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Vitamin D deficiency in athletes: Laboratory, clinical and field integration

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ABSTRACT

Vitamin D deficiency is highly prevalent in athletes. Increased utilisation and storage depletion may be key contributing factor. We found a higher prevalence of vitamin D inadequacy (deficiency/ insufficiency) in power than endurance sport athletes, which may be related to vitamin D utilisation and reserve in skeletal muscles.

1. Introduction

Nutrition is an important element in sports medicine. Vitamin D is a fat-soluble sterol nutrient and hormone precursor required for many essential functions in overall health. It is synthesised in the skin, produced in the body upon 15–30 min of sunlight exposure, or absorbed from fatty fish, egg yolk, dairy products and/or fortified foods.

An individual's vitamin D status is defined by the serum 25(OH) D concentration.[1–3] The Endocrine Society Committee (ESC) has defined concentration of ≥30 ng/mL (≥75 nmol/L) as sufficient, 21–29 ng/mL (52.5–72.5 nmol/L) as insufficient, and ≤20 ng/ml (≤50 nmol/L) as deficient.[4] Concentration of 100 ng/mL may contribute to vitamin D toxicity.[5] The recommended daily vitamin D intake for ages 18–70 is 1500–2000 IU[6] or 600 IU[7] according to the ESC and Institute of Medicine respectively. Actual dosage depends on age, geographical location, skin pigmentation, physical activity and season.

In the past decade, growing research interest into the role of vitamin D in sports medicine has unveiled a high prevalence of vitamin D deficiency in athletes.[8] Low vitamin D levels have been demonstrated to have negative effects on muscle strength, power, and endurance; increase stress fractures and other musculoskeletal injuries; and affect acute muscle injuries and inflammation following high-intensity exercises.[9] Nevertheless, currently there is no evaluation of vitamin D screening and supplementation protocol among elite athletes in the literature.

To address the problem of vitamin D deficiency in athletes, this perspective article will first provide a succinct background on the biochemistry and physiology of vitamin D, and then proceed to detail the evidence for vitamin D relevancy in athletes through pre-clinical and clinical lenses. We aim to provide biomedical scientists with a new perspective to investigate the causes of vitamin D deficiency in athletes; to athletes, coaches and sport nutritionists the knowledge on vitamin D source identification and optimal level maintenance; and to sports medicine practitioners and authoritative bodies more information on who and when to screen for vitamin D deficiency, and the possibility of supplementation. Knowledge exchange and collaborative effort among diverse experts will hopefully maximize the potential medical, social and economic benefits of treating vitamin D deficiency in athletes.

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2. Vitamin D in athletes: Basic sciences

2.1. Factors contributing to vitamin D deficiency in athletes

Despite a presumably leaner physique and higher health consciousness in athletes, the high prevalence of vitamin D deficiency in athletes (56%[10]) as compared to the age-matched general population (24–40%[11]) is alarming. Vitamin D deficiency is supposedly caused by low bioavailability from sunlight and dietary intake,[12] but to the best of our knowledge, there is no evidence to suggest a lower sun exposure nor dietary vitamin D intake in athletes when compared to non-athletes. On the other hand, a high prevalence of vitamin D deficiency has been documented in athletes who train outdoor and at latitudes favourable for sun exposure.[13–15] Therefore, other factors may account for athletes' unusual vulnerability to vitamin D deficiency. In particular, the role of vitamin D reserve and how exercise mobilises this reserve may be highly relevant.

2.2. General metabolic pathway

2.2.1. Regulation of circulating vitamin D levels

Major vitamin D metabolites include the precursor form (vitamin D_2 and D_3), circulating pre-hormone form (25(OH)D), bioactive form ($1\alpha,25(OH)_2D$) and excreted form ($24,25(OH)_2D$).

