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Nutritional status and weakness following pediatric hematopoietic cell transplantation

Sandra Bouma[1] | **Mark Peterson**[2] | **Erin Gatza**[1] | **Sung Won Choi**[1]

[1]Department of Pediatrics, Blood and Marrow Transplantation Program, University of Michigan, Ann Arbor, MI, USA

[2]Department of Physical Medicine and Rehabilitation, University of Michigan, Ann Arbor, MI, USA

Correspondence
Sung Won Choi, Department of Pediatrics and Communicable Diseases, Blood and Marrow Transplantation Program, Ann Arbor, MI, USA.
Email: sungchoi@med.umich.edu

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Abstract

Survivorship after pediatric HCT has increased over the past decade. Focus on long-term care and well-being remains critical due to risk of poor dietary habits and exaggerated sedentary behavior, which can lead to muscle weakness, increased risk for obesity, and cardiometabolic disorders. Nutrition and physical activity are key factors in survivorship; however, data are limited. Comprehensive nutritional assessments, including nutrition-focused physical examination, grip strength, and food/activity surveys, were completed in 36 pediatric HCT survivors (aged 2-25 years). Patients were divided into undernutrition, normal-nutrition, and overnutrition categories. Fifty percent of participants were classified as normal nutrition, 22% undernutrition, and 28% overnutrition. Few patients met the U.S. Dietary Guidelines recommended intake for vegetables, fiber, saturated fat, and So FAS. Patients in the undernutrition group demonstrated significantly lower grip strength than those in the normal- and overnutrition groups. When grip strength was normalized to body mass, patients in the overnutrition group had the highest prevalence of weakness. Using NHANES reference data, maximum grip strength and NGS cutoffs were identified that could significantly distinguish the nutrition groups. Comprehensive nutritional assessments and grip strength measurements are feasible, non-invasive, easy to perform, and inform both under- and overnutrition in pediatric HCT survivors.

KEYWORDS
child malnutrition, hematopoietic stem cell transplantation, nutrition assessment, pediatrics

1 | INTRODUCTION

Children who receive HCTs are at high nutritional risk due to comorbidities and complications that are likely to develop before, during, and after transplant.[1,2] Energy imbalances from poor dietary habits and exaggerated sedentary behavior can result in substantial losses of lean body mass, muscle weakness, and functional impairments, placing survivors at risk for malnutrition, obesity, and cardiometabolic disorders.[3–6] While mounting evidence suggests that body habitus, nutritional status, dietary intake, and physical activity throughout the HCT process are key factors in survivorship, there is a paucity of data in pediatric HCT patients.

BMI is the conventional method for determining body habitus, medication dosing, and nutritional status in HCT patients. Obesity, on the basis of BMI at the time of transplant, was associated with higher non-relapse mortality among pediatric and adult allogeneic HCT patients at our institution. Of the 101 pediatric patients included in the study, 32% were determined to be overweight or obese based on their BMI (>85th percentile).[7] Although BMI is a valid metric for stratifying the general population into different risk categories, it does not discriminate adipose tissue and muscle, nor does it allow identification

Abbreviations: BMI, body mass index; CONSEPT, clinical outcomes, nutrition, exercise, and psychosocial factors in pediatric hematopoietic cell transplant; GVHD, graft-versus-host disease; HCT, hematopoietic cell transplant; MVPA, moderate-to-vigorous physical activity; NGS, normalized grip strength; NHANES, National Health and Nutrition Examination Survey.So FAS, solid fat and added sugars.

of non-obese individuals with excess body fat.[8,9] These shortcomings may be especially relevant among pediatric patients after HCT, as shorter stature and stunting are documented latent outcomes.[4,6]

Alternative anthropometric and body composition measures, along with nutrition-focused physical examination (ie, assessment of fat and muscle wasting) and simple functional assessments, can more accurately determine nutritional status (under-, normal-, and overnutrition) and muscle weakness in children.[10–16] Grip strength is a functional assessment with excellent criterion validity and intra- and inter-rater reliability[17–21] and is correlated with nutritional status in adults.[22–25] In children and adolescents, grip strength is feasible to measure[26–30] and is highly correlated with total muscle strength.[31] NGS (grip strength/body mass) helps to identify weakness in overweight and obese adolescents and has been associated with cardiometabolic disorders.[15] New guidelines for diagnosing adult malnutrition (undernutrition) include both grip strength measurement and nutrition-focused physical examination.[32] The pediatric malnutrition indicators do not yet include grip strength or nutrition-focused physical examination, partly due to a lack of pediatric reference data at the time of development.[10,14] However, reference charts for grip strength and NGS using NHANES data from 2011 to 2012 (aged 6-80 years, by gender) recently became available, allowing standardized measure of grip strength in pediatric patients.

