

Five-Year Surveillance of Vitamin D Levels in NCAA Division I Football Players

Risk Factors for Failed Supplementation

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Background: Monitoring vitamin D levels in athletes and determining their response to supplementation in cases of deficiency is thought to be necessary to modulate the risks associated with vitamin D deficiency.

Hypothesis/Purpose: To report the results of a 5-year-long surveillance program of vitamin D in the serum of football players on a National Collegiate Athletic Association (NCAA) Division I team and to examine whether factors including age, body mass index (BMI), race, position played, and supplement type would affect the response to 12-month oral vitamin D replacement therapy in athletes with deficiency. We hypothesized that yearly measurements would decrease the proportion of athletes with vitamin D insufficiency over the years and that the aforementioned factors would affect the response to the supplementation therapy.

Study Design: Cohort study; Level of evidence, 3.

Methods: We measured serum 25(OH)D levels (25-hydroxyvitamin D) in 272 NCAA Division I football players from our institution annually between 2012 and 2017. Athletes with insufficient vitamin D levels (<32 ng/mL) received supplementation with vitamin D3 alone or combined vitamin D3/D2. The percentage of insufficient cases between the first 2 years and last 2 years of the program was compared, and yearly team averages of vitamin D levels were calculated. Associations between player parameters (age, BMI, race, team position, supplement type) and failed supplementation were evaluated.

Results: The prevalence of vitamin D insufficiency decreased significantly during the study period, from 55.5% in 2012-2013 to 30.7% in 2016-2017 ($P = .033$). The mean 25(OH)D level in 2012 was 36.3 ng/mL, and this increased to 40.5 ng/mL in 2017 ($P < .001$); however, this increase was not steady over the study period. Non-Hispanic athletes and quarterbacks had the highest average 25(OH)D levels, and Black players and running backs had the lowest overall levels. There were no significant differences in age, BMI, race, or playing position between athletes with and without failed vitamin D supplementation. Athletes receiving vitamin D3 alone had a more successful rate of conversion (48.15%) than those receiving combined vitamin D3/D2 (22.22%; $P = .034$).

Conclusion: To decrease the prevalence of vitamin D deficiency in football players, serum vitamin D measurements should be performed at least once a year, and oral supplementation therapy should be provided in cases of deficiency. Black players might be at increased risk of vitamin D insufficiency. Oral vitamin D3 may be more effective in restoring vitamin D levels than combined vitamin D3/D2 therapy.

Keywords: vitamin D; 25(OH)D; athletes; football; risk factor

Vitamin D insufficiency, which can be diagnosed by measuring the levels of 25(OH)D (25-hydroxyvitamin D) in the blood, is prevalent and well-documented in athletes.^{3,4,7,27,37,42} A previous study reported the prevalence of vitamin D insufficiency to be 48% in outdoor athletes and 80% in indoor athletes who competed at a high

level and participated in various sports.² It is unknown whether athletes need to maintain the circulating level of vitamin D within a specific range to avoid the risks associated with vitamin D deficiency.¹ A previous study showed a relatively high prevalence (33.6%) of vitamin D insufficiency (serum 25(OH)D level <32 ng/mL) among National Collegiate Athletic Association (NCAA) athletes across a variety of sports.⁴² Significant variation has been reported in the practice patterns for the diagnosis and treatment of vitamin D deficiency among NCAA Division I athletes.³⁰

The Orthopaedic Journal of Sports Medicine, 9(1), 2325967120975100
DOI: 10.1177/2325967120975100
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Previous studies in high-level athletes showed an association between vitamin D insufficiency and increased risk of stress fractures, hormonal imbalance (testosterone, cortisol, and parathyroid hormone), infection, and elevated blood pressure.^{4,5,8,11,26,35,36,40} In collegiate football players, an association was found between vitamin D insufficiency and inability to maintain glucose homeostasis, and the same authors reported an inverse relationship between serum 25(OH)D levels and hepatic lipid content in these athletes.^{35,36} Rebolledo et al²⁹ found an association between low vitamin D levels and history of lower extremity and core muscle injury in National Football League players.

