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A multi-center, randomized, controlled trial of parenteral nutrition titrated to resting energy expenditure in children undergoing hematopoietic stem cell transplantation (“PNTREE”): Rationale and design

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Abstract

Background—Children undergoing hematopoietic stem cell transplantation (HSCT) frequently require prolonged courses of parenteral nutrition (PN) as a consequence of gastrointestinal dysfunction related to preparative chemotherapy and radiation. PN has been associated with shorter engraftment time and decreased mortality during HSCT, however, it is also linked with complications, including infections, liver disease, and metabolic disturbances. Some of these complications may be a result of providing PN in excess of nutrient requirements. We previously described significant reductions in resting energy expenditure (REE), as measured by indirect calorimetry, over the course of HSCT. We also documented a decline in mid-arm muscle area, suggesting depletion of muscle mass, while triceps skinfold, a marker of fat stores, was unchanged. These results suggested the need for further study of energy expenditure, body composition and nutritional intake in this group of high risk patients.

Design and hypothesis—We hypothesize that changes in body composition affect REE during HSCT, and that standard nutritional support may lead to overfeeding. We are performing a randomized controlled trial of parenteral nutrition among children undergoing allogeneic HSCT. Subjects are randomized to receive PN designed to provide 100% of measured REE, or standard PN, i.e., 140% of estimated energy expenditure. The primary outcome variable is change in percent body fat. Secondary outcomes include glycemic control and frequency of infections, changes in REE and body composition.

Conclusion—This study will provide unique and comprehensive nutritional data and its results will guide nutritional therapy for children undergoing HSCT and possibly other catabolic patients.

Keywords

Hematopoietic stem cell transplantation; Parenteral nutrition; Body composition; Energy expenditure

1. Introduction

The nutritional management of children undergoing hematopoietic stem cell transplantation (HSCT) is largely based on empirical estimates of energy and nutrient needs during a catabolic illness. High dose chemotherapy and total body irradiation as conditioning for HSCT frequently causes painful mucositis and gastrointestinal sequelae that can reduce oral intake for days to weeks [1]. Parenteral nutrition (PN) is often utilized during HSCT since it has been associated with faster engraftment and improved survival [2,3]. Despite the recognition that the cost and complication rates of PN can be substantial, few clinical trials have been performed since studies in the 1980s suggested the efficacy of PN after HSCT. Moreover, well-known complications of PN, including infections, hepatotoxicity, suppression of oral intake, and metabolic abnormalities [4], are also common among HSCT patients.

Providing optimal PN support while minimizing potential risks associated with overfeeding [5] or underfeeding [6] has been difficult without a clearer understanding of the energy and nutrient needs of children undergoing HSCT. Our study employs a unique and detailed approach to study energy requirements in these medically complex patients, the results of which will guide clinicians in the optimal nutritional management of HSCT and potentially other highly catabolic pediatric patients.

2. Scientific rationale

2.1. Parenteral nutrition and HSCT

High dose chemotherapeutic regimens and total body irradiation, used in preparation for HSCT, are known to cause severe mucositis and enteritis that interfere with oral intake and gastrointestinal absorption of nutrients. In a study of 22 patients undergoing HSCT and receiving prophylactic PN, marrow engraftment occurred significantly sooner, compared to age- and diagnosis-matched historical controls who received varying amounts of intravenous calories in response to severe wasting or prolonged fasting. There was no significant difference in other clinical outcomes including survival [2]. In a subsequent prospective trial, patients were randomized to receive either PN or a 5% dextrose solution (containing electrolytes, minerals, trace elements, and vitamins) for one week prior to and four weeks following HSCT. Although engraftment was not different between the two groups, overall survival, time to relapse, and disease-free survival were significantly better in the group receiving PN [3]. These studies were instrumental in making PN an integral part of supportive care to adults and children undergoing HSCT.

