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Vitamin D status among long-term survivors of hematopoietic cell transplantation

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Conflict of Interest

The authors have no conflicts of interest to report.

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Abstract

Little is known about serum vitamin D levels following hematopoietic cell transplantation (HCT). Patients are instructed to avoid sun exposure due to an increased risk of skin cancers. Altered gastrointestinal absorptive capacity as a result of GVHD, bile acid or pancreatic enzyme insufficiency, or bacterial overgrowth may lead to difficulty absorbing the fat soluble vitamin D. This study was undertaken to determine the prevalence of serum 25-hydroxyvitamin D (25(OH)D) deficiency, and factors associated with 25(OH)D deficiency, among children and adults who were at least one year following HCT. A total of 95 participants (54 males, 41 females) completed a questionnaire on usual diet and lifestyle, and provided a blood sample for 25(OH)D determinations between November 2008 and July 2009. The majority of participants had serum 25(OH)D levels ≥75 nmol/L (n=62, 65%), 23 had insufficient levels (50–75 nmol/L), and 10 participants were deficient (<50 nmol/L). The majority of participants reported regular vitamin D supplement use (n=58, 61%). Prednisone use was significantly inversely associated with serum 25(OH)D concentrations. Total vitamin D intake was the strongest single predictor of 25(OH)D concentrations. These findings suggest that 400–600 IU vitamin D/day appear to be required to achieve optimal serum 25(OH)D concentrations following HCT.

Keywords

hematopoietic cell transplantation; vitamin D; serum 25(OH)D; cancer survivors; diet; dietary supplements

Introduction

Vitamin D, a sterol hormone precursor, is well known for its role in maintaining calcium homeostasis and normal bone structure. Recent evidence suggests that in addition to calcium homeostasis, the vitamin may also play a role in cancer incidence and recurrence (1), risk of infectious diseases (2), and modulation of inflammatory pathways (3–5). Thus, for cancer survivors treated with hematopoietic cell transplantation (HCT), there is the possibility that maintaining adequate vitamin D status throughout the course of HCT may decrease risk of graft-vs-host disease (GVHD), graft rejection, infectious complications and disease relapse,

which in turn, could result in improved survival rates compared to individuals who are vitamin D deficient. In fact, several recent studies have reported an association between higher serum 25-hydroxyvitamin D (25(OH)D) levels and improved survival among individuals with colon (6), breast (6), prostate (6), and non-small cell lung cancers (7), as well as Hodgkin's lymphoma (6). Vitamin D deficiency has been associated with muscle weakness (8, 9), musculoskeletal pain (10), and impaired cognition (11); all issues common among cancer survivors which may contribute to diminished quality of life.

The 25(OH)D metabolite is the primary circulating form of vitamin D, and is considered the more clinically relevant form for assessing overall vitamin D status. A consensus has emerged that a serum 25-hydroxyvitamin D (25(OH)D) concentration of at least 75 nmol/L (30 ng/mL) is needed to prevent increases in parathyroid hormone or impaired calcium absorption (12), but it is unclear whether this level is optimal for prevention of other health related issues. Season, age, race, sex, obesity and dietary vitamin D intake have been previously reported to influence serum 25(OH)D concentrations in the general population (13). Vitamin D_3 (cholecalciferol) is available in fortified foods and dietary supplements, and is produced endogenously in the skin upon exposure to UV radiation. Vitamin D_2 (ergocalciferol) is only available exogenously through fortified foods and dietary supplements.

Little is known about serum vitamin D levels after HCT, although there is reason to believe that vitamin D deficiency is common, given reports of high prevalence of vitamin D insufficiency/deficiency in the US population (14), as well as among cancer survivors (15–18) and the critically ill (19). Following HCT, patients are instructed to avoid sun exposure and to use sunscreen due to an increased risk of skin cancers (20). Use of certain medications, such as glucocorticoids commonly used to treat GVHD, have been associated with lower serum vitamin D levels (21–23), although it is unclear whether this is due to the drug itself, or concurrent lack of vitamin D exposure from diet, supplements or ultraviolet (UV) exposure. Also some individuals develop altered gastrointestinal absorptive capacity following HCT as a result of gastrointestinal GVHD, intestinal bile salt deficiency, pancreatic enzyme insufficiency, or bacterial overgrowth; consequently, these individuals may have difficulty absorbing dietary fat and fat soluble vitamins such as vitamin D (24). Osteoporosis is a common complication among long-term HCT survivors, again suggesting that vitamin D deficiency may be present.