There has been increased awareness of vitamin D insufficiency in athletes during the past decade.^{18,30} Reported factors that increase the risk of vitamin D insufficiency in football players include Black race and male sex.^{3,33,44} In terms of therapy, oral vitamin D supplementation has been shown to successfully raise levels of 25(OH)D in high-level athletes.^{2,10,20,43} Although it is still controversial whether vitamin D sufficiency is correlated with improved athletic performance, maintaining adequate levels of 25(OH)D in serum is important for the athlete's general health and might also help with injury prevention.^{10,13,20,29,32,34,43} Given that normal levels of vitamin D have been shown to be associated with the athlete's general health, examining the factors that may be associated with poor response to therapy would help to improve the current treatment strategies.

The purpose of this study was to report the results of a 5-year surveillance program for maintaining adequate levels of vitamin D in the serum of football players on an NCAA Division I team. We also sought to examine whether factors including player age, body mass index (BMI), race, position in the field, and type of supplement would affect the response to 12-month oral supplementation therapy for vitamin D insufficiency. We hypothesized that yearly measurements would decrease the proportion of athletes with vitamin D insufficiency over the years and that the aforementioned factors would affect the response to the supplementation therapy.

METHODS

Data Collection

A vitamin D surveillance program was implemented in our institution to diagnose and treat 25(OH)D insufficiency in collegiate athletes. Per our standardized protocol, all athletes on the institution's football team had their serum

25(OH)D levels measured at the beginning of each season from June 2012 to August 2017. Each athlete's level was categorized as either sufficient (≥ 32 ng/mL) or insufficient (< 32 ng/mL). The definition of vitamin D insufficiency was based on a previous publication.⁴² All athletes with insufficient vitamin D levels were supplemented with either vitamin D3 (50,000 IU weekly) or a combination of vitamin D3 (2000 IU daily) and vitamin D2 (50,000 IU weekly). Preference of one supplementation regimen over the other was based on the recommendation of the primary care physician of each athlete. After each full year of supplementation, the vitamin D levels were remeasured at the beginning of the following season. All athletes would continue the supplementation regimen based on their vitamin D levels and undergo reanalysis annually during their time with the team. If an athlete had normal vitamin D levels they were given the option to continue to take vitamin D supplement at a lower than the therapeutic dose (for maintenance) dose or they stopped taking the supplement. All measurements were conducted and prospectively recorded by the team physician and/or the institution's medical staff, who were also responsible for administering the supplement to all athletes and ensuring compliance with therapy. This study received institutional review board approval.

Additional parameters were collected for each player retrospectively, using our institutional database. These parameters included age, race (White, Black, Asian/Pacific Islander, Hispanic, Native American, multiracial), field position (quarterback, running back, wide receiver, tight end, offensive lineman, defensive lineman, defensive back, kicker, punter, long snapper), and type of supplement taken (vitamin D3 alone vs vitamin D3/D2).

Study Methodology and Statistics

Statistical analysis comparing the athletes' descriptive characteristics and vitamin D levels was performed using STATA Version 13.0 (StataCorp LP). To determine the overall efficacy of the vitamin D surveillance program, the percentage of athletes who had vitamin D insufficiency during the first 2 years was compared with the percentage of athletes who had vitamin D insufficiency in the last 2 years of program implementation. The yearly team averages of vitamin D levels were calculated to identify the trend of vitamin D levels during the study period. Subgroup analysis was conducted in a group of athletes with deficiency to identify potential factors that may have affected the response to 12-month oral supplementation therapy. Specifically, age, race, BMI, team position, and type of supplement received (vitamin D3 vs D2/D3) were compared

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Final revision submitted July 5, 2020; accepted July 29, 2020.

One or more of the authors has declared the following potential conflict of interest or source of funding: A.E.W. has received educational support from Arthrex, nonconsulting fees from Arthrex, and hospitality payments from Stryker. J.E.T. has received educational support from Arthrex and Micromed, nonconsulting fees from Arthrex and Pacira Pharmaceuticals, and royalties from Arthrex. S.C.G. has received educational support from Arthrex, consulting fees from Zimmer Biomet, and nonconsulting fees from Arthrex. AOSSM checks author disclosures against the Open Payments Database (OPD). AOSSM has not conducted an independent investigation on the OPD and disclaims any liability or responsibility relating thereto.