Since the publication of these studies in the mid-1980s, however, few studies have evaluated the role of PN support in HSCT patients. Some reports have suggested that avoiding parenteral overfeeding might be beneficial during HSCT [7,8], as has been documented in other acutely ill adults [9]. However, substantial confounding variables, including unknown oral dietary intake and altered lipid intake, as well as suboptimal study design, limit the interpretation of these findings, particularly in the pediatric setting.

2.2. Energy expenditure in HSCT

Total energy expenditure (TEE) is comprised of basal energy expenditure (BEE) plus energy required for activity, growth, obligatory losses in urine and stool, and digestion and absorption of food. Resting energy expenditure (REE) is a clinically measurable approximation of BEE. Since lean body mass is the major determinant of BEE, the largest component of TEE, alterations in REE are closely linked with energy imbalance, weight change, and body composition changes. Loss of lean body mass is associated with reduced muscle strength, decreased immune function, decreased pulmonary function, increased

disability, and death [10–14]. Elevations in body fat mass [15–18] accompanied by reductions in lean body mass [19] have been reported in several studies of cancer survivors. Changes in body composition and REE in children undergoing HSCT may impact clinical and nutritional outcomes but few studies have examined these outcomes. Previous cancer treatment, underlying nutritional health, and regimen related toxicity contribute to changes in energy expenditure. Wide variability in REE has been reported in adults and children during HSCT, including measurements both higher and lower than that estimated by standardized equations [20–23]. As a consequence, energy expenditure during HSCT remains poorly described.

In a previous study, we performed longitudinal indirect calorimetry measurements, dietary intake analysis, and arm anthropometric measurements in 25 children undergoing HSCT [24]. At baseline, mean % predicted REE was 96%, but by week 3 REE had declined to 80% predicted ($p = 0.002$). In addition, there was a strong correlation between mid-arm muscle area, a surrogate marker of lean body mass, and baseline REE ($r = 0.82$, $p < .001$). At hospital discharge, a significant decline in mid-arm muscle area, with no change in triceps skinfold, indicated preservation of fat stores with muscle mass depletion. These results suggest that REE changes in children throughout the transplant course, and that reductions in REE may correspond with reductions in lean body mass. These changes may predispose to complications associated with overfeeding, such as increased weight gain and fat gain, hyperglycemia [25–27], suppression of oral intake and metabolic abnormalities, if standard amounts of PN are used. Our trial will further examine REE in children, with more detailed measurements of body composition and nutritional outcomes.

3. Study design

3.1. Hypotheses

We hypothesize that children receiving PN titrated to measured REE will have a smaller change in percent body fat than those provided PN using standard estimation equations. Secondly, we hypothesize that children receiving titrated PN will have improved glycemic control and fewer infections. We expect that children undergoing HSCT have alterations in measured REE compared with published norms, and that these changes will correlate with changes in body composition. We anticipate that children receiving titrated PN will have earlier resumption of oral intake.

3.2. Specific aims

1. To compare the effects of standard vs. titrated nutritional support in pediatric HSCT patients on percent body fat, as measured by DXA.
2. To compare the effects of standard vs. titrated nutritional support in pediatric HSCT patients on glycemic control, insulin resistance, and incidence of infections.
3. To measure serial changes in REE over the course of HSCT with indirect calorimetry.
4. To correlate anticipated changes in REE with changes in body composition.
5. To measure resumption of oral dietary intake after HSCT.

3.3. Description of study outcomes

Accurate provision of parenteral energy may reduce complications related to underfeeding (e.g., immunosuppression, hypoalbuminemia, and weight and bone loss) [5] or overfeeding (e.g., hepatic steatosis, hyperglycemia, and overweight) [6]. In our previous study, we observed a significant and substantial reduction in REE [24], likely related to lean body

mass depletion with chemotherapy and radiation in preparation for HSCT. If titrating energy intake to measured REE leads to less overfeeding, more optimal body composition will result. We will judge this based on differences in percent body fat as measured by dual energy X-ray absorptiometry (DXA). Differences in percent body fat, as measured by DXA, between the two groups will be compared at baseline, day + 30, and day + 100.

