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Prevalence of Vitamin D Deficiency in Patients With Foot and Ankle Injuries

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Abstract

Background: Vitamin D deficiency has been identified as one of the most common causes of fragility fractures and poor fracture healing. Although rates of vitamin D deficiency have been delineated in various orthopaedic populations, little is known about the prevalence of vitamin D deficiency in patients with foot and ankle disorders. The goal of this study was to identify the prevalence of vitamin D deficiency in patients with a low energy fracture of the foot or ankle.
Methods: Over a 6-month period, a serum 25-OH vitamin D level was obtained from consecutive patients with a low energy ankle fracture, fifth metatarsal base fracture, or stress fracture of the foot or ankle. For comparative purposes, vitamin D levels in patients with an ankle sprain and no fracture were also examined.
Results: The study cohort included 75 patients, of which 21 had an ankle fracture, 23 had a fifth metatarsal base fracture, and 31 had a stress fracture. The mean age was 52 (range, 16–80) years. Thirty-five of the fracture patients (47%) had an insufficient vitamin D level (below the recommended level of 30 ng/mL), and 10 of the patients (13%) had a level that was deficient (< 20 ng/mL). Vitamin D levels were significantly lower in those with a fracture than in those with an ankle sprain ($P = .02$). In the fracture cohort, the factors significantly associated with vitamin D insufficiency in the multivariate analysis were smoking ($P = .03$), obesity ($P = .003$), and other medical risk factors for vitamin D deficiency ($P = .03$).
Conclusion: Hypovitaminosis D was common among patients with a foot or ankle injury seen at our institution. Patients with a low energy fracture of the foot or ankle were at particular risk for low vitamin D, especially if they smoked, were obese, or had other medical risk factors. Given that supplementation with vitamin D (± calcium) has been shown to reduce the risk of fragility fractures and improve fracture healing, monitoring of 25-OH vitamin D and supplementation should be considered in patients with fractures.
Level of Evidence: Level III, prospective case control.

Keywords: Vitamin D deficiency, hypovitaminosis D, ankle fracture, metatarsal fracture, stress fracture

Introduction

Fragility fractures are associated with considerable morbidity, mortality, and cost to the health care system and are increasingly common in our society. Vitamin D deficiency has been identified as one of the most common causes of these fractures,[20,26,28] as serum 25-hydroxyvitamin D [25(OH) D] levels persistently below 20 ng/mL may lead to hypocalcemia, secondary hyperparathyroidism, osteoporosis, and osteomalacia in adults or rickets in children.[13,24] Evidence suggests that low vitamin D levels may also be implicated in fracture nonunions.[4,14] In addition, it has been suggested that maintenance of adequate vitamin D levels may reduce the risk of cancer, falls, and cardiovascular disease.[1,17,19,31]

Vitamin D deficiency is estimated to affect more than 1 billion people globally and more than 25% of individuals in the United States.[14,21,32] Studies have shown low levels of vitamin D in elective orthopaedic surgery patients in New York City (15% with vitamin D < 20 ng/mL),[3] healthy Boston adolescents (42% with vitamin D < 20 ng/mL),[12] patients undergoing total hip replacement in Boston (22% with vitamin D < 15 ng/mL)[10] and the United Kingdom (24% with vitamin D < 16 ng/mL),[22] patients with an unexplained fracture nonunion (51% with vitamin D < 20 ng/mL),[4] patients undergoing spinal fusion (27% with vitamin

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D < 20 ng/mL),[27] and orthopaedic trauma patients (39% with vitamin D < 20 ng/mL).[6]

Although the rate of vitamin D deficiency has been identified in these various orthopaedic populations,[3,10–12,22] little is known about the prevalence of vitamin D deficiency in patients with foot and ankle disorders. The goals of this study were to identify the prevalence of vitamin D deficiency in patients with a low energy fracture of the foot or ankle and to determine if patients with a foot and ankle fracture were at greater risk of hypovitaminosis D than a control population of foot and ankle patients without fracture.

