Current Problems in Cancer 43 (2019) 421–428

Contents lists available at ScienceDirect

Current Problems in Cancer

journal homepage: www.elsevier.com/locate/cpcancer

# Vitamin D deficiency in cancer patients and predictors for screening (D-ONC study)

Ali Alkan[a,*], Elif Berna Köksoy[b]

[a] Department of Medical Oncology, Osmaniye Public Hospital, Osmaniye, Turkey
[b] Department of Medical Oncology, Kastamonu Public Hospital, Kastamonu, Turkey

## ABSTRACT

*Introduction:* Vitamin D is a prohormone that is vital for calcium/phosphate balance, bone structure, and physiological functioning. Vitamin D deficiency (VDD) is an important clinical problem worldwide. However, there are no standardized protocols for screening of patients with a diagnosis of cancer. The purpose of this study is to define the prevalence of VDD in cancer patients and establish the predictors of VDD to address a specific group of patient for screening.
*Material/Methods:* The study was designed as a retrospective case-control study. The patients cared in the outpatient clinic between December 2016 and May 2018 with a diagnosis of cancer were evaluated. The clinical properties and the 25(OH) D levels were evaluated. Logistic regression was used to compute odds ratios (ORs) and 95% confidence intervals (CIs) for the association between VDD and clinical parameters.
*Results:* In 2 cancer centers, 706 patients with a diagnosis of cancer were evaluated. Median 25(OH) D level was 12.2 ng/mL (2.1-96.4). VDD was present in 509 (72.0%) of patients. The multivariate analysis of factors associated with VDD showed that female gender (OR: 1.5 [95% CI: 1.05-2.4], $P = 0.026$), low sun light exposure (OR: 1.4 [95% CI: 1.009-2.1], $P = 0.045$), being under palliative (OR: 1.5, [95% CI: 1.008-2.4] $P = 0.04$) or adjuvant setting (OR: 2.6 [95% CI: 1.3-5.1], $P = 0.006$), and history of gastrointestinal surgery (OR: 1.8, [95% CI: 1.03-3.2] $P = 0.03$) were associated with VDD. The female patients with headscarf had lower 25(OH) D levels than without group (10.5 ng/mL vs 23.4 ng/mL, $P < 0.001$) and they had more VDD (77.2% vs 29.4%, $P < 0.001$).
*Conclusion:* Our study concluded that prevalence of VDD is high in cancer patients and female gender, low sun light exposure, being under palliative or adjuvant setting, and history of gastrointestinal surgery are associated with VDD. These parameters should be used for selecting patients for screening.



## ARTICLE INFO

*Keywords:* Vitamin D deficiency; Risk factors; Prevalence; 25(OH) D; Cancer

☆ Conflict of interest: There is no conflict of interest. The study has not been supported or funded by any organization, group, or society. The report has been written with contributions of all authors, and all of the authors are in agreement with the content of the manuscript.

* Correspondence to: Ali Alkan, Department of Medical Oncology, Osmaniye Public Hospital, Osmaniye 80350, Turkey.
*E-mail address:* alkanali@yahoo.com (A. Alkan).

https://doi.org/10.1016/j.currproblcancer.2018.12.008
0147-0272/

## Introduction

Vitamin D is a prohormone that is vital for calcium/phosphate balance, bone structure, and physiological functioning. It is obtained from foods consumed and synthesized by skin exposed to ultraviolet B. In clinical practice, total serum 25(OH) D concentration is used for evaluation of vitamin D status. Vitamin D deficiency (VDD) is defined as a 25(OH) D below 20 ng/mL (50 nmol/L), and vitamin D insufficiency as a 25(OH) D of 21-29 ng/mL (525-725 nmol/L).[1] VDD is an important clinical problem. Worldwide, 1 in 7 people (14%) are estimated to have either insufficient or deficient vitamin D status.[2] The clinical impacts of VDD have been documented in numerous studies. VDD has been associated with cardiovascular diseases, increased risk of fracture, dyslipidemia, increased inflammation, glucose metabolism disorders, weight gain, infectious diseases, multiple sclerosis, mood disorders, cognitive dysfunction, impaired physical functioning, and all-cause mortality.[3]

