ORIGINAL RESEARCH ARTICLE

Anthropometric profile of pediatric patients undergoing allogeneic hematopoietic stem cell transplantation: a single center one-year follow-up study

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Abstract

Introduction: Hematopoietic stem cell transplantation (HSCT) is an aggressive form of therapy which leads to malnutrition requiring nutritional support. The aim of our study was to evaluate if the growth of children is affected by HSCT and what the relevant factors are.

Methods: We analyzed changes in anthropometric measures of 79 pediatric patients who underwent allogeneic HSCT. Nutritional status was assessed based on weight and height measurements collected prior to HSCT and within 12 months post-transplantation. Body weight and height were referred to the age of patients using available z-score calculators.

Results: Compared to the first measurement, the weight-for-age and height-for-age z-scores were significantly reduced in all following measurements within a 1-year follow-up. The most severe weight loss occurred on the last day of hospitalization related to HSCT, while the height gain declined progressively after HSCT. The presence of acute graft versus host disease (GvHD) and the use of a total body irradiation-based regimen were found to be risk factors for a severe slowdown of weight gain, while acute GvHD of the gastrointestinal tract, chronic GvHD and the use of parenteral nutrition were risk factors for a decline in height gain.

Conclusions: Patients treated with allogeneic HSCT demonstrate a reduction in the pace of growth. HSCT recipients complicated by GvHD require prolonged and close weight and height monitoring.

Key words: children, hematopoietic stem cell transplantation, nutritional assessment, anthropometric profile

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Introduction

Hematopoietic stem cell transplantation (HSCT) is an aggressive form of therapy used for malignant and non-malignant disorders of the hematopoietic system. Over recent years, the annual numbers of both allogeneic and autologous HSCTs have been continuously increasing [1]. Early- and long-term survival rates have improved, and are expected to continue to improve in the coming decades due to the enhancement in human leukocyte antigen (HLA)

typing, conditioning regimens, supportive and post-transplant care [2]. Today, the probability of 10-year survival is 85% in 2-year survivors [3].

Nevertheless, there is strong evidence that childhood HSCT survivors carry a significantly higher burden of chronic health conditions related to therapeutic exposures than do patients treated with conventional therapies and non-cancer patients [4]. Taken together, all these factors underscore the need for effective long-term surveillance for screening, prevention and maintaining good quality of life. The nutritional status of HSCT recipients has long been of interest to clinicians. Due to ablative therapy, the intensity of conditioning regimen and underlying disease, the catabolism of the patient increases and leads to malnutrition, which usually requires nutritional support [5]. Other factors contributing to impaired weight and height gain are transplant-related complications such as: mucositis, diarrhea, nausea, vomiting, and anorexia. These are usually related to graft-versus-host disease (GvHD), which interferes with the digestion and absorption of nutrients [5].

Several longitudinal studies have reported a significant decline in final growth of adult cancer survivors, including HSCT recipients [6–8]. The use of total body irradiation and certain conditioning regimens have been associated with the most severe growth deterioration due to their impact on the hypothalamic-pituitary axis and damage to bone epiphyses [9–11]. Moreover, the Childhood Cancer Survivor Study found that patients with certain malignancies are more likely to be underweight as adults and to suffer from serious medical conditions. This demonstrates the need for close surveillance [12].

Since the most dynamic part of the HSCT involves the early period after the HSCT [13, 14], patients are at risk of malnutrition, and often require nutritional support. Despite this fact, there is a paucity of data concerning the impact of HSCT on the short-term growth of children, indicating a need for further research on an adequate population. A significant heterogeneity of patient groups is challenging, since malnutrition and short stature are included in the phenotype of some genetic disorders that are treated with HSCT. Therefore, studies reporting short-term anthropometric profiles of patients often include different populations, making proper comparisons problematic [15, 16].

Thus, the purpose of this analysis was to assess the changes of anthropometric measures (weight, height) of children who underwent HSCT in a one-year follow-up and to evaluate any potentially relevant risk factors contributing to growth disturbances in this population.