To date, using these alternative measures as part of a comprehensive nutritional assessment has not been reported in children undergoing HCT. Thus, we aimed to test the feasibility of incorporating nutrition-focused physical examination and measures of grip strength and NGS as part of a comprehensive nutritional assessment in pediatric HCT patients.

2 | METHODS

An exploratory, quality improvement investigation was conducted in survivors of pediatric HCT (aged 2-25 years). Patients were eligible to participate if they came to at least one regularly scheduled visit at a single university-affiliated outpatient clinic during a study period of 30 consecutive clinic days. Participants provided written consent/assent for this feasibility study that was approved by our institutional review board in compliance with institutional regulations for the protection of human research participants. Comprehensive nutrition assessments were performed by a single registered dietitian with expertise in diagnosing adult and pediatric malnutrition, who also received advanced training on performing nutrition-focused physical examination and measuring grip strength. http://www.eatrightpro.org/resource/career/professional-development/face-to-face-learning/nfpe-workshop. Last accessed June 23, 2016.[33] Nutrition assessment included the following: collecting anthropometric data (height, weight, mid-upper arm circumference), obtaining medical and nutritional history, performing a nutrition-focused physical examination, measuring grip strength, and having participants fill out an online food-frequency questionnaire (BLOCK by NutritionQuest) http://www.nutritionquest.org/.[33] If participants were too young (typically <10 years old), caregivers filled out the BLOCK surveys on their behalf. Using BMI, nutrition-focused physical examination and age-appropriate adult or pediatric characteristics of undernutrition, patients were divided into three nutritional status categories: undernutrition, normal nutrition, and overnutrition.[34] Medical and nutrition history was obtained through the medical chart and by interview with the participant and their family, if present at the appointment. A head-to-toe nutrition-focused physical examination was performed by the registered dietitian who was trained using previously described techniques.[12,35,36] Nutrition-focused physical examination was performed prior to measuring grip strength so as to minimize examination bias.

Grip strength was measured using a calibrated Jaymar Plus digital hand dynamometer (Patterson Medical, Warrenville, IL, USA), according to the American Society of Hand therapists measurement protocol, which has high intratest and intertest reliability.[17] Participants were encouraged to squeeze harder until the number on the digital readout stopped rising.[37] The average of the three measurements (kg) for each hand was compared to the reference data provided with the dynamometer.[38,39] The highest measurement from either hand was used to determine the age- and gender-specific percentile for maximum grip strength and NGS (maximum grip strength/body mass) from the Peterson NHANES charts as per the NHANES protocol.[33] If a child was between an age and percentile category, the closest age or percentile category was selected. If the age or grip strength value was exactly midway between an age or percentile category, the lower category was selected. Because age and gender are the largest determinants of muscle strength,[23,25] age- and gender-specific percentiles were calculated from NHANES reference data to allow comparisons across age groups. Cutoffs of <25th percentile and <10th percentile were used to assess significant differences between the nutritional status groups. The conventional method of determining undernutrition using a cutoff of more than 2 SD below the mean for age and gender per dynamometer manufacturer reference data was also used.[40]

Participants or their parents filled out online, validated food and activity screeners (BLOCK by NutritionQuest)[41,42] using a laptop computer before the end of their clinic visit. Children, aged 2-17, used the BLOCK Kids food and activity screener, which is designed to assess usual dietary intake over the past 7 days. Young adults (18-25 years of age) used the BLOCK Alive! food and physical activity screener, which is designed to assess usual dietary intake over the past 3 months. The screeners assessed intake of fruit and fruit juices, vegetables, potatoes, whole grains, meat/poultry/fish, dairy, legumes, saturated fat, added sugars, glycemic load, and glycemic index. The screeners also estimate daily calories (kcals), protein and sugary beverage (both kcal and frequency) intake based on patient-reported intake. The physical activity portion of the BLOCK Kids screener queries frequency and duration of activities and the amount of screen time (television, video games, computer) per day, over the past week. The adult screener includes the frequency and duration of job-related, daily life, and leisure activities during the past 3 months. The participants were provided with a summary printout of the online screener results. Participant data were downloaded from the password-protected NutritionQuest research portal for analysis.

