Journal of Multidisciplinary Healthcare

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Nutritional and Body Composition Changes in Paediatric β-Thalassemia Patients Undergoing Hematopoietic Stem Cell Transplantation: A Retrospective Study Using Bioelectrical Impedance Analysis

Luyang Zhang[1,*], Li Wang[2,*], Jiewen Long[1], Yan Yin[1], Sandip Patil[1]

[1]Department of Haematology and Oncology, Shenzhen Children's Hospital, Shenzhen, Guangdong Province, 518000, People's Republic of China; [2]Department of Clinical Nutrition, Shenzhen Children's Hospital, Shenzhen, Guangdong Province, 518000, People's Republic of China

*These authors contributed equally to this work

Correspondence: Sandip Patil; Yan Yin, Department of Haematology and Oncology, Shenzhen Children's Hospital, 7019 Yitian Road, Shenzhen, Guangdong Province, 518000, People's Republic of China, Tel +86-755-83008283, Email sandippatil1309@yahoo.com; yinyan0915@sina.com

Journal of Multidisciplinary Healthcare downloaded from https://www.dovepress.com/
For personal use only.

Objective: This retrospective study evaluated nutritional status and body composition changes in paediatric β-thalassemia (β-TM) patients before and after hematopoietic stem cell transplantation (HSCT), using bioelectrical impedance analysis (BIA), and explored their relationship with HSCT outcomes.

Methods: A cohort of 40 paediatric β-TM patients undergoing allogeneic HSCT was assessed for their nutritional status, anthropometric parameters, including body mass index (BMI), weight, and height, and body composition parameters pre-and post-HSCT, focusing on BIA measurements, including intracellular water (ICW), extracellular water (ECW), fat mass (FAT), fat-free mass (FFM), Skeletal Muscle Mass (SMM), soft Lean Mass (SLM), percent body fat (PBF), Body Cell Mass (BCM), Phase angle (PA) and muscle balance pre- and post-HSCT. Post-HSCT clinical outcomes, including acute graft-vs-host disease (aGVHD), engraftment time, oral mucositis (OM), sinusoidal obstruction syndrome (SOS), and diarrhoea in relation to nutrition status after HSCT were analysed.

Results: After HSCT, 28.21% experienced diminished nutritional status, with 71.43% of those who were wasting before HSCT showing diminished nutritional status, significantly higher than the normal group (18.75%, $P = 0.012$). Anthropometric changes included significant weight reduction (87.5%, 22.15 ± 7.46 vs 20.74 ± 6.57, $P < 0.001$) and BMI decrease (90%, 15.19 ± 1.70 vs 14.05 ± 1.48, $P < 0.001$). Body composition parameters, which are FFM, SMM, SLM, ICW, ECW, BCM, and PA (18.26 ± 5.71 vs 17.27 ± 5.19, 8.68 ± 3.30 vs 7.93 ± 3.02, 17.11 ± 5.28 vs 16.06 ± 4.84, 8.19 ± 2.54 vs 7.62 ± 2.31, 5.15 ± 1.58 vs 4.94 ± 1.47, 11.74 ± 3.63 vs 10.92 ± 3.32, 4.42 ± 0.50 vs 3.90 ± 0.57, respectively, $P < 0.001$) analysis revealed significant decreases. No significant differences in clinical outcomes were observed based on nutritional status.

Conclusion: Paediatric β-TM patients undergoing HSCT exhibit significant changes in nutrition status and body composition, emphasizing the need for focused attention on malnourished children who are more prone to diminished nutritional status. Comprehensive BIA aids in understanding the impact, urging consideration for extended follow-up and larger cohorts in future research.

Keywords: paediatric β-thalassemia, hematopoietic stem cell transplantation, HSCT, bioelectrical impedance analysis, BIA, nutritional status, malnourished children

Introduction

The term "thalassemia" refers to a group of inherited disorders characterized by defective production of haemoglobin (Hb).[1] Among these, β-thalassemia (β-TM) necessitates lifelong blood transfusions for survival. Allogeneic hematopoietic stem cell

Received: 11 February 2024
Accepted: 29 April 2024
Published: 9 May 2024

© 2024 Zhang et al. This work is published and licensed by Dove Medical Press Limited. The full terms of this license are available at https://www.dovepress.com/terms.php and incorporate the Creative Commons Attribution – Non Commercial (unported, v3.0) License (http://creativecommons.org/licenses/by-nc/3.0/). By accessing the work you hereby accept the Terms. Non-commercial uses of the work are permitted without any further permission from Dove Medical Press Limited, provided the work is properly attributed. For permission for commercial use of this work, please see paragraphs 4.2 and 5 of our Terms (https://www.dovepress.com/terms.php).

transplantation (HSCT) stands as the sole definitive cure for addressing defective erythropoiesis in children with β-TM. It offers respite from the lifelong demands of treatment and mitigating long-term complications associated with the disease or its therapeutic intervention.[2,3] The success of HSCT is intricately linked to the nutritional status of patients, with poor nutrition correlating with adverse outcomes such as relapse, non-relapse mortality, delayed engraftment, and an increased risk of acute graft-vs-host disease (aGVHD).[4–7] While the majority of HSCT patients exhibit good nutritional status prior to the procedure, with ~10% to 15% experiencing malnutrition.[8,9] Notably, β-TM patients often manifest growth retardation symptoms prior to HSCT, including shorter stature, being underweight, wasting away, and diminished bone mineral density.[10] The initiation of treatment, however, precipitates rapid deterioration of nutritional status, exposing patients to the perils of malnutrition.[7] Recognizing malnutrition through validated screening tools before HSCT and implementing timely interventions are pivotal in optimizing HSCT outcomes. Conventional Indicators like albumin, transferrin, and pre-albumin, while commonly used to assess nutritional status, are susceptible to interference from non-nutritional factors, complicating their interpretation.[11]

Traditional anthropometric measurements such as weight and body mass index (BMI), often employed in malnutrition assessment, exhibit inconsistent impacts on transplantation outcomes,[7,12–14] possibly due to their inability to detect changes in body composition accurately.[15,16] In this context, bioelectrical impedance analysis (BIA) emerges as a portable, easy-to-use, non-invasive, low-cost, and reproducible tool for assessing body composition and fluid distribution with fewer physical demands, offering advantages in health care and disease management.[17–19] As well as coupled with children's comfort and cooperation, BIA is significantly appropriate for children in daily clinical practice.[18] BIA works mainly through the measurement of body resistance (R) and reactance (Xc) to alternate electrical current.[20] Resistance depends on the fluid and electrolyte content of the body. Cell membranes produce capacitance (reactance) by storing parts of the charge as a capacitor.[21–23] BIA provides insights into total body water (TBW), intracellular water (ICW), extracellular water (ECW), fat mass (FAT), fat-free mass (FFM), Phase angle (PA), etc.[24] Meanwhile, BIA-derived PA was calculated using the following equation: $PhA = (Xc/R) \times (180/\pi)$. It can reflect the integrity of the cellular membrane, total body cell mass, and hydration status of the body.[25] Moreover, PA, as one of the BIA parameters, reflecting muscle mass, has shown promise in identifying malnutrition more sensitively than traditional criteria in this population.[26] The European Working Group on Sarcopenia in Older People (EWGSOP) 2019 consensus on sarcopenia suggested that PA could be regarded as an index of overall muscle quality.[27] PA has been established as an independent predictor for nutritional status, non-relapse mortality (NRM), 2-year overall survival (OS), and progression-free survival (PFS) in allogeneic HSCT recipients.[28,29]