Ethical approval for this study was obtained from the University of Southern California (No. HS-13-00560-CR001).

between athletes who did and did not undergo successful conversion to sufficient levels of vitamin D after receiving oral supplementation therapy for 12 months. Fisher exact and chi-square analysis was performed to compare categorical variables—namely, the percentages of athletes with abnormal vitamin D levels or those whose supplementation failed. Significance was set at $P < .05$.

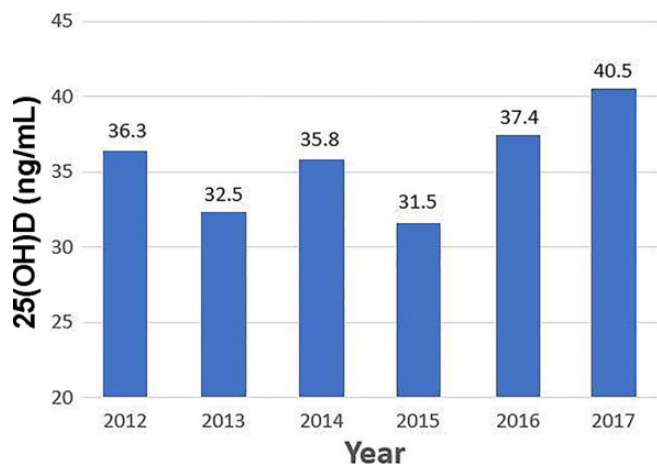


Figure 1. Mean 25(OH)D levels (ng/mL) of all team athletes by year. 25(OH)D, 25-hydroxyvitamin D.

RESULTS

Evaluation of Program Efficacy

A total of 272 NCAA Division I football players were analyzed. At the time of the first serum 25(OH)D level measurement, the mean \pm SD age of the athletes was 19.6 ± 1.7 years (range, 17-27 years), and the mean BMI was 29.2 ± 4.4 kg/m². The prevalence of athletes with vitamin D insufficiency was significantly decreased during the study period, from 55.5% in 2012-2013 to 30.7% in 2016-2017 ($P = .033$). The yearly team averages of vitamin D levels are depicted in Figure 1. The overall annual average 25(OH)D level in 2012 was 36.3 ng/mL and increased to 40.5 ng/mL in 2017 ($P < .001$); however, this increase was not steady throughout the study period. The annual differences between incoming and returning athletes is presented in Figure 2. During the initial year, 51.4% of the incoming athletes had insufficient vitamin D levels, and 48.7% of the returning athletes had insufficient vitamin D levels. However, by the final measured year, the percentage of returning athletes with insufficient levels (16.2%) was significantly lower than that of the incoming athletes (55.6%; $P < .001$). The prevalence of vitamin D insufficiency was decreased $>50\%$ over the 5-year period, from 49.6% in 2012 to 20.8% in 2017.

Analysis by Race

White athletes had consistently the highest measured average 25(OH)D levels among all races, ranging from 38.8 to