Methods

Study design

In this single-institution, retrospective cohort study, we enrolled 79 pediatric (under the age of 18) patients who received hematopoietic stem cells (HSC) at the Transplantation Center, Children's University Hospital in Krakow, Poland between December 2005 and March 2019. The medical records of eligible patients were reviewed and the results were drawn up based on a database created by the authors. This study was designed and described according to the STROBE guidelines for observational studies (Table S1 in Supplement 1) [17].

Treatment protocol

The transplant procedure was conducted according to institutional procedures and a suitable treatment protocol.

Anthropometric profile

The anthropometric profile of patients was assessed based on body weight and height measurements (SECA 799 Class III Approved Electronic Column Scale with BMI function). Calculations based on Center for Diseases Control (Medscape, CDC) growth charts were used to determine weight-for-age and height-for-age percentiles and z-scores in all children. The measurements were made during scheduled medical check-ups as part of the post-transplant surveillance process. Data concerning patients' body weight and height were collected at four time points:
1) up to seven days before HSCT — on admission
2) on the last day of hospitalization related to HSCT — on discharge
3) 100 (±14) days post-HSCT
4) 365 (±30) days post-HSCT.

The nutritional status of patients was described based on percentile values. Patients were classified as underweight (<5 percentile), healthy weight (≥5 and <85 percentile), overweight (≥85 and <95 percentile), or obese (≥95 percentile) according to their weight; and as short stature (<5 percentile), normal stature (≥5 and <95 percentile), or tall stature (≥95 percentile) according to their height.

Eligibility criteria

Eligible patients were those who underwent allogeneic HSCT between December 2005 and March 2019 and whose weight and height measurements were collected at all the designated time points. To reduce the risk of confounding factors, patients with primary immunodeficiencies or other genetic conditions associated with short stature were excluded. Other exclusion criteria were: subsequent HSCT, death for any reason before the fourth measurement, insufficient information in the medical records, HSCT-related hospitalization longer than 86 days, or a period between second and third measurements shorter than two weeks. None of the patients had received growth hormone (GH) therapy within the 12 months prior to HSCT nor in the 12 months after HSCT. A flowchart outlining the inclusion process is presented in Figure 1.
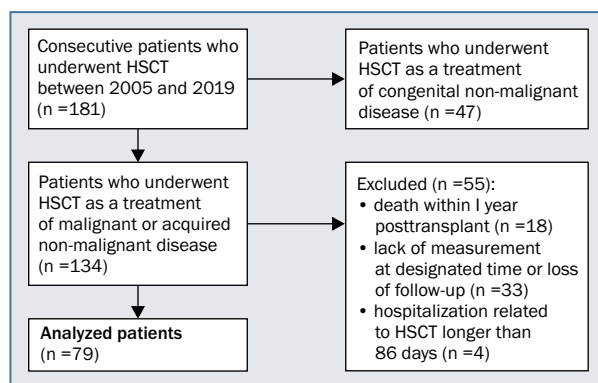
Figure 1. Flowchart of patient inclusion

Measured outcomes

The primary endpoints of our study included an evaluation of patients' anthropometric profiles within one year after transplantation, i.e. changes of weight-for-age and height-for-age z-scores in four time points.

The secondary endpoints comprised analysis of potentially relevant factors contributing to growth slowdown. We analyzed differences between first and fourth measurements in weight-for-age and height-for-age z-scores in subgroups derived from selected baseline characteristics of patients and transplant complications. These included: age (<10 and ≥10 years), sex, type of disease, type of pre-transplant conditioning, the use of total body irradiation (TBI)-based regimen and parenteral nutrition, the presence of stage III–IV mucositis, acute GvHD (graded according to Keystone Consensus [18]), acute GvHD of the gastrointestinal (GI) tract, chronic GvHD (diagnosed within 365 days after transplantation), and chronic GvHD of the GI tract.

Statistical analysis

Prior to statistical analysis, all patients with missing data or who were lost to follow-up were excluded. Continuous variables are presented as mean ±standard deviation (SD) or median and interquartile range [IQR], as appropriate. Categorical variables are expressed as numbers and percentages. For normality assessment, the Shapiro–Wilk test was used. Continuous variables were compared between two related and non-related groups using the Wilcoxon signed-rank test and Mann-Whitney U test, respectively. *P*-values of less than 0.05 were considered statistically significant. Data analysis was done with STATISTICA 13.0 software (StatSoft Inc., Tulsa, OK, USA).

