Hypovitaminosis D in Patients Scheduled to Undergo Orthopaedic Surgery

A Single-Center Analysis

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Background: Vitamin D is essential for optimal bone health and muscle function. An alarmingly high rate of vitamin-D deficiency in the general population has been reported recently. The purpose of the present study was to characterize the extent of low serum levels of vitamin D among orthopaedic surgery patients.

Methods: We performed a retrospective chart review of 723 patients who were scheduled for orthopaedic surgery between January 2007 and March 2008. Preoperative serum 25-hydroxyvitamin D (25[OH]D) levels were measured. The prevalence of normal (≥32 ng/mL), insufficient (<32 ng/mL), and deficient (<20 ng/mL) vitamin-D levels was determined. Logistic regression was used to assess risk factors for insufficient (<32 ng/mL) 25(OH)D levels.

Results: Overall, 43% of all patients had insufficient serum vitamin-D levels, and, of these, 40% had deficient levels. Among the orthopaedic services, the highest rates of low serum vitamin-D levels were seen in the trauma and sports services, in which the rates of abnormal (insufficient and deficient) vitamin-D levels were 66% and 52%, respectively. The lowest rate of abnormal vitamin-D levels was seen in the metabolic bone disease service. Patients between the ages of fifty-one and seventy years were 35% less likely to have low vitamin-D levels than patients between the ages of eighteen and fifty years ($p = 0.018$). The prevalence of low vitamin-D levels was significantly higher in men ($p = 0.006$). Individuals with darker skin tones (blacks and Hispanics) were 5.5 times more likely to have low vitamin-D levels when compared with those with lighter skin tones (whites and Asians) ($p < 0.001$).

Conclusions: The prevalence of low serum levels of vitamin D among patients undergoing orthopaedic surgery is very common. Given the importance of vitamin D in musculoskeletal health, such low levels may negatively impact patient outcomes.

An alarmingly high prevalence of vitamin-D deficiency has been described in numerous segments of the global population. Numerous studies have characterized the scope of the problem. Vitamin D (25[OH]D) deficiency has been seen in all races, age groups, and ethnic backgrounds, and it is estimated to affect >1 billion people worldwide[1]. In a group of American postmenopausal women taking medication for osteoporosis, more than half were found to have inadequate levels of vitamin D[2]. Among a group of women with osteoarthritis undergoing total hip arthroplasty, two in five had suboptimal levels of vitamin D[3]. High rates of hypovitaminosis D have also been reported in young, healthy cohorts. In a group of black and Hispanic adolescents in Boston, 52% were found to be vitamin D-deficient[4]. Another study demonstrated that 36% of healthy adolescents from Northern Ireland were vitamin D-deficient[5]. A wintertime prevalence study in Beijing demonstrated that 89.2% of young Chinese girls were vitamin D-deficient[6].

Despite these reports on the prevalence of hypovitaminosis D in the general population, there is a paucity of studies focusing on orthopaedic surgery patients. Moreover, while the majority of studies of this nature have involved postmenopausal women with fragility or hip fractures, to our knowledge, no studies to date have described the prevalence of hypovitaminosis D in the adult orthopaedic population, irrespective of age or sex. Given the critical role of vitamin D in musculoskeletal

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health and function as well as the potential negative consequences of vitamin-D deficiency in the operative and postoperative settings, data revealing the prevalence of vitamin-D deficiency in this patient population may be of value.

The purpose of the present study was to characterize the extent of vitamin-D inadequacy among orthopaedic surgery patients across a number of specific services encompassing a spectrum of musculoskeletal problems including fracture, acute soft-tissue injury, overuse injury, degenerative joint disease, and chronic/progressive deformity.

Materials and Methods

Subjects

We performed a retrospective chart review of 723 patients who were scheduled to undergo orthopaedic surgery at our institution in New York, NY (+40.76°N), between January 2007 and March 2008, following approval by our institutional review board. Study subjects were identified by monitoring the surgery schedules of participating surgeons who obtain serum 25(OH)D levels for all of their patients prior to surgery as part of routine preoperative care. All patients who were included in the study had been cleared for elective orthopaedic surgery by a specialist in internal medicine. Patients with comorbid medical conditions that precluded surgery were not included. Only patients with musculoskeletal conditions requiring surgical intervention were included. Given these parameters, patients from the following orthopaedic services were included in the study: Trauma (all patients), Foot and Ankle (all patients), Sports Medicine (patients undergoing anterior cruciate ligament and/or meniscal repair, including meniscectomy), Arthroplasty (patients undergoing primary total hip and knee arthroplasty), Hand (patients with distal radial or ulnar fracture), and Metabolic Bone Disease (patients with vertebral compression fracture).