Undernutrition for young adult participants (18-25 years of age) was determined using the American Society of Parenteral and Enteral Nutrition (A.S.P.E.N.)/Academy of Nutrition and Dietetics (Academy) workgroup's adult characteristics of malnutrition, as previously described.[32] Participants who were 2-17 years old were assessed for undernutrition using MTool™, the University of Michigan Health System's pediatric malnutrition diagnostic tool.[11] MTool™ is based on the evidence-informed, consensus-derived definition of pediatric malnutrition endorsed by A.S.P.E.N., the Academy and the American Academy of Pediatrics.[14] MTool™ assesses *z-scores* for BMI/weight-for-length ratio, weight, height and mid-upper arm circumference, weight loss, growth velocity, dietary intake, and illness-related metabolic stress. The indicators used with MTool™ are closely aligned with the indicators of pediatric malnutrition published in a consensus statement of the A.S.P.E.N./Academy pediatric malnutrition workgroup,[10] but MTool™ additionally includes nutrition-focused physical examination, and markers for diagnosing overweight and obesity associated with stunting.[11] Overnutrition was defined in young adults (aged 18-25 years) as BMI≥25 kg/m^2 and in children (aged 2-17 years) as a *z-score*≥1 along with evidence of subcutaneous body fat on physical examination.[43]

All statistical analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC, USA). Differences across nutritional status categories were tested using two-sample *t* tests and chi-squared tests for continuous and categorical variables, respectively. A *P* value <.05 was considered statistically significant.

3 | RESULTS

Thirty-eight patients were approached to participate in the comprehensive nutrition assessments, and all agreed to participate. Two could not complete the assessment, and one patient could not complete the food survey due to time constraints (ie, having to get to another medical appointment). In total, 36 patients were included in our study. Patient and transplant characteristics are reported in Table 1. Twenty-four (66.7%) participants were male, 12 (33.3%) were female. Participants had a median age of 16 years with a median time since transplant of 636 days. Seventy-five percent (n=27) of participants were white and non-Hispanic. The majority of patients received an HLA-matched HCT from a related (n=10) or unrelated (n=20) donor after full-intensity conditioning (n=22). Sixty-one percent of participants received a HCT as treatment for a malignant diagnosis; 39% (n=14) had a diagnosis that was non-malignant. Seventeen participants (47.2%) had a history of acute GVHD, 21 had a history of chronic GVHD, and 9 (25%) never had GVHD. Twenty participants (55.6%) had active GVHD, requiring therapy with corticosteroids, at the time of this study. No statistically significant differences in age, race, malignant or non-malignant diagnosis, HCT donor or conditioning, or GVHD were detected between male and female participants (*P*>.05).

The weight status, nutritional status, and dietary intake for study participants are summarized in Table 1. Only two male participants were underweight. Fifty-six percent of the group were normal weight (n=20); however, more female than male participants were normal weight (83.3% vs 41.7%; *P*<.05). Conversely, more male than female participants were overweight or obese (50.0% vs 16.7%; *P*<.05). Correspondingly, significantly more male than female participants were categorized as overnutrition (37.5% vs 8.3%; *P*<.05). No significant differences between male and female participants were observed in the normal-nutrition and undernutrition categories. In all, 50% of participants were categorized as normal nutrition, 28% as overnutrition, and 22% as undernutrition.

Overall, dietary intake was below the 2015 U.S. Dietary Guideline's recommended amounts. Only one-quarter of participants met the 2015 U.S. Dietary Guideline's recommended intake for fruit (n=9; 25.7%). An even smaller percentage of participants met the recommended intake for vegetables (11.4%), fiber (2.9%), saturated fat (8.6%), and solid fat and added sugars (8.6%). However, female participants were more likely than male to meet the recommended intake for fruit (45.5% vs 16.7%), vegetables (36.4% vs 0.0%), and saturated fat intake (27.3% vs 0.0%). Less than half of the cross-sectional cohort ate as well as 50% of those in the U.S. population of the same age and gender as reported in the National Health And Nutrition Survey of 2007–2011. http://epi.grants.cancer.gov/diet/usualintakes/pop/2007-10/index.html. Last accessed June 23. 2016.

Participants' grip strength differed significantly by nutrition status (Table 2). Grip strength among individuals in the undernutrition group was significantly lower than the other two groups, with 75% of the undernutrition group having a grip strength <25th percentile for age/gender compared to a U.S. reference population.[33] Using recently published NHANES reference data, a maximum grip strength cutoff of less than the 10th percentile for age/gender significantly distinguished the undernutrition group from the normal- and overnutrition groups (62.5% vs 26.7% and 25.0%, respectively; *P*<.05). This difference was also significant using the conventional cutoff point of >2 standard deviations (SD) below the mean of age- and gender-matched dynamometer reference data.