Methods

This was a prospective case control study. The approval of our institutional review board was obtained. All patients who presented to our institution in Boston (USA, latitude +42.35° N) with a low energy ankle fracture, fifth metatarsal base fracture, or stress fracture of the foot or ankle were included in the study. Low energy mechanism of injury was defined as a fall from standing, twisting injury, dance or sports injury, or repetitive stress injury. Patients with a high energy mechanism of injury, such as a fall from greater than 5 feet or motor vehicle collision, were excluded. The period of enrollment was May to November 2012. Seventy-five patients with a low energy foot or ankle fracture were enrolled in this study. The mean age was 52 years (range, 16–80), and the study sample was 69% Caucasian. Additional characteristics of the patient cohort are presented in Table 1.

At the time of initial evaluation, a serum 25(OH)D was obtained from our hospital laboratory under standard automated conditions by Mayo Medical Laboratories of New England using Liquid Chromatography-Tandem Mass Spectrometry. Vitamin D sufficiency was defined as a serum 25(OH)D greater than or equal to 30 ng/mL. Insufficiency was defined as a serum 25(OH)D less than 30 ng/mL but greater than or equal to 20 ng/mL. Deficiency was defined as a serum 25(OH)D less than 20 ng/mL.[14,15]

Information recorded for each patient included sex, age, race or ethnicity, fracture type, smoking status, obesity, history of osteopenia or osteoporosis, vitamin D supplementation at time of injury, and a history of prior foot or ankle fracture and/or prior fragility fracture (hip fracture, distal radius fracture, proximal humerus fracture). Additional independent medical risk factors for vitamin D deficiency recorded included actively breastfeeding mothers, history of hereditary rickets, glucocorticoid medication, anticonvulsant medication, HAART (AIDS treatment), chronic renal insufficiency, liver failure, gastrointestinal malabsorption syndromes, and primary hyperparathyroidism.

For comparison, we estimated the baseline prevalence of vitamin D insufficiency in our practice by examining 25(OH)D levels in patients with an ankle sprain and no fracture. Patients for this portion of the study were identified retrospectively. Those seen for an ankle sprain from May to November over the past 10 years who had a 25(OH) D level drawn by our multi-specialty physician group during this same period were included. Vitamin D levels had been obtained either for routine screening or because of a particular medical condition. Any patient with a fracture associated with the injury was excluded from this group. The patient information and independent risk factors for vitamin D deficiency outlined above were gathered for the ankle sprain patients as well.

Table 1. Patient Characteristics.

Variable	No. (%)
Sex	
Female	55 (73.3%)
Male	20 (26.7%)
Age	
30 or younger	10 (13.3%)
31–59	38 (50.7%)
60 or older	27 (36.0%)
Race/ethnicity	
Caucasian	52 (69.3%)
Hispanic	9 (12.0%)
African American	7 (9.3%)
Asian or Middle-Eastern	4 (5.4%)
Other	3 (4.0%)
Diagnosis	
Fifth metatarsal fracture	23 (30.7%)
Stress fracture	31 (41.3%)
Ankle fracture	21 (28.0%)
Smoker	
No	68 (90.7%)
Yes	7 (9.3%)
Body mass index[a]	
Normal (25 or below)	24 (35.3%)
Overweight (25–30)	21 (30.9%)
Obese (30 or above)	23 (33.8%)
Osteopenia/osteoporosis	
No	59 (78.7%)
Yes	16 (21.3%)
Currently on Vitamin D supplementation	
No	58 (77.3%)
Yes	17 (22.7%)
Prior fracture[b]	
No	59 (78.7%)
Yes	16 (21.3%)
Other medical risk factors	
No	63 (84.0%)
Yes	12 (16.0%)
Total	75 (100.0%)

[a]Excludes 7 patients for whom body mass index was unknown.
[b]All prior fractures were foot or ankle fractures. There were no other prior fragility fractures.

Table 2. Prevalence of Hypovitaminosis D and Mean 25(OH)D in Patients with a Low Energy Fracture or Ankle Sprain.