The prevalence of VDD in cancer patients has been reported to be ranging between 14% and 92%.[4,5] The clinical impacts of VDD have been studied both as a risk factor for cancer and its consequences in cancer patients. It has been found to be associated with a variety of cancers, including prostate, multiple myeloma, colorectal, and breast cancer.[6-8] Higher levels of 25(OH) D levels have been associated with increased survival in breast, colorectal, prostate, and melanoma patients.[9] However, the studies evaluating the clinical effects of vitamin D in cancer patients have showed conflicting results. So in guidelines, the patients who should be screened or replaced have not been well defined.

The screening for VDD in asymptomatic patients is another issue under debate. In healthy population, there is not a study examining the effects of vitamin D screening vs no screening on clinical outcomes. The data in literature concluded that current evidence is insufficient to assess the benefits and harms of screening for VDD in asymptomatic adults.[3,10] However, the guidelines recommend screening for VDD in individuals at risk for deficiency. In oncology practice, there are no standardized protocols for screening and supplementation for individuals found to have VDD. However cancer patients are generally exposed to “risk factors” which were defined for noncancer patients, such as hepatic/renal dysfunction, malabsorption, exposure to anti-seizure medication, glucocorticoids, and antifungals.[1] The purpose of this study is to define the prevalence of VDD in cancer patients and establish the predictors of VDD to address a specific group of patient for screening.

## Material/methods

The study was conducted in medical oncology units in Osmaniye Public Hospital and Kastamonu Public Hospital. Institutional Ethics Committee approved the study protocol, and the study was in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. The study was designed as a retrospective study. The patients cared in the outpatient clinic between December 2016 and May 2018 with a diagnosis of cancer were evaluated. The patients who were more than age of 18, and had a 25(OH) D level at the initial evaluation were included. The ones without 25(OH) D at the initial workup, appropriate clinical data, and who had a history of calcium/ vitamin D replacement therapy in the last 6 months, history of parathyroid disease, calcium disturbance, and presence of renal dysfunction were excluded.

The age, gender, weight, height, history of smoking, Eastern Cooperative Oncology Group performance score, comorbidities, presence of polypharmacy ($\geq$5 drugs), presence of anticonvulsant, steroid medication, enteral nutritional supplements, and history of gastrointestinal surgery were recorded. In addition, primary diagnosis, the disease status at the initial presentation to medical oncology unit, and the presence of hepatic metastases were noted. To evaluate the effect of sun exposure, the dates of the workup were put into analysis. The laboratory work-up at the initial evaluation was searched for 25(OH) D, albumin, calcium, phosphate, creatinine, and alanine

aminotransferase. Creatinine and alanine aminotransferase levels were used to exclude patients with renal and hepatic dysfunction.

The 25(OH) D levels below 20 ng/mL were defined as VDD. The age of the patients were grouped as ≥65 years of age and <65. The body mass index (BMI) was calculated and BMI was grouped as underweight (<18.5 kg/m$^2$), normal weight (18, 5-25 kg/m$^2$), overweight (25-30 kg/m$^2$), and obese as more than 30 kg/m$^2$. The primary diagnoses of the patients were grouped according to their frequencies. "Disease status" was defined as the clinical picture when the patient was evaluated for 25(OH) D. The patients who were admitted after curative surgery and who were referred to unit with an intent to have adjuvant therapy were grouped as "adjuvant setting." As an indirect parameter for nutritional status, we used albumin levels. The levels less than 3.5 g/dL was defined as "low albumin level." The patients with a diagnosis of advanced cancer and treated with palliative chemo/radiotherapy or the ones under palliative care were grouped as "palliative setting." The months were used to evaluate the effects of the seasons. In addition, as recommended by the Society of Endocrinology and Metabolism of Turkey guidelines, the months of the year were further grouped as "sun exposure—low" (December-April) and "sun light exposure––high" (May-November). It was determined according to angle of the sun lights reaching to Turkey (zenith angle).[11]

