Assessing Vitamin D Status in African Americans and the Influence of Vitamin D on Skeletal Health Parameters

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KEYWORDS

• Vitamin D • African American • 25-Hydroxyvitamin D • Calcium absorption
• Parathyroid hormone • Bone mineral density

KEY POINTS

- Despite having lower total 25-hydroxyvitamin D (25OHD) levels compared with white Americans (WAs), African Americans (AAs) have higher bone mineral density and lower fracture risk.
- It was previously proposed that this may be explained by the possibility that AAs may have lower total, but comparable free, 25OHD levels compared with WAs; these earlier findings may have resulted from vitamin D binding protein isoform-dependent variations in assay performance.
- AAs have higher intestinal calcium absorption efficiency and lower urinary calcium excretion compared with WAs.
- AAs may have skeletal resistance to secondary hyperparathyroidism. The threshold 25OHD level below which PTH secretion increases substantially is generally lower in AAs than in WAs.
- AAs have higher BMD and lower fracture risk. Epidemiologic studies suggest an inverse relation between vitamin D status and BMD in WAs, but not in AAs.

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INTRODUCTION

The classical endocrine function of vitamin D is to facilitate intestinal calcium absorption, prevent secondary hyperparathyroidism, and maintain skeletal strength. Vitamin D status is assessed clinically by measuring serum 25-hydroxyvitamin D (25OHD) concentrations.[1,2] In epidemiologic studies, lower 25OHD levels are associated with increased parathyroid hormone (PTH) secretion, decreased bone mineral density (BMD), and increased fracture risk.[3–10] Randomized clinical trials have confirmed that adequate vitamin D intake in combination with calcium prevents fragility fractures in those most at risk for nutritional deficiency.[11]

In the United States, there is a significant disparity in vitamin D status among individuals of African versus European descent. In particular, African Americans (AAs) consistently have lower 25OHD levels compared with white Americans (WAs) throughout the life cycle.[12] Despite these lower 25OHD levels, AAs tend to have greater BMD and lower fracture risk than their WA counterparts.[13,14] Given the importance of vitamin D in helping to maintain skeletal health, this finding has been described as a paradox.[12]

In recent years, it has been proposed that this paradox may be explained by the possibility that although total 25OHD levels (protein-bound 25OHD + free 25OHD) are lower among AAs, free 25OHD levels are comparable with those in WAs.[15,16] This article begins with a review of classical and nonclassical vitamin D physiology. The theoretic rationale for using total versus free 25OHD as a marker of vitamin D status is discussed, and whether total versus free 25OHD is a better marker of vitamin D status in racially/ethnically diverse populations is reviewed. Finally, the effects of vitamin D status and vitamin D supplementation on markers of vitamin D bioactivity (intestinal calcium absorption, PTH secretion, BMD, fracture risk) are described.

VITAMIN D PHYSIOLOGY

Sources of Vitamin D

Vitamin D is obtained through sunlight exposure and oral intake (food or supplement). With sunlight exposure, solar ultraviolet B (UVB) radiation (wavelength spectrum 280–320 nm) penetrates the skin and converts 7-deydrocholesterol to pre–vitamin D_3. Pre–vitamin D_3 is then converted to vitamin D_3 in a thermosensitive, but nonenzymatic, reaction.[17] The rate of endogenous vitamin D_3 synthesis is determined by intensity of UVB and skin pigmentation. UVB intensity varies depending on season (less in winter) and latitude (less with greater distance from equator).[18] Increased melanin in the skin limits UVB access to 7-deydrocholesterol.[19] Dietary sources of vitamin D are limited (vitamin D_3 from fatty fish and egg yolks; vitamin D_2 from shiitake mushrooms). Supplemental vitamin D can also be obtained as vitamin D_2 (ultraviolet irradiation of ergosterol from yeast) and vitamin D_3 (ultraviolet irradiation of 7-dehydrocholesterol from lanolin).[20] Most clinical guidelines treat vitamin D_2 and vitamin D_3 as therapeutically equivalent based on early reports that both analogues reverse vitamin D-deficient rickets in children.[1,2,21]

Classical Endocrine Vitamin D Physiology

The canonical endocrine function of vitamin D is to facilitate intestinal calcium absorption. Under the classical paradigm, vitamin D (D_2 or D_3) is converted to 25OHD (produced in nanogram per milliliter concentrations) in the liver by the CYP2R1 hydroxylase. 25OHD is then converted to 1,25-dihydroxyvitamin D ($1,25(OH)_2D$) in the kidney by the CYP27B1 hydroxylase (produced in picogram per milliliter concentrations). The latter reaction occurs when filtered 25OHD, bound to the vitamin D