The specific aim of this pilot study was to determine the prevalence of 25-hydroxyvitamin D (25(OH)D) deficiency among long-term (≥1 year) cancer survivors who received HCT. We hypothesized that the majority of these individuals would have suboptimal serum vitamin D levels due to avoidance of sun exposure, regular use of sunscreen, suboptimal dietary/supplemental intake, and treatment-related factors.

Materials and methods

Study population

Study participants for this observational study were recruited from patients scheduled for clinic visits in the Blood and Marrow Transplant (BMT) Clinic, the Adult BMT Long-Term

Follow-Up (BMT LTFU) Clinic and the Pediatric Long-Term Follow-Up Clinic (LTFU) at the University of Minnesota between November 2008 and July 2009. Patients were eligible to participate in the study if they were at least one year from the date of HCT for any diagnosis, except multiple myeloma. Patients who had undergone HCT for multiple myeloma were excluded from the present study due to the potential for alterations in skeletal metabolism and renal function, and the likelihood of concurrent treatment with bisphosphonates and higher doses of vitamin D supplementation. This study was approved by the University of Minnesota Institutional Review Board, and all participants (or their guardians) provided written informed consent.

Data collection

Medical records and the HCT databases were used to abstract diagnostic and treatment-related data for each participant. Data collected included original cancer diagnosis, pre-treatment height (adults) and current height (children), current weight, date of transplant, HCT conditioning regimen, donor matching status, GVHD prophylaxis regimen, history of acute and chronic GVHD, current medications, and comorbidities.

Dietary vitamin D intake was obtained from a self-administered questionnaire adapted from a validated short screening instrument by Blalock et al (25). The questionnaire asked participants about usual intake of food sources high in vitamin D (milk, salmon, tuna, eggs, fortified cereals) over the past month. For dietary vitamin D intake, micrograms of vitamin D per serving of milk as a beverage, milk on cereal, salmon, tuna and eggs, were calculated using a 100g reference value for each food from the United States Department of Agriculture National Nutrient Database for Standard Reference. Recent supplemental vitamin D intake data was collected at the time of the clinic visit. Participants were asked to bring dietary supplements that they were currently taking to the clinic visit. Information on the type and amount of vitamin D provided was collected from the Supplement Facts label, and the study participant was asked to report frequency of use over the past month. Participants were also asked to report their average number of hours of daily sun exposure on weekdays and on weekend days over the previous month, and frequency of sunscreen use.

For study participants less than 18 years of age at the time of the study, study paperwork, including the questionnaire, was provided to the parents or legal guardians. In most cases, it was the parent who completed of the study questionnaire on behalf of their child.

Serum for the 25(OH)D determinations was obtained during the routine blood draw for the participant’s clinic visit. Fairview Diagnostic Laboratories (Minneapolis, MN) performed the serum 25(OH)D determinations using liquid chromatography/tandem mass spectrometry (LC-MS/MS) methods.

Statistical analysis

For this analysis, serum 25(OH)D deficiency was defined as serum levels <50 nmol/mL (20 ng/mL), insufficiency as 50–74.9 nmol/L (20–29.9 ng/mL), and sufficient as ≥ 75 nmol/L (30 ng/mL) (26). The distribution of serum 25(OH)D concentrations were skewed toward higher values, therefore these values were log-transformed for use in the statistical analyses.

Geometric means and 95% confidence intervals (CI) are presented, which were obtained by taking the anti-log of the mean and 95% CIs. We evaluated whether seasonal variation in serum 25(OH)D concentrations was present in this cohort by comparing mean 25(OH)D concentrations by month and season (March–May, June–August, September–November, December–February) of blood draw.