Baseline characteristics of the patients were described by using proportions for dichotomous and categorical variables. The chi-square or Fisher exact tests were used to compare categorical variables. Univariate analysis of the predictors of VDD was performed with chi-square or Fisher exact tests. Multivariate analysis was performed using a logistic regression model. The parameters that were found statistically significant in univariate analysis were used in logistic model. Female gender, low performance score, enteral supplement, gastrointestinal surgery, disease status, low albumin levels, and sun exposure were further tested with logistic regression analysis. All analyses were performed using SPSS 17.0 for Windows (IBM Corp., Armonk, NY). *P* value of less than 0.05 was considered as statistically significant.

## Results

In 2 cancer centers, 706 patients with a diagnosis of cancer were evaluated. Median age was 63 years (23-91) and most of them were female (416, 58.9%; Table 1). The BMI could be evaluated only in 234 patients (33.1%) and 32.5% of them were obese. While 52.4% of patients had at least 1 comorbidity, most common disease was hypertension (238, 33.7%). One hundred twenty-five (17.7%) of the patients were exposed to polypharmacy. 60.1% of them were nonsmoker. The Eastern Cooperative Oncology Group performance scores at the initial evaluation were (0-1-2) in 89.7% and (3-4) in 10.3%. There were anticonvulsant medications in 3.7%, steroids in 2.4%, and enteral supplements in 7.2% of them. In 556/706 (78.8%) patients albumin levels could be found and only 54 patients (9.7%) had low albumin levels. The information if the female patients wore headscarf could be documented in 389 (93.5% of female patients) and 372 (95.6%) of them were wearing headscarf in their daily lives.

Median 25(OH) D level was 12.2 ng/mL (2.1-96.4). In 509 (72.0%) of patients VDD was present. The analysis of factors associated with VDD concluded that female gender (75.2% vs 67.6%, $P=0.01$), low performance score (86.3% vs 70.5, $P=0.002$), and low sun exposed months (December-May) were associated with more VDD (Table 2). While patients who were under remission had less VDD (65.4%); patients under palliative therapy (76.0%) and the patients under adjuvant setting (83.3%) were more exposed to VDD. In the subgroup analysis of comorbidities: there were more VDDs in hypertension (73.1% vs 71.6, $P=0.36$), diabetes mellitus (75.6% vs 71.3, $P=0.31$) and less VDDs in cardiovascular disease (61.4% vs 73.5%. $P=0.21$) when compared with patients without comorbidities. However, these were not statistically significant. The multivariate analysis of factors associated with VDD showed that female gender (odds ratio [OR]: 1.5 [95% confidence interval {CI}: 1.05-2.4], $P=0.026$), low sun light exposure (OR: 1.4 [95% CI: 1.009-2.1], $P=0.045$), being under palliative (OR: 1.5, [95% CI: 1.008-2.4] $P=0.04$) or adjuvant setting (OR: 2.6 [95% CI: 1.3-5.1], $P=0.006$), and history of gastrointestinal surgery (OR: 1.8, [95% CI: 1.03-

