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ORIGINAL ARTICLE

Defining physiologically "normal" vitamin D in African Americans

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Abstract
Summary The relationship between serum 25(OH)D and intact parathyroid hormone (iPTH) was evaluated in the Multicenter Osteoarthritis Study (MOST). No further change in iPTH was observed for African Americans with 25(OH)D levels above 20 ng/ml, suggesting that compared to Caucasians, lower vitamin D targets for sufficiency may be appropriate for African Americans.
Introduction Vitamin D levels ≥30 ng/ml are commonly considered "normal" based upon maximal suppression of iPTH; however, this has recently been challenged and the optimal 25(OH)D level among non-Caucasians is unclear. We evaluated the cross-sectional relationship between serum 25(OH)D and iPTH in a sample of Caucasian and African American adults.
Methods We used baseline serum samples of participants from the Multicenter Osteoarthritis Study (MOST) for this analysis and used three methods to model the relationship between 25(OH)D and iPTH: ordinary least squares regression (OLS), segmented regression and Helmert contrasts.
Results Among Caucasians (n=1,258), 25(OH)D and iPTH ranged from 4 to 51 ng/ml and 2 to 120 pg/ml and from 3 to 32 ng/ml and 3 to 119 pg/ml in African Americans (n=423). We observed different thresholds between African Americans and Caucasians using each analytic technique. Using 25(OH)D as a categorical variable in OLS, iPTH was statistically higher at lower 25(OH)D categories than the 24–32 ng/ml referent group among Caucasians. However, in African Americans, the mean iPTH was only significantly higher at 25(OH)D levels below 15 ng/ml. Using segmented regression, iPTH appeared to stabilize at a lower 25(OH)D level in African Americans (19–23 ng/ml) compared to in Caucasians (>32 ng/ml). Helmert contrasts also revealed a lower threshold in African Americans than Caucasians.
Conclusion Among MOST participants, the 25(OH)D thresholds at which no further change in iPTH was observed was approximately 20 ng/ml in African Americans versus

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approximately 30 ng/ml in Caucasians, suggesting optimal vitamin D levels in Caucasians may not be applicable to African Americans.

Keywords African American · Osteoporosis · Parathyroid hormone · Racial differences · Thresholds · Vitamin D

Introduction

Vitamin D is an essential hormone in the maintenance of skeletal health. Based upon the prevention of rickets in children or osteomalacia in adults, historically, vitamin D deficiency was defined as a serum 25(OH)D level <10 g/ml [1]. With the increasing knowledge of vitamin D's role in a variety of physiologic functions and other organ systems, the assessment of vitamin D status has become important. Clinical thresholds to define vitamin D deficiency and insufficiency sometimes have been based on levels at which 25(OH)D maximally suppresses parathyroid hormone (PTH), an important regulator of calcium in systems throughout the body. Using this endpoint, most studies have shown that optimal levels of 25(OH)D range between 9 ng/ml and 44 ng/ml, with a cluster of values around 32 ng/ml or 80 nmol/L [2–7]. The World Health Organization defines vitamin D insufficiency as 25(OH)D levels below 20 ng/ml (50 nmol/l) [8]; however, others have defined vitamin D deficiency as 25(OH)D less than 20 ng/ml and insufficiency as 25(OH)D below 30 ng/ml [9]. Depending on the threshold used, vitamin D deficiency or insufficiency is extremely prevalent in the US [2, 10–12] with a significantly higher risk in obese individuals and people with darker skin pigmentation such as African Americans [13, 14].

Previous studies evaluating optimal 25(OH)D levels were largely performed in populations that were primarily Caucasians, were performed in special populations such as nursing homes or were performed with a relatively small number of participants [2–6]; however, two recent studies have included a diverse racial and ethnic population [15, 16]. In both studies, the 25 (OH)D level at which PTH was maximally suppressed in African Americans was lower than in Caucasians, suggesting a different "normal" or "optimal" 25(OH)D levels among African Americans.

In 2010, the Institute of Medicine's (IOM) report on calcium and vitamin D updated the dietary reference intakes based on recent literature on bone health [17]. After their systematic review, the IOM defined vitamin D deficiency as <12 ng/ml 25(OH)D and considered levels between 12 and 20 ng/ml as inadequate vitamin D [17]. Though the deficiency and insufficiency/inadequate thresholds were lowered, the reference range for "normal" 25(OH)D at many commercial labs remains between 30 and 32 ng/ml [18], and many researchers are still in favor of the higher threshold as indicated by a recent debate at the American Society for Bone and Mineral Research annual conference [19].