Laboratory Studies

Calcium, phosphorus, and albumin levels were measured with use of standard automated laboratory methods. Measurement of serum 25(OH)D was not standardized and was dependent on the laboratory chosen by patients for preoperative testing. The hospital laboratory, used by 91% of the patients surveyed, employed liquid chromatography-tandem mass spectrometry that had an analytical sensitivity of 4 ng/mL for $25(OH)D_2$ and $25(OH)D_3$. Laboratory results were collected by means of a retrospective chart review of patient records. Only preoperative total 25(OH)D levels were collected and analyzed.

Background Data

Patient demographic and background variables considered to be risk factors for vitamin-D inadequacy were collected by means of a chart review and were evaluated for potential association with 25(OH)D levels. Variables included the primary musculoskeletal diagnosis, age, sex, race, and body-mass index. Age was further categorized into three groups (eighteen to fifty years, fifty-one to seventy years, and more than seventy years) to account for the different dietary habits and gastrointestinal absorptive capacities of these age groups and to investigate their potential effects on serum 25(OH)D levels. Body-mass index was also grouped into three categories: normal (18.5 to 24.9 kg/m^2), overweight (25.0 to 29.9 kg/m^2), and obese (≥30 kg/m^2)[7]. Race and body-mass index data were not available for the entire cohort of 723 patients and were collected for 599 and 429 patients, respectively. Despite well-established effects on serum 25(OH)D levels, a history of gastrointestinal disease, gastrointestinal surgery, or renal disease was not deemed to be relevant to the purpose of the present study in terms of characterizing the prevalence of and identifying novel risk factors for hypovitaminosis D, regardless of its etiology.

Outcome Measures

We defined vitamin-D sufficiency as a serum 25(OH)D level of ≥32 ng/mL. Vitamin-D inadequacy was defined as a serum 25(OH)D level of <32 ng/mL and was further divided into vitamin-D insufficiency (20 to <32 ng/mL) and vitamin-D deficiency (<20 ng/mL)[8].

Statistical Analysis

All patients with valid 25(OH)D measurements were included in the statistical analysis. The distribution of 25(OH)D (mean, standard deviation, median) and the percentages of patients with insufficient (20 to <32 ng/mL) and deficient (<20 ng/mL) 25(OH)D were determined, both for the overall population and for each individual service.

Univariate and multivariate logistic regression models were used to assess the independent relative risk for vitamin-D inadequacy (<32 ng/mL) for each potential risk factor (age, sex, race, body-mass index, and orthopaedic diagnosis/service). Serum 25(OH)D was the dependent variable, with the aforementioned risk factors as independent predictors. The level of significance was set at $p \leq 0.05$. The unadjusted odds ratio, 95% confidence interval, and p value were estimated for each risk factor.

A multivariate logistic regression analysis was then conducted to assess the association between upper extremity fractures and vitamin-D insufficiency. Vitamin-D status, patient age, and sex were the independent predictors that were included in the forward-stepwise model and were assessed for significance. The level of significance was set at $p \leq 0.05$. The adjusted odds ratio, 95% confidence interval, and p value were estimated for each risk factor.

All analyses were performed with use of two-tailed tests. The level of significance was set at $p \leq 0.05$.

Source of Funding

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Results

Subject Characteristics

Seven hundred and twenty-three patients were included in this retrospective study of the prevalence of vitamin-D deficiency (see Appendix). The average age (and standard de-