When grip strength was normalized to body mass (maximum grip strength/body mass; NGS), patients in both the undernutrition and overnutrition groups demonstrated weakness compared to patients in the normal-nutrition group (*P*<.05). A NGS cutoff of less than the 25th percentile for age/gender significantly differentiated the overnutrition group from normal-nutrition group (62.5% vs 13.3%, *P*<.05).

Finally, participants in the normal-nutrition group spent more time engaged in physical activity, while those in the undernutrition group spent significantly more hours of the day viewing a screen.

4 | DISCUSSION

Health maintenance behaviors, such as eating a nutrient-dense diet and participating in physical activity, have not traditionally been emphasized during pediatric HCT. In this study, HCT survivors consumed a diet that was well below recommended intakes and were at risk for significant muscle weakness. Less than 12% of our patients

TABLE 1 Weight, nutritional, and transplant characteristics of a cross-sectional sample of pediatric HCT survivors

Characteristic	Group n=36	Male n=24	Female n=12
Age, years[†]	16.0 (2-25)	14.5 (2-25)	19.0 (2-23)
Time post-transplant, days[†]	636.0 (84.0-3217.0)	636.0 (102.0-3217.0)	636.0 (84.0-1957.0)
	n (%)	n (%)	n (%)
Race			
Non-Hispanic white	27 (75.0)	20 (83.3)	7 (58.3)
Non-Hispanic black	5 (13.9)	2 (8.3)	3 (25.0)
Hispanic or Mexican American	2 (5.6)	1 (4.2)	1 (8.3)
Other race	2 (5.6)	1 (4.2)	1 (8.3)
Diagnosis			
Malignant	22 (61.1)	16 (66.7)	6 (50.0)
Acute lymphoblastic leukemia	13 (36.1)	10 (41.7)	3 (25.0)
Acute myelogenous leukemia	4 (11.1)	2 (8.3)	2 (16.6)
Myelodysplastic syndrome	4 (11.1)	3 (12.5)	1 (8.3)
Juvenile myelomonocytic leukemia	1 (2.8)	1 (4.2)	0 (0.0)
Non-malignant	14 (39)	8 (33.3)	6 (50.0)
XLP1	4 (11.1)	4 (16.7)	0 (0.0)
Sickle cell	3 (8.3)	1 (4.2)	2 (16.6)
Hemophagocytic lymphohistiocytosis	2 (5.6)	1 (4.2)	1 (8.3)
Hypomorphic artemis mutation	1 (2.8)	0 (0.0)	1 (8.3)
Idiopathic severe aplastic anemia	1 (2.8)	0 (0.0)	1 (8.3)
Paroxysmal nocturnal hemoglobinuria	1 (2.8)	1 (4.2)	0 (0.0)
SCIDS	1 (2.8)	0 (0.0)	1 (8.3)
Shwachman-Diamond syndrome	1 (2.8)	1 (4.2)	0 (0.0)
Donor			
Matched related	10 (27.8)	7 (29.2)	3 (25.0)
Matched unrelated	20 (55.6)	13 (54.2)	7 (58.1)
Mismatched related	0 (0.0)	0 (0.0)	0 (0.0)
Mismatched unrelated	6 (16.7)	4 (16.7)	2 (16.6)
Conditioning			
Full	22 (61.1)	16 (66.7)	6 (50.0)
Reduced	14 (38.9)	8 (33.3)	6 (50.0)
GVHD			
History of acute GVHD	17 (47.2)	10 (41.7)	7 (58.3)
History of chronic GVHD	21 (58.3)	14 (58)	7 (58.3)
Active GVHD at assessment	20 (55.6)	13 (54.2)	7 (58.3)
Never any GVHD	9 (25.0)	7 (29.2)	2 (16.7)
Weight status			
[a]Underweight	2 (5.6)	2 (8.3)	0 (0.0)
[b]Normal weight	20 (55.6)	10 (41.7)	10 (83.3)*
[c]Overweight or obese	14 (38.9)	12 (50.0)	2 (16.7)*
Nutritional status			
[d]Undernutrition	8 (22.2)	5 (20.8)	3 (25.0)
[e]Normal nutrition	18 (50.0)	10 (41.7)	8 (66.7)
[f]Overnutrition	10 (27.8)	9 (37.5)	1 (8.3)*
Dietary intake[g]			
[h]Met recommendations for:			