Insulin resistance, defined by HOMA (homeostasis model assessment) [28], will be compared at each time point between the two experimental groups. The HOMA model as a measure of insulin resistance is convenient, safe and feasible among sick, HSCT patients.

Measured resting energy expenditure will be compared at each time point to predicted norms [29]. Changes in percent predicted REE between the two groups will be calculated, since percent predicted takes into account weight, height and sex-based standards.

Resumption of oral intake will be measured as elapsed time in days until oral intake exceeds 50% energy requirements for age. Previous studies have linked prolonged PN use with a delay in resuming oral nutrition [30]. We therefore hypothesize that the experimental group may have a more rapid resumption of oral intake.

3.4. Schema

We are carrying out a randomized, double-blinded controlled clinical trial of two approaches to provide parenteral nutrition to pediatric HSCT patients: 1) the standard of care in which energy intake is provided in the amount of 130–150% of estimated BEE (as calculated by standard reference equations [29]) and 2) an experimental protocol in which energy intake is titrated to match resting energy expenditure (as measured by indirect calorimetry) (Fig. 1). Based on the likelihood of steroid exposure in children undergoing unrelated donor HSCT and the known influences of steroid use on body composition [31,32], we will stratify with respect to the type of donor (unrelated vs. related). Stratification will help distribute steroid exposures more equally between the two study arms.

3.5. Patient selection

Children being admitted for allogeneic HSCT at Children's Hospital Boston, UCLA Mattel Children's Hospital, and Texas Children's Hospital with the following inclusion criteria are enrolled: 1) First myeloablative allogeneic HSCT using either TBI (1400 cGy) or busulfan in addition to other chemotherapeutic agents, 2) graft versus host disease (GVHD) prophylaxis with a calcineurin-inhibitor and methotrexate+/-corticosteroids, 3) 6/6 HLA-matched, related or unrelated HSCT donor, 4) Age 6 years and older.

Children with the following conditions are excluded from participation: 1) Age less than age 6 years, or otherwise unable to comply with study procedures, 2) Underweight (body mass index (BMI) z -score < -2 for age and sex) at baseline, 3) Overweight (BMI z -score > 2 for age and sex) at baseline, 4) Unable or unwilling to return for day+100 studies, 5) Previous stem cell transplant, 6) Unmatched HSCT donor, 7) Current treatment for hypo- or hyperthyroidism, 8) Current insulin-dependent diabetes, 9) Current use of parenteral nutrition, 10) Allergy to egg or soy products, 11) Other contraindication to parenteral nutrition at baseline.

3.6. Description of study treatments

3.6.1. Standard of care—All enrolled subjects receive oncologic and medical care per institutional HSCT standard guidelines and protocols. Outpatient research visits take place in the General Clinical Research Center (GCRC) or Clinical and Translational Study Unit (CTSU) of each site at baseline, day 30, and day 100. The day 65 data are collected during a

routine clinic visit. While subjects are inpatients, research assessments take place at the bedside whenever feasible and consistent with the data collection schedule (Table 1). Medication guidelines during the first month after transplant include the use of oral non-absorbable antibiotics for gut decontamination, ursodeoxycholic acid and Vitamin E for veno-occlusive disease prophylaxis [33], and, in some centers, leucovorin calcium for recovery from methotrexate, if used for GVHD prophylaxis. Central venous catheters are used for administration of intravenous (IV) fluid and PN. Parenteral nutrition is initiated when and if oral energy intake declines to less than baseline REE measurement for more than 3–5 days, but no earlier than the day of transplant. Intravenous fluid from PN provide approximately 50% of calculated maintenance fluid requirements, with the remainder of fluid intake is provided from medications, blood products, oral intake, and other IV fluids as needed. Parenteral amino acids (20% ProSol™, Baxter International, Deerfield IL) are prescribed at 1.5 to 2.0 g/kg/day for 6–13 year old children and 1.0 to 1.5 g/kg/day for children older than 13 years [34]. Intravenous lipids (Intralipid® 20%, Baxter International, Deerfield IL) provide approximately 30–40% of total parenteral energy intake. Standard dosing of pediatric (age 6–11 years) and adult (age 11 and over) intravenous multivitamins are supplied. A combination pediatric trace mineral solution, including zinc, copper, manganese, and chromium, is provided daily at standard doses. Electrolytes and minerals are monitored and adjusted daily by HSCT physicians according to laboratory results and metabolic impression. The macronutrient composition of PN is titrated to match the total protein and energy goals of the group assignment based on the previous day's (calculated twice weekly) oral protexin and energy intake. PN is discontinued when oral energy intake reaches 50% of the measured REE, or at the time of preparation for hospital discharge, whichever comes first.