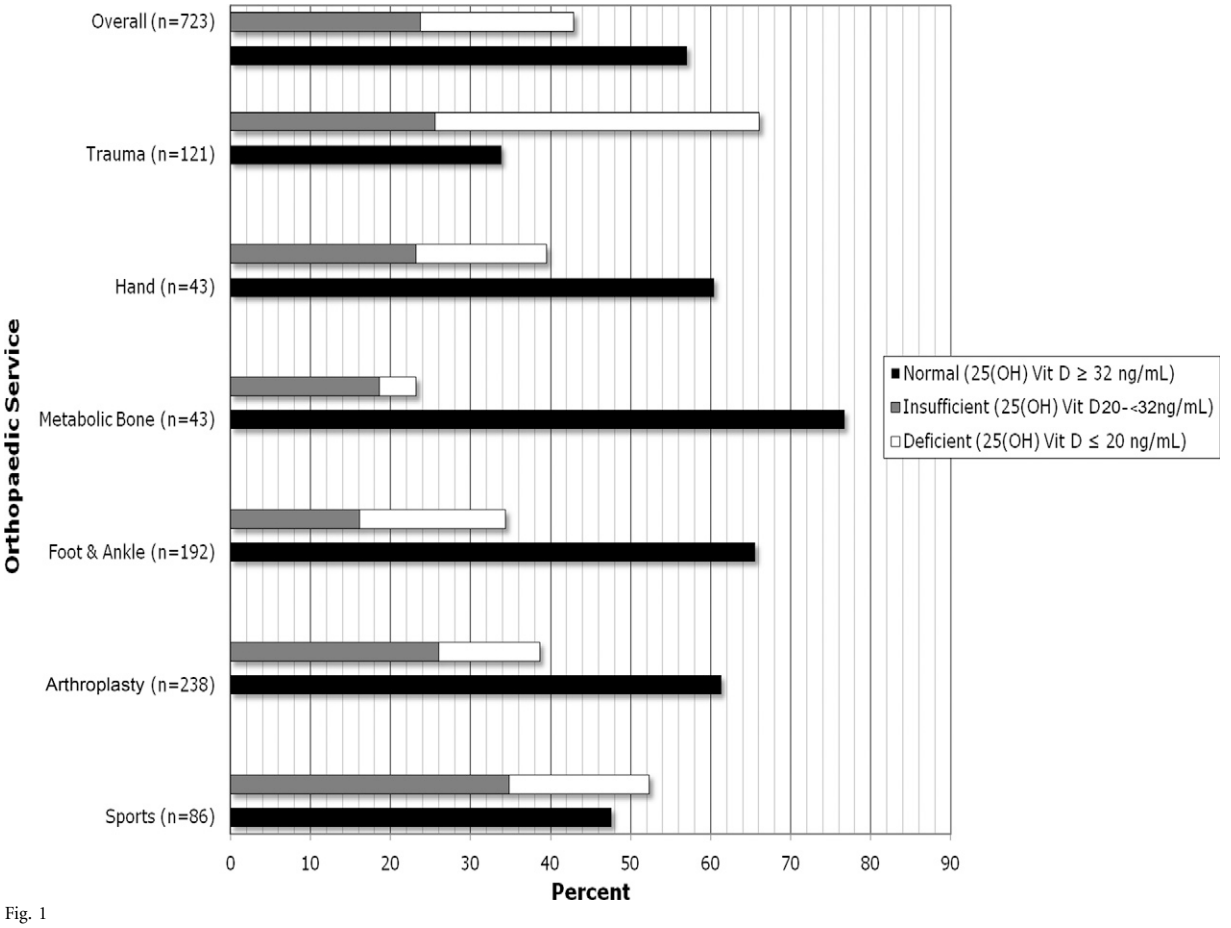

Fig. 1

Bar chart depicting the prevalence of 25(OH)D insufficiency and deficiency among the different orthopaedic services.

viation) of the study population was 60 ± 17.3 years. Five hundred and thirty-two patients (74%) were more than fifty years old, and 469 (65%) were female. Of the 599 patients for whom data on race were available, 546 (91%) were white. The average body-mass index for the 429 patients for whom data were available was 27.23 ± 6.38 kg/m^2, with 256 patients (60%) being overweight (body-mass index, ≥25.0 kg/m^2). Nearly half (105) of the overweight patients were obese (body-mass index, ≥30 kg/m^2). The service-specific patient census was as follows: Trauma (n = 121), Foot and Ankle (n = 192), Sports Medicine (n = 86), Arthroplasty (n = 238), Hand (n = 43), and Metabolic Bone Disease (n = 43).

Prevalence of Hypovitaminosis D

The serum 25(OH)D levels for the 723 subjects were normally distributed, with a mean of 35.2 ± 15.3 ng/mL, a median of 34 ng/mL, and minimum and maximum values of 6 and 116 ng/mL, respectively. Among all patients studied, 43% were vitamin D-insufficient, and among those, 40% were vitamin D-deficient (Fig. 1). Of the 723 vitamin-D serum levels measured in this study, fourteen were <9 ng/mL, ninety-six were between 9 and 19 ng/mL, eighty-one were between 20 and 24 ng/mL, eighty-three were between 25 and 29 ng/mL, thirty-eight were between 30 and 31 ng/mL, and 411 were ≥32 ng/mL.