Ethical statement

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was not required in this type of study. This study was approved by the Ethics Committee of Jagiellonian University.

Results

Patient characteristics

A total of 79 pediatric patients (54 male, 25 female) underwent allogeneic HSCT as a treatment for malignant disease (61; 77.22%) or acquired non-malignant disease (18; 22.78%). The mean ±SD age on admission was 116.32 ±58.79 months. Fifty-eight (73.42%) patients received pre-transplant myeloablative therapy, and in 31 (39.24%) of them a TBI-based regimen was used. Forty-seven (59.49%) patients received HSC from an unrelated donor and 32 (40.51%) from a related donor, comprising 28 from an HLA-matched sibling donor (35.44%), and four from an HLA-family donor (5.06%). Donors were men in 43 (54.43%) cases and women in 36 (45.57%) cases, with a mean age of 23.53 ±10.23 years. Bone marrow was a graft source in 74 (93.67%) patients, peripheral stem cells were used in four (5.06%) patients, and cord blood in one (1.27%) patient. Hematopoietic reconstitution was completed in all patients. The median (IQR) length of hospitalization related to HSCT was 36 (32–44) days. The time between first and third measurements was 97 (91–104) days, and between first and fourth measurements was 362 (356–373) days. Transplant-related complications included mucositis in 69 (87.34%) patients, acute GvHD in 26 (34.57%), chronic GvHD in 25 (31.65%), fever of unknown origin in 59 (74.68%), veno-occlusive disease in three (3.80%), and engraftment syndrome in 11 (13.92%). Patient and transplant characteristics are set out in Table I.

Primary endpoints

The anthropometric profiles of all eligible (n =79) patients were expressed as mean values with standard deviations of weight-for-age and height-for-age z-scores (Figures 2A and 2B).

Weight

At baseline, four (5.06%) patients were classified as underweight, 52 (65.82%) as healthy weight, 16 (20.25%) as overweight, and seven (8.86%) as obese. The mean values of weight were 36.37 kg, 33.89 kg, 34.71 kg and 37.66 kg at the first, second, third and fourth measurements, respectively. The weight-for-age z-scores in subsequent measurements were: 0.11, –0.39, –0.35 and –0.21, respectively. Compared to the first measurement (on admission), the weight-for-age z-scores were significantly reduced in all following measurements within the 1-year follow-up (Table II). The lowest value of weight-for-age z-scores was noted at the second measurement (on discharge).

Table I. Demographics of patients and hematopoietic stem cell transplantation (HSCT) characteristics

Parameter	n	Number of patients	Parameter	n	Number of patients
Sex, n (% of males)	79	54 (68.35%)	Peripheral blood stem cells	79	4 (5.06%)
Age on admission (months), mean ±SD	79	116.32 ±58.79	Cord blood	79	1 (1.27%)
Age group, n (%)			**HLA-matching**, n [%]	79	62 (78.48%)
<10 years	79	40 (50.63%)	**Myeloablative conditioning**, n [%]	79	58 (73.42%)
≥10 years	79	39 (49.37%)	**TBI-based regimen**, n [%]	79	31 (39.24%)
Transplant indication, n (%)			**Hematopoietic reconstitution**, n [%]	79	79 (100.00%)
Malignant	79	61 (77.22%)	**Parenteral nutrition in HSCT period**, n [%]	79	50 (63.29%)
Non-malignant	79	18 (22.78%)	**Time between HSCT and second measurement** (days), median [IQR]	79	36.00 [32.00–44.00]
Disease, n (%)			**Time between HSCT and third measurement** (days), median [IQR]	79	97.00 [91.00–104.00]
Acute lymphoblastic leukemia (ALL)	79	32 (40.51%)	**Time between HSCT and fourth measurement** (days), median [IQR]	79	362.00 [356.00–373.00]
Severe aplastic anemia (SAA)	79	19 (24.05%)	**Transplant complications**, n [%]		
Acute myeloid leukemia (AML)	79	13 (16.46%)	Mucositis:	79	69 (87.34%)
Myelodysplastic syndrome (MDS)	79	4 (5.06%)	• stage I–II		35 (44.30%)
Juvenile chronic myeloid leukemia (JMML)	79	3 (3.80%)	• stage III–IV		34 (43.04%)
Autoimmune disease	79	2 (2.53%)	Acute GvHD:	79	26 (34.57%)
Chronic myeloid leukemia (CML)	79	2 (2.53%)	• stage I–II		19 (24.05%)
Hemophagocytic lymphohistiocytosis (HLH)	79	2 (2.53%)	• stage III–IV		7 (8.86%)
Non-Hodgkin's lymphoma (NHL)	79	2 (2.53%)	• gastrointestinal tract		13 (17.28%)
Disease stage before HSCT, n [%]			• liver		3 (4.94%)
No remission	79	34 (43.04%)	• skin		25 (33.33%)
CR I	79	21 (26.58%)	Fever of unknown origin	79	59 (74.68%)
CR II	79	23 (29.11%)	Veno-occlusive disease	79	3 (3.80%)
CR >II	79	1 (1.27%)	Engraftment syndrome	79	11 (13.92%)
Donor type, n [%]			Chronic GvHD:	79	25 (31.65%)
MSD	79	28 (35.44%)	• gastrointestinal tract		12 (15.19%)
MUD	79	47 (59.49%)	• skin		19 (24.05%)
MFD	79	4 (5.06%)	• liver		11 (13.92%)
Donor age (years), mean ±SD	79	23.53 ±10.23	• lungs		9 (11.39%)
Donor sex, n (% of males)	79	43 (54.43%)			
Source of stem cells, n [%]					
Blood marrow	79	74 (93.67%)			