Descriptive statistics, including geometric means, standard deviations, frequencies and ranges, were obtained for the entire cohort, and stratified by age group at the time of the blood draw: children/adolescents (<20 years old), young adults (20–40 years old), and adults (>40 years old). Where sufficient numbers were present, analyses were also stratified on key covariates such as sex, years since transplant (1–1.9, 2–4.9, ≥5), type of transplant (autologous vs. allogeneic), conditioning regimen (myeloablative vs. non-myeloablative), history of acute and chronic GVHD, use of immunosuppressive medications (yes/no), and vitamin D supplement use (yes/no). Analyses were also stratified by body weight category according to BMI-for-age for children and adolescents less than 20 years of age (27) and BMI for adults. Body weight was categorized as: underweight (< 5^{th} percentile BMI-for-age or BMI < 18.5), normal weight (5^{th}–84^{th} percentile BMI-for-age or BMI 18.5 – 24.9), overweight (85^{th}–94^{th} percentile BMI-for-age or BMI 25.0–29.9), and obesity (≥ 95^{th} percentile BMI-for-age or BMI ≥ 30).

Multivariable linear regression was used to model the predictors of 25(OH)D concentration. Current age (continuous), sex, month of blood draw, BMI or BMI-for-age percentile (continuous), self-reported race (white/other), self-reported average daily hours of sun exposure, usual dietary vitamin D intake, usual supplemental vitamin D intake, clinical serum chemistry concentrations at the same blood draw (calcium, creatinine, albumin, ALT, AST, alkaline phosphatase), type of HCT (allogeneic/autologous), conditioning regimen (myeloablative/non-myeloablative), history of acute and chronic GVHD and current use of immunosuppressants (yes/no) and prednisone (yes/no) were considered as potential predictors. Each potential predictor was examined individually by assessing its effect on the overall model fit (R^2, F-test).

Statistical significance for all analyses was defined as a p-value of <0.05. Statistical analyses were performed using SAS 9.1 data analysis software (SAS Institute Inc., Cary, NC).

Results

A total of 95 long-term HCT survivors (44 children/adolescents, 12 young adults and 39 adults), out of a total of 170 (56%) potentially eligible individuals, agreed to participate in this study. Non-participation most commonly occurred via passive refusal (non-response to study mailings or telephone contact by the study coordinator prior to the scheduled clinic visit); only 5 individuals actively declined participation. Non-participants did not differ from participants by sex, time since HCT, or original diagnosis (p>0.05), however non-participants tended to be younger than participants (mean: 21.8 vs. 31.7 years respectively, p<0.01). The characteristics of the study population are described in Table 1. Slightly more than half the participants were male, and the majority (87%) were Caucasian. Most study participants resided in northern US states at the time of the study (Minnesota, Wisconsin,

North and South Dakota, Michigan, Iowa, Illinois, New Jersey, Rhode Island), although 4 (4%) of study participants resided in southern US states (Florida, Georgia, California).

Overall, more than half of the participants were using vitamin D supplements. However, a significantly higher percentage of young adults and adults used supplements compared to children/adolescents (78 vs 41%, $p<0.01$). Likewise, mean supplemental vitamin D intake was statistically significantly higher among young adults and adults than among children (mean: 259 vs. 85 IU/day, $p<0.01$). Mean dietary vitamin D intake was 144 IU/day, and was not statistically significantly different across age groups.

No statistically significant differences in mean 25(OH)D by month or season of blood draw were observed in this cohort. Mean self-reported hours of sun exposure was 1.1 hours/day for the entire cohort, with no statistically significant differences by age group. The majority of participants reported rarely or never using sunscreen, although a greater percentage of young adults (50%) reported always using sunscreen compared to the percentages of children/adolescents (16%) or adults (21%). No statistically significant differences in average daily sun exposure by sunscreen use category was observed, even when stratified by age category (data not shown).

Contrary to our original hypothesis, the majority of study participants had sufficient serum 25(OH)D concentrations, with a mean of 88nmol/L (35.2 ng/mL). Despite the overall lack of seasonal variation in 25(OH)D concentrations, all 10 individuals who were categorized as having deficient 25(OH)D concentrations (<50 nmol/mL) had their blood drawn between November and March, the point in the year in which the lowest 25(OH)D concentrations would be expected at higher latitudes. Eight of the 25(OH)D deficient individuals (80%) were not taking vitamin D supplements at the time of the blood draw, and mean total vitamin D intake (diet and supplements) was significantly lower for the deficient individuals (119 IU/day) compared to 25(OH)D sufficient individuals (399 IU/day, $p<0.0001$).

Stratification by transplant and patient characteristics (Table 2) indicates that type of transplant (autologous or allogeneic) was not associated with significant differences in serum 25(OH)D concentrations. Adults who received non-myeloablative conditioning regimens had significantly higher serum 25(OH)D concentrations than adults who underwent myeloablative regimens ($p=0.01$). Conditioning regimen was not associated with significant differences in serum 25(OH)D concentrations among children/adolescents. History of acute or chronic GVHD was not associated with significant differences in serum 25(OH)D concentrations.