Vitamin D, ng/mL	Low Energy Fracture (n = 75)	Ankle Sprain (n = 41)
Sufficient (> 30)	40 (53%)	29 (71%)
Insufficient (20–30)	25 (34%)	8 (19%)
Deficient (< 20)	10 (13%)	4 (10%)
Mean (SD)	31.3 (11.8) ng/mL	36.8 (13.4) ng/mL

With regard to the statistical analyses, a 2-tailed Student t test with a predetermined level of significance of $P < .05$ was used for categorical variables. For the comparison between patients who sustained a fracture and those who did not, a post hoc power analysis (parameters: $P < .05$, power = 80%) using a vitamin D difference of 5.5 ng/mL indicated that a minimum sample size of 40 patients would be necessary to detect an effect between groups. To determine the factors associated with hypovitaminosis D, logistic regression was performed. Factors with $P < .10$ in the univariate analysis were retained in the multivariate model. In the multivariate analysis, multiple logistic regression was used to adjust for all variables simultaneously. Associations were estimated on the basis of odds ratios (ORs) and 95% confidence intervals (CIs). $P < .05$ was considered statistically significant, and all tests were 2-sided. Statistical analysis was performed with use of SAS (Version 9; SAS Institute, Cary, NC).

Results

Among patients in the study cohort, the mean serum 25(OH) D level was 31.3 ± 11.8 ng/mL. Thirty-five patients (47%) had a vitamin D level below the recommended level of 30 ng/mL, including 25 patients (34%) who had a level that was insufficient (20–30 ng/mL) and 10 patients (13%) who were deficient (< 20 ng/mL) (Table 2).

For comparison, 41 patients with an ankle sprain and no fracture were identified. There were no statistically significant differences between this group and the low energy fracture group with respect to the factors examined (Table 3). In this comparison group, 29% were found to have a vitamin D level below the recommended level. The mean serum 25(OH)D was 36.8 ± 13.4 in this group, which was significantly higher than the fracture group ($P = .02$).

Within the fracture group, the risk factors for vitamin D insufficiency were determined. In the multivariate analysis, the factors associated with vitamin D insufficiency in this group were smoking ($P = .03$), obesity ($P = .003$), and other medical risk factors for vitamin D deficiency ($P = .03$) (Table 4). In the ankle sprain group, none of the risk factors were associated with vitamin D insufficiency.

Table 3. Demographics of Patients with a Low Energy Fracture or Ankle Sprain[a].

	Fracture (n = 75)	Ankle Sprain (n = 41)	*P* Value
Age, mean (SD)	51.5 (15.9)	56.3 (12.8)	.11
Race/ethnicity			
Caucasian	52 (69.3)	34 (82.9)	.11
Hispanic	9 (12)	1 (2.4)	.08
African American	7 (9.3)	3 (7.3)	.71
Asian or Middle-Eastern	4 (5.4)	2 (4.8)	.94
Unknown	3 (4)	1 (2.4)	.66
Sex			
Male	20 (26.7)	8 (19.5)	.39
Female	55 (73.3)	33 (80.5)	.39
Current smoker	7 (9.6)	7 (18.4)	.19
Other medical risk factor	19 (34.7)	21 (51.2)	.08
Body mass index	28.3 kg/m^2	27.8 kg/m^2	.73

[a]Percentage of cohort is shown in parentheses, unless otherwise indicated.

Discussion

Vitamin D has a central role in bone health and mineral homeostasis.[16] This fat-soluble hormone regulates calcium and phosphate levels by affecting gastrointestinal absorption and bone turnover. With deficient vitamin D (< 20 ng/mL), there is decreased calcium absorption and up-regulation of parathyroid hormone, which leads to increased bone resorption and subsequent osteoporosis, osteomalacia in adults, rickets in children, and impaired bone healing.[8,9,14]

This study identified a 47% prevalence of hypovitaminosis D in patients with a low energy fracture of the foot or ankle. By comparison, a well-matched group of patients with an ankle sprain in the absence of fracture, seen during the same time of year and same geographic location after a similar mechanism of injury, had a hypovitaminosis D prevalence of 30%. The prevalence of vitamin D insufficiency in this comparison group provides an estimate of baseline hypovitaminosis D during the sunny months of the year in our geographic location (Boston). These data suggest that a large number of patients seen at our institution have hypovitaminosis D, regardless of whether they present with a fracture. However, our data also suggest that those who present with a low energy fracture are even more likely to be vitamin D deficient.