Assessment of Risk Factors for Hypovitaminosis D

Univariate analysis was performed to assess the independent associations between age, sex, race, skin tone, and body-mass index and subnormal levels of vitamin D (see Appendix). The analysis showed that patients between the ages of fifty-one and seventy years were 35% less at risk for having inadequate vitamin-D levels in comparison with patients between the ages of eighteen and fifty years ($p = 0.018$). Female sex appeared to be protective as the mean 25(OH)D levels were significantly higher in women as compared with men ($p < 0.001$). There also was an association between race/skin tone and 25(OH)D levels; in general, patients with darker skin tone (black and Hispanic) had a higher risk of having a low vitamin-D level and were 5.5 times more likely to have a low vitamin-D level in comparison with patients with lighter skin tone (white and Asian) (odds ratio = 5.53; 95% confidence interval = 2.34 to 13.05; $p < 0.001$). Finally, with regard to body-mass index, obese patients were twice as likely to have abnormal vitamin-D levels when compared with patients of normal weight ($p = 0.004$).

Following the univariate analysis, multivariate logistic regression was performed to evaluate the effects of age, sex, race, skin tone, and body-mass index while controlling for possible confounding effects of other variables (see Appendix). All variables (including service group) were deemed eligible for evalu-

ation because they had p value levels of ≤0.15 on univariate analysis or because they were considered to be clinically relevant risk factors. With use of a stepwise-forward method, variables were considered to be significant predictors if they had a final p value of ≤0.05 after adjusting for all other variables in the model.

Age was treated as a continuous variable in the regression model (but was examined as a categorical variable in the univariate analysis). Even after controlling for all other variables in the model, age was not a significant predictor of the outcome in question. Female sex was found to have a protective effect in the initial analysis ($p = 0.006$) and continued to do so when entered into the regression model. The protective effect remained relatively unchanged, with female sex being associated with a 35% decrease in risk after adjusting for all other variables ($p = 0.047$). Like age, body-mass index was entered into the model as a continuous variable. After adjustment for potential confounders, body-mass index remained a significant risk factor, with a one-unit increase in body-mass index resulting in an approximately 5% increase in the odds of having abnormal vitamin-D levels ($p = 0.008$). Dark skin tone was also found to be significantly associated with abnormal levels of vitamin D ($p < 0.001$). After adjusting for all other variables, dark skin tone continued to be a significant risk factor, with an almost eight times increased likelihood for low vitamin-D levels. When race was entered into the model, it was not considered to be a significant risk factor as it was in the initial analysis. Tests of collinearity demonstrated that the effect of skin tone and race were similar, and therefore race was dropped from the model.

Service Data

Trauma

The trauma service had the highest prevalence of hypovitaminosis D. Of the 121 patients identified, 66.1% had inadequate vitamin-D levels, and, among those, 61% were vitamin D-deficient. Higher rates of inadequate vitamin D were found in the older populations (fifty-one to seventy years [$p = 0.082$] and more than seventy years [$p = 0.035$]) compared with the younger population (eighteen to fifty years), whereas sex and low-energy mechanism of trauma were not significant predictors of abnormal vitamin-D levels. Sixteen patients with an upper extremity fracture were identified, of whom fifteen (94%) had abnormal vitamin-D levels. Univariate logistic regression showed that the sixteen patients with upper extremity fractures were nearly nine times more likely to have inadequate levels of vitamin D compared with ninety-four patients with lower extremity fractures (odds ratio = 8.90; 95% confidence interval = 1.13 to 70.31; $p = 0.015$). Multivariate logistic regression analysis was performed to further determine the strength of association between fracture location and vitamin-D insufficiency while taking into consideration possible confounding due to patient age and sex. All three variables were included in the forward-stepwise model and were assessed for significance. In the adjusted multivariate regression model, both advanced patient age (odds ratio = 2.71; 95% confidence interval = 1.08 to 6.77; $p = 0.033$) and upper extremity fracture location (odds ratio = 8.97; 95% confidence interval = 1.12 to 71.85; $p = 0.039$) remained significant predictors of vitamin-D insufficiency.

Sports Medicine

The sports medicine service had the second-highest prevalence of inadequate vitamin-D levels despite having the youngest population (mean age, 45 ± 14.9 years). Among all eighty-six patients, 52.3% had insufficient serum vitamin-D levels, and, among these, one-third had deficient levels.

Arthroplasty

Thirty-eight percent of patients in the arthroplasty group were found to have inadequate levels of vitamin D, and, among these, nearly half (48%) had deficient levels. Women were 54% less likely to be vitamin-D inadequate as compared with men ($p = 0.021$). Vitamin-D deficiency was three times more prevalent among younger patients (those with an age of eighteen to fifty years).