**Table 1**
Characteristics of patients.

| Characteristics | N (%) |
|---|---|
| Median age (range) | 63 (23-91) |
| ≥65 y | 301 (42.6) |
| Female | 416 (58.9) |
| Body mass index (kg/m$^2$)* | |
| Low weight | 11 (4.7) |
| Normal | 67 (28.6) |
| Over weight | 80 (34.2) |
| Obese | 76 (32.5) |
| Smoking history | |
| Present | 88 (12.5) |
| Absent | 424 (60.1) |
| Exsmoker | 194 (17.5) |
| Performance score† | |
| 0-1-2 | 633 (89.7) |
| 3-4 | 73 (10.3) |
| Comorbidity present | 370 (52.4) |
| Hypertension | 238 (33.7) |
| Diabetes mellitus | 135 (19.1) |
| Cardiovascular disease | 83 (11.8) |
| Drugs used | |
| Polypharmacy (≥5 drugs) | 125 (17.7) |
| Anticonvulsants | 26 (3.7) |
| Steroids | 17 (2.4) |
| Enteral supplements | 51 (7.2) |
| Gastrointestinal surgery | 118 (16.7) |
| Diagnosis | |
| Breast | 271 (38.4) |
| Gastrointestinal | 142 (20.1) |
| Lung/head & neck | 108 (15.3) |
| Genitourinary | 58 (8.2) |
| Lymphoma | 38 (5.4) |
| Gynecological | 43 (6.1) |
| Other | 46 (6.5) |
| Disease status | |
| Remission/follow-up | 324 (45.9) |
| Adjuvant setting | 90 (12.7) |
| Palliative setting | 292 (41.4) |
| Liver metastasis | 73 (10.3) |
| Albumin level (g/dL, median, range) | 4.2 (1.9-5.3) |
| Low albumin level(<3.5 g/dL) | 54 (9.7) |
| Season of evaluation | |
| Summer | 95 (13.3) |
| Autumn | 227 (28.9) |
| Winter | 204 (28.9) |
| Spring | 181 (25.6) |
| Sun light exposure | |
| Low | 319 (45.2) |
| High | 387 (54.8) |

* The body mass index could be evaluated in 234 patients.
† Eastern Cooperative Oncology Group performance score.

3.2] $P = 0.03$) were associated with VDD. The female patients with headscarf had lower 25(OH) D levels than without group (10.5 ng/mL vs 23.4 ng/mL, $P < 0.001$) and they had more VDD (77.2% vs 29.4%, $P < 0.001$).

## Discussion

In the present study, we evaluated the prevalence of VDD in cancer patients and tried to establish the predictors of VDD to address a specific group of patient for screening. We demon-

**Table 2**
The factors associated with VDD.

| Characteristics | VDD (n, %) | *P* |
|---|---|---|
| Age | | |
| ≥65 y | 216 (71.8) | |
| <65 y | 293 (72.3) | 0.46 |
| Gender | | |
| Male | 196 (67.6) | |
| Female | 313 (75.2) | 0.01 |
| Body mass index (kg/m$^2$) | | |
| Low weight | 7 (63.6) | |
| Normal | 53 (79.1) | |
| Over weight | 53 (66.3) | |
| Obese | 60 (78.9) | 0.18 |
| Smoking history | | |
| Present | 70 (79.5) | |
| Absent | 307 (72.4) | |
| Exsmoker | 132 (68.0) | 0.13 |
| Performance score | | |
| 0-1-2 | 446 (70.5) | |
| 3-4 | 63 (86.3) | 0.002 |
| Comorbidity | | |
| Present | 266 (71.9) | |
| Absent | 243 (72.3) | 0.48 |
| Polypharmacy | | |
| Present | 91 (72.0) | |
| Absent | 418(71.9) | 0.47 |
| Anticonvulsants | | |
| Present | 21 (80.8) | |
| Absent | 488 (71.8) | 0.22 |
| Steroids | | |
| Present | 13 (76.5) | |
| Absent | 496 (72.0) | 0.46 |
| Enteral supplements | | |
| Present | 42 (82.4) | |
| Absent | 467 (71.3) | 0.058 |
| Gastrointestinal surgery | | |
| Present | 92 (78.0) | |
| Absent | 417 (70.9) | 0.07 |
| Diagnosis | | |
| Breast | 193 (71.2) | |
| Gastrointestinal | 110 (77.5) | |
| Lung/head & neck | 80 (74.1) | |
| Genitourinary | 33 (56.9) | |
| Lymphoma | 28 (73.7) | |
| Gynecological | 32 (74.4) | |
| Other | 33 (71.7) | 0.16 |
| Disease status | | |
| Remission/follow-up | 212 (65.4) | |
| Adjuvant setting | 75 (83.3) | |
| Palliative setting | 222 (76.0) | 0.001 |
| Liver metastasis | | |
| Present | 59 (80.8) | |
| Absent | 450 (71.1) | 0.50 |
| Albumin level | | |
| Low (<3.5 g/gl) | 45 (83.3) | |
| Normal | 357 (71.1) | 0.057 |