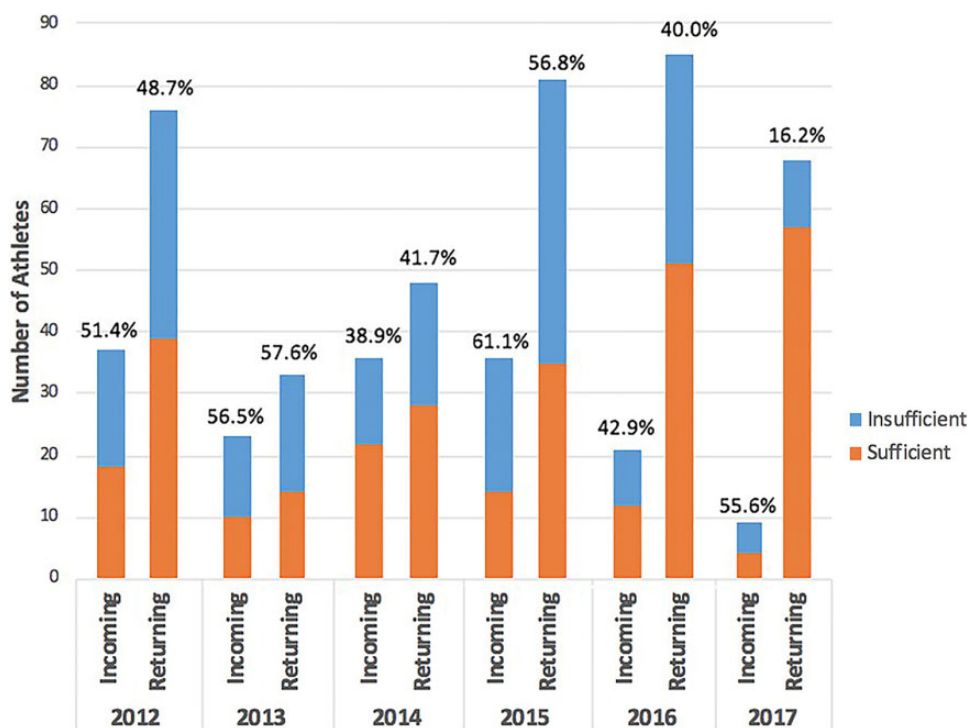


Figure 2. Athletes with insufficient (<32 ng/mL) and sufficient (≥ 32 ng/mL) levels of 25(OH)D by incoming status (first time measured) or returning status (had previously been tested). The percentage at the top of the column is the percentage of athletes with vitamin D insufficiency. 25(OH)D, 25-hydroxyvitamin D.

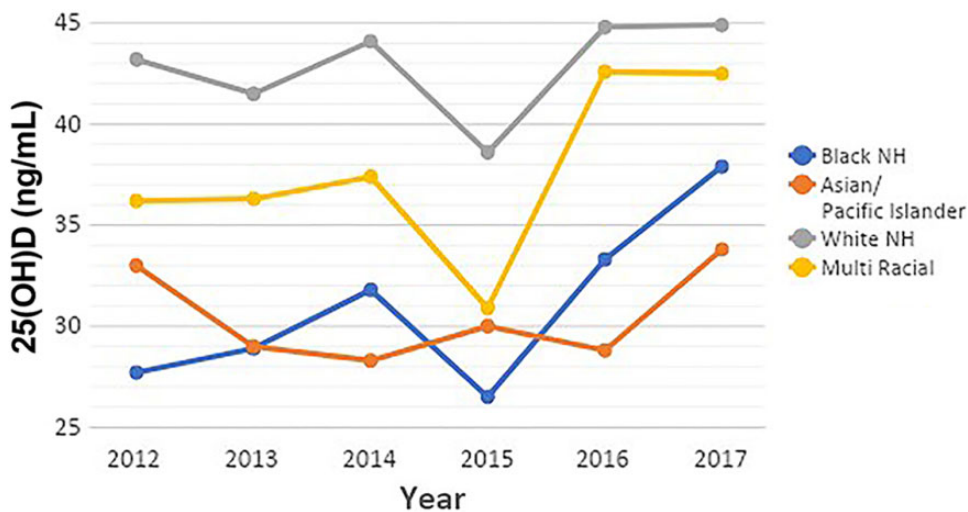


Figure 3. Mean yearly 25(OH)D levels by race. 25(OH)D, 25-hydroxyvitamin D; NH, non-Hispanic; NH, non-Hispanic.