Despite the wealth of research focusing on HSCT recipients, a significant gap exists in understanding the nutritional status of β-TM child patients before and after HSCT. Given the predisposition of most children with β-TM to malnutrition and growth retardation symptoms before HSCT, independent studies in this population are imperative. This retrospective study aims to employ BIA to investigate changes in various parameters of body composition before and 1 month after HSCT in pediatric patients, considering the presence or absence of aGVHD, engraftment time, and other relevant clinical outcomes.

Methods

This study was conducted in accordance with the guidelines of the Declaration of Helsinki and approved by the Institutional Ethics Committee of Shenzhen children's hospital (SZCH), reference number: 202313302 which complies with international ethical standards. All patients provided informed consent before undergoing HSCT, permitting the use of their data for research, in accordance with the Declaration of Helsinki.

Study Population

The medical records from the Haematology and Oncology Department of SZCH system for the period between 2022 and 2023 were retrospectively reviewed. Inclusion criteria encompassed 40 patients diagnosed with β-TM who underwent allo-HSCT within the specified timeframe and were aged between 3 and 18 years. The donor type included matched related donors, haploidentical donors, and matched unrelated donors.

Data Collection

Clinical outcomes with the first 30 days post HCT, including oral mucositis (OM), aGVHD, engraftment, intestinal infection, sinusoidal obstruction syndrome (SOS), and engraftment time were systematically collected. Time to neutrophil, haemoglobin, and platelet engraftment was separately determined as the time from stem cell infusion (day 0) to the first of three consecutive days with a neutrophil count of at least $0.5*10^9$/L, 7 consecutive days with a haemoglobin count of at least 90g/L, 7 consecutive days with a platelet count of at least $20*10^9$/L. Nutrition status which was assessed by the new growth standards and growth reference published by WHO in 2006[30] and 2007[31] and body composition by BIA at baseline (before the use of conditioning regimen), and 30 days post-transplantation was collected. This included measurements of FFM, Skeletal Muscle Mass (SMM), soft Lean Mass (SLM), FAT, percent body fat (PBF), ICW, ECW, Body Cell Mass (BCM), PA, and muscle balance.

The BIA analysis was performed by using a tetrapolar multi-frequency BIA InBodyS10 (Biospace, Seoul, Korea), with gradual electric current frequency of 1, 5, 50, 250, 500 and 1000 kHz for the measurement. Heights and weights were measured before the measurement of body composition. The children was required fasting for 4 hours, with the bladder empty, and lying in a supine position for 15 minutes. After 15 minutes, the electrodes were placed on specific parts of the thumbs and middle fingers of the right and left hands as well as on the ankles of the right and left lower limbs, and the analysis were performed.

Statistical Analysis

In the statistical analysis of the study, SPSS 26.0 software was employed. Descriptive statistics were utilized for presenting general characteristics, with categorical data expressed as $\bar{x} \pm s$, paired *t*-tests and Wilcoxon Signed Ranks Test (WRST) were performed to analyze the parameters' alteration pre- and post-HSCT. Proportion's 95% confidence intervals (CI) was estimated using Wilson score method. The WRST compared differences in engraftment time of neutrophils, haemoglobin, and platelets between groups. Categorical data, represented as the number of cases, rate or percentage (%), underwent chi-square or Fisher's exact test to compare between-group differences of clinical outcome with baseline data. To Investigate the relationship between pre-HSCT wasting and clinical outcomes, as only one child categorizes as overweight pre-HSCT was excluded. All statistical analyses were two-sided and $P < 0.05$ was considered statistically significant. These rigorous analyses allowed for a comprehensive exploration of the data, enabling the identification of meaningful trends and relationships within the study variables.

Results

A cohort comprising 40 paediatric patients was selected for this study. Among these, 55% (n=22/40) of individuals are male while 45% of individuals (n=18/40) are female which is lower than male, as depicted in Table 1. The age distribution of the cohort ranged from 2 to 15 years, with a calculated average age of 3.03 years (Mean) and a median age of 8.4 years. It is noteworthy that all children underwent therapeutic interventions while confined to bed, abstaining from any form of physical activity during the treatment period. The transplantation procedures employed allogeneic peripheral blood stem cell transplantation (PBSCT), utilizing diverse donor types. Specifically, PBSCT from unrelated donors with matched human leukocyte antigen (HLA) constituted 20% of cases (n=8/40). The predominant approach involved PBSCT from haploidentical donors, accounting for 62.5% of cases (n=25/40), whereas PBSCT from matched related donors was administered in 17.5% of cases (n=7/40) (Table 1). All patients received a myeloablative conditioning regimen, comprising cyclophosphamide (CY), busulfan (BU), fludarabine (Flu), and thyroglobulin (TT). The difference is that for prophylaxis of graft-versus-host disease (GVHD), matched related recipients received cyclosporin A (CsA), methotrexate (MTX) and mycophenolate mofetil (MMF),[32] while haploidentical and matched unrelated recipients received tacrolimus, cyclophosphamide (CY), and MMF simultaneously[33] (Table 1).