To add to the small literature base on optimal vitamin D in non-Caucasian populations and to provide more information on racial and ethnic differences in the relationship between calcium and vitamin D identified as a need by the IOM [17], we conducted a cross-sectional study examining the relationship between serum 25(OH)D and intact PTH (iPTH) among older community dwelling adults participating in the Multicenter Osteoarthritis Study (MOST), a large observational study which study population comprised 15% of African Americans. We hypothesized that there would be a different relationship between 25(OH)D and iPTH between African Americans and Caucasians, with African Americans exhibiting a lower "optimal" threshold for 25(OH)D based on change in iPTH.

Methods

Study population

MOST is a longitudinal observational study of individuals with or at high risk for knee osteoarthritis (OA). Participants included those with preexisting knee OA or who were considered to be at high risk for knee OA indicated by the presence of overweight/obesity, a history of knee OA symptoms, a history of knee injuries or a history of knee operations [20]. MOST enrolled 3,026 women and men aged 50 to 79 years from two clinical centers (Iowa City, Iowa and Birmingham, Alabama), and 15% of the participants self-reported to be African American. Subjects were excluded from the MOST cohort if they had other arthritic conditions including: rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis or chronic reactive arthritis; if they needed hemodialysis or peritoneal dialysis; if they had a history of cancer (excluding nonmelanoma skin cancer); if they had bilateral knee replacement surgery; if they were unable to walk without the help of another person or walker; or if they were planning to move out of the area in the next 3 years [20]. The MOST study protocols were approved by the University of Iowa, the University of Alabama at Birmingham, the University of California at San Francisco and the Boston University Medical Center institutional review boards.

Measurement of vitamin D and intact parathyroid hormone

Baseline 25(OH)D and iPTH measurements were performed on a selection of 1,830 participants, which included all African Americans (n=461) with available samples. Serum 25(OH)D was measured at Tufts University using commercially available radioimmunoassay (RIA) kits (Diasorin). Previous studies have shown good correlation between

RIA and gold standard high performance liquid chromatography (HPLC) results [21, 22]. Commercially available solid phase, two-site chemiluminescent immunometric assay (Immulite 1000 Diagnostic Products Corp) was used to measure iPTH. The intraassay coefficient of variation (CV) for 25(OH)D was 10.8%, and the interassay CV was 9.4%. The intraassay CV for iPTH ranged from 5.5 to 6.6%, and the inter assay CV ranged from 7.9 to 8.6%.

Covariates

The following baseline variables were considered as covariates in the analysis: age, gender, body mass index (BMI), education, season of baseline visit and supplemental calcium and vitamin D intake. Age was reported in years by the participant. Standing height (cm) and weight (kg) were measured using standardized procedures and used to calculate BMI in kilogram per meter squared. The highest level of education completed was reported by the participants, and the results were categorized into the following: completed high school, completed college or completed graduate school. The season of baseline visit was recorded and categorized as: winter (Dec–Feb), spring (Mar–May), summer (Jun–Aug) and autumn (Sept–Nov). Participants were categorized as calcium or vitamin D supplement users if they reported use on the baseline medication inventory.

Statistical analysis

Descriptive statistics of the study population were performed by race. *T*-tests were used to compare continuous variables, and χ^2 tests were used to compare categorical variables. A race-specific scatter plot of the crude and log-transformed relationship between 25(OH)D and iPTH was produced and a LOWESS curve used for smoothing. The relationship between 25(OH)D and iPTH by race was modeled in three ways: 1) ordinary least squares (OLS) regression, 2) segmented regression with grid search [23] and 3) Helmert contrasts [24, 25].

For the OLS regression, six categories of 25(OH)D were created based on the Caucasian data, and the relationship between 25(OH)D and iPTH was tested after adjusting for age, gender, body mass index, education, supplemental calcium use, supplemental vitamin D use and season. The potential effect modification of gender, BMI and both calcium and vitamin D supplementation on the 25(OH)D and iPTH relationship was tested using traditional interaction methods. Interactions terms were considered statistically significant if $p<0.10$.