As has been commonly reported (28–30), overweight and obesity was associated with lower 25(OH)D concentrations compared to individuals who were underweight or in the normal weight range. Adults with current BMI ≥ 25 kg/m^2 had significantly lower 25(OH)D concentrations compared to individuals with current BMI of <25 kg/m^2 (71.0 vs. 91.5 nmol/L, $p=0.04$). However, differences in 25(OH)D concentrations by body weight categories among children and adolescents did not reach statistical significance. Neither BMI nor BMI-for-age percentile contributed significantly to the multivariate model

predicting serum 25(OH)D concentrations for the respective age groups after adjustment for total vitamin D intake and current prednisone use (yes/no).

Current use of prednisone was associated with significantly lower serum 25(OH)D concentrations compared to individuals not on prednisone (64.0 vs. 86.5 nmol/L, p=0.002). Similarly, current use of any immunosuppressive medications (prednisone, cyclosporine, mycophenolate mofetil, or FK506) was also associated with lower serum 25(OH)D concentrations; however, the majority of study participants in this category were receiving prednisone. Of the 5 individuals on an immunosuppressive medication other than prednisone (4 cyclosporine, 1 mycophenolate mofetil) at the time of the blood draw, the mean serum 25(OH)D concentration was 81.2 ng/mL (95% CI: 75.2–88.2 nmol/L) after adjusting for total vitamin D intake, suggesting that prednisone use was the primary immunosuppressive agent associated with lower 25(OH)D concentrations. The final multivariate model for predictors of serum 25(OH)D concentrations in this population included only total daily vitamin D intake and prednisone use (R^2=0.30, p<0.0001).

Total daily vitamin D intake was the most significant predictor of serum 25(OH)D concentrations, and explained 22% of the variation between participants. Among participants who reported using vitamin D supplements, supplements comprised, on average, 65% of total vitamin D intake. Individuals who reported any vitamin D supplement use had significantly higher serum 25(OH)D concentrations compared to those who did not use vitamin D supplements (94.0 vs. 65.2 nmol/L, p<0.001). Table 3 describes mean 25(OH)D concentrations by total vitamin D intake (dietary and supplemental) after adjusting for prednisone use. Our data suggest that 400–600 IU vitamin D/day is required for mean 25(OH)D concentrations to be in the normal range (≥75 nmol/L) for the majority of individuals in each age group (i.e. entire 95% confidence interval within the normal range).

Discussion

In this cohort of long-term HCT survivors, the majority (64%) of study participants had sufficient vitamin D levels, likely as a result of vitamin D supplement use, which was highly prevalent in the study population. Total dietary and supplemental vitamin D intake was the strongest single predictor of 25(OH)D concentrations, and 400–600 IU/day appear to be required to achieve optimal serum 25(OH)D concentrations across 95% of the study population. The lack of seasonal variation in 25(OH)D concentrations suggests that study participants were generally adhering to recommendations to minimize UV exposure following HCT. Prednisone use was significantly inversely associated with serum 25(OH)D concentrations.

While the inverse association between prednisone use and serum 25(OH)D concentrations may indicate a direct effect of prednisone on either vitamin D absorption or metabolism, the prednisone use variable may also be acting a surrogate for an individual’s heightened awareness of the need to limit UV exposure, or decreased appetite limiting dietary and supplemental vitamin D intake. In our study, no statistically significant differences in dietary vitamin D intake, supplemental vitamin D intake or average hours of sun exposure were observed between those who were currently taking prednisone, and those who were not.

Participants on prednisone were likely receiving the medication due to active chronic GVHD, and vitamin D absorptive capacity may have been reduced among those with gastrointestinal GVHD. We did not collect data on prednisone dose; future studies are needed to determine whether a dose-effect relationship exists between prednisone and vitamin D status.