3.6.2. Blinding—The patients, parents, physicians and nurses are blinded to treatment allocation, i.e., they are not informed of the energy composition of the parenteral nutrition. The pharmacist prepares PN solutions and remains unblinded to treatment assignments, but will not otherwise be directly involved in the conduct of the study. A single member of the clinical care team at each site, a clinical dietitian or clinical pharmacist, is also unblinded. This clinician is responsible for calculating each patient's daily regimen and writes fluid and macronutrient orders to the pharmacy, using either the standard method or the experimental method as fitting to the subject's assignment. The ordering clinician is responsible for clinical care, but no study measurements. The research coordinator is responsible for collection of data, study measurements, and storage of data, but no inpatient clinical care. We are therefore confident that neither the intervention nor the data will be compromised by the single clinician's unblinded status.

3.6.3. Randomization—A serially numbered sequence of treatment assignments in randomly permuted blocks of 2, 4, and 6 is generated for each site and kept in locked file cabinets by the Clinical Research Program (CRP) of Children's Hospital Boston, the data coordinating site. Each list is divided into two balanced strata, one for unrelated donors and one for related donors. A separate enrollment log for each site, similarly numbered but without treatment assignments, is maintained by the study coordinator. Upon enrollment, the unblinded clinician enters the patient into the randomization log, thus committing the patient to that position in the randomization sequence. Only the unblinded clinician and pharmacy staff is informed of the patient's treatment assignment.

3.6.4. Experimental protocol—All subjects continue to receive standard of care nutritional support, as detailed above, but the energy goal of each group differs. The goal for patients in the standard arm is 140% of estimated basal energy expenditure, calculated using the Schofield method [29]. For patients in the experimental arm, the parenteral energy

prescription is adjusted so that the energy goal is equal to the 100% of the most recent measured REE. This is accomplished by alterations in dextrose and lipid; total protein goals in both groups are kept constant.

3.6.5. Data collection methods, assessments, and schedule—Measurements are performed at specified intervals (Table 1).

3.6.5.1. Demographic and clinical assessment: Standardized demographic and clinical assessments of all study participants are performed via medical record review concomitant with the hospitalization and selected clinic visits. Data include medical record number, underlying diagnosis, type of donor, date of transplant, date of birth, gender, pubertal status, conditioning and prophylactic medication regimen, routine laboratory tests (serum chemistries, white blood cell counts), medications used. Because of their known influence on body composition and glycemic control, the use of corticosteroids (dose, route, and duration) is documented throughout the study intervention period. Presumed and confirmed infections [35] from blood, urine, and cerebrospinal fluid are recorded during each subject's hospitalization. Stool volume and quality, when available, are recorded daily while subjects are hospitalized. Severity of oral mucositis and mouth pain are assessed at baseline and twice weekly throughout the hospitalization by qualified dentists or physicians using established scoring methods [36–38]. Grade of graft versus host disease and diagnosis and severity of veno-occlusive disease, as determined by the attending oncologist, are also recorded.