Two segmented regression with grid search models were performed after adjustment for the above-mentioned variables included in the OLS regression. First, a knot was placed sequentially at 0.1 unit increments of 25(OH)D from 5 to 50 ng/ml, and the comparative fit of the models that varied the knot was evaluated by determining mean squared error (MSE) of each model, looking for local minimums. Secondly, knots were placed at each of the previously defined 25(OH)D categories, and the relationship between 25(OH)D and iPTH between each knot was compared between Caucasian and African Americans.

The final statistical method utilized Helmert contrasts to identify thresholds of 25(OH)D. Helmert contrasts are a type of orthogonal contrast that sequentially compares the mean outcome (iPTH) at levels of an exposure (25(OH)D). Helmert contrasts incorporate adjustment for multiple comparison at the time of analysis and do not require additional posthoc tests [24, 25]. For each level used in the contrasts, we grouped 25(OH)D into 2 ng/ml categories. For each racial group, the contrasts compared the mean iPTH of the highest 25(OH)D group to the mean iPTH of the next lowest 25(OH)D group and so on until the mean iPTH of all 25 (OH)D groups were compared to the mean iPTH of the lowest 25(OH)D group. The level at which the mean iPTH significantly differed ($p<0.05$) between the levels was considered the 25(OH)D threshold. All analyses were done using SAS v. 9.2, Cary, NC.

Results

Serum 25(OH)D and iPTH values were missing for 11 of the 1,830 participants. We excluded persons with self-reported chronic kidney disease (CKD) ($n=96$) and further excluded participants with iPTH >120 pg/ml (~2× the upper limit of lab normal) ($n=24$) due to concern that the elevated iPTH was not solely due to vitamin D deficiency. A small proportion of patients excluded for CKD were African American ($n=18/96$); however a larger proportion ($n=15/24$) of those excluded for elevated iPTH were African American. The baseline characteristics of the remaining participants are shown in Table 1. No statistically significant differences were seen in the percentage of women or the season of baseline visit between the two groups; however, there were significant differences in other baseline variables. The Caucasian participants were on average 3 years older ($p<0.0001$) and had a higher proportion reporting completion of college or higher (75% versus 68%) than the African American participants. The mean BMI was larger in the African American compared to the Caucasian participants ($p<0.0001$). The mean±SD serum 25(OH)D was 21.7± 7.0 ng/ml and 13.9±6.1 ng/ml in Caucasian and African American participants, and the mean serum iPTH was 46.8±22.4 pg/ml and 60.0±30.5 pg/ml, respectively. 25 (OH) D <30 ng/ml was observed in 88% of Caucasians and 99% of African Americans.

Table 1 Baseline characteristics of eligible MOST participants by race

	Caucasian (n=1,258) Mean±SD (min, max)	African American (n=423) Mean±SD (min, max)	p-Value
Age (years)	62.8±7.9 (50, 79)	59.8±8.2 (50, 79)	<0.0001
BMI (kg/m^2)	29.9±5.2 (16.7, 55.8)	33.2±6.8 (18.3, 71.9)	<0.0001
iPTH (pg/ml)	46.8±22.4 (2.0, 239.0)	60.0±30.5 (3.0, 213.0)	<0.0001
25(OH)D (ng/ml)	21.7±7.0 (4.0, 51.0)	13.9±6.1 (3.0, 37.0)	<0.0001
	N (%)	N (%)	p-Value
Women	775 (61.4)	277 (63.4)	0.450
Clinic site			<0.0001
UAB	624 (49.4)	426 (97.5)	
Iowa	639 (50.6)	11 (2.5)	
Education			<0.0001
High school	322 (25.5)	142 (32.5)	
College	571 (45.2)	213 (48.7)	
Graduate	370 (29.3)	82 (18.8)	
Season of baseline visit			0.190
Spring (Mar–May)	268 (21.2)	296 (23.4)	
Summer (Jun–Aug)	309 (24.5)	125 (28.6)	
Autumn (Sep–Nov)	390 (30.9)	130 (29.8)	
Winter (Dec–Feb)	296 (23.4)	85 (19.5)	
Vitamin D supplement user			<0.0001
No	984 (78.2)	394 (93.1)	
Yes	274 (21.8)	29 (6.9)	
Calcium supplement user			<0.0001
No	659 (52.4)	325 (76.8)	
Yes	599 (47.6)	98 (23.2)	
25(OH)D category (ng/ml)			<0.0001
<12	113 (9.0)	197 (46.6)	
12–15	121 (9.6)	81 (19.2)	
15–19	265 (21.1)	69 (16.3)	
19–23	284 (22.6)	39 (9.2)	
23–32	386 (30.7)	37 (8.8)	
>32	89 (7.1)	0 (0.0)	

