data (17). The gama, linear or tweedie distributions models were individually tested for all outcomes. The gama with log link model was chosen because showed the lower quasi-likelihood under the independence model criterion (QIC). Bonferroni post hoc test was used to adjustment method for multiple comparisons. The treatment was grouped into three categories: 1- chemotherapy, 2- chemotherapy and radiotherapy and 3- surgery and chemotherapy and radiotherapy. Sex and cancer diagnosis were considered as adjustment factors. All statistical analyzes were performed in the Statistical Package for Social Science (SPSS Statistics for Windows, version 20.1, SPSS®, Inc., Chicago, USA), considering a 95% confidence interval and a significance level of $p \leq 0.05$.

3. RESULTS

The sample was composed of 73 patients included in this study, 54.8% (40) were male, 30.1% (22) were> 5 and ≤ 10 years old, 52.1% (38) were diagnosed with hematologic malignancies and 52.9% (36) underwent chemotherapy. The frequency of oral supplementation ranged from 5.5% (4) at T0 to 21.3% (10) at T3, showing an increase over time. Regarding nutritional enteral therapy, there was a higher incidence of T0 8.2% (6) and decreased throughout treatment, reaching T3 in 2.2% (1). Underweight was high all the time after treatment, with higher values of malnourished patients at T1 18.6% (11) **(Table 1)**.

The evolution of anthropometric parameters during treatment was also verified, comparing the nutritional status at diagnosis (T0) with the other times. All indicators showed a significant association ($p = 0.004$ for BMI over 10 years and other $p < 0.001$) **(Table 2)**.

Considering the GEE analyzes, (Table 3), the WFA was associated with time in children under two years old ($p = 0.031$) and between 2 and 5 years old ($p < 0.001$). HFA is also associated with type and time of treatment for children under 2 years old ($p < 0.001$), and with time for children from 2 to 5 years old ($p = 0.047$) and above 10 years old ($p < 0.001$ and $p = 0.002$). The BMI was associated with type and time of treatment and for children under 2 years old ($p = 0.018$ and $p < 0.001$), and children 2 to 5 years old ($p = 0.013$ and $p < 0.001$). In this sense, children with under 2 years old presented a growth deficit at T0-T1 ($p = 0.002$), T0-T2 ($p = 0.001$) and T1-T2 ($p = 0.005$). In patients For children with 2 to 5 years old, there was a negative impact on growth between times T0-T3 ($p = 0.017$) and T1-T3 ($p = 0.043$). Besides that, a deficit of WFA ($p < 0.001$) and BMI ($p < 0.001$) were observed in T1-T2. In patients over 10 years old, a significant decreased was found in HFA when comparing T0-T3 ($p = 0.004$) and T1-T3 ($p=0.002$), showing negatively impact in development **(Table 4)**.

4. DISCUSSION

Our study showed the high prevalence of underweight and shortness in 3, 6 and 12 months after oncology treatment in children and adolescents with cancer, especially the impact in growth (HFA). In general, there was a decrease in the percentiles at T1 (3 months), modest recovery at T2 (6 months) and more evident recovery at T3 (12 months), as expected. On the other hand, there is a negative impact on height growth, which shows the deficit in all age groups. Even when there were no significant variations in the percentiles for HFA over time, it is already indicative of growth deficit, since the increase of percentiles are expected in this age group. Still, chemotherapy and radiotherapy or the combination of surgery, chemotherapy and radiotherapy were the most impacting treatments on nutritional indicators. In the literature, there are few longitudinal studies related to nutritional deficits in pediatric cancer patients and the most of them just to assess and describe the nutritional status (10,18,19).

The nutritional needs of children and adolescents are higher compared to adults due to the expenditure for development and growth, and with the disease and oncology treatment, the energy expenditure is even higher. So, the patients have greater energy and protein needs, contributing to challenge in achieve their needs. Thus, the malnutrition is common (11,20) and could contribute to clinical growth deficits, clinical complications and death. The shortness ranged from 13% to 18,6%, like other studies follow the values of 10%, 11.5% to 20.7% (21–23).

Genetic and a poor diet (negative nitrogen and energy balance) for a long term could be lead the shortness and an important growth deficit. Treatment over time contributes to lower dietary intake due to adverse effects such as mucositis, poor diet, vomiting and diarrhea (5,16,19).