(Continues)

TABLE 1 (Continued)

Characteristic	Group n=36	Male n=24	Female n=12
Fruit intake	9 (25.7)	4 (16.7)	5 (45.5)*
Vegetable intake	4 (11.4)	0 (0.0)	4 (36.4)*
Fiber intake	1 (2.9)	1 (4.2)	0 (0.0)
Saturated fat intake	3 (8.6)	0 (0.0)	3 (27.3)*
Solid fat and added sugar intake	3 (8.6)	1 (4.2)	2 (18.2)
[i]>50th percentile of the U.S. population for:			
Fruit intake	17 (48.6)	9 (37.5)	8 (72.7)
Vegetable intake	12 (34.3)	6 (25.0)	6 (54.6)
Fiber intake	10 (28.6)	5 (20.8)	5 (45.5)
[i]<50th percentile of the U.S. population for:			
Saturated fat intake	4 (11.4)	0 (0.0)	4 (36.4)*
Solid fat and added sugar intake	16 (45.7)	11 (45.8)	5 (45.5)

*Significant difference between males and females (*P*<.05).
[†]Median (range).
[a]BMI<18.5 kg/m^2 (≥18 y old) or BMI z-score< -1 (<18 y old).
[b]BMI 18.5-24.9 kg/m^2 (≥18 y old) or BMI z-score −0.99 to +0.99 (<18 y old).
[c]BMI≥25 kg/m^2 (≥18 y old) or BMI z-score≥1 (<18 y old).
[d]Per the previously described adult undernutrition characteristics[14] and pediatric undernutrition indicators.[23,27]
[e]No undernutrition or overnutrition.
[f]BMI=BMI≥25 kg/m^2 (≥ 18 y old) or BMI z-score ≥ 1 (<18 y old) PLUS no PCM, no evidence of strong, lean body habitus on physical examination and no report of engaging in intense physical activity training.
[g]n=35.
[h]U.S. Department of Health and Human Services and U.S. Department of Agriculture. *2015 – 2020 Dietary Guidelines for Americans*, 8[th] Edition, December 2015. Available at http://health.gov/dietaryguidelines/2015/guidelines/. Accessed June 23, 2016.
[i]Usual Dietary Intakes: Food Intakes, U.S. Population, 2007-2010. Epidemiology Research Program Web site. National Cancer Institute. http://epi.grants.cancer.gov/diet/usualintakes/pop/2007-10/index.html Updated May 20, 2015. Accessed June 23, 2016.

TABLE 2 Muscle strength and physical activity stratified for nutritional status in patients aged > 6 y

	Undernutrition *n=8*	Normal nutrition *n=15*	Overnutrition *n=8*
Grip strength, kg	20.71±14.74	33.08±14.74*	33.99±14.04[†]
[a]Grip strength<25th percentile (for age & sex), %	75.0	40.0	37.5
[a]Grip strength<10th percentile (for age & sex), %	62.5	26.7*	25.0[†]
NGS	0.47±0.17	0.56±0.16*[,§]	0.40±0.14
[a]NGS<25th percentile (for age and sex), %	37.5	13.3[§]	62.5
[a]NGS<10th percentile (for age and sex), %	25	6.7[§]	62.5
Grip strength, right hand, >2 SD below the norm, %	87.5	6.7*	12.5[†]
Grip strength, left hand, >2 SD below the norm, %	50.0	13.3*	12.5[†]
Moderate-to-vigorous physical activity (MVPA), min	8.62±9.20	88.22±69.66*[,§]	39.10±30.82
[b]Television/screen viewing time, hours	5.67±0.58*	4.00±1.00	4.40±1.52

*Significant difference between undernutrition and normal-nutrition groups (*P*<.05).
[†]Significant difference between undernutrition and overnutrition groups (*P*<.05).
[§]Significant differences between normal-nutrition and overnutrition groups (*P*<.05).
[a]Percentiles from NHANES 2011-2012 population-level reference data, as reported by Peterson and Krishnan, 2015.
[b]Among children/adolescents aged <18 y (n=17).

met the 2015 U.S. Dietary Guidelines for key dietary components. Males and females had significant differences in intake for a few key nutrients; however, there were no statistically significant differences in dietary intake across nutritional status (data not shown). To discern these differences, a larger, sufficiently powered study using the BLOCK screeners or perhaps using the "gold standard" dietary intake method, that is, a three- to five-day day 24-hour recall, would be required (e.g., Automated Self-Administered 24-hour recall; ASA24-2016, National Cancer Institute).