(*continued on next page*)

**Table 2** (*continued*)

| Characteristics | VDD (n, %) | *P* |
|---|---|---|
| Season of evaluation | | |
| Summer | 63 (67.0) | |
| Autumn | 148 (65.2) | |
| Winter | 157 (77.0) | |
| Spring | 141 (77.9) | 0.007 |
| Sun light exposure | | |
| Low | 246 (77.1) | |
| High | 263 (68.0) | 0.004 |

VDD, vitamin D deficiency.

**Table 3**
Multivariate analysis of factors associated with vitamin D deficiency.

| | Vitamin D deficiency | | |
|---|---|---|---|
| | OR | CI (95%) | *P* |
| Female | 1.5 | 1.05-2.4 | 0.026 |
| PS 3-4 | 2.0 | 0.7-5.3 | 0.16 |
| Sun exposure—low | 1.4 | 1.009-2.1 | 0.045 |
| Disease status | | | |
| Adjuvant vs remission | 2.6 | 1.3-5.1 | 0.006 |
| Palliative vs remission | 1.5 | 1.008-2.4 | 0.04 |
| Enteral supplement | 0.8 | 0.3-2.4 | 0.78 |
| Gastrointestinal surgery | 1.8 | 1.03-3.2 | 0.03 |
| Low albumin level | 1.6 | 0.7-3.7 | 0.20 |

CI, confidence interval; OR, odds ratio.

strated a 72.0% prevalence of VDD. Female gender, Low sun light exposure, being under palliative or adjuvant setting, and history of gastrointestinal surgery were found to be associated with VDD (Table 3).

The central role of vitamin D in calcium metabolism and skeletal health has been recognized for nearly 100 years. The effects of vitamin D on differentiation, proliferation, and apoptosis of cancer cells have been shown both in vitro and in preclinical animal models.[12] Since then "cause and effect" studies, the studies trying to evaluate the effects of hypovitaminosis and clinical results of replacement have emerged. Unfortunately, the studies about breast cancer,[4,13,14] colorectal cancer,[15,16] and prostate cancer[17,18] have conflicting data. Further studies are needed to clarify the VDD in cancer.

Some of the literature has tried to define the patients to highlight the group of patients who should be screened for VDD. The risk factors defined for VDD in noncancer population are increased age, dark pigmented skin, obesity, presence of osteopenia, avoiding sun exposure, living in highly polluted environment, and disease causing fat malabsorption.[19] Cancer patients are more exposed to VDD due to insufficient dietary intake, malnutrition, and being homebound because of fatigue and a poor performance status. However, the data evaluating prevalence and risk factors for VDD is limited. Helou et al found a VDD prevalence of 72%.[20] Gillam et al worked with breast cancer patients who were under bisphosphonate therapy either for bone metastases or osteoporosis.[21] They reported a prevalence of 27.3%. They also pointed out the low rates of VDD screening in metastatic disease. Demille et al studied a population with different types of cancer (mostly breast cancer; 55.9%) and reported a prevalence of 18.1%.[22] Male gender, winter/spring seasons, esophagogastric cancer, and metastatic disease were found to be risk factors of VDD. Our data is consistent with the 1 data presented by Demille et al. Gastrointestinal cancers had more VDD (77.5%) than the average. In addition, we showed an increased risk for VDD in patients with a history of gastrointestinal surgery. Gastrointestinal pathologies and surgery are important risk factors VDD, due to malabsorption.[23] In the study, being under adjuvant or palliative therapy were associated with high VDD. The data are consistent with the findings presented