Foot and Ankle

Thirty-four percent of patients undergoing foot and ankle surgery had inadequate vitamin-D levels. Of these, 32% had a frank deficiency. Women were 52% less likely to have low vitamin-D levels in comparison with men ($p = 0.024$). Older patients (those with an age of more than fifty years) were also more likely to have normal vitamin-D levels ($p = 0.036$). Compared with patients with a normal body-mass index (18.5 to 29.9 kg/m^2), patients with a body-mass index of ≥30 kg/m^2 were four times more likely to have inadequate vitamin-D levels.

Hand

Forty percent of hand surgery patients, mostly those scheduled to undergo operative treatment of distal radial fractures, had insufficient vitamin-D levels, and, among these, 41% had deficient levels.

Metabolic Bone Disease

The lowest rates of inadequate vitamin-D levels were found in the metabolic bone disease service, where all patients had undergone treatment for previously detected hypovitaminosis D before surgery. The prevalences of insufficiency and deficiency were 18.6% and 4.6%, respectively. Included in this category were patients who were scheduled to undergo operative treatment of a vertebral compression fracture.

Discussion

Extremely low vitamin-D levels, especially those of ≤9 ng/mL, have been associated with osteomalacia and impaired muscle function[8]. There is a high prevalence of low serum levels of vitamin D within the adult orthopaedic surgery population. Of the 723 study participants who were scheduled to undergo orthopaedic surgery, 43% had low levels of vitamin D (25[OH]D, <32 ng/mL). Two of every five of these patients with low levels had frank deficiency (25[OH]D, <20 ng/mL), placing them at increased risk for osteomalacia and secondary hyperparathyroidism. Our results are consistent with those of similar studies

investigating the prevalence of vitamin-D deficiency. A high body-mass index and dark skin tone were identified as risk factors in the present study, findings that are consistent with those that have been documented previously. In particular, high concentrations of melanin in darker-skinned individuals increase ultraviolet B radiation absorption, which can reduce vitamin-D3 synthesis by as much as 99%[9]. The present study also identified a higher prevalence of vitamin-D deficiency in men. The association between sex and vitamin-D deficiency varies throughout the literature, with some studies demonstrating higher rates in women and others in men. Our results are similar to those reported by Guardia et al. in a prevalence study that identified male sex as a risk factor for vitamin-D deficiency[10].

The high rate of vitamin-D deficiency among fracture patients, as seen in our trauma population, has been well-described in the literature. In a study of elderly community-dwelling women who had been admitted to the hospital because of an acute hip fracture and had no secondary cause for bone loss, more than half had vitamin-D deficiency and elevated parathyroid hormone levels[11]. A unique finding in the present study was the increased prevalence of inadequate vitamin-D levels among patients with upper extremity fractures as compared with those with lower extremity fractures. This finding suggests that fractures involving long bones of the upper extremity may indicate an underlying bone disorder and warrant an assessment of vitamin-D levels. Contrary to previously observed trends of increased rates of vitamin-D deficiency among patients with fractures, a low rate of hypovitaminosis D was observed in the metabolic bone disease service, and the lowest levels of vitamin-D deficiency were observed in patients scheduled to undergo surgical treatment of vertebral compression fractures. A low prevalence of vitamin-D deficiency in this patient population is not surprising, as many of these patients have an established diagnosis of osteoporosis and likely have been managed with calcium and vitamin-D supplementation.

Limitations

First, a disproportionately large number of white patients comprised the subject pool for the present study. Given the predisposition of darker skin-toned individuals toward low vitamin-D levels, the prevalence of hypovitaminosis D among darker skin-toned orthopaedic surgery patients may be underreported in the present study. Second, serum 25(OH)D levels were measured during various seasons for all patients. Therefore, it is possible that seasonal variability in serum 25(OH)D levels may have affected the findings of this study to a certain extent. To complicate matters further, individuals vary in their physiologic responses to sunlight and serum 25(OH)D levels[12]. Third, serum 25(OH)D levels were not standardized among the various laboratories chosen by patients for preoperative testing, although 91% of the patients used the laboratory at our hospital. Nevertheless, we were unable to account completely for variations in serum 25(OH)D measurements among the various laboratories. All of the aforementioned limitations underscore the need for further studies to define the precise extent of hypovitaminosis D in the orthopaedic surgery patient population. The purpose of the present study was to raise awareness among orthopaedic surgeons about hypovitaminosis D by presenting compelling but raw data that would spur future in-depth investigations as well as early detection and treatment.

Appendix

eA Tables showing patient characteristics and the univariate and multivariate analyses are available with the electronic version of this article on our web site at jbjs.org (go to the article citation and click on "Supporting Data"). ■

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