The LOWESS plot of the raw measurements revealed a steep lowering in iPTH as 25(OH)D reached 9 ng/ml in both Caucasians and African Americans, consistent with the threshold associated with osteomalcia and rickets (Fig. 1). In African Americans, the iPTH levels were slightly lower as 25(OH)D levels reached 20 ng/ml and then appeared to stabilize with no further lowering in iPTH with 25(OH)D levels ≥20 ng/ml. However, in Caucasians, a slight but consistent lowering in iPTH was observed as 25(OH)D levels reached 30 ng/ml at which no further lowering was observed. Similar patterns in the 25(OH)D and iPTH relationship were observed when using log-transformed values, and no additional improvement in fit was observed with the transformation.

The six categories of 25(OH)D created included <12 ng/ml, 12–15 ng/ml, 15–19 ng/ml, 19–23 ng/ml, 23–32 ng/ml

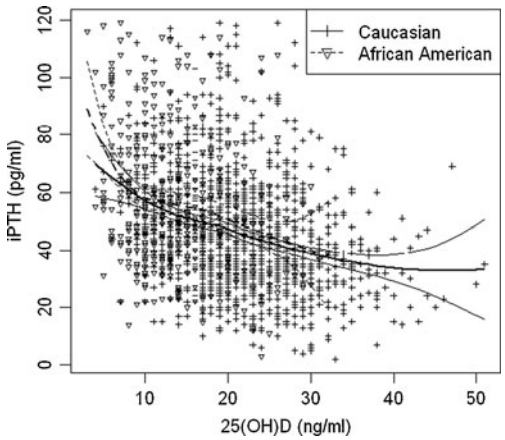

Fig. 1 The relationship between 25(OH)D and iPTH by race—LOWESS plot

and >32 ng/ml. These categories were based primarily on the Caucasian data and with categories reflecting commonly used cut-points for 25(OH)D deficiency and insufficiency levels [8, 9]. Approximately 9%, 9.6%, 21.1%, 22.6%, 30.7% and 7.0% of the Caucasian population fell within each of these categories. The proportion of African Americans in each category was different; there were no African Americans with 25(OH)D in the >32 ng/ml range and 46.6%, 19.2%, 16.3% , 9.2% and 8.8% of the African Americans in the <12, 12–15, 15–19, 19–23 and 23–32 categories, respectively.

Ordinary least squares regression

The mean iPTH at each 25(OH)D category was compared by race after adjusting for age, gender, BMI, education, calcium and vitamin D supplement use, and season of blood draw. Within each race, the adjusted mean iPTH at each 25(OH)D category was compared to the mean iPTH of the 24–32 ng/ml 25(OH)D referent category (Table 2). In Caucasians, the mean iPTH at each 25(OH)D category up to the referent category was significantly higher than that of the 23–32 ng/ml referent category, and the mean iPTH of those with 25(OH)D >32 ng/ml was significantly lower than the referent group (Table 2). There was a significant trend of lower iPTH with higher 25(OH)D ($p<0.0001$) in African Americans as well; however, in contrast to the Caucasian participants, the mean iPTH was only significantly higher in the <12 ng/ml and the 12–15 ng/ml categories compared to the referent 24–32 ng/ml (Table 2). There was no significant difference between the mean iPTH at 19–23 ng/ml 25(OH)D and 23–32 ng/ml 25(OH)D categories. For both races, no significant interaction by gender, BMI category or supplement use on the relationship between 25(OH)D and iPTH was observed.

Segmented regression

Using the first segmented regression approach, the slope of the relationship between 25(OH)D and iPTH differed at four levels or knots of 25(OH)D in Caucasians at 12, 24, 31 and 40 ng/ml. The MSE at each of the four knots for Caucasians were minimized indicating better model fit with knots at these values. In African Americans, only one knot at 9 ng/ml was associated with a minimum MSE in the 25(OH)D iPTH association.