A review of the literature provides additional estimates of baseline vitamin D deficiency. The most comparable baseline level from the literature is from a study by Bogunovic et al, which reported a 43% insufficiency rate (< 32 ng/mL) and a 15% deficiency rate (< 20 ng/mL) in elective orthopaedic surgery patients. Although this study population is well-matched to our cohort in terms of age (mean age 60 years) and geography (New York City, latitude

Table 4. Factors Associated with Hypovitaminosis D.

Variable	Rate of Vitamin D Insufficiency	Univariate		Multivariate	
		OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Sex				NA	NA
Female[a]	45.5% (25/55)	1.00	—		
Male	50.0% (10/20)	1.20 (0.43–3.34)	.73		
Age				NA	NA
30 or younger[a]	40.0% (4/10)	1.00	—		
31–59	50.0% (19/38)	1.50 (0.36–6.18)	.57		
60 or older	44.4% (12/27)	1.20 (0.27–5.25)	.81		
Race/ethnicity					
Caucasian[a]	38.5% (20/52)	1.00	—	1.00	—
Hispanic	77.8% (7/9)	5.60 (1.06–29.7)	**.04**	5.58 (0.84–36.9)	.07
African American	71.4% (5/7)	4.00 (0.71–22.6)	.11	3.02 (0.33–27.3)	.32
Asian or Middle-Eastern	50.0% (2/4)	1.60 (0.21–12.3)	.65	0.62 (0.07–5.61)	.67
Other	33.3% (1/3)	0.80 (0.07–9.41)	.85	0.52 (0.01–19.1)	.72
Diagnosis				NA	NA
Fifth metatarsal fracture[a]	34.8% (8/23)	1.00	—		
Stress fracture	48.4% (15/31)	1.76 (0.58–5.33)	.32		
Ankle fracture	57.1% (12/21)	2.50 (0.74–8.45)	.14		
Smoker					
No[a]	42.7% (29/68)	1.00	—	1.00	—
Yes	85.7% (6/7)	8.07 (0.92–70.7)	.06	14.2 (1.22–164.8)	**.03**
Body mass index[b]					
Normal (25 or below)[a]	20.8% (5/24)	1.00	—	1.00	—
Overweight (25–30)	52.4% (11/21)	4.18 (1.13–15.4)	**.03**	3.67 (0.85–15.9)	.08
Obese (30 or above)	69.6% (16/23)	8.69 (2.31–32.7)	**.001**	9.70 (2.09–45.1)	**.003**
Osteopenia/osteoporosis				NA	NA
No[a]	45.8% (27/59)	1.00	—		
Yes	50.0% (8/16)	1.19 (0.39–3.58)	.76		
Currently on vitamin D supplementation				NA	NA
No[a]	51.7% (30/58)	1.00	—		
Yes	29.4% (5/17)	0.39 (0.12–1.25)	.11		
Prior fracture				NA	NA
No[a]	49.2% (29/59)	1.00	—		
Yes	37.5% (6/16)	0.62 (0.20–1.93)	.41		
Other medical risk factors					
No[a]	41.8% (26/63)	1.00	—	1.00	—
Yes	75.0% (9/12)	4.27 (1.05–17.3)	.04	5.97 (1.11–32.1)	**.03**

Abbreviations: CI, confidence interval; NA, not available; OR, odds ratio. *P* values < .05 are shown in bold.
[a]Reference.
[b]Excludes 7 patients for whom body mass index was unknown.

