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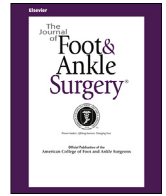

Association of Vitamin D With Stress Fractures: A Retrospective Cohort Study

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A R T I C L E I N F O

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A B S T R A C T

Vitamin D is an essential, fat-soluble nutrient that is a key modulator of bone health. Despite the gaining popularity throughout published medical studies, no consensus has been reached regarding a serum vitamin D level that will guarantee adequate skeletal health in a patient with an increased functional demand. The purpose of the present investigation was to examine the serum concentrations of vitamin D in patients with confirmed stress fractures. A total of 124 patients were included in our retrospective cohort study. Of the 124 patients, 53 had vitamin D levels measured within 3 months of diagnosis. An association was seen in patients with a stress fracture and vitamin D level measured, as 44 (83.02%) of the 53 patients had a serum 25-hydroxyvitamin D level <40 ng/mL. Although an association was seen at our institution in patients with stress fractures and a serum vitamin D concentration <40 ng/mL, a larger and prospective investigation is warranted to further understand the effect of vitamin D level and stress fracture prevention in an active, nonmilitary population.

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The role of vitamin D in the body has recently become a subject of increasing interest in current medical studies owing to its many physiologic effects throughout multiple organ systems. In brief, vitamin D is an essential nutrient that can behave as a hormone that is obtained through diet and cutaneous synthesis by ultraviolet B radiation (1–4). Vitamin D has been linked to effects on mood and behavior, innate and acquired immune responses, metabolic function, and individually affecting the pancreas, heart, parathyroid, and skeletal muscles (1,2).

The primary physiologic function of vitamin D and its activated metabolites is to maintain serum calcium and phosphorus levels and to support bone mineralization and turnover (1,3). Vitamin D is essential for bone development and remodeling, as demonstrated by a direct correlation with rickets in children (3). Furthermore, a significant correlation has also been shown with adequate vitamin D and appropriate bone mass density. In contrast, it has been reported that hypovitaminosis D can lead to osteoporosis, osteomalacia, decreased bone mineral density, and, subsequently, the risk of acute fracture (4–8). Vitamin D insufficiency has been associated with increased age, obesity, female gender, geographic region and season predilection, pregnancy and lactation, and malabsorption syndromes (7,9).

Less known is the quantitative importance of vitamin D concentrations in the delicate balance of bone turnover and healing in the context of osseous loading and physiological stresses. The goal of the present investigation was to examine the serum concentrations of vitamin D in patients with confirmed stress fractures. By assessing the average serum vitamin D concentrations of those with stress fractures and evaluating the prevalence of deficiency or insufficiency according to the current guidelines, we wish to encourage a discussion of the possibility that a higher "norm" concentration of serum vitamin D should be recommended for active patients who may be at risk of stress fractures.

Patients and Methods

A single-center, retrospective medical record review was performed from the senior authors' (J.R.M., L.J.C.) practice during a 3-year period (July 31, 2011 to August 1, 2014). All patients who initially presented with lower extremity pain, with a suspected

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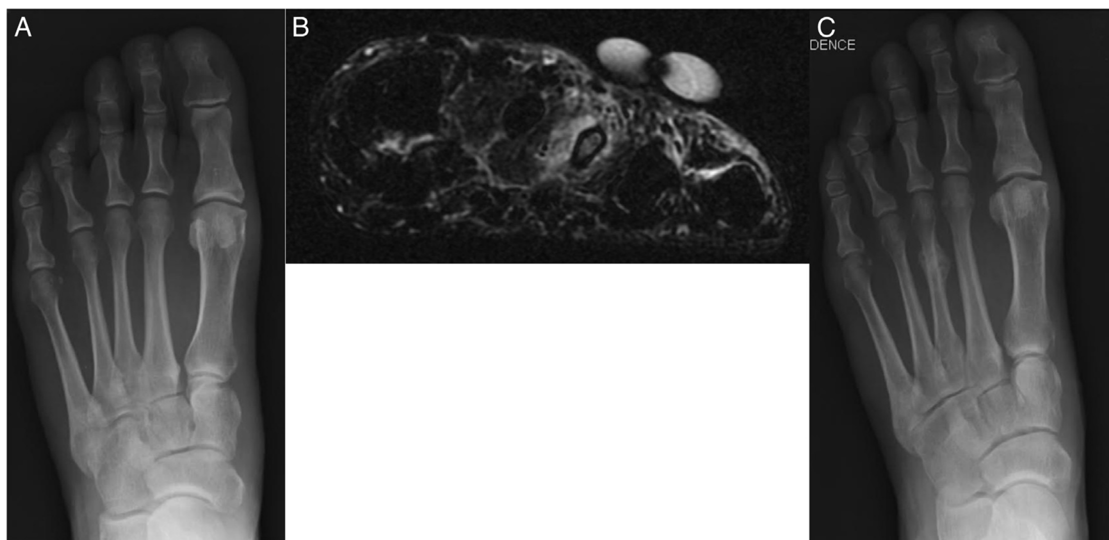