Inadequate food intake and some diseases may contribute to malnutrition, weight loss and child growth deficit. The impact on growth is more prevalent in the age group of 2 years and is considered a critical and very important period for proper development, being related to diet and environmental factors (16,24). Not much knowledge about the impact on pediatric cancer patients' growth over time, but studies had shown the underweight since treatment (4,8,25,26).

In our study, we found that patients also had a growth deficit in the age group of less than 2 years old, between 2 and 5 years old and above 10 years old. These are the

age groups where the speed of child growth is highest, so they had the biggest impact on growth. The largest growth deficit has been in patients younger than two years since the beginning of treatment, presenting impact since the first months (16).

The greatest impact on growth of children less than two years is showed in the rare studies of literature (26,27). There are a positive correlation between a low growth hormone secretion and the age of irradiated children at diagnosis, suggesting that younger children are more vulnerable to central nervous system damage due to irradiation of treatment (25). These effects also contribute to a reduction weight gain, which, as with height, is of great impact to pediatric patients, because it is expected that proper development will occur with weight gain and growth expected. Thus, these patients may have irreparable damage to development and growth. In addition, another consequence is the overweight or obesity that patients may develop due to altered body composition, metabolic syndrome and the use of corticosteroids during treatment (16,27–29).

BMI for age and weight for age were impacted by moment and type of treatment, and the impact of weight loss was evident between 3 and 6 months of treatment of patients between 2 and 5 years of age. Many associations had no significant difference between the times according to GEE, however, weight maintenance is also a negative impact for these patients, which cannot be assessed in this context. Just as height, moment and treatment also negatively impact weight gain, it can contribute to weight loss due to catabolism and low food intake (19,30).

Despite weight loss, the results presented in children less than two years of age have recovered weight over time, as expected (31,32). Corticosteroids are known to be involved in regulating energy intake, storage and mobilization. Prolonged use has shown effects on increased energy intake and body fat percentage in patients, and may contribute to weight gain for this reason, and not necessarily due to better nutritional status (10,32).

Although weight gain is expected due to child development, it can also have other causes such as the use of large doses of corticosteroids for treatment (28,29). Corticosteroids are known to be involved in regulating energy intake, storage and mobilization. Prolonged use has shown effects on increased energy intake and body fat percentage in patients, and may contribute to weight gain for this reason, and not necessarily due to better nutritional status (33).

Among the limitations of the study, we have a heterogeneous sample, which hinders the establishment of more accurate data, but that was softened with the stratification according to the age group. Secondly the retrospective study could have lack of data in the medical record, which may cause information bias, however, the medical records with patient follow-up data were reviewed and evaluated, with all information recorded.

Cancer patients tend to intake less energy and protein than necessary to meet the body's demands, but we do not know the exact amount. So, it is uncertain about the contribution of this point in nutritional indicators. However, the strengths of our study included the assessment of nutritional status for one year and at four different moments through the variables: anthropometric parameters, cancer treatment and nutritional therapy, which gives us a better idea of the patient's outcome throughout treatment. Some studies have also evaluated over time, but unlike ours, they did not investigate the time and type of treatment, neither stratifying the patients by age, which is extremely important because they have different growth rates and weight gain. Finally, further investigations are needed to elucidate intake through 24-hour recall and to better assess nutritional status during treatment, along with anthropometric, biochemical, and other parameters such as body composition (9,16,28,29).

5. CONCLUSION

Children and adolescents undergoing oncology treatment had high percentage of shortness and underweight, especially those under 2 years. Therefore, it is important that nutritional status is monitored during the treatment, not only the most usual weight, but also height, contributing to better nutritional monitoring, planning, good nutritional status and better disease prognosis.

REFERENCES

1. INCA. Estimativa 2018 - Síntese de Resultados e Comentários. 2018. Available in: http://www1.inca.gov.br/estimativa/2018/sintese-de-resultados-comentarios.asp. Accessed on January 10, 2020.

2. INCA. ABC do câncer: abordagens básicas para o controle do câncer. ABC do câncer: abordagens básicas para o controle do câncer. Instituto Nacional de Câncer José Alencar Gomes da Silva, Organização Mário Jorge Sobreira da Silva, 2018;(4):111.

3. Steliarova-Foucher E, Colombet M, Ries LAG, Moreno F, Dolya A, Bray F, et al. International incidence of childhood cancer, 2001–10: a population-based registry study. The Lancet Oncology,2017;18(6):719–31.