Nutritional Status Pre- to Post-HSCT Transition

A total of 40 children were included to explore the nutritional status before and after HSCT. Prior to HSCT, the cohort of 40 pediatric patients exhibited a nuanced spectrum of nutritional and growth parameters. The incidence of wasting pre-HSCT

Table 1 Demographic and Clinical Characteristics of 40 Pediatric Patients Undergoing Haematopoietic Stem Cell Transplantation (HSCT)

Patients Characteristics	n	Proportion (95% CI)
Median age (range)	8.4 (2 to 15 years)	
Gender		
Male	22	55.00% (0.40%, 0.70%)
Female	18	45.00% (0.31%, 0.60%)
Type of HSCT		
Haploidentical donor	25	62.50% (0.47%, 0.76%)
Matched related donor	7	17.50% (0.09%, 0.32%)
Matched unrelated donor	8	20.00% (0.11%, 0.35%)
Condition regimen		
CY + BU + Flu + TT	40	100.00% (0.91%, 1.00%)
GVHD prophylaxis		
CsA + MTX+MMF	7	17.50% (0.09%, 0.32%)
Tacrolimus+CY+MMF	33	82.50% (0.68%, 0.91%)
W/H or BMI/A-Z score		
Normal	32	80.00% (0.65%, 0.90%)
Moderately wasted	6	15.00% (0.07%, 0.29%)
Severe wasted	1	2.50% (0.01%, 0.13%)
Over weight	1	2.50% (0.01%, 0.13%)
H/A-Z score		
Normal	25	62.50% (0.47%, 0.76%)
Moderately stunted	10	25.00% (0.14%, 0.40%)
Severely stunted	5	12.50% (0.05%, 0.26%)

Note: Proportion's 95% confidence intervals (CI) was estimated using Wilson score method.
Abbreviations: CY, cyclophosphamide; BU, busulfan; Flu, fludarabine; TT, thyroglobulin; CsA, cyclosporin A; MTX, methotrexate; MMF, mycophenolate mofetil.

was 17.5% (n=7/40), with subcategories indicating 15% (n=6/40) experiencing moderate wasting, and 2.5% (1/40) demonstrating severe wasting. Additionally, 2.5% (1/40) of patients were categorized as overweight before HSCT, and maintain the same after HSCT. Following HSCT, the nutritional landscape of the cohort underwent notable changes. A trend towards diminished nutritional status after HSCT in children was observed both in the normal group and the wasting group. The incidence of diminished nutritional status after HSCT in the normal group was 18.75%, while in the wasting group, it notably increased to 71.43%. Children who experienced wasting were significantly more likely to undergo a decline in nutritional status compared to those in normal nutrition status pre-HSCT (P = 0.011) (Table 2). Simultaneously, the study involved 40 children to investigate changes in stunting before and after HSCT. Stunting was observed, with an overall incidence of 37.5% (n=15/40). Further analysis revealed that 25% (n=10/40) were moderately stunted, and 12.5%

Table 2 Nutritional Status Changes Pre- and Post-Haematopoietic Stem Cell Transplantation (HSCT)

	W/H or BMI/A-Z Rank Change			P-value***
	Improved/Sustained (%)*	Deteriorated (%)**	Total (%)	
Normal	26 (81.25%)	6 (18.75%)	32 (100%)	0.011
Wasting	2 (28.57%)	5 (71.43%)	7 (100%)	
Overweight	1 (2.5%)	0 (97.5)	1 (100%)	

Notes: *Compare with pre HSCT, W/H or BMI/A-Z rank improved or sustained, including severely wasted to moderately wasted or normal, and moderately wasted to normal. **Compare with pre HSCT, W/H or BMI/A-Z rank deteriorated, including normal to moderately wasted or severely wasted, and moderately wasted to severely wasted. ***Fisher's exact test was performed.

(n=5/40) presented with severe stunting. Interestingly, no significant change was found in stunting before and after HSCT, and the stunting rank remained consistent with the pre-HSCT status.

Anthropometric Changes Pre- and Post-HSCT

In the post-HSCT period, a significant weight reduction was observed in 87.5% (n=35/40, 22.15 ± 7.46 vs 20.74 ± 6.57, respectively, $P < 0.001$) of the children. In 55% (n=22/40, 119.63 ± 16.97 vs 120.38 ± 17.05, respectively, $P < 0.001$) of cases, height increased. The BMI experienced a decrease in 90% (n=36/40, 15.19 ± 1.70 vs 14.05 ± 1.48, respectively, $P < 0.001$) of the cases (Table 3).

Body Composition Analysis Pre- and Post-HSCT

After HSCT, the analysis of body composition in 40 pediatric patients with β-TM revealed significant changes. The FFM decreased by 87.5% (n=35/40, 18.26 ± 5.71 vs 17.27 ± 5.19, respectively, $P < 0.001$). Similarly, SMM showed a decrease in 90% of cases (n=36/40, 8.68 ± 3.30 vs 7.93 ± 3.02, respectively, $P < 0.001$). Furthermore, SLM exhibited an 87.5% decrease (n=35/40, 17.11 ± 5.28 vs 16.06 ± 4.84, respectively, $P < 0.001$). The ICW exhibited a 90% decrease (n=36/40, 8.19 ± 2.54 vs 7.62 ± 2.31, respectively, $P < 0.001$). While ECW decreased by 72.5% (n=29/40, 5.15 ± 1.58 vs 4.94 ± 1.47, respectively, $P < 0.001$). BCM showed an 87.5% decrease (n=35/40, 11.74 ± 3.63 vs 10.92 ± 3.32, respectively, $P < 0.001$). Additionally, the PA demonstrated an 80% decrease (n=32/40, 4.42 ± 0.50 vs 3.90 ± 0.57, respectively, $P < 0.001$). However, FAT decreased in 47.5% of cases (n=19/40, 3.64 ± 2.27 vs 3.455 ± 2.23, respectively, $P = 0.352$). PBF decreased by 65% (n=26/40, 16.74 ± 6.84 vs 16.04 ± 7.56, respectively, $P = 0.397$) (Table 3).

Muscles Balance

After HSCT, 40 children experienced a significant decrease in muscle mass from baseline to 30 days ($P < 0.001$), with an 87.5% reduction in right arm (RA) muscle (n=35/40, 0.66 ± 0.22 vs 0.53 ± 0.19, respectively, $P < 0.001$). Similarly, the left arm (LA) muscle exhibited a 90% decrease (n=36/40, 0.65 ± 0.22 vs 0.53 ± 0.19, respectively, $P < 0.001$). Trunk (TR) showed a 90% decrease in muscle mass (n=36/40, 7.39 ± 2.38 vs 6.63 ± 2.32, respectively, $P < 0.001$). The right leg (RL) muscle experienced a 92.5% decrease (n=37/40, 2.07 ± 0.90 vs 1.72 ± 0.90, respectively, $P < 0.001$). Left leg (LL) muscle displayed a 65% decrease (n=26/40, 2.31 ± 1.13 vs 2.09 ± 1.27, respectively, $P < 0.001$) (Table 4).