Fig. 1. A 51-year-old female presented with forefoot pain associated with weightbearing. The initial radiograph (*A*) did not display an acute fracture. The patient underwent subsequent magnetic resonance imaging (*B*), in which an increased signal in the bone marrow of the third metatarsal and surrounding soft tissues, consistent with a stress fracture, was seen on T_2-weighted and short T_1-weighted inversion recovery images (shown on coronal T_2-weighted images). The patient's serum 25-hydroxyvitamin D level was 33 ng/mL, and she was prescribed vitamin D_3 4000 IU daily. A follow-up radiograph (*C*) displayed circumferential callus formation after the patient had been placed in a fixed-walking boot for 6 weeks.

stress fracture, underwent plain film radiographs of the affected extremity. The patients were then sent for magnetic resonance imaging (MRI) for a confirmatory diagnosis if no acute fracture was seen, yet concern for the presence of a stress fracture remained based on the physical examination findings (Fig. 1). Musculoskeletal radiologists independently reviewed all the MRI scans, and the senior authors (J.R.M., L.J.C.) confirmed the diagnosis of a stress fracture after a review of the images based on an MRI (short T_1-weighted inversion recovery and T_2-weighted images) sequence displaying a high-signal intensity of the bone marrow (bone marrow edema) and the adjacent soft tissues.

The following clinical data were obtained from the private practice electronic database of the senior authors (J.R.M., L.J.C.): patient age, gender, body mass index, location of stress fracture, serum 25-hydroxyvitamin D [25(OH)D] levels within 3 months of the positive MRI diagnosis. The data identified were recorded and statistically analyzed for the investigation by 1 of us (K.W.D.), using the "International Classification of Diseases, version 9," codes 733.93, 733.94, and 733.95. All the patients with a positive diagnosis of an acute stress fracture from the MRI findings were included in the present study, for a total of 124 consecutive patients. No patient was excluded from the present study once a diagnosis of a stress fracture had been confirmed and supported by the electronic medical record data.

Results

Of the 124 patients, 42 (33.9%) were male and 82 (66.1%) were female. Their mean age was 43.92 ± 17.47 years, and the mean body mass index of those with it recorded (120 [96.8%] of 124 patients) was 26.81 ± 6.30 kg/m^2. The most common bone with a stress fracture was the second metatarsal (n = 42 [33.9%]), followed by the third metatarsal (n = 22 [17.7%]). The stress fracture anatomic locations are presented in Fig. 2. The serum 25(OH)D level was recorded within 3 months of diagnosis for 53 (42.74%) of the 124 patients. The mean serum 25(OH)D of all patients was 31.14 ± 14.71 ng/mL. Similar serum levels were reported for the males (31.0 ± 15.66 ng/mL) and females (31.21 ± 14.23 ng/mL) (Mann-Whitney U test p value = .58).

Using the standards recommended by the Vitamin D Council (San Luis Obispo, CA; sufficient range 40 to 80 ng/mL; Fig. 3), 44 (83.02%) of the 53 patients would have been classified as having insufficient or deficient vitamin D levels. According to the standards set by the Endocrine Society (Washington, DC; sufficient range 30 to 100 ng/mL), 28 (52.83%) of the 53 patients would have been classified as having insufficient or deficient vitamin D levels.

Discussion

An individual's vitamin D concentration is intimately linked to the absorption of dietary calcium and phosphorus. In a vitamin D-deficient state, only 10% to 15% of dietary calcium and 50% to 60% of dietary phosphorus will be absorbed. Thus, a decrease occurs in the serum-ionized calcium levels. This is recognized by the calcium sensor in the parathyroid glands, resulting in an increase in the secretion of parathyroid hormone. In turn, parathyroid hormone enhances the expression of RANKL on osteoblasts to increase the production of mature osteoclasts to mobilize skeletal calcium stores (3). Thus, a decrease in bone mineralization and structural integrity can develop.

Although several guidelines have been published to determine the vitamin D status, the current thresholds are considered estimates, which were largely observationally and determined from the occurrence of secondary hyperparathyroidism in vitamin D deficiency through the use of serum parathyroid hormone levels as a surrogate parameter for the optimal 25(OH)D serum level. Furthermore, no minimum 25(OH)D serum level has been defined that can guarantee adequate skeletal health in a patient with an increased functional demand (10).

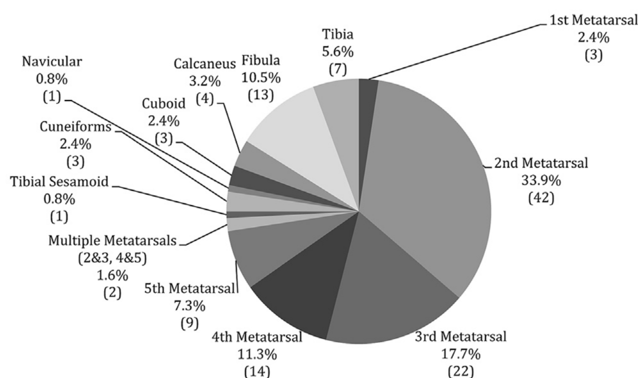

Fig. 2. Anatomic location of stress fractures (N = 124 patients).

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