4. Brinksma A, Roodbol PF, Sulkers E, Hooimeijer HL, Sauer PJJ, van Sonderen E, et al. Weight and height in children newly diagnosed with cancer: Weight and Height in Children With Cancer. Pediatric Blood Cancer,2014;62(2):269–73.

5. Triarico S, Rinninella E, Cintoni M, Capozza MA, Mastrangelo S, Mele MC, et al. Impact of malnutrition on survival and infections among pediatric patients with cancer: a retrospective study. European Review for Medical and Pharmacological Sciences, 2019;23:1165–75.

6. Pribnow AK, Ortiz R, Báez LF, Mendieta L, Luna-Fineman S. Effects of malnutrition on treatment-related morbidity and survival of children with cancer in Nicaragua. Pediatric Blood Cancer, 2017;64(11):e26590.

7. Schiavetti A A, Fornari C, Bonci E, Clerico A, Guidi R. Nutritional Status in Childhood Malignancies. Nutrition and Cancer,2002;44(2):153–5.

8. Viana MB, Vilela MIOP. Height deficit during and many years after treatment for acute lymphoblastic leukemia in children: A review. Pediatric Blood Cancer, 2008;50(S2):509–16.

9. Brinksma A, Sanderman R, Roodbol PF, Sulkers E, Burgerhof JGM, de Bont ESJM, et al. Malnutrition is associated with worse health-related quality of life in children with cancer. Support Care Cancer, 2015;23(10):3043–52.

10. Garófolo A, Caran EM, Silva NS, Lopez FA. Prevalência de desnutrição em crianças com tumores sólidos. Revista de Nutrição, 2005;18(2):193–200.

11. Belle FN, Wenke-Zobler J, Cignacco E, Spycher BD, Ammann RA, Kuehni CE, et al. Overweight in childhood cancer patients at diagnosis and throughout therapy: A multicentre cohort study. Clinical Nutrition, 2019;38(2):835–41.

12. Revuelta Iniesta R, Paciarotti I, Davidson I, McKenzie JM, Brougham MFH, Wilson DC. Nutritional status of children and adolescents with cancer in Scotland: A prospective cohort study. Clinical Nutrition ESPEN, 2019;32:96–106.

13. Yoruk MA, Durakbasa CU, Timur C, Sahin SS, Taskin EC. Assessment of Nutritional Status and Malnutrition Risk at Diagnosis and Over a 6-Month

Treatment Period in Pediatric Oncology Patients With Hematologic Malignancies and Solid Tumors. Journal of Pediatric Hematology/Oncology, 2019;41(5):e308–21.

14. Chaves AL, Campos CK, Navarro AC. Relação da Síndrome de Down com a obesidade. Revista Brasileira de Obesidade, Nutrição e Emagrecimento, 2008; 2(11): 412-22.

15. WHO. World Health Organization. Expert Committe on Physical Status: the use and interpretation of anthropometry physical status. WHO Technical Report Series, 1995; 463p.

16. SOCIEDADE BRASILEIRA DE PEDIATRIA. Avaliação nutricional da criança e do adolescente – Manual de Orientação / Sociedade Brasileira de Pediatria. Departamento de Nutrologia, 2009; 112.

17. Wu W, Wang Z, Xu K, Zhang X, Amei A, Gelernter J, et al. Retrospective Association Analysis of Longitudinal Binary Traits Identifies Important Loci and Pathways in Cocaine Use. Genetics, 2019, 213 (4): 1225-36.

18. Gregório EL, Caldeira PT, Silva LÁ e, Rocha AMS. Avaliação do perfil nutricional dos pacientes internados na oncologia pediátrica do Hospital Santa Casa De Misericórdia De Belo Horizonte – MG. HU Revista, 2016;42(1): 75-81.

19. Tazi I, Hidane Z, Zafad S, Harif M, Benchekroun S, Ribeiro R. Nutritional status at diagnosis of children with malignancies in Casablanca. Pediatric Blood Cancer, 2008;51(4):495–8.

20. Coradine AVP, Pianovski MAD, Rabito EI. Medidas Antropométricas para o Acompanhamento do Estado Nutricional de Crianças e Adolescentes com Câncer, o que utilizar na Prática Clínica? Revista Brasileira de Cancerologia, 2015;61(3):269–76.