Table 3 Comparative Analysis of Body Composition Parameters Before and After Haematopoietic Stem Cell Transplantation (HSCT) in Pediatric Patients

	Pre-HSCT ($\bar{x} \pm s$)	Post-HSCT ($\bar{x} \pm s$)	t	P
Weight (kg)	22.152±7.459	20.735±6.569	6.313	<0.001
Height	119.625±16.972	120.382±17.054	−5.066	<0.001
BMI	15.189±1.699	14.05±1.477	8.846	<0.001
FFM (Kg)	18.26±5.712	17.273±5.194	4.871	<0.001
SMM (Kg)	8.68±3.304	7.938±3.019	6.397	<0.001
SLM (Kg)	17.105±5.285	16.063±4.836	5.55	<0.001
FAT (Kg)	3.64±2.267	3.455±2.234	0.942	0.352
PBF (%)	16.738±6.843	16.035±7.563	0.856	0.397
ICW (L)	8.19±2.543	7.618±2.309	6.401	<0.001
ECW (L)	5.153±1.582	4.935±1.47	3.599	0.001
BCM (Kg)	11.738±3.633	10.923±3.322	6.431	<0.001
PA (°)	4.415±0.504	3.905±0.565	5.388	<0.001

Note: Paired *t*-tests and Wilcoxon Signed Ranks Test (WRST) were performed.
Abbreviations: BMI, body mass index; FFM, fat-free mass; SMM, Skeletal Muscle Mass; SLM, soft Lean Mass; FAT, fat mass; PBF, percent body fat; ICW, intracellular water; ECW, extracellular water; BCM, Body Cell Mass; PA, Phase angle.

Table 4 Comparative Analysis of Muscle Measurements (RA, LR, TR, RL, LL) Pre- and Post-Hematopoietic Stem Cell Transplantation (HSCT) in Pediatric Patients

	Pre-HSCT ($\bar{x} \pm s$)	Post-HSCT ($\bar{x} \pm s$)	t	P
RA	0.664±0.22	0.535±0.194	6.546	<0.001
LR	0.646±0.22	0.526±0.193	5.476	<0.001
TR	7.393±2.382	6.635±2.321	7.705	<0.001
RL	2.072±0.902	1.722±0.898	7.756	<0.001
LL	2.692±2.577	2.093±1.265	1.540	0.132

Note: Paired *t*-tests and Wilcoxon Signed Ranks Test (WRST) were performed.
Abbreviations: RA, right arm; LR, left arm; TR, trunk; RL, right leg; LL, left leg.

Nutritional Status of Pre-HSCT and Engraftment Time of Neutrophil, Haemoglobin, and Platelet

The time to engraftment of neutrophils, haemoglobin, and platelets in the normal and wasting groups were 18.09 vs 19.43 (P = 0.260), 14.47 vs 13.14 (P = 0.955), and 16.78 vs 14.14 (P = 0.985), respectively (Table 5). Regarding stunting, the engraftment time of neutrophils, haemoglobin, and platelets in the normal group was 17.84, 13.56, and 16.68 days, respectively, and an increase in the engraftment time was observed in the stunting group compared to the normal group, with the engraftment time of neutrophils, haemoglobin, and platelets being 19.20, 15.40, and 17.93 days, respectively; however, this difference was not statistically significant (P > 0.05) (Table 6).

Pre-HSCT Wasting and Stunting and Clinical Outcomes

Table 7 demonstrates the relationship between pre-HSCT wasting and stunting and clinical outcomes, including aGVHD, oral mucositis (OM), sinusoidal obstruction syndrome (SOS), and diarrhoea within one month post-HSCT. Among the 40 children, the incidence of aGVHD, OM, SOS, and diarrhoea was 5%, 52.5%, 25%, and 45%, respectively, which revealed no significant differences between pre- and post-HSCT groups (P > 0.05). Being wasted or Stunted before HSCT is not a risk factor for developing the above clinical outcomes in the month following HSCT. The co-infection identified in this study involves a diverse array of microbial pathogens, including *Candida albicans, Escherichia coli, Enterococcus avium, Klebsiella pneumoniae, Proteus mirabilis, Rhizobium radiobacter, Clostridium difficile, Salmonella typhimurium, Lactobacillus casei, Lactobacillus paracasei*, and *Enterococcus faecium*.

Table 5 Engraftment Time of Neutrophil, Haemoglobin, and Platelet in Normal (n = 32) and Wasting Group (n = 7) Pre HSCT

	Normal (95% CI)	Wasted (95% CI)	Z*	P
Granulocyte	18.09 (17.00, 19.19)	19.43 (17.17, 21.68)	1.126	0.260
Haemoglobin	14.47 (12.79, 16.15)	13.14 (7.38, 18.90)	0.055	0.956
Platelet	16.78 (12.66, 20.90)	14.14 (8.98, 19.30)	0.018	0.985

Note: *Wilcoxon rank-sum test (WRST) was used to analysis.

Table 6 Engraftment Time of Neutrophil, Haemoglobin, and Platelet in Normal (n = 25) and Stunting Group (n = 15) Pre HSCT

	Normal (95% CI)	Stunted (95% CI)	Z*	P
Granulocyte	17.84 (1.76, 18.92)	19.20 (16.40, 21.00)	−0.973	0.331
Haemoglobin	13.56 (12.04, 15.08)	15.40 (11.89, 18.91)	−1.026	0.305
Platelet	16.68 (11.35, 22.01)	17.93 (12.47, 23.40)	−1.294	0.196

Note: *Wilcoxon rank-sum test (WRST) was used to analysis.

Table 7 The Relationship Between Nutritional Status of Pre-HSCT and Four Clinical Outcomes

	Wasting group (W/H or BMI/A-*Z* score)						Stunting group (H/A-*Z* score)					
	Agvhd	**Normal**	**Total**	**OR**	**OR 95% CI**	**P value**	**Agvhd**	**Normal**	**Total**	**OR**	**OR 95% CI**	**P value**
Wasting/Stunted	0 (0%)	7 (18.9%)	7	0.82*	0.04, 18.79	1	1 (50%)	13 (34.2)	14	1.92	0.11, 33.30	1
Normal	2 (100%)	30 (81.1%)	32				1 (50%)	25 (65.8)	26			
Total	2	37	39				2	38	40			
	OM	**Normal**	**Total**	**OR**	**OR 95% CI**	**P value**	**OM**	**Normal**	**Total**	**OR**	**OR 95% CI**	**P value**
Wasting/Stunted	5 (71.4%)	2 (28.6%)	7	2.50	0.42, 14.83	0.42	10 (66.7%)	5 (33.3%)	15	2.55	0.68, 9.51	>0.05
Normal	16 (50%)	16 (50%)	32				11 (44%)	14 (56%)	25			
Total	21 (53.9)	18 (46.1%)	39				21 (52.5)	19 (47.5%)	40			
	SOS	**Normal**	**Total**	**OR**	**OR 95% CI**	**P value**	**SOS**	**Normal**	**Total**	**OR**	**OR 95% CI**	**P value**
Wasting/Stunted	1 (10%)	6 (20.7%)	7	0.43	0.04, 4.05	0.65	6 (60%)	9 (30%)	15	3.5	0.54, 22.49	>0.05
Normal	9 (90%)	23 (79.3%)	32				4 (40%)	21 (70%)	15			
Total	10	29	39				10	30	40			
	Diarrhea	**Normal**	**Total**	**OR**	**OR 95% CI**	**P value**	**Diarrhea**	**Normal**	**Total**	**OR**	**OR 95% CI**	**P value**
Wasting/Stunted	3	4	7	0.96	0.18, 5.03	1	6	9	15	0.85	0.23, 3.11	>0.05
Normal	14	18	32				11	14	25			
Total	17	22	39				17	23	40			

Notes: Chi-square or Fisher's exact test were performed. *Haldane-Anscombe correction was applied to calculating the odds ratio and its 95% CI for the zero cell. Fisher's exact test was used to calculate the P value for contingency tables with smaller sample sizes.
Abbreviations: Agvhd, acute graft-vs-host disease; OM, oral mucositis; SOS, sinusoidal obstruction syndrome.