Three major enzymatic conversion steps are involved: 25-hydroxylation, 1α-hydroxylation and 24-hydroxylation.[12] The main circulating form of vitamin D, 25(OH)D, is generated by 25-hydroxylation of vitamin D_2 and D_3 in the liver. 25(OH)D is then hydroxylated to $1\alpha,25(OH)_2D$, the biologically active form of vitamin D, in the kidneys. Renal 1α-hydroxylation is tightly regulated by three hormones to maintain calcium and phosphate homoeostasis: the parathyroid hormone (PTH), fibroblast growth factor 23 (FGF23) and $1,25(OH)_2D$. PTH stimulates while FGF23 and $1,25(OH)_2D$ inhibits the 1α-hydroxylase.[12] Thus, the regulation of circulating $1\alpha,25(OH)_2D$ level is under a close negative feedback mechanism. Finally, vitamin D metabolites are cleared from the circulation via 24-hydroxylase-initiated catabolism, where biologically inactive $24,25(OH)_2D$ is produced and excreted mainly through the bile (refer to Fig. 1).

Traditionally, we refer to serum 25(OH)D concentration as the best biochemical marker of an individual's vitamin D status because of its relatively longer half-life than $1\alpha,25(OH)_2D$.[16] Majority of circulating 25(OH)D is bound to vitamin D binding protein (DBP). Though only free 25(OH)D is bioactive for renal conversion and responsible for subsequent biological effects of vitamin D, unresolved issues regarding their measurement and result interpretation hinder clinical application of bound/free form of 25(OH)D as marker for vitamin D status.[17] Total circulating 25(OH)D (DBP-bound and free forms) is thus used as the measure to define vitamin D deficiency.

There are three sources of vitamin D and hence circulating 25(OH)D after hepatic conversion. The major source is endogenous synthesis in the skin, where upon exposure to ultraviolet B (UVB) radiation from the sun, 7-dehydrocholesterol, a liver-derived vitamin D precursor stored inside the plasma membrane of skin cells, eventually isomerizes to D_3.[12] Nutritional sources include fatty fish, fortified foodstuffs and supplements, where vitamin D_2 and D_3 can be obtained.[18] Finally, despite less explored, the storage and release of D_2, D_3 and 25(OH)D from tissue reserve such as fat and muscle, may represent the third source of 25(OH)D in the circulation (refer to Fig. 1).

Taken together, there could theoretically be four possible causes of low serum 25(OH)D: (1) insufficient source from sunlight exposure and diet, (2) pathological deregulation in liver and renal conversion, (3) increased utilisation that depletes the storage, and (4) difficulties in mobilisation from reserve (refer to Fig. 1). As mentioned before, the high prevalence of vitamin D deficiency in athletes is less likely to be attributed solely to insufficient sources from sunlight or diet. Defective liver modification or exaggerated renal conversion are rare and may only happen in certain diseases. While the excreted form ($24,25(OH)_2D$) is highly correlated to the circulating pre-hormone form (25(OH)D),[19] to the best of our knowledge, no evidence has demonstrated vitamin D deficiency due to exaggerated excretion. Therefore, though less investigated, increased utilisation and mobilisation of vitamin D reserve may be a key determinant for vitamin D deficiency in athletes.

2.2.2. Vitamin D storage in fat and muscle

There are two principal storage sites of vitamin D in human: adipose tissues and skeletal muscle.[20] As vitamin D reserve, fat stores the highest concentration of vitamin D metabolites among all body tissues, skeletal muscle is second.[20]

Vitamin D_2 and D_3, being more lipophilic than other vitamin D metabolites, are the major storage forms in fat.[20] Long-term