When using the second segmented regression approach that placed five knots associated with the six 25(OH)D categories, different iPTH 25(OH)D relationships were observed between Caucasians and African Americans (Fig. 2). Similar to the LOWESS plot, inverse slopes were observed in both Caucasian and African Americans as 25(OH)D reached 12 ng/ml. The slope of the iPTH and 25(OH)D relationship appeared to be flat between the <12 ng/ml and the 12–15 ng/ml knots in African Americans, whereas a slight declining slope was observed in Caucasians between these two knots. Between the 12–15 ng/ml and 15–19 ng/ml knots, flat slopes were observed in both Caucasian and African Americans; however, a noticeable declining iPTH slope was observed in both African Americans and Caucasians in the 19–23 ng/ml category. Although the slope appeared to decline as 25(OH)D increased beyond the knot at 19–23 ng/ml in Caucasians, no additional decline in the iPTH slope was seen in African Americans above the knot at the 19–23 ng/ml category.

Helmert contrasts

Based on the range of data, 22 contrasts were performed in Caucasians and 14 in African Americans starting at the highest level of 25(OH)D [Caucasian: 50–51 ng/ml; African Americans: 31–32 ng/ml]. The 25(OH)D level at

Table 2 Comparison of mean iPTH by 25(OH)D category and race using ordinary least squares regression

Caucasian (n=1,258)			African American (n=423)		
25(OH)D (ng/ml)	Mean iPTH (pg/ml)[a]	p-Value	25(OH)D (ng/ml)	Mean iPTH (pg/ml)[a]	p-Value[b]
<12 (n=113)	56.5	<0.001	<12 (n=197)	59.7	<0.001
12–15 (n=121)	51.5	<0.001	12–15 (n=81)	55.1	0.018
15–19 (n=265)	48.4	<0.001	15–19 (n=69)	52.6	0.070
19–23 (n=284)	45.5	0.004	19–23 (n=39)	41.5	0.600
23–32 (n=386)	41.2	Ref.	23–32 (n=37)	44.3	Ref.
>32 (n=89)	36.3	0.029	>32 (n=0)	–	–
P for trend		<0.0001	P for trend		<0.0001

[a] Mean iPTH values after adjustment for age, gender, BMI, education, season of blood draw, baseline supplemental calcium use and baseline supplemental vitamin D use in ordinary least squares regression models

[b] p-Value comparing mean iPTH at each 25(OH)D category to the 23–32 ng/ml referent category

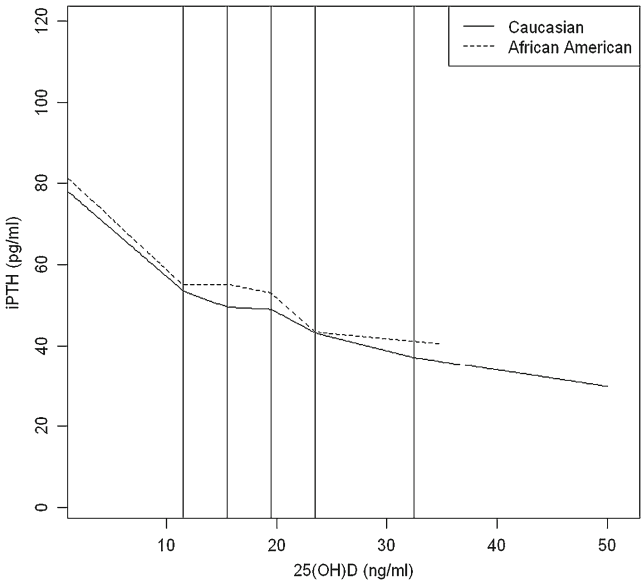

Fig. 2 The relationship between iPTH and 25(OH)D by race—results from segmented regression