21. Córdova ME, Gottschall CBA; da Cruz LB; Gregianin LJ. Comparison of the nutritional status of children and adolescents with malignancy at diagnosis and follow-upfrom invasive mechanical ventilation. Revista HCPA, 2012; 32 (2):154-160.

22. Mendes TG, Benedetti FJ. Fatores nutricionais associados ao câncer em crianças e adolescentes. Disciplinarum Scientia, 2013; 14(2): 265-72.

23. Sousa TS, Santos LTG, Sousa P, Sousa RML, Martins ICVS, Dias LPP et al . Indicadores antropométricos em crianças com câncer em um hospital de referência. Revista de Pesquisa em Saúde, 2016; 17(3):151-53.

24. Kasaye HK, Bobo FT, Yilma MT, Woldie M. Poor nutrition for under-five children from poor households in Ethiopia: Evidence from 2016. Demographic and Health Survey. PLOS ONE, 2019;14(12):e0225996.

25. Brauner R, Czernichow P, Rappaport R. Greater susceptibility to hypothalamopituitary irradiation in younger children with acute lymphoblastic leukemia. Journal of Pediatric, 1986;108(2):332.

26. Dalton VK, Rue M, Silverman LB, Gelber RD, Asselin BL, Barr RD, et al. Height and Weight in Children Treated for Acute Lymphoblastic Leukemia: Relationship to CNS Treatment. Journal of Clinical Oncology, 2003;21(15):2953–60.

27. Vilela MIOP, Viana MB. Longitudinal growth and risk factors for growth deficiency in children treated for acute lymphoblastic leukemia. Pediatric Blood Cancer, 2007;48(1):86–92.

28. Chow EJ, Pihoker C, Hunt K, Wilkinson K, Friedman DL. Obesity and hypertension among children after treatment for acute lymphoblastic leukemia. Cancer, 2007;110(10):2313–20.

29. Esbenshade AJ, Simmons JH, Koyama T, Koehler E, Whitlock JA, Friedman DL. Body mass index and blood pressure changes over the course of treatment of pediatric acute lymphoblastic leukemia. Pediatric Blood Cancer, 2011;56(3):372–8.

30. Mauer AM, Burgess JB, Donaldson SS, Rickard KA, Stallings VA, Van Eys J, et al. Reviews: Special Nutritional Needs of Children with Malignancies: A Review. Journal of Parenteral Enteral and Nutrition, 1990;14(3):315–24.

31. Ezgu FS, Tumer L, Cinasal G, Hasanoglu A, Gunduz M. Effect of Enteral and Parenteral Nutrition on Growth Parameters of Hospitalized Turkish Children. Indian Pediatrics, 2005;42 (5):469-72.

32. Maciel Barbosa J, Pedrosa F, Coelho Cabral P. El estado nutricional y la adecuación de la nutrición enteral em pacientes de oncología pediátrica em um centro de referencia del noreste de Brasil. Nutrición Hospitalaria, 2012; 27(4):1099–105.

33. Zhang FF, Parsons SK. Obesity in Childhood Cancer Survivors: Call for Early Weight Management. Advances in Nutrition, 2015;6(5):611–9.

Table 1: Demographic, clinical and nutritional data of children and adolescent cancer patients from 2013 to 2015

VARIABLES		TOTAL % (n)
Sex	Male	54.8 (40)
	Female	45.2 (33)
Age group (years)	≤ 2	21.9 (16)
	>2 and ≤ 5	27.4 (20)
	>5 and ≤ 10	30.1 (22)
	> 10	20.5 (15)
Clinical diagnosis	Hematologic malignancies	52.1 (38)
	Solid tumors	46.6 (34)
Type of treatment	Chemotherapy	52.9 (36)
	Chemotherapy + Radiotherapy	22.1 (15)
	Surgery + Chemotherapy + Radiotherapy	25.0 (17)
Nutrition Therapy	T0	5.5 (4)
	T1	12.7 (8)
Oral Supplement	T2	15.3 (9)
	T3	21.3 (10)
	T0	8.2 (6)
Enteral Nutrition	T1	6.3 (4)
	T2	3.4 (2)
	T3	2.2 (1)
Nutritional Status	T0	13.8 (9)
	T1	18.6 (11)
Malnourished	T2	13.0 (7)
	T3	15.0 (6)