+40.71° N),[3] these patients were examined in part during the winter months and therefore would be expected to have lower vitamin D levels than patients in our study. Although these previous studies provide good historic controls, our ankle sprain control group provides a better baseline value because vitamin D fluctuates by time of year and geographic location. Our control group was from the same geographic location and was matched to time of year.

A number of independent factors either impair adequate vitamin D bioavailability or blunt the effects of this hormone.[14] These include skin color (race/ethnicity), sex, age, dietary intake, sunlight exposure, breastfeeding, smoking, obesity, hereditary disorders that cause rickets, certain medications such as glucocorticoids and anticonvulsants, and medical conditions such as renal failure, liver failure, gastrointestinal malabsorption syndromes, and primary hyperparathyroidism. Although we were unable to measure sun exposure or vitamin D dietary intake, we attempted to determine if any of these other factors posed an additional risk for hypovitaminosis D.

Among the fracture cohort, we identified smoking, obesity, and having a medical risk factor for vitamin D insufficiency as strongly correlated to a lower vitamin D level. Smoking may lead to low vitamin D by attenuating calcium absorption and promoting bone loss[18] and may represent an indicator for poor dietary habits and generalized health. Obesity is a known risk factor for low vitamin D due to sequestration of this lipid soluble hormone in adipose tissue.[14] The medical conditions that contribute to hypovitaminosis D do so by a variety of mechanisms. Our ability to assess the effect of all of these risk factors was limited by our study numbers, which may explain the lack of significance seen in the ankle sprain group. Nevertheless, these data suggest that a particular concern for hypovitaminosis D is warranted in patients with a low energy foot or ankle fracture who smoke, are obese, or have an additional medical risk factor for hypovitaminosis D.

Our data showed a trend within both the fracture and ankle sprain groups of those receiving vitamin D supplementation having a lower rate of hypovitaminosis D. It is somewhat surprising that this trend was not statistically significant as it has been documented elsewhere that vitamin D supplementation increases vitamin D serum levels.[14] Possible explanations for this include an insufficient sample size, too brief a duration of supplementation in these individuals to effect a change, or that patients were profoundly deficient and had already corrected considerably.

The high percentage (21%) of patients in this study who had a prior foot or ankle fracture raises the question of whether a low energy fracture of the foot or ankle portends other fragility fractures, such as a hip fracture or distal radius fracture. It is interesting that none of the patients in this study had a prior hip, distal radius, or proximal humerus fracture. A larger cohort would be needed, potentially prospectively followed, to thoroughly evaluate the relationship between these injuries and other fragility fractures.

It is important to note that the level of hypovitaminosis D we observed was during the sunniest months of the year (May to November) in New England. Lack of sun exposure is a known risk factor for vitamin D deficiency. It is generally thought that the bulk of vitamin D produced by people living north of approximately 37° latitude occurs between March and November.[16] Seasonal fluctuations of vitamin D exist, and during less sunny times of year, vitamin D levels fall and we rely more heavily upon dietary sources (oily fish, fortified milk, daily vitamin supplements).[16] Due to the time of year of this study, the observed prevalence of hypovitaminosis D may be lower than exists during the rest of the year in our community.

The general consensus is that an optimal vitamin D level is greater than 30 ng/mL.[7,13–15,24] Holick concluded that a serum concentration of greater than 20 ng/mL but less than 30 ng/mL should be considered relatively insufficient.[14] This is explained biologically as the level of serum vitamin D is inversely proportional to parathyroid hormone (PTH) level until 25(OH)D reaches a serum concentration of 30 to 40 ng/mL, at which point PTH levels do not decline any further.[5,30] Bischoff-Ferrari has suggested that a level as high as 36 to 48 ng/mL may be desirable for cancer prevention, whereas others have suggested that a level above 30 ng/mL is adequate to prevent falls, reduce cardiovascular disease, and prevent fractures.[2,17,19,31] We did not obtain calcium, phosphorus, or parathyroid hormone levels. This decision was made because there is already a well-established relationship between vitamin D, calcium, phosphorus, and parathyroid hormone[14] and we did not expect these laboratory values to impact our ability to answer the principle questions of the study.