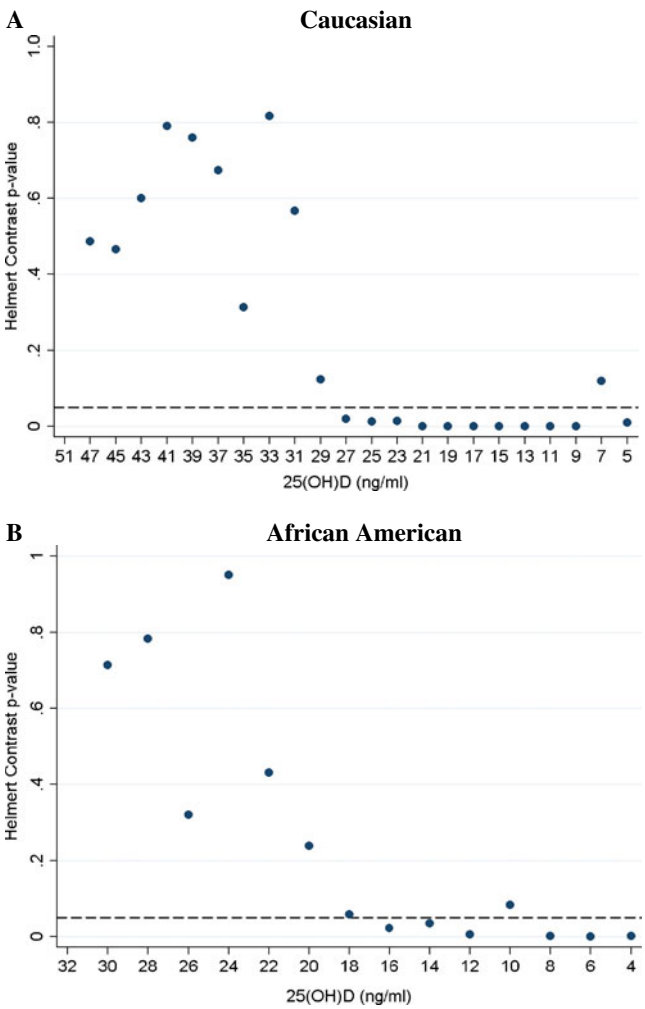

Fig. 3 The level of 25(OH)D where the Helmert contrast *p*-value first transitions below the reference line at $p=0.05$ shows the value at which the mean iPTH of the higher 25(OH)D points combined is significantly different than the mean iPTH at that level, indicating a threshold

which the mean iPTH differed significantly ($p<0.05$) from the previous levels combined in Caucasians was at 26–27 ng/ml (Fig. 3a). In African Americans, the 25(OH)D level at which the mean iPTH differed significantly ($p<0.05$) from the previous levels was at 15–16 ng/ml; however, marginal significance was observed at 17–18 ng/ml (Fig. 3b). Similar to the previous results, the Helmert contrast results indicate that the point of 25(OH)D at which iPTH is significantly different was lower in African Americans than Caucasians.

Discussion

In this sample of community dwelling older adults, we observed a similar inverse relationship between iPTH and 25(OH)D in both Caucasians and African Americans as 25(OH)D increased from nadir to 12 ng/ml. Unlike Caucasians, both OLS and segmented regression results showed a statistically significant inverse relationship until 25(OH)D levels >32 ng/ml; however, the inverse relationship between 25(OH)D and iPTH was only observed at 25(OH)D levels <23 ng/ml of 25(OH)D in African Americans. Helmert contrast results also indicated a lower iPTH threshold in African Americans than Caucasians.

These findings are consistent with those presented by Aloia et al. (2006) and Gutierrez et al. (2010) [15, 16]. Aloia et al. examined the association between vitamin D and PTH in a sample of African American postmenopausal women randomized to 800 IU of oral vitamin D3 or placebo [15]. Because of the effect of calcium deficiency on the vitamin D/PTH feedback loop, all participants received calcium supplements to ensure a calcium intake between 1,200 and 1,500 mg/day [15]. The authors assessed 25(OH)D and iPTH longitudinally for 36 months and found that 25(OH)D levels between 40 and 50 nmol/l (16–20 ng/ml), with a specific threshold at 44 nmol/l (17.6 ng/ml), was optimal in preventing a rise in PTH level in the population [15]. Both the current and the Aloia studies used segmented or spline regression to model the association between 25(OH)D and PTH and included a higher level modeling approach. Our study included men, pre- and postmenopausal women and was only able to examine the relationship cross-sectionally; however, a similar threshold, specifically the peak around 20 ng/ml, was observed.

Through utilization of the National Health and Nutrition Examination Study (NHANES) participants, Gutierrez et al. were able to conduct the largest assessment of 25(OH)D and iPTH in a diverse population

including 4,305 Whites, 2,025 Mexican-Americans and 2,081 African Americans [16]. In each of the groups, lower levels of 25(OH)D was associated with higher levels of serum PTH, and after taking into account age, gender, BMI, creatinine, calcium intake, and season of blood draw, the authors found in the total population a significant decrease in iPTH of [coefficient (95% CI)] −0.80 (−1.00, −0.60) for each unit increase in 25(OH)D when 25(OH)D was ≤20 ng/ml; however, when 25(OH)D levels were >20 ng/ml, significant decreases in iPTH for each unit increase in 25(OH)D were only statistically significant in Whites [−0.29 (−0.37, −0.21)] and Mexican-Americans [−0.52 (−0.71, −0.34)], and no significant association was seen in African Americans [0.09 (−0.41, 0.59)]. Though the NHANES population was considerably larger, the results of the Gutierrez study are comparable to ours, suggesting a threshold of the effect of 25(OH)D on iPTH to be around 20 ng/ml in African Americans, adding another study to the evidence that there is a lower 25(OH)D threshold in African Americans.