To our knowledge, this is the first study to report vitamin D status among long-term survivors following HCT. A small study of 48 patients undergoing allogeneic HCT found that 25(OH)D declined significantly from pre-treatment levels to time of engraftment (approximately one month after transplant) (31). Prior to HCT, mean serum 25(OH)D_3 (the D_3 specific fraction of 25(OH)D) was 36.4 ± 2.2 nmol/L. Mean serum 25(OH)D_3 at time of engraftment was 27.8 ± 1.3 nmol/L. At 10 weeks post-engraftment, significant differences in serum 25(OH)D_3 were observed between patients who had not experienced GVHD and those who had experienced grades 3–4 GVHD (mean ± standard error not presented, although p=0.03). Details of the 25(OH)D_3 assay methodology and total 25(OH)D levels (both ergocalciferol, D_2, and cholecalciferol, D_3, specific fractions) were not provided in this report. Thus, it is difficult to determine whether these patients would have met the accepted definitions for vitamin D insufficiency (<75 nmol total vitamin D/L) or deficiency (<50 nmol total vitamin D/L).

In this study, 400–600 IU dietary or supplemental vitamin D/day appears to be required to achieve optimal serum 25(OH)D concentrations across 95% of the study population after adjusting for prednisone use. The current Dietary Recommended Intakes for adequate intake of vitamin D among healthy individuals is 200 IU/day for individuals up to 50 years of age, 400 IU/day for individuals aged 51–70 years, and 600 IU/day for those 71 and older (32). Thus, our findings suggest that following HCT, vitamin D requirements may be higher than the current recommendations. However, the Institute of Medicine has convened an expert panel to reevaluate the current Dietary Recommended Intakes for calcium and vitamin D, and the adequate intake recommendations are expected to increase when the committee releases their report which is expected to be made publically available in November 2010 (33).

Our study had several strengths and limitations. One strength is that this is the first study to consider dietary and supplemental vitamin D intake, as well as UV exposures, as potential predictors of vitamin D status among patients with a history of HCT. Despite our relatively large study population, we did not have sufficient numbers to fully evaluate the effect of potential confounding factors for differences by age group. We were also limited in having only one measurement of vitamin D status, which may not have been reflective of long-term vitamin D status. Another limitation is that there is considerable heterogeneity in overall health status and health issues among patients who have undergone HCT, and healthier patients (who might be more likely to be vitamin D sufficient) may have been more likely to participate in the study. A larger study population would have allowed for restriction to specific sub-populations (e.g. specific underlying diagnoses, treatment regimens, comorbid conditions, time since transplant, etc.) to isolate these factors with regard to effect on vitamin D status. We also lacked sufficient numbers to fully explore potential effects of medications on vitamin D status.

Further prospective studies are needed to confirm our findings related to specific adequate vitamin D intake recommendations for this population. Additionally, similar studies are needed to determine the prevalence of vitamin D deficiency, and factors predicting vitamin D deficiency, during the early post-transplant period, and the effects of vitamin D status on treatment related outcomes.

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Table 1

Characteristics of the study population

	All (n=95)	Children/ Adolescents (n=44)	Young Adults (n=12)	Adults (n=39)	p *
Current age, years, mean (range)	32.2 (2.7–72.2)	9.0 (2.7–14.8)	29.6 (20.1–37.7)	57.5 (43.1–72.2)	
Male, yes	54 (57%)	26 (59%)	3 (25%)	25 (64%)	0.05
White, yes	82 (87%)	36 (82%)	11 (92%)	35 (92%)	0.34
Current BMI-for-age percentile, mean (range)		59.4 (1 – 99)	-	-	
Current BMI, mean (range)		-	21.3 (17.7–26.8)	28.2 (20.6–46.3)	<0.01
Current weight category					
Under weight	5 (6%)	3 (8%)	2 (17%)	0	<0.01
Normal weight	41 (49%)	22 (59%)	8 (67%)	11 (32%)	
Overweight	27 (33%)	6 (16%)	2 (17%)	13 (38%)	
Obese	10 (12%)	6 (16%)	0	10 (29%)	
Years since transplant, mean (range)	4.2 (1.0–23.6)	3.8 (1.0–10.6)	6.4 (1.0–23.6)	3.9 (1.0–13.0)	0.12
Donor Type					0.05
Autologous	12 (13%)	3 (7%)	4 (33%)	5 (13%)	
Allogeneic	83 (87%)	41 (934%)	8 (67%)	34 (87%)	
Conditioning regimen					<0.01
Myeloablative	70 (75%)	34 (97%)	11 (92%)	18 (47%)	
Non-myeloablative	24 (26%)	1 (3%)	1 (8%)	20 (53%)	
Usual time outdoors between 10 AM–4 PM, mean hours/day (range)	1.1 (0–6.0)	0.9 (0–6.0)	0.9 (0–2.0)	1.4 (0–5.4)	0.13
Self-reported sunscreen use					0.12
Almost always	21 (22%)	7 (16%)	6 (50%)	8 (21%)	
More than half the time	12 (13%)	7 (160%)	1 (8%)	4 (10%)	
About half the time	5 (5%)	3 (7%)	1 (8%)	1 (3%)	
Less than half the time	4 (4%)	4 (9%)	0	0	
Rarely	10 (11%)	3 (7%)	2 (17%)	5 (13%)	
Never	43 (45%)	20 (45%)	2 (17%)	21 (54%)	
Vitamin D supplement use	58 (61%)	18 (41%)	10 (83%)	30 (77%)	<0.01
Dietary vitamin D intake, daily IU, mean (range)	144 (0–380)	148 (0–360)	124 (22–282)	144 (0–380)	0.53