SD — standard deviation; CR — complete remission; MSD — matched-sibling donor; MUD — matched-unrelated donor; MFD — matched-family donor; HLA — human leukocyte antigen; TBI — total body irradiation; IQR — interquartile range; GvHD — graft-versus-host disease

Height

In the first measurement, four (5.06%) patients were classified as short stature, 71 (89.87%) as normal stature, and four (5.06%) as tall stature. Patients' mean height expressed in meters was 1.34, 1.34, 1.35 and 1.38 in the first, second, third and fourth measurements, respectively. The mean height-for-age z-scores were: –0.03, –0.15, –0.15, –0.34. Similarly to weight, the height-for-age z-scores in the second, third and fourth measurements were significantly diminished compared to the first measurement (Table II). But in contrast to the weight profile, the greatest drop in height-for-age values occurred at one year post-transplant.
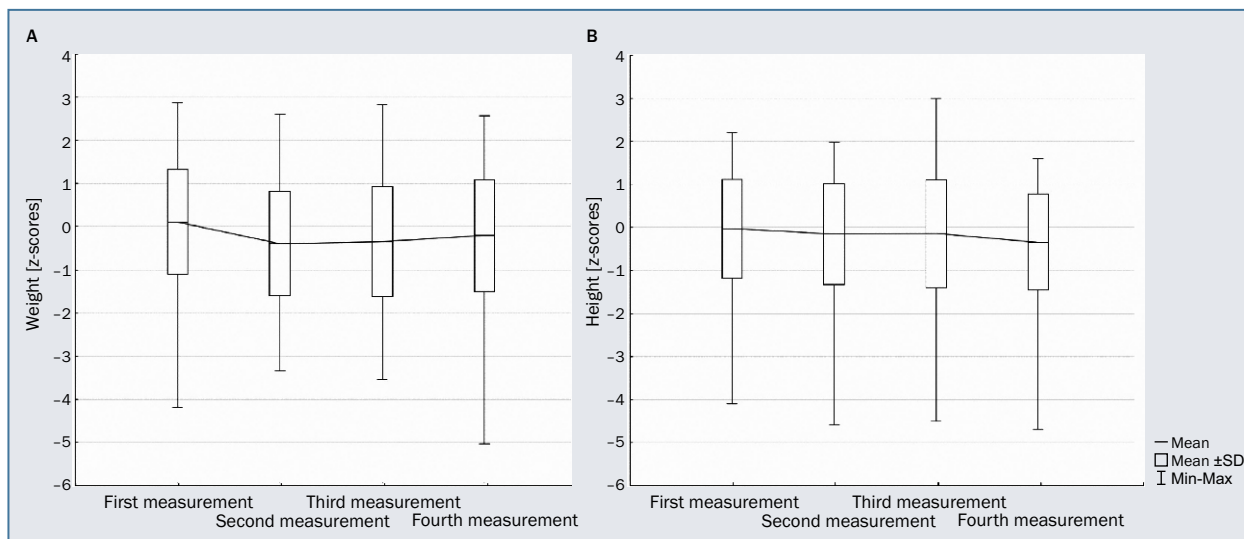
Figure 2. Charts presenting mean ±standard deviation (SD) values of z-scores of **A** — weight, **B** — height, measured at designated time points