Early biochemical assessment studies examining 25(OH)D, calcium and PTH have reported that despite lower 25(OH)D levels and higher PTH levels in African Americans, calcium excretion is lower in African Americans [26–31]. Lower levels of 25(OH)D and higher levels of PTH is typically associated with an increase in calcium excretion, which is associated with a decrease in bone formation markers such as osteocalcin. Several studies have found that despite the lower 25(OH)D and higher PTH levels, African Americans have higher bone formation markers, when comparing to Caucasians, which has lead to the hypothesis that African Americans have reduced sensitivity to the catabolic skeletal effects of PTH [26, 29, 31–33]. In a more recent study examining calcium metabolism by vitamin D status in adolescent girls, Weaver et al. found an inverse relationship between 25(OH)D and PTH only in Caucasian and not African American girls [34]. Despite having lower levels of 25(OH)D, calcium retention was higher in African American girls than Caucasian girls [34]. These biochemical studies agree with the findings from this and other studies that African Americans may not need as high levels of 25(OH)D to maintain skeletal health.

Recently, the use of PTH in the definition of optimal vitamin D has been questioned, as increases in PTH are associated with a variety of other factors. Several studies have shown that PTH increases with age [35, 36] and is modified by calcium intake [37] or the presence of other comorbidities such as renal disease. Because of this, the IOM report suggested that PTH not be used [17]; however, this remains under debate, and the IOM lowered the deficiency threshold to <12 ng/ml and considered 25(OH)D levels between 12 and 20 ng/ml as inadequate vitamin D. These new levels complement the threshold we observed in African Americans, but our study did find the threshold for Caucasians to be closer to the level at 30 ng/ml, which is traditionally used to define normal 25(OH)D level by many commercial labs [18].

Strengths and limitations

Though consistent with the Aloia and Guitierrez studies, our study is not without limitations. First, the results are based on a cross-sectional analysis. Though a longitudinal analysis or a more experimental design such as a controlled trial would provide more information on the causal effect of 25(OH)D on PTH status, in most clinical situations, physicians make treatment decisions based on one assessment of vitamin D status, so a cross-sectional approach to the study may not be a large limitation to the conclusion that normal 25(OH)D levels are different between Caucasians and African Americans. The second largest limitation is that there were no African Americans in the highest category of vitamin D, so we were unable to examine how 25(OH)D at levels ≥33 ng/ml might alter iPTH in African Americans.

Our study did not examine serum calcium levels making it possible that some of our findings could be related to calcium deficiency/insufficiency. We were able to adjust for calcium supplementation use as a binary variable, but assessing the amount of calcium intake from dietary and supplemental sources or having serum levels may have provided more complete assessment of calcium exposure for assessing confounding or effect modification. It is possible that the low proportion of calcium supplement used in African Americans contributed to the overall lower levels of 25(OH)D in the population. Persons self-reporting chronic kidney disease were excluded from this study; however, measurement of glomerular filtration rate (GFR) or creatinine were not conducted, and it is possible that people with stage 3 or 4 chronic kidney disease were included, accounting for the increased iPTH observed in the study. The MOST study participants were derived from two clinical centers, and the majority of African Americans were enrolled at one of the two centers (AL), so these results may not be generalizable to Africans Americans and Caucasians from other locations.

Despite these limitations, our study joins a very small literature base on the examination of 25(OH)D and PTH in African Americans. The study used simple and complex statistical methods in this examination and had a sufficient sample size and power to find statistically significant associations in Caucasians. Although only 9% of the African Americans fell within the two highest 25(OH)D categories, the proportions are very similar to those reported in the larger and more nationally representative NHANES study, which only had 10% of the African American in their highest two

25(OH)D categories. Our study found that 20 ng/ml of 25 (OH)D appears to be the threshold at which significant differences in iPTH levels are observed in African Americans compared to higher levels in Caucasians. Studies like ours provide additional evidence that there indeed may be different optimal vitamin D levels in African Americans for bone health.

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Conflicts of interest None.

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