Discussion

The present study focused on a cohort of 40 pediatric patients undergoing HSCT for β-TM. The demographic distribution revealed a male preponderance, aligning with previous studies.[34] The age range of 2 to 15 years underscores the relevance of HSCT across different pediatric age groups, with an average age of 3.03 years. PBSCT from haploidentical donors emerged as the predominant approach, reflecting the development of haplo-HSCT, patients who previously had no donor have the opportunity to receive HSCT. This approach effectively addresses the challenge of finding matched donors.[35]

The nutritional status of the patients was assessed pre- and post-HSCT, revealing significant changes. Post-HSCT, 28.21% of children experienced a diminished nutritional status. It is essential to note that 71.43% of children who experienced wasting before HSCT experienced a diminished nutritional status after HSCT, which was much higher than the normal group, which was 18.75%. These results demonstrated that compared with the children who are in the normal nutrition status pre-HSCT, the children who experienced wasting are more prone to experience a decline in their nutritional status. These changes in nutritional status suggest a potential impact of the transplantation process on the patients' nutritional well-being. Stunting remained consistent with pre-HSCT, the lack of change in the stunting aspect may be attributed to the limited one-month observation period, which may not be sufficient to detect alterations in growth and development.

Our observation has shown that there were significant anthropometric changes post-HSCT, including a notable weight reduction in 87.5% of children, and a height increase in 55% of cases, but the BMI decreased in 90% of cases. These alterations underscore the substantial physiological impact of HSCT on pediatric patients with β-TM. Studies have revealed that most children undergoing HSCT have normal BMI at admission,[36] however, decreases in BMI, and weight loss during the post-transplant weeks have been detected.[37] The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N) and the European Society for Parenteral and Enteral Nutrition (E.S.P.E.N) have stated that children undergoing HSCT are at nutritional risk and that all children undergoing HSCT should be evaluated for nutrition status.[38,39] Additionally, malnutrition pre- and post-HSCT has been found to be an independent risk factor for complications.[40] For this reason, growth monitoring and evaluation of nutritional status are very important factors in detecting children at risk of malnutrition, and nutritional treatment should be prioritized in pediatric patients.

In terms of nutritional status, the administration of immunosuppressants and anti-tumour drugs during hospitalization can induce toxic effects, manifesting as gastrointestinal symptoms like OM, nausea, and vomiting.[41] These symptoms contribute to challenges in nutritional intake, causing reduced appetite and inadequate energy consumption. Consequently, insulin levels decrease while glucagon levels increase in the body.[42] The diminished insulin effect leads to the breakdown of muscle protein, resulting in weight loss and a decrease in basal metabolic rate.[43] This cascade of effects contributes to muscle loss in children and establishes a negative nitrogen balance in the body.[44] However, regular measurements of mid-upper arm circumference and triceps skinfold thickness can only provide insights into changes in local fat mass. Relying solely on BMI, and weight and height for assessing malnutrition may not accurately reflect nutritional status due to potential chemotherapy-induced dehydration.[45,46] Weight loss may not necessarily indicate a reduction in SLM, and a decrease in muscle mass does not necessarily reflect a decrease in FAT.[47] Therefore, the integration of BIA technology to measure changes in body composition enables a more accurate evaluation of nutritional status in children before and after HSCT.

We found significant decreases in various body composition parameters; however, FAT and PBF showed no significant change after HSCT aligned with the previous research.[15,48] These findings suggest a shift in body composition towards a less favourable state, potentially reflecting the catabolic effects of the transplantation process.[49] Although BCM represents the number of cells containing water and protein in the body's organs and is a sensitive indicator of nutritional status, no specific studies have focused on BCM, ICW, and ECW in patients with β-TM. Insufficient energy intake attributable to the immunosuppressants and anti-tumour drugs affects the sodium, potassium, and ATP function of the cell membrane. This effect disrupts the concentration gradient and cannot maintain the concentration difference between sodium and potassium ions inside and outside the cell at a constant level leading to sodium retention which causes hypotonic dehydration, hypokalemia, and decreased ICW, indirectly indicating cellular malnutrition.[50] PA assessment, encompassing both cell quality and quantity along with muscle proportion.[51] Our findings revealed a significant decrease in PA after HSCT which is consistent with previous studies.[29,52] Meanwhile, a decline in muscle mass, including FFM, SMM, and SLM were been found. SMM experienced a substantial reduction in the Right Arm (RA), Left Arm (LA), Trunk (TR), Right Leg (RL), and Left Leg (LL) muscles. These observations indicate a systemic impact on muscle health, possibly influenced by factors such as reduced physical activity and insufficient intake during the treatment period.[53] The imbalance in muscle mass distribution could contribute to functional limitations and underscores the importance of post-transplant rehabilitation programs to address muscle atrophy.[54]

Our study shows being wasted or Stunted before HSCT did not increase the risk of developing clinical outcomes, such as aGVHD, engraftment time, OM, SOS, and diarrhoea, in the month following HSCT. aGVHD is the most common complication for HSCT patients and is the major cause of mortality during the first year after HSCT.[55] Some reports reported that nutrition might contribute to preventing aGVHD[6,56] which did not be proved in our finding. No significant differences were observed in aGVHD, suggesting a more complex relationship between nutritional status and specific clinical outcomes. The inconsistent result could be attributed to aGVHD being particularly undesirable in patients with β-TM. The post-transplant CY (PTCY) as part of GVHD prophylaxis for haploidentical HSCT achieved favourable outcomes which caused the increasing number of haploidentical HSCT performed. Especially our center performs PTCY plus a small dose of ATG which further reduces the incidence of aGVHD. Therefore, the main reason for the negative results may be related to the low incidence of aGVHD resulting in a limited number of aGVHD patients that can be analyzed; however, the influence of other factors cannot be ruled out. If the association between nutritional status and aGVHD wants to be clarified, expanding the sample size could be considered.