Table II. Patient weight in kilograms and height in meters with z-scores at four time points. All values expressed as mean ±standard deviation (SD

Variable	Before HSCT			On discharge				100 days post-HSCT				1 year post-HSCT			
	n	[kg]	[z-score]	n	[kg]	[z-score]	p-value*	n	[kg]	[z-score]	p-value**	n	[kg]	[z-score]	p-value***
Weight	79	36.37 ±19.16	0.11 ±1.21	79	33.89 ±17.83	–0.39 ±1.21	<0.001	79	34.71 ±17.63	–0.35 ±1.28	<0.001	79	37.66 ±18.14	–0.21 ±1.3	<0.001
	n	[m]	[z-score]	n	[m]	[z-score]	p-value*	n	[m]	[z-score]	p-value**	n	[m]	[z-score]	p-value***
Height	79	1.34 ±0.29	–0.03 ±1.15	79	1.34 ± 0.29	–0.15 ±1.18	<0.001	79	1.35 ±0.28	–0.15 ±1.25	0.002	79	1.38 ±0.27	–0.34 ±1.12	<0.001

*Second vs. first measurement in z-scores; **third vs. first measurement in z-scores; ***fourth vs. first measurement in z-scores; HSCT — hematopoietic stem cell transplantation

The differences in the weight-for-age and height-for-age z-scores between the fourth and the first measurements are shown in Figure 3.

Secondary endpoints

At one year post-transplant, declines in weight-for-age and height-for-age z-scores had occurred in all analyzed subgroups. Acute GvHD and the use of a TBI-based conditioning regimen were the significant factors influencing weight (mean ±SD difference in weight-for-age z-scores values: –0.53 ±1.19 vs. –0.22 ±0.83, for patients with and without acute GvHD, respectively, and –0.59 ±0.88 vs. –0.14 ±0.98, for patients who received and did not receive TBI, respectively). Other analyzed factors, which were sex, age (<10 years vs. ≥10 years), type of disease (malignant vs non-malignant), parental nutrition in HSCT period, the presence of III–IV mucositis, acute GvHD of the GI tract, chronic GvHD, as well as chronic GvHD of
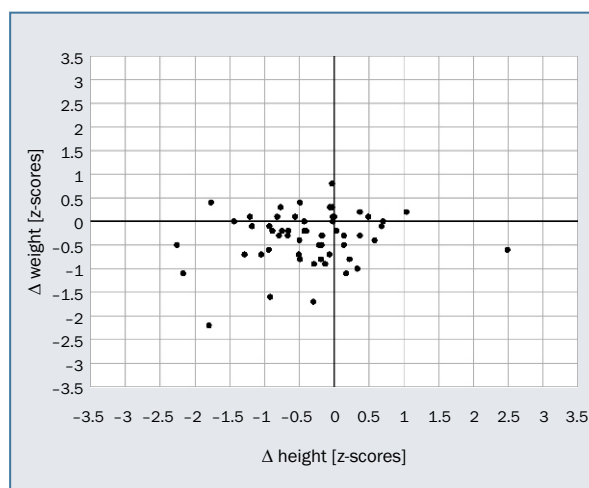

Figure 3. Differences between fourth [365 days after hematopoietic stem cell transplantation (HSCT)] and first (on admission) measurements expressed in z-scores. Each point refers to one patient

the GI tract, were not significantly associated with the weight difference.