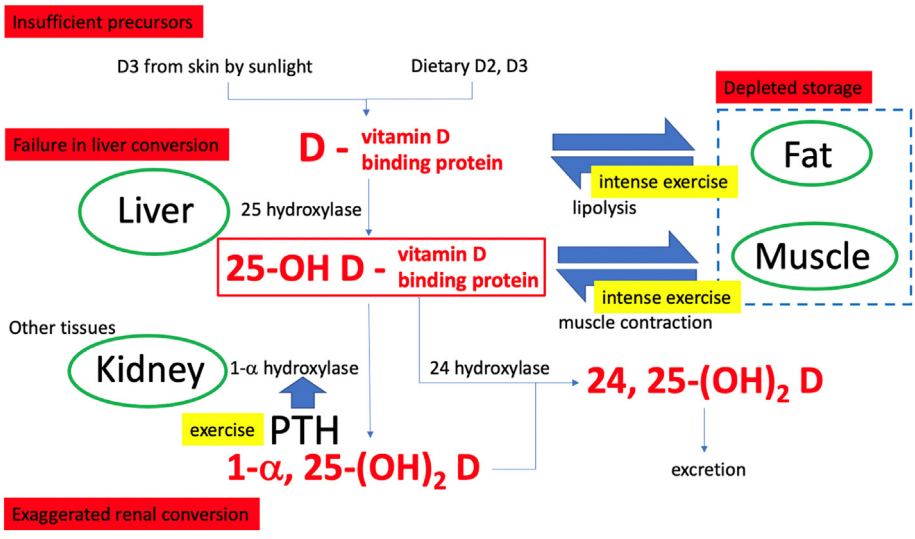

Fig. 1. Possible causes of vitamin D deficiency.

vitamin D_3 supplementation leads to a substantial accumulation in adipose tissues.[21] What regulate the storage of vitamin D_2 and D_3 in adipose tissues remains unknown. It could be by simple passive diffusion with an equilibrium between vitamin D_2 and D_3 in serum and fat globules,[22] or by active processes which are yet to be confirmed. Lipolysis may be a mechanism of mobilising this reserve for hepatic conversion,[23] but the release appears to be slow[21] and exercise-dependent,[24] while the exact trafficking remains largely unknown. Fat may represent a site of sequestration where once uptaken, vitamin D_2 and D_3 do not readily contribute to the circulating 25(OH)D level, especially in obese subjects[23] (refer to Fig. 1). On the other hand, 1α,25$(OH)_2$D stimulates its own degradation[25] and reduces adipocyte fat contents,[26] it may be inferred that increased vitamin D utilisation also reduces the storage in fat.[21]

Alternatively, skeletal muscle cells uptake and accumulate 25(OH)D through the DBP-mediated megalin-cubulin membrane transport process.[27] DBP has two specific, high affinity binding sites: one for vitamin D and its metabolites, another for actin.[28] The cell membrane receptor megalin and its associated protein cubulin mediate extracellular uptake of DBP, which is retained in the cell by its specific binding to actin; such a retention provides high affinity binding sites for 25(OH)D.[29] It has been demonstrated that exercise leads to an immediate transient increase in serum 25(OH)D level.[30] Intense exercise may trigger a quick release of 25(OH)D from skeletal muscle (refer to Fig. 1), though further investigation is required to confirm this process. In short, skeletal muscle and adipose tissues play important roles as vitamin D reserve; the extent of exercise-induced vitamin D metabolites mobilisation varies.

2.3. Exercise-induced changes related to vitamin D metabolism

First, exercise indirectly activates renal hydroxylation of 25(OH)D to 1α,25$(OH)_2$D, increasing vitamin D metabolite utilisation (refer to Fig. 1). Second, the increased 1,25$(OH)_2$D level activates 24-hydroxylase conversion even in the pre-hormone forms (D_2 and D_3), increased excretion of vitamin D may further aggravate storage depletion on top of mobilising 25(OH)D reserve to circulation (refer to Fig. 1). Overall, intense exercise represents higher physiological demands for 25(OH)D and 1,25$(OH)_2$D, which may be met by increased recruitment of circulating or muscle-stored 25(OH)D (fat storage unknown).

3. Vitamin D in athletes: Clinical implications

3.1. Assessment of athletes

3.1.1. Clinical feature of athletes with Vitamin D deficiency

Of particular relevance to sports medicine practitioners, the clinical feature of athletes with vitamin D deficiency serves as a guide to screen for further investigation and/or intervention. This include: (1) female athletes with amenorrhea (low energy availability,[31,32] on hormonal contraceptives[32]), (2) jumping sport athletes with a history of previous stress fracture[33,34] (high vitamin D utilisation, low reserve), (3) indoor sport athletes who require weight-maintenance,[35] and (4) collegiate athletes with busy schedules[32,34] (decreased vitamin D supplementation via food intake).