Animal models suggest that vitamin D supplementation facilitates fracture healing.[5,9,23] In addition, a randomized clinical trial after proximal humerus fracture in humans showed increased fracture callus formation with vitamin D and calcium supplementation when compared with placebo supplementation.[8] For patients diagnosed with vitamin D deficiency, the diagnosing orthopaedist may either treat the patient or refer the patient to his or her primary care physician or endocrinologist. Patients in this study with a low vitamin D level were referred to their primary care physicians. The Institute of Medicine released a report in 2010 outlining the recommended daily intake of vitamin D for healthy individuals, which is 600 IU (international units) for those younger than 70 and 800 IU after age 71.[25] In 2011, a clinical practice guideline by the Endocrine Society recommended that adults with vitamin D deficiency (< 20 ng/mL) receive 50 000 IU of vitamin D2 or D3 orally once per week for 8 weeks, followed by a typical dose of 1500 to 2000 IU daily thereafter to maintain a level greater than 30 ng/mL. For vitamin D insufficiency (20–30 ng/mL), a daily dose of 600 to 800 IU of vitamin D3 may be sufficient to raise levels above 30 ng/mL.[15] Vitamin D intoxication is extremely rare.[14]

Conclusion

This study demonstrated that hypovitaminosis D is common among patients with a foot or ankle injury seen at our institution, particularly among those with a low energy fracture of the foot or ankle. Additional predictors of hypovitaminosis D include smoking, obesity, and having a medical risk factor for vitamin D insufficiency. Given that supplementation and repletion are relatively simple and that vitamin D supplementation has been shown in 2 separate meta-analyses to cause a greater than 20% risk reduction in all nonvertebral fractures[2,29] and has been linked to improved fracture healing,[5,8,9,23] we recommend identifying at-risk patients, obtaining a 25(OH)D level, and considering vitamin D supplementation or repletion.