Our analysis of differences in height-for-age z-scores revealed that patients with GI manifestation of acute GVHD and with chronic GVHD presented significantly greater decreases in height gain than did patients without these complications (mean ±SD difference in height-for-age z-scores values: −0.51 ±1.31 vs. −0.23 ±0.53 for patients with and without acute GvHD of GI tract, respectively, and −0.41 ±1.08 vs. −0.22 ±0.45 for patients with and without chronic GvHD, respectively). Moreover, patients who received parenteral nutrition during the peritransplant period presented a greater decline in height gain than did those without parenteral nutrition (mean ±SD difference in height-for-age z-scores values: −0.39 ±0.83 vs. −0.08 ±0.39 for patient with and without parenteral nutrition, respectively; p =0.006). Sex, age (<10 years vs. ≥10 years), type of disease (malignant vs non-malignant), the use of TBI, the presence of III–IV mucositis, acute GvHD and GI manifestation of chronic GvHD were not significantly associated with height differences. The results of the comparisons are set out in Table III.

Discussion

Our study aimed to assess the influence of HSCT on the growth and body mass of children with malignant or acquired non-malignant diseases in a one-year follow-up. We found that patients treated with allogeneic HSCT demonstrated a severe reduction in the pace of growth, and were unable to achieve their baseline z-score values one-year post-transplant.

Moreover, we demonstrated that the presence of acute and chronic GvHD, GI manifestation of acute GvHD, as well as the use of TBI-based regimens and parenteral nutrition, are potential risk factors for a severe slowdown of growth. HSCT is a commonly used therapeutic procedure for malignant and non-malignant disorders of the hematopoietic system. In most cases, it comprises myeloablative radio- or chemotherapy, infusion of hematopoietic stem cells, and complex immunosuppression [19]. The most dynamic part of the procedure involves the early period after HSCT [13, 14]. As a result of ablative therapy, the intensity of the conditioning regimen, and the underlying disease, the catabolism of the patient increases and can lead to malnutrition, often requiring nutritional support [5]. Other factors contributing to possible weight loss are transplant-related complications such as: mucositis, diarrhea, nausea, vomiting, and anorexia. These are usually related to GvHD, which interferes with the digestion and absorption of nutrients [5]. Since nutritional status is an essential factor in determining the proper development and health status of children, it is of interest to many clinicians. Several studies have assessed the impact of nutritional status prior to HSCT on its

outcomes, but their results remain ambiguous, particularly in pediatric populations.

The aim of our study was to analyze the anthropometric profile of patients before and up to one year after HSCT. We found a significant weight loss and a slowdown in height gain in the early period after transplantation. The height gain continued to slow down until one year post-transplant, but a catch-up in weight occurred. Despite that, children did not reach their baseline z-score values one-year post-transplant. To date, only a few studies have reported the short-term follow-up nutritional profiles of pediatric HSCT recipients with various underlying conditions. Some of them have aimed to determine the efficacy and outcomes of enteral and/or parenteral nutrition and reported short-term evaluations of nutritional status [20–23]. Patients receiving enteral nutrition had lower weight-for-height z-scores than those receiving parenteral nutrition on admission and 30 days post-transplant [20]. Analysis of the anthropometric profile of patients with Fanconi anemia showed a significant decline in nutritional status (weight loss and decrease in height-for-age and BMI-for-age z-scores) at 30 days after HSCT [16]. Campos et al. [24] found no significant reduction in z-scores for weight-for-age, height-for-age, or body mass index (BMI)-for-age in 25 children at 12-months post-transplant. A recent study on 27 children with primary immunodeficiencies showed a progressive catch up for weight (−0.27) but no catch up for height (−0.93) in a one-year follow up after a primary decrease in anthropometric measures soon after HSC [15]. This is wholly consistent with our findings. Nonetheless, before transplantation mean weight and height z-scores of those patients were below average, and one-third of children had a weight and/or height ≤−2 SD, in contrast to our population which was above average (0.11 z-score for height and −0.03 z-score for weight), with only 5% of our patients being below the 5th percentile of weight and height. Given that we excluded patients with genetic non-malignant conditions, our study group would seem to reflect a healthy population and to be a good model to show alterations in growth patterns.