Although the majority of vitamin D deficiency cases are asymptomatic, some athletes may present with non-specific symptoms, such as muscular weakness (predominantly of the proximal limb muscles), chronic musculoskeletal pain, or fatigue.[36] Physical examination is usually unremarkable.

3.1.2. Risk factors for Vitamin D deficiency in athletes

Intrinsic factors that place athletes at increased risks of vitamin D deficiency include young age (under 18 year-old),[37] lean body mass,[38] and darker pigmented skin.[38] Extrinsic risk factors include winter and early spring seasons, >40°N latitude, and indoor sport activities.[10] Noteworthy though, with prolonged restriction to home-training under COVID-19, outdoor sport athletes may also be at increased risk of vitamin D deficiency.

3.2. Investigation

3.2.1. Degree of vitamin D deficiency and the type of sport

In addition to the aforementioned intrinsic and extrinsic factors, significant difference in serum 25(OH)D concentration is observed between sport disciplines in the literature. Due to study heterogeneity, it was not feasible to adjust for the different sport types when investigating into athletes' vitamin D status.[8]

To fill this gap, we have done a preliminary review by including relevant studies which would contribute to a diverse pool of sport activities (Table 1). Outcome is the prevalence of vitamin D inadequacy [insufficiency (21–29 ng/mL) or deficiency (≤20 ng/mL)] in different types of sport (endurance, power, water, and jumping sport) (Table 2). This information serves as a general concept for future investigators to save time and effort when trying to answer this particular question.

To the best of our knowledge, only indoor and outdoor sport is recognised in the literature which demonstrates a statistically significant association with vitamin D status.[55] We furthered our investigation into the relationship between degree of vitamin D deficiency and type of sport base on two sets of evidence-based criteria – cardiovascular effects (endurance and power sport) and impact of weight-bearing (water and jumping sport). Cardiac-remodelling is greater in endurance sport (higher heart rate and cardiac output, lower blood pressure during exercise) than power sport. Jumping sport entails greater bone stimulation by mechanical forces than water sport.

Result in Table 2 suggests that vitamin D inadequacy is more prevalent in power sport (65.4%) than endurance sport (32.9%). Same association is found in a single study done on basketball, cross-country, soccer and track and field athletes, where track and field (power sport) athletes demonstrated a higher degree of vitamin D deficiency than cross-country (endurance sport) athletes.[33] The higher prevalence of vitamin D inadequacy in power than endurance sport athletes may be related to vitamin D utilisation and reserve in skeletal muscles.

On the other hand, the correlation between impact of weight-bearing and vitamin D inadequacy in athletes is inconclusive. Table 2 shows a higher prevalence of vitamin D inadequacy in water sport (68.5%) than jumping sport (44.4%), but Constantini et al.[56] demonstrated that vitamin D deficiency was more prevalent in dancers (94%) and basketball players (94%) than swimmers (33%), and Williams et al.[33] and Constantini et al.[56] reported the highest prevalence of vitamin D deficiency in track and field athletes, basketball players and dancers. These findings are inconsistent with our result in Table 2.

Of note, different sports have different effects on the body systems, physical and mental demands, and rates of impairing vitamin D status. Current meta-analyses can only minimize heterogeneity by stratification, adjusting for latitudes and season of serum 25(OH)D measurement. The populations being studied were also very diverse in terms of nationalities and living/training latitudes. Readers should interpret any findings with caution.

3.2.2. Timing of vitamin D measurement and the type of sport

There are two approaches to decide on the timing of serum 25(OH)D measurement in athletes. The traditional approach is to assess serum 25(OH)D concentrations with reference to seasonal

Table 1
Characteristics of included studies.