In terms of engraftment time, although no significance be found in the present study, however, there is a trend suggesting a nuanced interplay between stunting and time to engraftment time. The engraftment time of neutrophils, haemoglobin and platelets in the normal group was 17.84, 13.56, and 16.68 days, respectively, and an increase in the engraftment time was observed in the stunting group compared to the normal group, with the engraftment time of neutrophils, haemoglobin, and platelets being 19.20, 15.40, and 17.93 days, respectively. One study showed that high-risk malnutrition patients experienced a longer time for platelet engraftment but not time for neutrophil engraftment.[57] Additionally, researchers pointed out that albumin was associated with time to platelet engraftment, days of total parenteral nutrition (TPN) correlated with time to neutrophil engraftment[58] and time to platelet

engraftment.[58,59] However, study demonstrated that nutrition support was not associated with neutrophil engraftment time.[59] As above, nutritional status could have potential association with neutrophil and platelet engraftment. Further investigation was warranted to understand the interplay which could contribute to refining patient care strategies.

The co-infection analysis identified a diverse array of microbial pathogens, emphasizing the complexity and challenges associated with combating multiple pathogens simultaneously. This multi-species infection underscores the need for a comprehensive understanding of the intricate dynamics of co-infections in the context of clinical management and therapeutic interventions.

The study populations of majority studies on the nutritional status of HSCT patients before and after HSCT have included both malignant and non-malignant patients. The present study only focused on the nutritional status transition of TM patients pre- and post-HSCT. We will expand our study increase the sample size and include another centre to overcome the validity of the results. We accept that reliance on historical medical records may limit the accuracy and comprehensiveness of certain variables. However, we consider the long-term follow-up and complications associated with HSCT. Longitudinal studies with extended follow-up periods which is essential for a more comprehensive understanding of patient outcomes. The present study relies on BIA as a more accurate method to measure anthropocentric parameters compared to other nutritional parameters, such as blood indices, which may be influenced by chemotherapy drugs or other factors. Our other group working on co-infection and finding specific microbial interactions and their correlation with clinical manifestations. The study provides valuable insights into the multifaceted effects of HSCT on pediatric patients with β-TM, encompassing changes in nutritional status, body composition, muscle balance, and complications.

Conclusion

In summary, our study on pediatric patients undergoing HSCT for β-thalassemia major reveals significant post-transplant changes in nutritional status, body composition, and muscle balance, emphasizing potential vulnerability to nutritional challenges. Focusing on malnourished children is essential due to they are more likely to undergo a decline in nutritional status compared to those in normal nutrition status pre-HSCT. Anthropometric changes, including weight reduction and BMI decrease, underscore the physiological impact on these young patients. Despite the nuanced information provided by BIA, our study found limited significant correlations between nutritional status assessed by BIA and clinical outcomes. However, intriguing trends observed in BIA parameters warrant further exploration to better elucidate their clinical implications and predictive value in this population. Comprehensive body composition analysis shows systemic shifts, notably in muscle health. While the relationship between nutritional status and clinical outcomes lacks significance in our study, intriguing trends suggest further investigation. Acknowledging limitations such as modest sample size and single-centre design, these findings offer valuable insights into the effects of HSCT, advocating for extended follow-up and larger cohorts in future research.

Data Sharing Statement

The datasets generated during and/or analysed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

Ethics Approval

This study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Ethics Committee of SZCH, reference number: 202313302 dated 2023/03/31, which complies with international ethical standards.

Consent for Publication

Informed consent was obtained from all participants in the study.

Author Contributions

LZ: Writing—original draft, Formal analysis, Investigation, Methodology. LW: Formal analysis, Investigation, Methodology, Writing—original draft. JL: Investigation, Methodology, Resources, Project administration, Writing—

original draft. YY: Conceptualization, Formal analysis, Resources, Writing—original draft. SP: Conceptualization, Methodology, Resources, Supervision, Validation, Writing—Final review & editing. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by funding from Sanming Project of Medicine in Shenzhen SZSM202211033; Shenzhen Fund for Guangdong Provincial High-level Clinical Key Specialties (SZGSP012); Shenzhen Key Medical Discipline Construction Fund (SZXK034); Guangdong High-level Hospital Construction Fund; Shenzhen High-level Hospital Construction Fund; and Shenzhen Science and Technology Program (SGDX20201103095404018).

Disclosure

Luyang Zhang and Li Wang are co-first authors for this study. The authors declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