HSCT is a factor demonstrated as altering final height of children in a longitudinal follow-up [6–8]. Growth deficits have been associated with cranial radiotherapy, spinal irradiation of ≥7 vertebrae, administration of certain conditioning regimens (lomustine, busulfan), pre-transplant body height, and young age [9, 25]. Among these factors, conditioning regimens (total body irradiation, busulfan, cyclophosphamide, melphalan) have been found to be one of the most important factors affecting final height of cancer survivors, as they exert an effect on the hypothalamic-pituitary axis, endocrine glands function, and cause damage to bone epiphyses [9–11]. Since GH deficiency is one of the most common endocrinopathies among childhood cancer survivors, GH therapy offers possible beneficial

Table III. Evaluation of anthropometric profile of patients according to weight-for-age and height-for-age z-scores differences between fourth (365 days post-transplant) and first (on admission) measurements

Parameter	n	Difference in weight-for-age z-score values*	p-value	Difference in height-for-age z-score values*	p-value
All patients	79	–0.32 ±0.96		–0.28 ±0.72	
Age group			0.17		0.12
<10 years	39	–0.44 ±1.07		–0.38 ±0.91	
≥10 years	40	–0.20 ±0.83		–0.18 ±0.46	
Sex			0.16		0.26
Male	54	–0.24 ±1.01		–0.23 ±0.79	
Female	25	–0.49 ±0.83		–0.38 ±0.55	
Type of disease			0.16		0.95
Malignant	61	–0.38 ±1.03		–0.26 ±0.77	
Non-malignant	18	–0.09 ±0.66		–0.34 ±0.51	
Type of pretransplant conditioning			0.09		0.11
Myeloablative	58	–0.44 ±0.9		–0.37 ±0.58	
Non-myeloablative	21	0.03 ±1.05		–0.02 ±0.98	
TBI-based regimen			0.01		0.48
Yes	31	–0.59 ±0.88		–0.33 ±0.53	
No	48	–0.14 ±0.98		–0.24 ±0.82	
Parenteral nutrition in HSCT period			0.56		0.01
Yes	50	–0.33 ±1.14		–0.39 ±0.83	
No	29	–0.30 ±0.54		–0.08 ±0.39	
Stage III–IV mucositis			0.71		0.49
Yes	34	–0.30 ±0.88		–0.22 ±0.53	
No	45	–0.33 ±1.03		–0.33 ±0.85	
Acute GvHD			0.047		0.75
Yes	26	–0.53 ±1.19		–0.27 ±1.00	
No	53	–0.22 ±0.83		–0.30 ±0.54	
Acute GvHD of gastrointestinal tract			0.17		0.01
Yes	13	–0.38 ±1.50		–0.51 ±1.31	
No	66	–0.31 ±0.54		–0.23 ±0.53	
Chronic GvHD			0.2		0.04
Yes	25	–0.42 ±1.31		–0.41 ±1.08	
No	54	–0.27 ±0.76		–0.22 ±0.45	
Chronic GvHD of gastrointestinal tract			0.11		0.05
Yes	12	–0.79 ±0.88		–0.69 ±0.72	
No	67	–0.23 ±0.96		–0.2 ±0.7	

*Fourth vs. first measurement; TBI — total body irradiation; HSCT — hematopoietic stem cell transplantation; GvHD — graft versus host disease

management of decreased growth [10]. Additionally, only a few studies have aimed to investigate nutritional status and body composition abnormalities in cancer survivors. A report of the Childhood Cancer Survivor Study showed that underweight HSCT survivors are more likely to suffer from major medical conditions, and need to be monitored for negative health consequences of abnormal BMI [12].

Our study is one of the first to investigate the risk factors for early growth retardation in children treated with HSCT. So far, few studies have focused on this issue. A short-term follow-up study comprising 123 adult patients found that being male, an allogeneic transplant, and a length of stay in hospital >21 days were all factors associated with greater deterioration of nutritional status [26]. Moreover, Campos et al. found that total dose of corticosteroids, length of their use, and the type of HSCT donor were all risk factors for lean body mass changes in a 6-month follow-up period [24]. We found the presence of acute GvHD to be a possible factor impeding weight gain, and we found acute GvHD of the GI tract or chronic GvHD to affect height gain. Acute and chronic GvHD include multiple manifestations and can affect any segment of the GI tract, causing a variety of GI symptoms. Mucosal injury of intestines results in protein loss, which subsequently leads to malabsorption and malnutrition [27]. To date, the results describing the association between acute GvHD and weight and height changes are inconsistent. Contrary to our study, a report on 45 children treated with HSCT showed no association between the presence of GI symptoms in patients with GvHD and anthropometric measurements four months after HSCT; however, this study group was relatively small, which might have impeded analysis [28]. Chronic GvHD is a leading cause of long-term mortality in HSCT recipients and can occur at any time after HSCT. To date, a few studies have shown that patients with chronic GVHD were more likely to report shorter final height and significant weight loss [10, 29].