	All (n=95)	Children/ Adolescents (n=44)	Young Adults (n=12)	Adults (n=39)	p *
Supplemental vitamin D intake, daily IU, mean (range)	182 (0–573)	91 (0 – 573)	272 (0–573)	255 (0–573)	<0.01
Total vitamin D intake (diet + supplement), daily IU, mean (range)	325 (6–910)	239 (28–637)	397 (100–715)	400 (6–910)	<0.01
Serum 25(OH)D, nmol/L, mean (range)	88.0 (12.5–206.3)	83.8 (43.8–206.3)	80.3 (23.8–157.5)	79.3 (12.5–171.3)	0.98
Serum 25(OH)D status					0.07
Sufficient (≥75 nmol/L)	62 (65%)	27 (61%)	8 (67%)	27 (69%)	
Insufficient (50–74.9 nmol/L)	23 (24%)	15 (34%)	3 (25%)	5 (13%)	
Deficient (<50 nmol/L)	10 (11%)	2 (5%)	1 (8%)	7 (18%)	

Data reported as n (%) unless otherwise noted.

Abbreviations: BMI = body mass index, IU = International Units, kg = kilogram, L = liter, m = meters, nmol = nanomoles.

* for comparison between age categories. From X^2 statistic, Fischer exact test, and 1-way analysis of variance *F*-test statistic.

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Table 2

Effect of transplant and patient characteristics on 25(OH)D concentrations*

	All			Children / Adolescents			Young Adults / Adults		
	n (%)	Mean 25(OH)D nmol/L (95% CI)	p	n (%)	Mean 25(OH)D nmol/L (95% CI)	p	n (%)	Mean 25(OH)D nmol/L (95% CI)	p
Sex									
Female	41 (43%)	86.0 (76.5–96.8)	0.23	18 (41%)	92.5 (81.2–105.5)	0.05	23 (45%)	80.8 (67.5–96.8)	0.81
Male	54 (57%)	78.3 (70.5–86.8)		26 (59%)	78.2 (70.2–87.2)		28 (55%)	78.5 (66.5–92.5)	
Years since transplant									
1–1.9	23 (24%)	75.3 (64.3–88.0)	0.33	10 (23%)	79.2 (65.8–95.2)	0.68	13 (25%)	74.8 (58.5–95.8)	0.72
2–4.9	46 (48%)	86.3 (77.3–96.5)		24 (55%)	86.0 (76.2–96.8)		22 (43%)	84.0 (69.8–101.2)	
≥ 5	26 (27%)	79.0 (68.0–91.8)		10 (23%)	83.5 (69.2–100.8)		16 (31%)	77.5 (62.2–96.2)	
Type of transplant									
Autologous	12 (13%)	77.0 (61.5–96.0)	0.59	3 (7%)	61.0 (44.2–84.5)	0.05	9 (18%)	82.8 (61.5–111.5)	0.77
Allogeneic	83 (87%)	82.0 (75.5–89.3)		41 (93%)	85.8 (78.8–93.5)		42 (82%)	78.8 (69.0–90.0)	
Conditioning regimen									
Myeloablative	70 (74%)	78.5 (71.8–86.0)	0.15	41 (93%)	83.2 (76.0–91.0)	0.53	29 (58%)	69.5 (59.8–80.8)	0.01
Non-myeloablative	24 (26%)	89.5 (76.8–104.5)		**3** (7%)	92.8 (66.2–129.8)		21 (42%)	94.5 (79.0–112.8)	
History of acute GVHD									
no	53 (56%)	84.5 (76.0–93.8)	0.31	27 (61%)	85.0 (76.0–95.0)	0.69	26 (51%)	82.5 (69.8–97.8)	0.53
yes	42 (44%)	77.8 (69.3–86.8)		17 (39%)	82.0 (71.2–94.2)		25 (49%)	76.5 (64.2–90.8)	
History of chronic GVHD									
no	54 (57%)	85.0 (76.8–94.5)	0.22	36 (82%)	86.2 (78.5–95.0)	0.19	18 (35%)	75.0 (61.0–91.8)	0.47
yes	41 (43%)	77.0 (68.3–86.8)		6 (18%)	73.5 (59.0–91.2)		33 (65%)	82.0 (70.8–95.2)	
Currently on immunosuppression									
no	71 (74%)	87.0 (79.8–94.8)	0.004	40 (91%)	85.0 (77.5–93.0)	0.35	31 (61%)	86.0 (74.0–100.0)	0.10
yes	24 (25%)	67.3 (57.8–78.0)		4 (9%)	73.2 (54.5–99.0)		20 (39%)	70.2 (58.2–84.8)	
Currently on prednisone									
no	76 (80%)	86.5 (79.8–94.0)	0.002	43 (98%)	83.8 (76.8–91.5)	0.97	33 (65%)	86.5 (74.8–100.0)	0.06
yes	19 (20%)	64.0 (54.3–75.5)		**1** (2%)	82.8 (45.2–151.8)		18 (35%)	68.0 (56.0–83.0)	
Vitamin D supplement use									