3.6.5.2. Anthropometric assessment: Body weight is measured by an electronic digital scale accurate to 0.1 kg. Standing height is measured by stadiometer to the nearest 0.1 cm. Triceps, biceps, iliac, and subscapular skinfold thicknesses is measured to the nearest 0.5 mm using Lange skin calipers. Mid-arm circumference is measured to the nearest 0.1 cm using a flexible non-stretchable plastic tape. Mid-arm muscle area is calculated according to standard equations. Body density and percent body fat are calculated from published equations using skinfold thickness measurements [39]. All skinfold measurements are made by a single observer at each site, and are performed in triplicate, with the average of these three measurements recorded. Measurement technique across all sites is standardized through exercises performed at site visits, using volunteer and dual measurements by the study coordinator and the site specific anthropometrist. Measurements with greater than 10% variation are repeated until they are within the target range.

3.6.5.3. Dietary intake assessment: Oral intake during the inpatient admission period of the study is recorded through the use of calorie counts, which require bedside providers to record all oral intake from observation and review with the patient and family. Nutrient intake is tabulated from 24-h recall at outpatient study visits. Total intake of calories, protein, carbohydrate, fat, and selected micronutrients is determined using nutrient analysis software and known specifications for the parenteral solutions.

3.6.5.4. Energy expenditure: REE is measured using the Vmax Encore indirect calorimeter (Viasys Healthcare, Yorba Linda, CA). Patients are studied in a modified fasted state, i.e. 6 h without any oral/enteral intake; intravenous fluids/nutrition as needed. The test is accomplished in the supine position, with a transparent canopy placed over the head. A constant airflow brings the expired gas to a monitor. The indirect calorimeter measures the inspiratory concentration of O₂ (FiO₂) and the difference between FiO₂ and expiratory concentrations of O₂ (FeO₂) with a paramagnetic differential oxygen sensor. The expiratory carbon dioxide (FeCO₂) is measured continuously with an infrared sensor. The inspiratory concentration of room air (FiCO₂) is measured every two minutes. Carbon dioxide output

and oxygen consumption are calculated each minute and then converted to standard temperature and pressure using dry gas equations. REE is calculated using the modified Weir equation and is expressed as kcal/day. The average values of VO₂, VCO₂, REE and respiratory quotient ($RQ = VCO_2 / VO_2$) over a 20–30 min study period are recorded. To normalize the data for age, gender, and growth stage, percent predicted REE is calculated [29].

3.6.5.5. Dual energy X-ray absorptiometry (DXA): DXA is a radiographic technique that measures the composition, distribution, and density of different body compartments (fat mass, lean tissue, fat free mass, and bone mineral content). All measurements are made in the anterior posterior position by a certified densitometry technologist using a Hologic Discovery A (Hologic, Inc.) scanner, which generates X-rays at 2 energy levels (100 and 70 kV). A series of transverse scans are made from the head to toe at 2 mm intervals, while the child is lying supine for approximately 15 min. Data is expressed as grams of total mass, fat mass, lean tissue mass, and percent fat. Bone mineral density (g/cm²) and bone mineral content (g) will also be recorded.

The DXA scanners were cross-calibrated with a single whole body phantom shipped to each site. Weekly whole body phantom scans are performed for quality control. Body composition data is sent quarterly on optical disks from each site to Children's Hospital Boston for centralized analysis and interpretation using Hologic Pediatric Upgrade for children and adolescents up to age 20 years.

3.6.5.6. Biochemical assessment: Measures of visceral protein status (prealbumin, albumin), micronutrients (calcium, magnesium, phosphorus, zinc, vitamin A, 25 hydroxy-vitamin D, and vitamin E), hormones (ghrelin, leptin, GLP-2), bone turnover markers (parathyroid hormone, bone-specific alkaline phosphatase, urinary N-telopeptide), glycemic control (hemoglobin A1C, insulin, glucose, C-peptide), triglycerides, and inflammatory status (CRP, IL-6, TNF-alpha) are performed at regular intervals (Table 1). Associations between measures of inflammation and micronutrient status will be made with dietary intake and body composition variables.