TBI remains a well-known factor altering final height of HSCT recipients due to its impact on endocrine and skeletal systems [8, 11]. Our study found it to be also an important risk factor for weight loss in short-term follow-up. Furthermore, we demonstrated that the use of parenteral nutrition in the peritransplant period is a risk factor for a severe deterioration in height gain. According to the ESPEN Guidelines, parenteral nutrition is recommended as nutritional support where oral and enteral nutrition is insufficient or unfeasible [30]. As far as we know, there has been no study evaluating the height of patients who underwent HSCT and who were fed with parenteral nutrition. A recent systematic review found that patients receiving enteral nutrition had lower weight-for-height z-scores than those receiving parenteral nutrition on admission and 30 days post-transplant. However, it did not evaluate the height of patients [20].

Our study has several limitations. Firstly, due to the low number of pediatric HSCT recipients, our study group (79 patients) is relatively small. Secondly, our study included only Polish children; the anthropometric profile may differ in other populations. Our results cannot be easily extrapolated to patients with primary immunodeficiencies and short stature phenotype, since they were excluded from the study.

Nevertheless, thanks to this criterion, our study group seems to present a healthy population and to be a good model to show alterations in growth patterns. Another downside is the retrospective character of this study and the limitations linked to that. Due to this fact, we were confronted by missing data, and as a result had to exclude some patients.

Conclusions

In conclusion, we demonstrated that weight-for-age and height-for-age z-scores of pediatric patients significantly declined throughout a one-year follow-up. Patients who received TBI before HSCT, who were fed with parenteral nutrition, or who were complicated with GvHD, especially localized in the GI tract, require prolonged and close weight and height monitoring, since we have found them to be at increased risk for deteriorations in weight and height gain. Future larger studies are warranted to validate these findings.

Data availability statement
The data that supports the findings of this study is available from the corresponding author upon request.

Author's contributions
All authors confirm they had full access to data and contributed to the drafting of this paper. MK and JG designed and coordinated the study. MK, AK, AAS and AC analyzed the data and wrote sections of the manuscript. All authors were responsible for the integrity and accuracy of the data, and approved the submitted version.

Conflict of interest
None.

Financial support
None.

Ethics
The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform Requirements for Manuscripts submitted to Biomedical Journals.

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Supplement 1

Table S1. STROBE Statement

	Item no.	Recommendation	Reported on page
aABS Title and abstract	1	*(a)* Indicate study's design with commonly used term in title or abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3, 4
Participants	6	*(a)* Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4, 5
		(b) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4, 5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	4, 5
Study size	10	Explain how the study size was arrived at	Figure 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	*(a)* Describe all statistical methods, including those used to control for confounding	5
		(b) Describe any methods used to examine subgroups and interactions	5
		(c) Explain how missing data was addressed	5
		(d) If applicable, explain how loss to follow-up was addressed	5
		(e) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study — e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Figure 1
		(b) Give reasons for non-participation at each stage	Figure 1
		Consider use of a flow diagram	Figure 1

cd. →

Table S1 (cont.). STROBE Statement

	Item no.	Recommendation	Reported on page
Descriptive data	14*	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	6, 7, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) Summarize follow-up time (e.g. average and total amount)	Table 1
Outcome data	15*	Report numbers of outcome events or summary measures over time	7, Table 2, Table 3
Main results	16	*(a)* Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g. 95% confidence interval). Make clear which confounders were adjusted for and why they were included	NA
		(b) Report category boundaries when continuous variables were categorized	4, 5 (described in Methods section)
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done — e.g. analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarize key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9–12
Generalisability	21	Discuss the generalizability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

*Give information separately for exposed and unexposed groups

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the websites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org