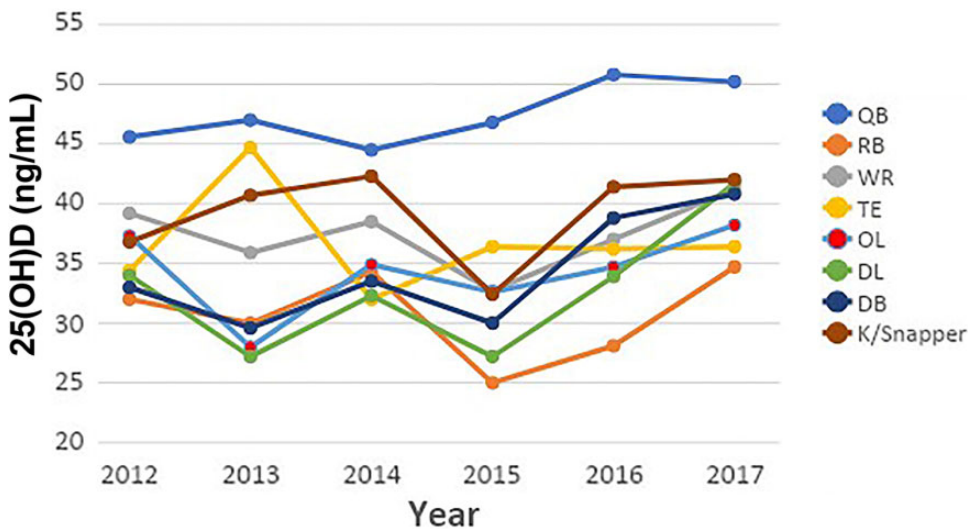


Figure 4. Yearly average 25(OH)D levels by player position. 25(OH)D, 25-hydroxyvitamin D; DB, defensive back; DL, defensive lineman; K, kicker; OL, offensive lineman; QB, quarterback; RB, running back; snapper, long snapper; TE, tight end; WR, wide receiver.

45.1 ng/mL (mean, 43.47 ± 11.91 ng/mL; *P* < .001). Black players had the lowest overall average vitamin D levels as compared with other races (mean, 31.02 ± 7.66 ng/mL; *P* < .001). A complete breakdown of mean annual vitamin D levels by race is presented in Figure 3 (only a single player over all 5 years was listed as Hispanic and thus was not included in the figure).

Analysis by Player Position

When vitamin D levels were analyzed by position, quarterbacks consistently had the highest mean levels, ranging from 44.5 to 50.8 ng/mL (47.48 ± 10.94 ng/mL; *P* < .001). Running backs, however, had the lowest overall mean vitamin D levels at 30.7 ± 7.49 ng/mL (*P* < .001) as well as the

lowest recorded annual mean vitamin D level (25 ng/mL in 2015). All positions showed an increase in vitamin D level from 2015 to 2017. A complete breakdown of mean annual vitamin D levels by player position is presented in Figure 4.

Failed Supplementation After Replacement Therapy

To identify factors that were associated with failed supplementation after 12 months of treatment, we analyzed a subgroup of patients who had complete measurements and no missing doses of therapy. After 1 year of oral supplementation, 27 athletes with insufficient vitamin D levels underwent successful conversion to sufficient levels, as opposed to 55 athletes whose conversion failed. There were no significant differences in age, BMI, position, or race between

TABLE 1
Successful vs Failed Conversion From Insufficient
to Sufficient Vitamin D Among Athletes

	Conversion, Mean \pm SD or No. (%)		P Value
	Failed (n = 55)	Successful (n = 27)	
Age, y	19.1 \pm 1.4	18.8 \pm 1.4	.208
Body mass index	30.4 \pm 4.9	29.4 \pm 4.2	.481
Race			.54
White non-Hispanic	4 (7.3)	4 (14.8)	
Black non-Hispanic	39 (70.9)	15 (55.6)	
Asian/Pacific Islander	4 (7.3)	2 (7.4)	
Hispanic	1 (1.8)	1 (3.7)	
Native American	0 (0)	1 (3.7)	
Multiracial	7 (12.7)	4 (14.8)	
Position			.319
Quarterback	0 (0)	0 (0)	
Running back	8 (14.6)	4 (15.4)	
Wide receiver	4 (7.3)	2 (7.7)	
Tight end	3 (5.5)	2 (7.7)	
Offensive lineman	10 (18.1)	4 (15.4)	
Defensive lineman	6 (10.9)	4 (15.4)	
Defensive back	24 (43.6)	7 (26.9)	
Kicker	0 (0)	1 (3.9)	
Punter	0 (0)	2 (7.7)	
Long snapper	0 (0)	0 (0)	
Type of supplement			.034 ^a
Vitamin D3 (50,000 IU/wk)	12 (21.8)	13 (48.1)	
Vitamin D3 (2000 IU/d) + D2 (50,000 IU/wk)	24 (43.6)	6 (22.2)	
Unspecified	18 (32.7)	8 (29.6)	

^aStatistically significant difference.

these groups (Table 1). However, athletes receiving vitamin D3 alone were more successful in rates of conversion (48.1%) versus those receiving combined vitamin D3/D2 (22.2%; $P = .034$).