References

1. Taher AT, Musallam KM, Cappellini MD. Beta-thalassemias. *N Engl J Med*. 2021;384(8):727–743. doi:10.1056/NEJMra2021838
2. De Simone G, Quattrocchi A, Mancini B, Di Masi A, Nervi C, Ascenzi P. Thalassemias: from gene to therapy. *Mol Aspects Med*. 2022;84:101028. doi:10.1016/j.mam.2021.101028
3. Strocchio L, Locatelli F. Hematopoietic stem cell transplantation in thalassemia. *Hematol Oncol Clin North Am*. 2018;32(2):317–328. doi:10.1016/j.hoc.2017.11.011
4. White M, Murphy AJ, Hastings Y, et al. Nutritional status and energy expenditure in children pre-bone-marrow-transplant. *Bone Marrow Transplant*. 2005;35(8):775–779. doi:10.1038/sj.bmt.1704891
5. Kerby EH, Li Y, Getz KD, et al. Nutritional risk factors predict severe acute graft-versus-host disease and early mortality in pediatric allogeneic hematopoietic stem cell transplantation. *Pediatr Blood Cancer*. 2018;65(2). doi:10.1002/pbc.26853
6. Hirose EY, de Molla VC, Goncalves MV, et al. The impact of pretransplant malnutrition on allogeneic hematopoietic stem cell transplantation outcomes. *Clin Nutr Espen*. 2019;33:213–219. doi:10.1016/j.clnesp.2019.05.005
7. Fuji S, Mori T, Khattry N, et al. Severe weight loss in 3 months after allogeneic hematopoietic sct was associated with an increased risk of subsequent non-relapse mortality. *Bone Marrow Transplant*. 2015;50(1):100–105. doi:10.1038/bmt.2014.228
8. Hadjibabaie M, Iravani M, Taghizadeh M, et al. Evaluation of nutritional status in patients undergoing hematopoietic sct. *Bone Marrow Transplant*. 2008;42(7):469–473. doi:10.1038/bmt.2008.188
9. Urbain P, Birlinger J, Lambert C, Finke J, Bertz H, Biesalski HK. Longitudinal follow-up of nutritional status and its influencing factors in adults undergoing allogeneic hematopoietic cell transplantation. *Bone Marrow Transplant*. 2013;48(3):446–451. doi:10.1038/bmt.2012.158
10. Soliman AT, Yassin M, Alyafei F, et al. Nutritional studies in patients with beta-thalassemia major: a short review. *Acta Biomed*. 2023;94(3):e2023187. doi:10.23750/abm.v94i3.14732
11. Gupta D, Lammersfeld CA, Vashi PG, et al. Bioelectrical impedance phase angle in clinical practice: implications for prognosis in stage iiib and iv non-small cell lung cancer. *BMC Cancer*. 2009;9:37. doi:10.1186/1471-2407-9-37
12. Gleimer M, Li Y, Chang L, et al. Baseline body mass index among children and adults undergoing allogeneic hematopoietic cell transplantation: clinical characteristics and outcomes. *Bone Marrow Transplant*. 2015;50(3):402–410. doi:10.1038/bmt.2014.280
13. Yang J, Xue SL, Zhang X, et al. Effect of body mass index on overall survival of patients with allogeneic hematopoietic stem cell transplantation. *Eur J Clin Nutr*. 2017;71(6):750–754. doi:10.1038/ejcn.2016.225
14. Rieger CT, Wischumerski I, Rust C, Fiegl M. Weight loss and decrease of body mass index during allogeneic stem cell transplantation are common events with limited clinical impact. *PLoS One*. 2015;10(12):e145445. doi:10.1371/journal.pone.0145445
15. Feng Y, Pan LY, Shen LY, Chang PP, Zhang BH, Hong L. Changes in body composition in children with acute graft-versus-host disease within the first 100 days after hematopoietic stem cell transplantation. *Eur J Clin Nutr*. 2018;72(8):1167–1175. doi:10.1038/s41430-017-0057-y
16. Murphy AJ, White M, Davies PS. The validity of simple methods to detect poor nutritional status in paediatric oncology patients. *Br J Nutr*. 2009;101(9):1388–1392. doi:10.1017/S0007114508076241
17. Jackson AA, Johnson M, Durkin K, Wootton S. Body composition assessment in nutrition research: value of bia technology. *Eur J Clin Nutr*. 2013;67(Suppl 1):S71–S78. doi:10.1038/ejcn.2012.167
18. Xiong ZH, Zheng XM, Zhang GY, Wu MJ, Qu Y. The use of bioelectrical impedance analysis measures for predicting clinical outcomes in critically ill children. *Front Nutr*. 2022;9:847480. doi:10.3389/fnut.2022.847480
19. Brunani A, Perna S, Soranna D, et al. Body composition assessment using bioelectrical impedance analysis (bia) in a wide cohort of patients affected with mild to severe obesity. *Clin Nutr*. 2021;40(6):3973–3981. doi:10.1016/j.clnu.2021.04.033
20. Wirth R, Volkert D, Rosler A, Sieber CC, Bauer JM. Bioelectric impedance phase angle is associated with hospital mortality of geriatric patients. *Arch Gerontol Geriatr*. 2010;51(3):290–294. doi:10.1016/j.archger.2009.12.002
21. Barbosa-Silva MC, Barros AJ. Bioelectrical impedance analysis in clinical practice: a new perspective on its use beyond body composition equations. *Curr Opin Clin Nutr Metab Care*. 2005;8(3):311–317. doi:10.1097/01.mco.0000165011.69943.39