Table 2: Association of nutritional indicators by different moments during treatment

AGE GROUP (years)		T0 Median (P25-P75)	T1 Median (P25-P75)	T2 Median (P25-P75)	T3 Median (P25-P75)	p-value
≤ 2	WFA	47.95 (14.30-91.45)	23.45 (3.22-70.57)	38.00 (8.30-77.40)	80.30 (39.80- 82.90)	<0.001
	HFA	58.80 (24.60-97.47)	28.40 (5.70-98.77)	12.60 (0.45-90.65)	39.85 (26.10-86.00)	<0.001
	WFH	45.80 (20.15-69.60)	19.50 (5.05-68.77)	43.00 (8.15-90.95)	79.25 (49.00-96.20)	<0.001
	BMI-for-age	36.90 (10.15-65.90)	12.40 (2.45-76.90)	35.30 (9.60-95.62)	78.05 (53.10-96.82)	<0.001
>2 and ≤ 5	WFA	44.00 (19.50-78.00)	66.65 (37.85-87.20)	40.60 (29.40-80.30)	60.10 (23.30-91.90)	<0.001
	HFA	69.60 (38.20-81.30)	63.20 (23.80-91.95)	67.70 (21.20-88.10)	46.10 (17.15-81.72)	<0.001
	WFH	54.10 (21.52-84.35)	67.35 (31.37-92.72)	49.75 (9.65-74.97)	54.7 (24.80-86.30)	<0.001
	BMI	40.90 (15.20-73.27)	57.90 (30.70-93.97)	48.60 (11.20-78.00)	56.85 (41.82-98.42)	<0.001
>5 and ≤ 10	WFA	40.55 (10.02-64.02)	43.60 (17.00-68.55)	58.80 (17.25-71.62)	68.80 (15.47-80.70)	<0.001
	HFA	43.30 (13.30-70.15)	28.35 (7.37-62.95)	45.70 (20.30-64.40)	52.40 (19.35-63.90)	<0.001
	BMI	29.90 (10.25-72.80)	43.20 (14.57-74.45)	49.20 (22.30-77.00)	42.35 (19.52-76.17)	<0.001
> 10	HFA	49.60 (24.45-84.75)	45.40 (24.25-90.10)	40.25 (20.77-75.77)	41.15 (7.62-56.27)	<0.001
	BMI	30.10 (3.95-57.3)	9.35 (1.70-64.85)	22.65 (0.47-67.47)	15.25 (0.13-70.30)	0.004

Note: Friedman Test; WFA: Weight-for-Age; HFA: Height-for-Age; WFH: Weight-for-Height; BMI-for-age: Body Mass Index-for-age.

Table 3: Association of moments and treatment on nutritional indicators in different age groups using modeling by Generalized Estimating Equations (GEE)

AGE GROUP (years)	Variables	WFA			HFA			WFH			BMI for age		
		Wald chi-square	gl	Sig.	Wald chi-square	gl	Sig.	Wald chi-square	gl	Sig.	Wald chi-square	gl	Sig.
≤ 2	Treatment	8.963	2	0.011	837.607	2	<0.001	2.155	2	0.340	8.063	2	0.018
	Time	8.841	3	0.031	309.287	3	<0.001	36.723	3	<0.001	56.647	3	<0.001
	Treatment * Times	48.630	5	<0.001	5106.730	5	<0.001	46.824	5	<0.001	3970.179	5	<0.001
>2 and ≤ 5	Treatment	3.705	2	0.157	4.869	2	0.088	3.513	2	0.173	8.680	2	0.013
	Time	20.117	3	<0.001	7.957	3	0.047	16.150	3	0.001	35.110	3	<0.001
	Treatment * Times	14.784	6	0.022	23.562	6	0.001	88.339	6	<0.001	67.437	6	<0.001
>5 and ≤ 10	Treatment	2.219	2	0.330	2.045	2	0.360	-	-	-	4.389	2	0.111
	Time	5.354	3	0.148	2.876	3	0.411	-	-	-	1.697	3	0.638
	Treatment * Time	28.909	6	<0.001	6.792	6	0.340	-	-	-	1.608	6	0.952
> 10	Treatment	-	-	-	64.769	2	<0.001	-	-	-	3.053	2	0.217
	Time	-	-	-	15.237	3	0.002	-	-	-	4.510	3	0.211
	Treatment * Times	-	-	-	17.426	6	0.008	-	-	-	32.878	6	<0.001

Note: Model Effect Test; Treatment: Surgery + Chemotherapy + Radiotherapy; Times: T0. T1. T2 e T3; WFA: Weight-for-Age; HFA: Height/-for-Age; WFH: Weight-for-Height; BMI for age: Body Mass Index-for-age: No data. Adjusted for sex and diagnosis.