DISCUSSION

This study showed that the prevalence of vitamin D insufficiency in a single team of elite football players was significantly decreased over 5 years by performing yearly measurements of 25(OH)D levels and providing the appropriate supplementation therapy to athletes with insufficiency. However, there was an indication that more frequent measurement of 25(OH)D might be necessary to sustain this outcome. After 12 months of oral replacement therapy, athletes with deficiency who received vitamin D3 alone had a more successful rate of conversion (48.1%) than those who received combined vitamin D3/D2 (22.2%). We noticed that athletes of Black race had the lowest levels of vitamin D during the study period and constituted >50% of the athletes whose 12-month supplementation therapy regimen failed. However, the player's age, BMI, and position in the field did

not seem to affect the response to treatment for vitamin D insufficiency.

Similar to our findings, previous studies have demonstrated that the prevalence of vitamin D deficiency is relatively high in competitive athletes, including football players.[‡] During the study period, the mean serum concentration of vitamin D in this group of NCAA Division I football players ranged between 31.5 and 40.5 ng/mL. Heller et al,¹⁴ in a study that included various intercollegiate teams, found that football athletes had significantly lower serum 25(OH)D concentration than nonfootball athletes. The mean level of vitamin D in this last group of football players (30 ng/mL) was similar to our lowest mean concentration of vitamin D recorded in 2015 (31.5 ng/mL). In a previous study, vitamin D levels were measured in athletes participating in 7 NCAA Division I sports, and basketball players (30.4 ng/mL) and football players (35.6 ng/mL) had lower mean concentrations of serum 25(OH)D than athletes in other sports.⁴²

Additional evidence is necessary to determine if vitamin D deficiency in elite football players (including collegiate athletes and National Football League players) affects the injury rate or athletic performance.^{7,22,23,29} As mentioned before, Sun et al^{35,36} found a correlation between vitamin D insufficiency and abnormal glucose homeostasis and changes in the hepatic lipid content in male collegiate football players. It has been reported that circulating 25(OH)D concentrations are negatively associated with fasting glucose concentration in young adults but also inversely correlated with the concentrations of 1-hour glucose, 2-hour glucose after oral glucose tolerance, the increments of the glucose area under the curve, and the increments of the insulin area under the curve.^{6,31} In addition, there is evidence that vitamin D may inhibit lipid accumulation and that higher levels of vitamin D are associated with reduced fat and weight gain.²¹ Another research group reported a higher prevalence of lower extremity muscle strains and core strains in National Football League players with abnormal vitamin D levels in serum.^{35,36} We suspect that the athlete's body composition and other factors, such as the training conditions, frequency of travel, hormonal changes, or dietary habits, might be implicated in metabolism of vitamin D in football players, but this is subject to further investigation.

Current literature agrees with the use of oral vitamin D3 for supplementation in athletes with vitamin D deficiency.^{9,38,39,41} The highest mean concentration of 25(OH)D in this group of football players (40.5 ng/mL) was achieved during the last year of the program implementation (2017). Based on the treatment protocol, vitamin D3 alone or in combination with vitamin D2 was given as replacement therapy. Our findings therefore corroborate the existing evidence on the effectiveness of vitamin D3-containing supplements to address 25(OH)D insufficiency in athletes.¹⁰ In addition, when the factors were examined for failed supplementation after 12 months of therapy for

[‡]References 7, 14, 18, 22, 23, 29, 30, 35, 36, 42.

vitamin D insufficiency in a subgroup of athletes, those who received vitamin D3 alone had a more successful rate of conversion (48.15%) than those who received the combined regimen (22.22%; $P = .034$).

A meta-analysis of 7 randomized trials evaluating the serum 25(OH)D concentration after supplementation with cholecalciferol (vitamin D3) versus ergocalciferol (vitamin D2) illustrated that vitamin D3 increased serum 25(OH)D more efficiently than vitamin D2.³⁸ These authors also showed the greatest differences in effectiveness in trials that used weekly or monthly dosing rather than daily dosing.³⁸ Our treatment protocol included 2 regimens: weekly administration of vitamin D3 or weekly administration of vitamin D2 in combination with oral vitamin D3 on a daily basis. The literature has not established a standard vitamin D dosing regimen.³⁰ A common approach is to treat with 50,000 IU of vitamin D2 or D3 weekly for 6 to 8 weeks, followed by 800 IU of vitamin D3 daily, based on the guidelines by the Endocrine Society.¹⁵ Based on our results, the prevalence of vitamin D insufficiency was relatively high in the returning athletes (supplemented), which highlights the need for optimization of the vitamin D supplementation protocol. In addition, standardization of the clinical practices to treat vitamin D insufficiency in young athletes is a necessary step to decrease the prevalence of this condition and the associated health consequences.