22. Schwenk A, Beisenherz A, Romer K, Kremer G, Salzberger B, Elia M. Phase angle from bioelectrical impedance analysis remains an independent predictive marker in HIV-infected patients in the era of highly active antiretroviral treatment. *Am J Clin Nutr*. 2000;72(2):496–501. doi:10.1093/ajcn/72.2.496
23. Bosy-Westphal A, Danielzik S, Dorhofer RP, Later W, Wiese S, Muller MJ. Phase angle from bioelectrical impedance analysis: population reference values by age, sex, and body mass index. *Jpen J Parenter Enteral Nutr*. 2006;30(4):309–316. doi:10.1177/0148607106030004309
24. Orsso CE, Gonzalez MC, Maisch MJ, Haqq AM, Prado CM. Using bioelectrical impedance analysis in children and adolescents: pressing issues. *Eur J Clin Nutr*. 2022;76(5):659–665. doi:10.1038/s41430-021-01018-w
25. Delshad M, Beck KL, Conlon CA, Mugridge O, Kruger MC, von Hurst PR. Validity of quantitative ultrasound and bioelectrical impedance analysis for measuring bone density and body composition in children. *Eur J Clin Nutr*. 2021;75(1):66–72. doi:10.1038/s41430-020-00711-6
26. Brotelle T, Lemal R, Cabrespine A, et al. Prevalence of malnutrition in adult patients previously treated with allogeneic hematopoietic stem-cell transplantation. *Clin Nutr*. 2018;37(2):739–745. doi:10.1016/j.clnu.2017.03.016
27. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;48(1):16–31. doi:10.1093/ageing/afy169
28. Urbain P, Birlinger J, Ihorst G, Biesalski HK, Finke J, Bertz H. Body mass index and bioelectrical impedance phase angle as potentially modifiable nutritional markers are independent risk factors for outcome in allogeneic hematopoietic cell transplantation. *Ann Hematol*. 2013;92(1):111–119. doi:10.1007/s00277-012-1573-4
29. Farias CL, Campos DJ, Bonfin CM, Vilela RM. Phase angle from bia as a prognostic and nutritional status tool for children and adolescents undergoing hematopoietic stem cell transplantation. *Clin Nutr*. 2013;32(3):420–425. doi:10.1016/j.clnu.2012.09.003
30. World Health Organization. Child Growth Standards based on length/height, weight and age. *Acta Paediatr Suppl*. 2006;450:76–85. doi:10.1111/j.1651-2227.2006.tb02378.x
31. World Health Organization. *Growth Reference Data for Children from 5 to 19 Years, 2007*. Geneva: World Health Organization; 2007. Available from: www.who.int/growthref/en/. Accessed May 1, 2024.
32. Li C, Wu X, Feng X, et al. A novel conditioning regimen improves outcomes in beta-thalassemia major patients using unrelated donor peripheral blood stem cell transplantation. *Blood*. 2012;120(19):3875–3881. doi:10.1182/blood-2012-03-417998
33. Anurathapan U, Hongeng S, Pakakasama S, et al. Hematopoietic stem cell transplantation for homozygous beta-thalassemia and beta-thalassemia/hemoglobin e patients from haploidentical donors. *Bone Marrow Transplant*. 2016;51(6):813–818. doi:10.1038/bmt.2016.7
34. Huang C, Qu Y, Liu S, Nie S, Jiang H. Hematopoietic stem cell transplantation for thalassemia major using hla fully-matched and mismatched donor grafts. *Transl Pediatr*. 2021;10(6):1552–1565. doi:10.21037/tp-20-415
35. Auletta JJ, Kou J, Chen M, et al. Real-world data showing trends and outcomes by race and ethnicity in allogeneic hematopoietic cell transplantation: a report from the center for international blood and marrow transplant research. *Transplant Cell Ther*. 2023;29(6):341–346. doi:10.1016/j.jtct.2023.03.007
36. Silva P, Schmit D, Bonfim C, Campos DJ, Rabito EI, Vilela RM. Body composition of Fanconi anemia patients after hematopoietic stem cell transplantation. *Rev Bras Hematol Hemoter*. 2017;39(4):318–324. doi:10.1016/j.bjhh.2017.06.004
37. Liu P, Wang B, Yan X, Cai J, Wang Y. Comprehensive evaluation of nutritional status before and after hematopoietic stem cell transplantation in 170 patients with hematological diseases. *Chin J Cancer Res*. 2016;28(6):626–633. doi:10.21147/j.issn.1000-9604.2016.06.09
38. August DA, Huhmann MB; American Society for Parenteral and Enteral Nutrition. Clinical guidelines: nutrition support therapy during adult anticancer treatment and in hematopoietic cell transplantation. *Jpen J Parenter Enteral Nutr*. 2009;33(5):472–500. doi:10.1177/0148607109341804
39. Arends J, Bachmann P, Baracos V, et al. Espen guidelines on nutrition in cancer patients. *Clin Nutr*. 2017;36(1):11–48. doi:10.1016/j.clnu.2016.07.015
40. Hacker ED, Larson J, Kujath A, Peace D, Rondelli D, Gaston L. Strength training following hematopoietic stem cell transplantation. *Cancer Nurs*. 2011;34(3):238–249. doi:10.1097/NCC.0b013e3181fb3686
41. Liu Y, Martin JH, Yan M. Editorial: therapeutic drug monitoring and clinical toxicology of anti-cancer drugs. *Front Oncol*. 2022;12:1053211. doi:10.3389/fonc.2022.1053211
42. Roder PV, Wu B, Liu Y, Han W. Pancreatic regulation of glucose homeostasis. *Exp Mol Med*. 2016;48(3):e219. doi:10.1038/emm.2016.6
43. Kalyani RR, Corriere M, Ferrucci L. Age-related and disease-related muscle loss: the effect of diabetes, obesity, and other diseases. *Lancet Diabetes Endocrinol*. 2014;2(10):819–829. doi:10.1016/S2213-8587(14)70034-8
44. Ong C, Lee JH, Puthucheary ZA. Narrative review of muscle weakness and wasting in pediatric critical illness. *Pediatr Med*. 2021;4:13. doi:10.21037/pm-20-83
45. Larson-Nath C, Goday P. Malnutrition in children with chronic disease. *Nutr Clin Pract*. 2019;34(3):349–358. doi:10.1002/ncp.10274
46. Richardson G, Dobish R. Chemotherapy induced diarrhea. *J Oncol Pharm Pract*. 2007;13(4):181–198. doi:10.1177/1078155207077335
47. Mccarthy D, Berg A. Weight loss strategies and the risk of skeletal muscle mass loss. *Nutrients*. 2021;13(7). doi:10.3390/nu13072473
48. Zong LL, Zhang X, Jiang SS, et al. Abnormal body composition related to the early clinical adverse outcome after HSCT. *Bone Marrow Transplant*. 2022;57(7):1191–1193. doi:10.1038/s41409-022-01687-6
49. El HW, Vendrely B, Chauveau P, et al. Early evolution of nutritional status and body composition after kidney transplantation. *Am J Kidney Dis*. 2002;40(3):629–637. doi:10.1053/ajkd.2002.34926
50. Li Z, Langhans SA. Transcriptional regulators of na, k-ATPase subunits. *Front Cell Dev Biol*. 2015;3:66. doi:10.3389/fcell.2015.00066
51. Ji W, Liu X, Zheng K, Yang H, Cui J, Li W. Correlation of phase angle with sarcopenia and its diagnostic value in elderly men with cancer. *Nutrition*. 2021;84:111110. doi:10.1016/j.nut.2020.111110
52. Hamada R, Murao M, Asano T, et al. Pre-transplant phase angle as a potential marker for predicting the development of infection after allogeneic hematopoietic stem cell transplantation. *Clin Nutr Espen*. 2023;58:122–127. doi:10.1016/j.clnesp.2023.09.925
53. Mori M, Flores RG, Kamimura H, Yamaura K, Nonaka H. An analytical investigation of body parts more susceptible to aging and composition changes using statistical hypothesis testing. *Healthc Anal*. 2024;5:100284. doi:10.1016/j.health.2023.100284
54. Mohammed J, Smith SR, Burns L, et al. Role of physical therapy before and after hematopoietic stem cell transplantation: white paper report. *Biol Blood Marrow Transplant*. 2019;25(6):e191–e198. doi:10.1016/j.bbmt.2019.01.018
55. Holler E, Greinix H, Zeiser R. Acute graft-versus-host disease. In: Carreras E, Dufour C, Mohty M, Krdger N, editors. *The EBMT Handbook. Hematopoietic Stem Cell Transplantation and Cellular Therapies*. Cham, Switzerland: Springer Open; 2019:323–330.

56. Masetti R, Zama D, Leardini D, et al. The gut microbiome in pediatric patients undergoing allogeneic hematopoietic stem cell transplantation. *Pediatr Blood Cancer*. 2020;67(12):e28711. doi:10.1002/pbc.28711
57. Lazarow H, Nicolo M, Compher C, Kucharczuk CR, Stadtmauer EA, Landsburg DJ. Nutrition-related outcomes for autologous stem cell transplantation patients. *Clin Lymphoma Myeloma Leuk*. 2019;19(7):e393–e398. doi:10.1016/j.clml.2019.04.002
58. Espinoza M, Perelli J, Olmos R, Bertin P, Jara V, Ramirez P. Nutritional assessment as predictor of complications after hematopoietic stem cell transplantation. *Rev Bras Hematol Hemoter*. 2016;38(1):7–14. doi:10.1016/j.bjhh.2015.10.002
59. Kuypers J, Simmance N, Quach H, Hastie K, Kiss N. Nutrition support use and clinical outcomes in patients with multiple myeloma undergoing autologous stem cell transplant. *Support Care Cancer*. 2022;30(11):9341–9350. doi:10.1007/s00520-022-07358-y

Journal of Multidisciplinary Healthcare Dovepress

Publish your work in this journal

The Journal of Multidisciplinary Healthcare is an international, peer-reviewed open-access journal that aims to represent and publish research in healthcare areas delivered by practitioners of different disciplines. This includes studies and reviews conducted by multidisciplinary teams as well as research which evaluates the results or conduct of such teams or healthcare processes in general. The journal covers a very wide range of areas and welcomes submissions from practitioners at all levels, from all over the world. The manuscript management system is completely online and includes a very quick and fair peer-review system. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: https://www.dovepress.com/journal-of-multidisciplinary-healthcare-journal