by Jacot et al.[24] In the study, they compared the 25(OH) D levels of patients who were under neoadjuvant therapy. They showed an increase in VDD, from 79.5% to 97.4% and concluded that chemotherapy drugs can cause a regulatory problem in calcium/RANKL/osteoprotegerin axis. The seasons with low sun light exposure were also found to be risk factors in our study.

In most of the studies held in noncancer patients, female gender has been reported as a risk factor. In the study, we showed that female gender is an important risk factor for VDD. However, most of the patients were wearing traditional clothes and headscarf. The negative effects of headscarf on VDD were reported by Farahati et al.[25] They showed that the mean 25(OH) D value in females with covered clothes was lower than that in Turk females with conventional clothing ($16.3 \pm 12.3$ vs $27.2 \pm 15.8$, $P < 0.001$). Vitamin D is actively secreted by skin, so sun light exposure is crucial. The negative effects of winter on VDD have been reported.[26] In consistent with the data, we found an increased risk of VDD in the months of December-April.

There are some limitations of the present study. First, like in every retrospective analysis, we were prone to selection bias and poor quality of data from patients' records. The study was held in 2 oncology centers. Although the number of patients studied was enough, more centers could provide us to analyze the effects of type of cancer and the effects of medication. In addition, we excluded the inhaler steroid medications. Inclusion of inhaler drugs and over the counter drugs should be more informative. In the study, we used albumin levels as a tool to evaluate the nutritional status indirectly. Patients with low albumin constituted a small part of the study population. Direct nutritional evaluation could have provided more exact data. We designed the study also to evaluate the effects of clinical characteristics of the patients. However, one-third of the population had a diagnosis of breast cancer. This unbalanced distribution of cancer diagnoses could have affected the analysis.

## Conclusion

There is limited data and no guideline recommendation for VDD screening in cancer patients. Our study concluded that prevalence of VDD is high in cancer patients and female gender, low sun light exposure, being under palliative or adjuvant setting, and history of gastrointestinal surgery are risk factors for VDD. In addition, we concluded that these parameters should be used to select patients for screening of VDD.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.currproblcancer.2018.12.008.

## References

1. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2011;96:1911–1930.
2. Holick MF. Vitamin D deficiency. *New Engl J Med*. 2007;357:266–281.
3. LeBlanc ES, Zakher B, Daeges M, et al. Screening for vitamin D deficiency: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2015;162:109–122.
4. Nogues X, Servitja S, Pena MJ, et al. Vitamin D deficiency and bone mineral density in postmenopausal women receiving aromatase inhibitors for early breast cancer. *Maturitas*. 2010;66:291–297.
5. Revuelta Iniesta R, Rush R, Paciarotti I, et al. Systematic review and meta-analysis: prevalence and possible causes of vitamin D deficiency and insufficiency in pediatric cancer patients. *Clin Nutr*. 2016;35:95–108.
6. Abbas S, Linseisen J, Slanger T, et al. Serum 25-hydroxyvitamin D and risk of post-menopausal breast cancer–results of a large case-control study. *Carcinogenesis*. 2008;29:93–99.
7. Gandini S, Boniol M, Haukka J, et al. Meta-analysis of observational studies of serum 25-hydroxyvitamin D levels and colorectal, breast and prostate cancer and colorectal adenoma. *Int J Cancer*. 2011;128:1414–1424.
8. Lee JE, Li HJ, Chan AT, et al. Circulating levels of vitamin D and colon and rectal cancer: the physicians' health study and a meta-analysis of prospective studies. *Cancer Prev Res*. 2011;4:735–743.