Table 4: Comparison of moments and treatment on nutritional indicators in different age groups using modeling by Generalized Estimating Equations (GEE)

AGE GROUP (years)	TIME (I)	TIME (J)	WFA		WFH		HFA		BMI for age	
			I-J	p-value (Bonferroni)	I-J	p-value (Bonferroni)	I-J	p-value (Bonferroni)	I-J	p-value (Bonferroni)
≤ 2	T0	T1	11.34	0.754	0.92	1.000	29.04	0.002	-1.88	1.000
		T2	3.26	1.000	-15.03	1.000	36.53	0.001	-18.97	0.685
		T3	-28.78	0.014	-38.30	<0.001	-3.35	1.000	-44.28	<0.001
	T1	T2	-8.07	0.195	-15.95	0.232	7.49	0.005	-17.08	0.172
		T3	-40.12	0.001	-39.23	<0.001	-32.40	0.001	-42.39	<0.001
	T2	T3	-32.05	<0.001	-23.27	0.254	-39.89	0.001	-25.31	0.177
	CT	CT+RT	-3.74	1.000	11.40	0.830	1.91	1.000	14.94	0.303
		Surgery + CT + RT	25.51	0.010	4.75	1.000	49.59	<0.001	0.44	1.000
>2 and ≤ 5	T0	T1	-17.16	0.003	-14.05	0.185	6.18	0.554	-20.46	<0.001
		T2	-3.66	1.000	3.91	1.000	10.92	0.145	-7.03	1.000
		T3	-9.66	1.000	-5.24	1.000	21.46	0.017	-18.92	0.146
	T1	T2	13.49	<0.001	17.96	0.002	4.74	0.244	13.43	<0.001
		T3	7.50	1.000	8.80	1.000	15.27	0.043	1.54	1.000
	T2	T3	-5.99	1.000	-9.15	1.000	10.53	0.106	-11.89	0.941
	CT	CT+RT	-27.86	0.276	-22.04	0.459	-11.80	1.000	-28.97	0.300
		Surgery + CT + RT	-12.16	1.000	-11.46	1.000	27.58	0.167	-16.01	0.188
>5 and ≤ 10	T0	T1	-7.65	0.761	-	-	4.93	1.000	-5.36	1.000

		T2	-9.14	1.000	-	-	-3.76	1.000	-6.75	1.000
		T3	-19.62	0.250	-	-	-8.34	1.000	-4.59	1.000
	T1	**T2**	-1.49	1.000	-	-	-8.69	0.596	-1.39	1.000
		T3	-11.97	0.752	-	-	-13.27	0.565	0.76	1.000
	T2	**T3**	-10.48	0.607	-	-	-4.58	1.000	2.16	1.000
	CT	**CT+RT**	4.99	1.000	-	-	-8.20	1.000	16.88	1.000
		Surgery + CT + RT	-26.26	0.737	-	-	-17.53	0.540	-23.18	1.000
> 10	**T0**	**T1**	-	-	-	-	-5.22	1.000	8.78	0.362
		T2	-	-	-	-	5.54	1.000	12.75	0.229
		T3	-	-	-	-	20.73	0.004	10.08	0.217
	T1	**T2**	-	-	-	-	10.76	0.075	3.97	1.000
		T3	-	-	-	-	25.96	0.002	1.30	1.000
	T2	**T3**	-	-	-	-	15.19	0.129	-2.66	1.000
	CT	**CT+RT**	-	-	-	-	18.82	0.068	23.25	0.571
		Surgery + CT + RT	-	-	-	-	-56.67	0.036	23.02	0.498

Note: Comparisons by Pairwise Method; CT: Chemotherapy; RT: Radiotherapy; WFA: Weight-for-Age; HFA: Height/-for-Age; WFH: Weight-for-Height; BMI for age: Body Mass Index-for-age: No data; Adjusted for sex and cancer diagnosis.