	All			Children / Adolescents			Young Adults / Adults		
	n (%)	Mean 25(OH)D nmol/L (95% CI)	p	n (%)	Mean 25(OH)D nmol/L (95% CI)	p	n (%)	Mean 25(OH)D nmol/L (95% CI)	p
no	37 (39%)	65.3 (57.3–74.0)	<0.001	26 (59%)	65.2 (57.2–74.0)	<0.001	11 (22%)	65.2 (57.2–74.0)	<0.001
yes	58 (61%)	94.0 (84.8–104.0)		18 (41%)	94.0 (84.8–104.0)		40 (78%)	94.0 (84.8–104.0)	
Current weight category[†]									
underweight / normal weight				25 (67%)	85.2 (75.8–95.8)	0.54	22 (48%)	91.5 (76.8–109.2)	0.04
overweight / obese				12 (32%)	79.8 (67.2–94.8)		24 (52%)	71.0 (60.0–84.2)	

Abbreviations: BMI = body mass index, CI = confidence interval, GVHD = graft-vs-host disease, kg = kilograms, L = liters, m = meters, nmol = nanomoles.

[*] Geometric means, adjusted for total vitamin D intake, except for vitamin D supplement and total vitamin D intake stratifications.

[†] According to Centers for Disease Control categorizations using sex-specific BMI-for-age for children and adolescents (2 – 19 years of age), and BMI for adults.

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Table 3

Geometric mean 25(OH)D concentration by total vitamin D intake

	All			Children/Adolescents			Young Adults / Adults		
Total vitamin D intake (diet and supplements)	**n**	**Mean 25(OH)D nmol/L (95% CI)**	**p**	**n**	**Mean 25(OH)D nmol/L (95% CI)**	**p**	**n**	**Mean 25(OH)D nmol/L (95% CI)**	**p**
0 – 200 IU/day	35	62.5 (55.3–70.5)	<0.001	24	74.8 (66.2–84.2)	0.02	11	44.0 (34.2–56.0)	<0.001
>200 – 400 IU/day	26	83.8 (72.5–96.5)		11	87.0 (72.8–104.0)		15	84.2 (68.2–103.8)	
>400 – 600 IU/day	20	101.8 (86.5–119.5)		6	102.0 (79.0–132.0)		14	97.0 (78.8–119.5)	
>600 – 1000 IU/day	14	109.8 (90.5–133.0)		3	123.2 (87.8–173.2)		11	103.0 (81.5–130.5)	

Abbreviations: CI = confidence interval, IU = International Units, L = liter, nmol = nanomoles.

*Geometric means, adjusted for prednisone use at the time of blood draw (yes/no).