	Data Collection				Participants					
Study	Study type	Country (latitude)	Season	Serum 25(OH)D measurement	Sport Activity	Sample size	Male (%)	Age [mean (SD)] (years)	Vitamin D status[a] (n)	Vitamin D inadequacy (deficient/insufficient)[b]
Barcal et al.[39]	Cohort	USA (43°N)	Fall, winter, spring	CLIA (DiaSorin Inc., USA)	Wrestling	18	100	20.9 (2.0)	Fall (19): Deficient: 2, Insufficient: 12 Winter & spring (16): Deficient: 4, Insufficient: 11	93.8%
Bescos Garcia et al.[40]	Cohort	Spain (41°N)	Spring	CLIA (DiaSorin Inc., USA)	Basketball	21	100	25 (4.3)	Deficient: 12 Insufficient: 0	57.1%
Dubnov-Raz et al.[41]	RCT	Israel (32°N)	Winter	NR	Swimming	80	NR	NR	Deficient/ insufficient: 53	66.3%
Ducher et al.[42]	Cohort	Australia (37°S)	Winter	CLIA (DiaSorin Inc., USA)	Ballet	18	100	16 (2.8)	Deficient: 2 Insufficient: 7	50.0%
Guillaume et al.[43]	Cross-sectional	France (46°N)	NR	NR	Swimming	29	59	NR	Deficient/ insufficient: 13	44.8%
Geiker et al.[44]	Cross-sectional	Denmark (56°N)	Spring	NR	Cycling	29	100	26.5 (5.3)	Deficient/ insufficient: 3	10.3%
Josh William et al.[45]	Cohort	UK (>51°N)	Fall	CLIA	Swimming	29	NR	21.0 (3.0)	Deficient: 3 Insufficient: 16	65.5%
Kim et al.[46]	Cohort	South Korea (37°N)	NR	CLIA (Roche Diagnostics, Switzerland)	Volleyball	52	100	23.8 (2.8)	Deficient: 14 Insufficient: 24	73.1%
Lovell et al.[47]	Cross-sectional	Australia (35°S)	Spring	NR	Gymnastics	18	0	13.6 (1.2)	Deficient: 1 Insufficient: 5	33.3%
Mielgo-Ayuso et al.[48]	RCT	Spain (43°N)	Spring	HPLC TMS	Rowing	36	100	27 (6)	Deficient: 4 Insufficient: 19	63.9%
Pollock et al.[49]	Cross-sectional	UK (53°N)	Summer, winter	CLIA (DiaSorin Inc., USA)	Track and field	63	51	24.9 (4.2)	Summer: Deficient: 8, Insufficient: 7 Winter: Deficient: 8, Insufficient: 6	22.2%
Umarov et al.[50]	Case-control	Republic of Uzbekistan (41°N)	Summer, winter	ELISA (DIAsource, Belgium and LLC)	Swimming	20	0	20.3 (0.6)	Summer: Deficient: 2, Insufficient: 16 Winter: Deficient: 6, Insufficient: 14	100%
					Synchronised swimming	20	0	21.1 (1.2)	Summer: Deficient: 0, Insufficient: 20 Winter: Deficient: 4, Insufficient: 16	100%
Vitale et al.[51]	Cohort	Italy (45°N)	Spring, summer, autumn, winter	CLIA (Siemens Healthcare Italy, Italy)	Alpine skiing	152	59	24.1 (3.2)	Deficient: 45 Insufficient: 77	80.3%
Wentz et al.[52]	Cross-sectional	USA (30°N)	NR	NR	Distance running	59	0	NR	Deficient: 3 Insufficient: 8	18.6%
Willis et al.[53]	Cohort	USA (30°N)	NR	CLIA (DiaSorin Inc., USA)	Distance running	19	47	28.3 (8.4)	Deficient: 2 Insufficient: 8	52.6%
Wolman et al.[54]	Cohort	UK (52°N)	Summer, winter	CLIA (Roche Diagnostics, Switzerland)	Ballet	19	32	26 (8.9)	Summer: Deficient: 2, Insufficient: 14 Winter: Deficient: 5, Insufficient: 14	100%

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; CLIA, Chemiluminescent immunoassay; ELISA, enzyme-linked immunosorbent assay; HPLC TMS, high-performance liquid chromatography tandem mass spectrometry; NR, not reported; RCT, randomized controlled trial.
[a] Defined by serum 25-hydroxyvitamin D levels. Deficient: ≤20 ng/ml (≤50 nmol/l); insufficient: 21–29 ng/ml (52–74 nmol/l).
[b] Defined by serum 25-hydroxyvitamin D levels. Deficient: ≤20 ng/ml (≤50 nmol/l); insufficient: 21–29 ng/ml (52–74 nmol/l).