The nutrition-focused physical examination, which includes a hands-on assessment of muscle and fat wasting, can be used to detect muscle tone and presence of body fat. Using nutrition-focused physical examination criteria, three patients that had been categorized as "overweight," by BMI or BMI *z-score*, were recategorized into the normal-nutrition group due to having a lean, muscular build on physical examination, plus reporting regular participation in resistance training and physical activity. Of interest, another patient in the normal-nutrition group, who was regaining weight after experiencing undernutrition, demonstrated continued mild-to-moderate muscle wasting, but also had early signs of fat accumulation. This patient also had low handgrip strength measurements, leading us to suspect normal weight obesity.

Measuring grip strength with a hand dynamometer is well received by individuals and takes less than 5 minutes to perform.[16,23] Grip strength has excellent criterion validity and intra- and inter-rater reliability.[17,18,20,21] This cross-sectional study showed that grip strength correlated with undernutrition, consistent with reports in the adult literature.[22–25] Because grip strength can vary by age and gender, reference tables that use percentiles are helpful in the clinical setting. Using a maximum grip strength cutoff of <10th percentile for age and gender may help detect patients who are undernourished. Even though a maximum strength cutoff of <10th percentile and the conventional method (average grip strength >2SD below the mean reference data provided with the dynamometer) were both statistically significant, percentiles may detect subtler changes in grip strength. Moreover, the NHANES data were drawn from a larger, more contemporary data set (7119 individuals, 2011-2012).[33] The reference data provided with the Jaymar Plus digital dynamometer were from a smaller, older sample (1109 individuals, mid-1980s).[38,39] In our study, the only patient in the undernutrition group who did not demonstrate weakness (<10th percentile for grip strength) had a grip strength in the 75th percentile and a NGS in the 90th percentile, leading us to suspect that perhaps he was not as malnourished as the pediatric malnutrition indicators suggested. A future study using a larger sample size could test whether a maximum grip strength of less than the 10th percentile for age/gender may be an indicator of pediatric undernutrition.

To our knowledge, this is the first study to compare NGS with nutritional status. We found that NGS distinguished between the normal- and overnutrition group, suggesting that NGS may be useful in determining weakness in overweight and obese pediatric HCT patients. NGS has been shown to help detect patients who are at risk of cardiometabolic diseases.[15] In our study, a NGS cutoff of 25th percentile for age and gender differentiated the overnutrition group from the normal-nutrition group.

Validated food-frequency questionnaires, such as Block by NutritionQuest, take little time to administer and were well received by our patients. Caregivers stated they appreciated having individualized nutrition education based on the results of the food-frequency questionnaires. While food-frequency questionnaires are not designed to compute exact calorie and protein information, they can be useful for determining dietary quality and to elucidate changes in an individual's dietary intake.

This study, although limited by the descriptive, cross-sectional design, showed the feasibility of using handgrip dynamometry, nutrition-focused physical examination, and online food and activity surveys as part of a comprehensive nutritional assessment. Future research is needed to determine which indicators are most correlated with nutritional status and weakness, and the temporal sequence of these changes throughout the HCT process. To that end, our institution is conducting a longitudinal study looking at clinical outcomes, nutrition, exercise and psychosocial factors in pediatric hematopoietic cell transplant (CONSEPT study, registered at ClinicalTrials.gov, NCT02734797). A larger sample size could potentially validate which grip strength and NGS cutoff values are best at detecting malnutrition and cardiometabolic risk in pediatric HCT patients. These data can be useful in designing individualized, targeted interventions to help prevent muscle loss and fat accumulation. Clinical trials are needed to determine whether health-enhancing behaviors can prevent malnutrition and weakness and improve clinical outcomes during survivorship.

CONFLICT OF INTEREST

None of the authors have any conflict of interests.

AUTHORS' CONTRIBUTIONS

Sandra Bouma: Enrolled participants into the study, performed all clinical assessments (including nutrition-focused physical examination, grip strength), administered food and activity online surveys, and managed participant data; Mark Peterson: Performed all statistical analyses; Sandra Bouma, Mark Peterson, Erin Gatza, and Sung Won Choi: Contributed to research study design, the analysis and interpretation of data, and to drafting, critical review, revising, and approval of the submitted version of the manuscript.

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