Declaration of Conflicting Interests

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References

1. Bischoff-Ferrari HA. Optimal serum 25-hydroxyvitamin D levels for multiple health outcomes. *Adv Exp Med Biol*. 2008;624:55–71.
2. Bischoff-Ferrari HA, Willett WC, Wong JB, et al. Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. *JAMA*. 2005;293(18):2257–2264.
3. Bogunovic L, Kim AD, Beamer BS, et al. Hypovitaminosis D in patients scheduled to undergo orthopaedic surgery: a single-center analysis. *J Bone Joint Surg Am*. 2010;92(13):2300–2304.
4. Brinker MR, O'Connor DP, Monla YT, et al. Metabolic and endocrine abnormalities in patients with nonunions. *J Orthop Trauma*. 2007;21(8):557–570.
5. Copp HD, Greenberg DM. Studies on bone fracture healing. *J Nutr*. 1945;4:261–267.
6. Crist B, Hood M, Murtha Y, et al. Prevalence of vitamin D deficiency in orthopaedic trauma patients. Paper presented at: Annual Meeting of the Orthopaedic Trauma Association; 2012.
7. Dawson-Hughes B, Heaney RP, Holick MF, et al. Estimates of optimal vitamin D status. *Osteoporos Int*. 2005;16(7):713–716.
8. Doetsch AM, Faber J, Lynnerup N, et al. The effect of calcium and vitamin D3 supplementation on the healing of the proximal humerus fracture: a randomized placebo-controlled study. *Calcif Tissue Int*. 2004;75(3):183–188.
9. Fu L, Tang T, Miao Y, et al. Effect of 1,25-dihydroxy vitamin D3 on fracture healing and bone remodeling in ovariectomized rat femora. *Bone*. 2009;44(5):893–898.
10. Glowacki J, Hurwitz S, Thornhill TS, et al. Osteoporosis and vitamin-D deficiency among postmenopausal women with osteoarthritis undergoing total hip arthroplasty. *J Bone Joint Surg Am*. 2003;85-A(12):2371–2377.
11. Glowacki J, LeBoff MS, Kolatkar NS, et al. Importance of vitamin D in hospital-based fracture care pathways. *J Nutr Health Aging*. 2008;12(5):291–293.
12. Gordon CM, DePeter KC, Feldman H, et al. Prevalence of vitamin D deficiency among healthy adolescents. *Arch Pediatr Adolesc Med*. 2004;158(6):531–537.
13. Holick MF. Resurrection of vitamin D deficiency and rickets. *J Clin Invest*. 2006;116(8):2062–2072.
14. Holick MF. Vitamin D deficiency. *N Engl J Med*. 2007;357(3):266–281.
15. 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(7):1911–1930.
16. Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. *Am J Clin Nutr*. 2008;87(4):1080S–1086S.
17. Kim DH, Sabour S, Sagar UN, et al. Prevalence of hypovitaminosis D in cardiovascular diseases (from the National Health and Nutrition Examination Survey 2001 to 2004). *Am J Cardiol*. 2008;102(11):1540–1544.
18. Krall EA, Dawson-Hughes B. Smoking increases bone loss and decreases intestinal calcium absorption. *J Bone Miner Res*. 1999;14(2):215–220.
19. LeBoff MS, Hawkes WG, Glowacki J, et al. Vitamin D-deficiency and post-fracture changes in lower extremity function and falls in women with hip fractures. *Osteoporos Int*. 2008;19(9):1283–1290.
20. McCabe MP, Smyth MP, Richardson DR. Current concept review: vitamin D and stress fractures. *Foot Ankle Int*. 2012;33(6):526–533.
21. Mithal A, Wahl D, Bonjour JP, et al. Global vitamin D status and determinants of hypovitaminosis D. *Osteoporos Int*. 2009;20(11):1807–1820.
22. Nawabi DH, Chin KF, Keen RW, et al. Vitamin D deficiency in patients with osteoarthritis undergoing total hip replacement: a cause for concern? *J Bone Joint Surg Br*. 2010;92(4):496–499.
23. Omeroğlu H, Ateş Y, Akkuş O, et al. Biomechanical analysis of the effects of single high-dose vitamin D3 on fracture healing in a healthy rabbit model. *Arch Orthop Trauma Surg*. 1997;116(5):271–274.
24. Rajakumar K. Vitamin D, cod-liver oil, sunlight, and rickets: a historical perspective. *Pediatrics*. 2003;112(2):e132–e135.
25. Ross AC, Taylor CL, Yaktine AL, et al. In: Ross AC, Taylor CL, Yaktine AL, Del Valle HB, eds. *Dietary Reference Intakes for Calcium and Vitamin D*. Washington, DC: The National Academies Press; 2011.
26. Sonneville KR, Gordon CM, Kocher MS, et al. Vitamin D, calcium, and dairy intakes and stress fractures among female adolescents. *Arch Pediatr Adolesc Med*. 2012;166(7):595–600.
27. Stoker GE, Buchowski JM, Bridwell KH, et al. Preoperative vitamin D status of adults undergoing surgical spinal fusion. *Spine*. 2013;38(6):507-515.
28. Sunyecz J. The use of calcium and vitamin D in the management of osteoporosis. *Ther Clin Risk Manag*. 2008;4(4):827–836.
29. Tang BM, Eslick GD, Nowson C, et al. Use of calcium or calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis. *Lancet*. 2007;370(9588):657–666.
30. Thomas MK, Lloyd-Jones DM, Thadhani RI, et al. Hypovitaminosis D in medical inpatients. *N Engl J Med*. 1998;338(12):777–783.
31. Wicherts IS, van Schoor NM, Boeke AJ, et al. Vitamin D status predicts physical performance and its decline in older persons. *J Clin Endocrinol Metab*. 2007;92(6):2058–2065.
32. Yetley E. Assessing the vitamin D status of the US population. *Am J Clin Nutr*. 2008;88(2):558S–564S.