variations. Serum 25(OH)D level should be assessed at least twice yearly in any athletes screened 'at-risk' – once in the early spring for the nadir, once in the late summer for a peak level.[57] Supplementation may be tailored according to athlete's serum 25(OH)D basal level and predicted seasonal variations throughout a competitive sporting season. Another approach is to base the assessment on actual training intensity and the schedule of a competitive sporting season, which would be more specific to each

Table 2
Prevalence of vitamin D inadequacy in different types of sport.

Type of sport (biophysical effect)	Sport activity	Included studies[a]	Sample size (total)	Vitamin D inadequacy (deficient/ insufficient)[b]
Endurance (high-cardiac remodelling)	Cycling, Rowing, Distance running	Guillaume et al.,[43] Mielgo-Ayuso et al.,[48] Wentz et al.,[52] Willis et al.[53]	143	32.9%; n = 47
Power (low-cardiac remodelling)	Alpine skiing, Track and field, Wrestling	Barcal et al.,[39] Pollock et al.,[49] Vitale et al.[51]	231	65.4%; n = 151
Jumping sport (high-impact)	Basketball, Ballet, Gymnastics, Track and field, Volleyball	Bescos Garcia et al.,[40] Ducher et al.,[42] Kim et al.,[46] Lovell et al.,[47] Pollock et al.,[49] Wolman et al.[54]	191	51.3%; n = 98
Water sport (low-impact)	Swimming, Synchronised swimming	Dubnov-Raz et al.,[41] Geiker et al.,[44] Josh et al.,[45] Umarov et al.[50]	178	68.5%; n = 122

[a] For study characteristics, refer to Table 1.
[b] Defined by serum 25-hydroxyvitamin D levels. Deficient: ≤20 ng/ml (≤50 nmol/l); insufficient: 21–29 ng/ml (52–74 nmol/l).

type of sport. Evidence from the literature favours the former approach.[58–62] Specifically, Vitale et al. reported that despite the physical effort spent, vitamin D follows a classical season-associated rhythm with a peak in summer and a nadir in winter for professional skiers.[51] Nevertheless, either way provides information of paramount importance to enable a more individualized supplementation regimen for athletes.

3.3. Management

To address vitamin D deficiency in athletes, three treatment modalities exist: (1) sunlight, (2) artificial ultraviolet B radiation, or (3) supplementation. All have their potential risks and benefits. Benefits of all treatment modalities outweigh their potential risks and greatly outweigh the risk of no treatment.[63]

3.3.1. Effects of Vitamin D supplementation to athletes

Vitamin D supplementation increases the serum 25(OH)D concentration in athletes. Fairbairn et al.[64] reported a significantly increased serum 25(OH)D concentration in supplemented professional rugby players compared to placebo (32 nmol/L difference between groups at 11–12 weeks). Jung et al.[65] reported a significant increase in serum 25(OH)D concentrations in the vitamin D group (96.0 ± 3.77 nmol/L) of collegiate taekwondo athletes after 4 weeks of supplementation, but no changes in the placebo group.

Correcting low serum vitamin D levels reduces the risk of stress fractures,[66] which are common in certain sport disciplines such as basketball, baseball, athletics, rowing, soccer, aerobics, and classical ballet.[67] Very recent studies suggested that the prevalence of stress fractures decreased when athletes are supplemented daily with 800 IU 25(OH)D and 2000 mg calcium.[34] High-risk collegiate athletes also demonstrated a statistically significant decrease in stress fracture rate from 7.51% to 1.65% with vitamin D_3 supplementation.[33]

In addition, vitamin D supplementation may play an important role in the prevention of skeletal muscle injuries following exercise with eccentric muscle contraction in athletes.[68] Żebrowska et al. reported that three weeks of vitamin D supplementation had a positive effect on serum 25(OH)D levels, and caused a marked decrease in post-exercise biomarkers (troponin, myoglobin, creatine kinase and lactic dehydrogenase) levels of ultra-marathon runners.