9. Autier P, Boniol M, Pizot C, et al. Vitamin D status and ill health: a systematic review. *Lancet Diabetes Endocrinol*. 2014;2:76–89.
10. Dimitrakopoulou VI, Tsilidis KK, Haycock PC, et al. Circulating vitamin D concentration and risk of seven cancers: mendelian randomisation study. *BMJ*. 2017;359:j4761.
11. http://temd.org.tr/admin/uploads/tbl_kilavuz/20180516162801-2018-05-16tbl_kilavuz162800.pdf.
12. Kennel KA, Drake MT. Vitamin D in the cancer patient. *Curr Opin Support Palliat Care*. 2013;7:272–277.
13. Scarmo S, Afanasyeva Y, Lenner P, et al. Circulating levels of 25-hydroxyvitamin D and risk of breast cancer: a nested case-control study. *Breast Cancer Res*. 2013;15:R15.
14. Mizrak Kaya D, Ozturk B, Kubilay P, et al. Diagnostic serum vitamin D level is not a reliable prognostic factor for resectable breast cancer. *Future Oncol*. 2018;14:1461–1467.
15. Avenell A, MacLennan GS, Jenkinson DJ, et al. Long-term follow-up for mortality and cancer in a randomized placebo-controlled trial of vitamin D(3) and/or calcium (RECORD trial). *J Clin Endocrinol Metab*. 2012;97:614–622.
16. Jenab M, Bueno-de-Mesquita HB, Ferrari P, et al. Association between pre-diagnostic circulating vitamin D concentration and risk of colorectal cancer in European populations: a nested case-control study. *BMJ*. 2010;340:b5500.
17. Gilbert R, Bonilla C, Metcalfe C, et al. Associations of vitamin D pathway genes with circulating 25-hydroxyvitamin-D, 1,25-dihydroxyvitamin-D, and prostate cancer: a nested case-control study. *Cancer Causes Control*. 2015;26:205–218.
18. Kristal AR, Arnold KB, Neuhouser ML, et al. Diet, supplement use, and prostate cancer risk: results from the prostate cancer prevention trial. *Am J Epidemiol*. 2010;172:566–577.
19. Khan QJ, Fabian CJ. How I treat vitamin D deficiency. *J Oncol Pract*. 2010;6:97–101.
20. Helou M, Ning Y, Yang S, et al. Vitamin D deficiency in children with cancer. *J Pediatr Hematol Oncol*. 2014;36:212–217.
21. Wang-Gillam A, Miles DA, Hutchins LF. Evaluation of vitamin D deficiency in breast cancer patients on bisphosphonates. *Oncologist*. 2008;13:821–827.
22. DeMille DM, Piscitelli M, Ocker A, et al. Vitamin D deficiency in the oncology setting. *J Community Support Oncol*. 2014;12:13–19.
23. Karefylakis C, Naslund I, Edholm D, et al. Vitamin D status 10 years after primary gastric bypass: gravely high prevalence of hypovitaminosis D and raised PTH levels. *Obes Surg*. 2014;24:343–348.
24. Jacot W, Pouderoux S, Thezenas S, et al. Increased prevalence of vitamin D insufficiency in patients with breast cancer after neoadjuvant chemotherapy. *Breast Cancer Res Treat*. 2012;134:709–717.
25. Farahati J, Nagarajah J, Gilman E, et al. Ethnicity, clothing style, and body mass index are significant predictors of vitamin D insufficiency in Germany. *Endocr Pract*. 2015;21:122–127.
26. Sham L, Yeh EA, Magalhaes S, et al. Evaluation of fall Sun Exposure Score in predicting vitamin D status in young Canadian adults, and the influence of ancestry. *J Photochem Photobiol B*. 2015;145:25–29.