3.7. Data and safety monitoring

Adverse events are reported as disease entities or syndromes whenever possible, rather than individual component symptoms [40], and classified according to the NCI Common Toxicity Criteria, v3.0. [41] The occurrence of significant weight loss (>15% of admission weight), or low visceral protein status (albumin <1.5 g/dL or prealbumin <10 mg/dl) after 7 days of PN are considered serious adverse events. Either is regarded as possible evidence of inadequate parenteral nutrition, and will trigger clinically relevant evaluations by the clinical care team (e.g. evaluation of gastrointestinal, renal or other causes of protein or energy loss). In either case, regardless of group assignment, the prescribed level of parenteral energy and protein intake are increased by 20%, and the study group assignment will remain blinded. If weight gain or improvement in visceral protein status does not ensue or if the patient's clinical management requires knowledge of the precise amount of parenteral energy, the attending oncologist may request unblinding at any time.

3.8. Data analysis

The primary test of hypothesis for the trial is a comparison of 30-day change in percentage body fat (%BF) between the experimental and control groups, which we will conduct by a two-sample Student *t*-test comparing mean changes in the two groups, or Wilcoxon rank-sum test if the distributions of change prove to be highly skewed. Confounding should not be a problem in a randomized trial, but adjusting for covariates is worthwhile nevertheless as

a way of reducing variance and elucidating mechanisms. As potential covariates we will examine, individually and in combination, the following variables with known relation to body composition: age, sex, pubertal status, prior steroid use, and diagnosis. Baseline %BF will not be used as a covariate because of its structural relation to 30-day change, which would induce a spurious correlation (“regression to the mean”). Collinearity among covariates will be investigated by examining pairwise associations (correlation, *t*-test, chi-square, or non-parametric equivalents as appropriate) and conducting principal-components analysis [42].

Secondary analyses will be performed on 100-day changes in %BF and on changes in weight, body mass index, skinfolds, HOMA, REE, dietary intake and biochemical measures. Further refinement will be made by use of repeated-measures ANOVA, which permits all time points to be modeled simultaneously (baseline, 30d, 100d in the case of %BF; varying schedules for other measures), taking account of diminishing within-subject correlation across time. The linear trend of each outcome variable can be determined from contrasts among time points in the repeated-measures model, appropriately weighted for unequal intervals. We will adjust for time-varying covariates such as REE and diet in the repeated-measures analysis of %BF and other secondary outcomes.

Analysis will follow the intention-to-treat principle. All available data will be attributed to the subject's assigned treatment group regardless of whether treatment was completed. A secondary analysis will be performed to examine the effect of actual treatment received since it is anticipated that patients will receive different amounts of PN due to variable oral intake. Missing data will be filled in with a conservative imputation, such as assigning the opposite group's mean change, extending the last observation, or assuming zero change [43]. We will test for selective attrition by comparing baseline data between dropouts and those completing the trial. For repeated-measures analysis, we can restrict the analysis to all available (not imputed) data, including baseline data on dropouts, without incurring bias if the data are “missing at random,” i.e., the likelihood of lost data is related only to variables accounted for in regression. For all analyses, a two-tailed *p*-value < 0.05 will be considered statistically significant.

3.9. Statistical power and sample size considerations

Power of the proposed trial can be estimated on the basis of published data for variability of %BF in children. Published norms put %BF at roughly $28 \pm 8\%$ (mean $\pm$ SD) in Caucasian and African-American girls aged 6–17 and $18 \pm 9\%$ in boys of the same age [44,45]. To determine the variance of change in %BF from the variance of %BF itself, we assume within-subject correlation to be 0.7, a conservative choice considering that anthropometric variables typically show within-subject correlation of 0.8–0.9 in healthy subjects. The lower correlation could apply to this study because of perturbations due to treatment and illness. Fig. 2 shows that with a sample of $n=20$ per arm we will have approximately 80% power to detect a differential of 6% (absolute) between arms, using $p < 0.05$ as critical value in a two-sided test, which would be a relative difference of about 20% in girls and 30% in boys. To compensate for losses to follow-up, we plan to enroll 24 subjects per arm to allow for loss of 20% of patients, in order to ensure a final sample near the planned $n=20$ per arm.