On the other hand, Han et al.[69] and Farrokhyar et al.[70] reported in their meta-analyses that there was no significant overall effect of vitamin D_3 intervention on muscle strength, despite achieving sufficiency in 25(OH)D concentrations. Fairbairn et al.[64] found that vitamin D supplementation had little impact on professional rugby players' physical performance outcomes despite a significant improvement in vitamin D status. Of note, though vitamin D supplementation has no significant direct effect on athletic performance, potential participation time lost from musculoskeletal injuries due to vitamin D inadequacy will indirectly affect performance.

Regarding vitamin D supplementation and immunity, Jung et al.[71] concluded from their randomized controlled trial that vitamin D_3 supplementation may be effective in reducing the symptoms of upper respiratory tract infection during winter training in vitamin D insufficient taekwondo athletes. Pereira et al.[72] reported in a recent systematic review and meta-analysis, that vitamin D deficiency was not associated with a higher chance of infection by COVID-19, but there is a positive association between vitamin D deficiency and the severity of the disease. A hypothesis now under scientific consideration is that taking vitamin supplements to raise serum 25(OH)D concentrations could quickly reduce the risk and/or severity of COVID-19.[73]

The target serum 25(OH)D levels should be above 40 ng/mL for fracture prevention, while optimal musculoskeletal benefits occur at levels above the current definition of sufficiency (>30 ng/mL), with no reported sports health benefits above 50 ng/mL.[74] However, there is no optimal vitamin D supplementation regimen reported in the literature for serum 25(OH)D maintenance.[75,76]

3.3.2. Recommendations on supplementation

To the best of our knowledge, there is no evaluation of vitamin D screening and supplementation protocol among elite athletes reported in the literature. The following discussion aims to help sports medicine practitioners caring for a wide-variety of athletes make appropriate recommendations to avoid excessive, inadequate, or unnecessary supplementation.

Regarding the type of prescription, we recommend oral vitamin

D_3 (cholecalciferol), which may be more effective in restoring vitamin D levels than combined vitamin D_3/D_2 (ergocalciferol) therapy,[77] since vitamin D_3 has a superior bioavailability compared to vitamin D_2 as a result of stronger association with vitamin D binding protein.[78,79]

Regarding the dosage and timing of administration, current evidence suggests that 2000–6000 IU of supplemental vitamin D_3 can be consumed daily,[9] a continuous consumption of <2000 IU may lead to sufficiency in vitamin D concentrations during spring and summer, and maintain sufficiency throughout the wintertime.[70] However, as we believe the increased vitamin D utilisation in athletes may play a significant role in vitamin D deficiency, the administration of vitamin D supplementation to athletes who have a low basal vitamin D level would be too simplistic. The vitamin D requirements of these professionals may vary depending on the duration, intensity, type of training, and the body composition for vitamin D storage. Potentially this explains why thus far the vitamin D guidelines and guidance papers published have heterogeneous and partially opposed opinions and recommendations regarding vitamin D requirements, as the increased utilisation leading to depletion of vitamin D had not been taken into consideration. Supplementing the athletes with vitamin D when the levels are not depleted may be of limited value and may increase the risk of vitamin D toxicity. To establish the appropriate timing and dosage of vitamin D supplement, the athletes' vitamin D deficiency status should be guided by the levels after different training intensities for the identification of the 'window period' of vitamin D deficiency post-exercise.

There are a few additional considerations. First, although intense exercise may lead to a transient deficiency of vitamin D, exercise remains crucial to maintain the serum levels of vitamin D. The highest concentration of vitamin D metabolites is stored in fat, while long-term vitamin D supplementation leads to a substantial accumulation in adipose tissues; exercise stimulates lipid mobilisation from adipose tissue, potentially playing a crucial role in releasing vitamin D 'trapped' in adipocytes. This would explain why higher activity levels have been associated with higher serum vitamin D levels. Second, the lipolytic response of adipose tissue to exercise is impaired in obese subjects, which should be taken into consideration when determining the effective dose for vitamin D supplementation in them. Third, despite the increased UVB radiation from sunlight, it is recommended to supplement athletes training at altitude with up to 4000 IU/day of vitamin D, especially in winter months.[70,80] Fourth, official recommendations should not limit the responsibility of clinicians to prevent or treat vitamin D deficiency in athletes. Current recommended daily intake values were not designed for and are not effective in preventing or treating vitamin D deficiency; instead, they are guidelines to prevent particular metabolic bone diseases.[63] Finally, it is important that the clinician recognizes that vitamin D supplementation requirements are highly individualized due to their dependence on diet, endogenous synthesis, and storage.