We also examined associations between player age, BMI, race, and team position and failed supplementation after 12 months of oral therapy for vitamin D insufficiency. There were no statistically significant differences in age, BMI, position, or race between the cohorts who underwent conversion to sufficient vitamin D and those who did not (Table 1). It is worth noting, however, that based on our findings, race might play a role in the response to oral replacement therapy. We noticed that the percentage of Black athletes in the cohort who did not achieve sufficient levels of vitamin D was higher than the corresponding percentage that had a successful treatment (71% and 56%, respectively). In addition, Black football players had the highest rate of insufficient vitamin D levels and also the lowest mean vitamin D levels in serum among all races analyzed.

This last finding was in congruence with previous literature showing that darker-skinned individuals have higher rates of vitamin D deficiency than other populations.^{12,19,28,42} The reasoning behind the concentration-level differences remains controversial. Using a monoclonal sandwich assay in a multiethnic cohort, Powe et al²⁸ found that low vitamin D-binding protein levels were more common in Black Americans than White Americans, but they had similar amounts of bioavailable vitamin D. However, when the vitamin D-binding proteins were measured using a different assay in a study by Hoofnagle et al,¹⁶ Black Americans did not display a higher rate of lower levels. Therefore, more research is needed to assess if Black race is a risk factor for vitamin D insufficiency in the general population and athletes and whether it affects the response to vitamin D supplementation. Until more evidence becomes available, we suggest close monitoring

of the vitamin D levels in Black athletes who participate in football and other sports, to protect them against the risks related to vitamin D insufficiency.^{2,3,17,24,25,33} Although the current study did not detect an association between player position and response to vitamin D supplementation in collegiate football players, more research is necessary to confirm this outcome. In theory, there could be a link between the athlete's body composition (which might be affected by position-specific training for prolonged periods) and the metabolism of vitamin D in football players. Further research is recommended to investigate this hypothesis.

Limitations

The results of this study are dependent on the athletes properly supplementing their vitamin D. To protect against improper dosing, we had the team nutritionist administer the pills to improve compliance. Failure of the athletes to follow the vitamin D supplementation program may underestimate the effect that supplementation has on the vitamin D levels. Two supplementation therapies were used (vitamin D3 only or combined vitamin D2/D3) based on the recommendation of the primary care physician of each athlete. In the body, both forms of the vitamin convert into calcifediol in the liver, so the effectiveness of both forms is thought to be similar on raising vitamin D levels. Furthermore, although this study illustrated the restorative effect of vitamin D supplementation, it did not include any clinical correlation. Future studies could investigate differences in peak performance, injury profiles, and injury prevalence between athletes with vitamin D deficiency and sufficiency, as well as before and after supplementation among athletes with deficiency.

While we analyzed race and team positioning as potential risk factors for vitamin D insufficiency, we did not take into consideration the amount of each athlete's sun exposure at the time of testing, which may have significantly affected the results. Last, we sought to identify any association between player parameters and response to vitamin D replacement therapy, but this was feasible only in a small subgroup of the study population who had complete data.

As mentioned previously, although the vitamin D measurement and supplementation information was collected prospectively, the players' age, BMI, race, and position were retrieved using our institutional database. The last parameter increased the risk of missing or incorrectly recorded data, which reduced the external validity of our results. We did not record whether any of the included athletes had left the team after their first year of vitamin D supplementation, which might have affected the accuracy of the reported prevalence of vitamin D insufficiency for the following year. The athletes' information regarding prior supplementation with vitamin D and/or other regimens was not recorded, which could have affected the circulating levels of vitamin D during the study period or the response to supplementation therapy.

CONCLUSION

To decrease the prevalence of vitamin D insufficiency in elite football players, serum vitamin D measurements should be performed at least once a year, and oral supplementation therapy must be provided in cases of deficiency. Black players might be at increased risk of vitamin D insufficiency as compared with other races, and closer monitoring is suggested. Oral vitamin D3 may be more effective in restoring the levels of vitamin D in athletes as compared with combined therapy with vitamin D2 and vitamin D3.

ACKNOWLEDGMENT

The authors acknowledge the Cappo Family Research Fund.

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