4. Baseline data

Baseline characteristics of our cohort enrolled to date are presented in Table 2. As expected and as consistent with our previous cohort [24], the subjects are well nourished upon study entry, as denoted by mean measures of BMI, percent body fat and bone mineral density. Oral intake provides all energy intake at baseline. A variety of diagnoses are represented leading to HSCT.

5. Summary

The nutritional management of pediatric patients undergoing HSCT has been largely based on empirical estimates of energy and nutrient needs. Both short term (metabolic instability, infections) and long term (liver disease, osteopenia) risks of overfeeding parenteral nutrition may contribute to poorer outcomes in HSCT patients. As survival rates improve for these patients, it is increasingly clear that nutritional issues are common, including obesity [46], short stature [47], and insulin resistance [48]. Precise provision of nutrition support has the potential to improve clinical outcomes in these and other medically complicated groups. We are carrying out a randomized, controlled trial to evaluate the safety and efficacy of titrated parenteral energy intake in children undergoing HSCT. Our trial will improve the clinical understanding of energy expenditure and body composition in this population, and advance the nutritional management of children undergoing HSCT.

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Fig. 1.
Study schema.

Fig. 2.

Power of proposed trial to detect difference between two parenteral nutrition strategies with respect to 30-d change in percentage body fat (BF) in children undergoing stem cell transplantation. Using 20 subjects per arm (leftmost curve) ensures 80% power to detect differential change of 6% BF between standard nutritional support and matching of energy intake to expenditure (•). Comparison between subgroups (15/arm, center; 10/arm, rightmost) carries less power. Calculation assumes 5% Type I error (2-sided); no adjustment for covariates; variance and correlation parameters as specified in text.

Table 1

Data collection schedule.

Day post HSCT						
Measurement	Baseline (-14 to -7)	Twice weekly to +30	Weekly to +30	+30 ^{c,d}	+65 ^d	+100 ^d
Height	X			X	X	X
Weight	X	X		X	X	X
Skinfolds	X			X	X	X
REE	X	X		X		X
DXA	X			X		X
Dietary intake	X	X		X	X	X
Prealbumin	X		X	X		X
Fasting insulin, C-peptide, glucose, inflammatory markers, hormones ^a	X		X	X		X
Hemoglobin A1C, albumin, triglyceride, micronutrients, bone markers ^b	X			X		X

^aC-reactive protein, IL-6, TNF-alpha, leptin, GLP-2, ghrelin.

^bSerum vitamin E, vitamin A, zinc, bone-specific alkaline phosphatase, 25 hydroxy-vitamin D, parathyroid hormone, urinary N-telopeptide, calcium, magnesium, phosphorus.

^cAfter engraftment occurs.

^d+/- 7 days.

Table 2

Baseline characteristics of 26 children undergoing HSCT.

Parameter, $n = 26$	Mean (SD), except where noted
Age (years)	14.8 (4.2)
BMI (Z-score)	0.29 (0.86)
Percent Body Fat at baseline (by DXA)	28.8 (8.4)
REE at baseline (kcal/day)	1313 (320)
Oral intake at baseline (kcal/day)	2022 (804)
Bone mineral density at baseline (Z-score)	-0.48 (1.09)
Gender	12 male, 14 female
Diagnosis	
Acute lymphoblastic leukemia	7
Acute myelogenous leukemia	7
Myelodysplastic syndrome	3
Aplastic anemia	1
Chronic myelogenous leukemia	3
Lymphoma	2
Other	3
Donor type	12 sibling/related, 14 unrelated