3.3.3. Vitamin D toxicity

Theoretically, prolonged and disproportionate consumption of vitamin D supplement could induce hyperphosphatemia, hypercalcemia and hypercalciuria, which may impair organ function.[81] Nevertheless, vitamin D toxicity which presents as asymptomatic hypercalcaemia, is exceedingly rare.[82] Cranney et al. looked into twenty-two trials that assessed the adverse events associated with vitamin D supplementation: biochemical abnormalities such as hypercalcemia and hypercalciuria were most frequently reported, but the rates between vitamin D and placebo groups were not significant nor clinically relevant.[83] Of note, most trials of higher vitamin D doses did not assess long-term adverse effects, extreme vitamin D supplementation may impair organ function (calcium and phosphorus dysregulation) even in hypovitaminosis D.[82] Overall, there is fair evidence that adults tolerate vitamin D at doses above current dietary reference intake levels. From a safety perspective, the evidence supports higher doses of vitamin D supplementation to athletes.

4. Vitamin D in athletes: Future research theme

4.1. Relationship between training and vitamin D utilisation

The mechanism and exact relationship between training, vitamin D bioavailability and reserve depletion remain largely unknown. We suggest the following investigations to check on their correlation:

(1) Investigation of exercise-induced changes in vitamin D metabolites to prove an increased utilisation. We postulate that all the excreted forms will increase, especially $24,25(OH)_2D$, which is the excreted form of active vitamin D.
(2) Investigation to monitor changes in vitamin D storage in muscle and fat following prolonged physical activities to prove a depletion of storage.
(3) Comparison of vitamin D deficiency status in athletes with different training intensities.

4.2. Degree of vitamin D deficiency and the type of sport

No observational studies have been done on this association. There were large inter-study heterogeneity in the data which we included (Table 1) for our preliminary review (Table 2). We may follow-up with a cross-sectional study on our local athletes at the Hong Kong Sports Institute. We postulate that the prevalence of vitamin D deficiency will be higher in power than endurance sport.

4.3. An update on the vitamin D3 supplementation guideline

Although the current 2000 IU tolerable upper limit (TUL) may be appropriate for young children, such limits in older children, adolescents and adults have both the effects of limiting effective treatment of vitamin D deficiency and impairing dose-appropriate interventional research. To support a revision of the official guidelines, more large-scale randomized controlled trials which study into the adverse effects of long-term high-dose vitamin D3 supplementation are warranted. Current epidemiological and open trials may not be sufficient to prompt government and medical bodies into reviewing the TUL and recommended daily allowance (RDA).

5. Conclusion

Vitamin D deficiency is highly prevalent in athletes. Increased utilisation and storage depletion may be an important contributing factor for the high prevalence of vitamin D inadequacy in power sport (65.4%) compared to endurance sport (32.9%) athletes. Clinical feature of athletes at risk of vitamin D deficiency include: (1) female athletes with amenorrhea, (2) jumping sport athletes with a history of previous stress fracture, (3) indoor sport athletes who require weight-maintenance, and (4) collegiate athletes with busy schedules. Ideally, serum 25(OH)D level should be assessed at least twice yearly in any athletes screened 'at-risk' – once in the early spring for the nadir and once in the late summer for a peak level. Supplemental oral vitamin D_3 (cholecalciferol) may be tailored according to athlete's serum 25(OH)D basal levels and predicted

seasonal variation throughout a competitive sporting season. Prescription at doses higher than the official recommendations are acceptable from a safety perspective.

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