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Vitamin D and Physical Activity

Nikolaos E. Koundourakis and Andrew N. Margioris

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Abstract

Vitamin D is synthesized in the skin following exposure to ultraviolet radiation, producing cholecalciferol, while only a small percentage of the circulating vitamin D is of exogenous origin deriving from food. Following two sequential hydroxylations, in the liver and in the kidneys, vitamin D is fully activated. Although its role in bone physiology and calcium homeostasis is well documented, there is emerging evidence that vitamin D exerts a plethora of additional effects on most tissues regulating the musculoskeletal, cardiovascular, and immune systems as well as energy homeostasis. Its deficiency/insufficiency poses a major public health problem observed in all age groups and regardless of latitude and insolation. In muscles, vitamin D deficiency is associated with a decline in neuromuscular function including muscular strength, walking speed, balance, jumping and sprinting performance, and aerobic capacity, although the evidence is still weak regarding its effects in the young and the athletes. Supplementation counteracts the negative effects of vitamin D deficiency on performance although in individuals with adequate levels of vitamin D, additional supplementation does not appear to enhance further physical capabilities. The aim of this chapter is to review our current understanding of diverse effects of vitamin D in physical performance in athletic and nonathletic populations.

Keywords: vitamin D, Physical activity, athletes, musculoskeletal system, cardiovascular system, immune system

1. Introduction

Vitamin D is synthesized in the skin from 7-dehydrocholesterol following exposure to ultraviolet radiation (cholecalciferol or D3), and only a small percentage is exogenous originating from food (ergocalciferol, D2) [1–3]. Following to sequential hydroxylations in the liver and the kidneys, vitamin D is activated (**Figure 1**). Vitamin D plays a crucial role in calcium
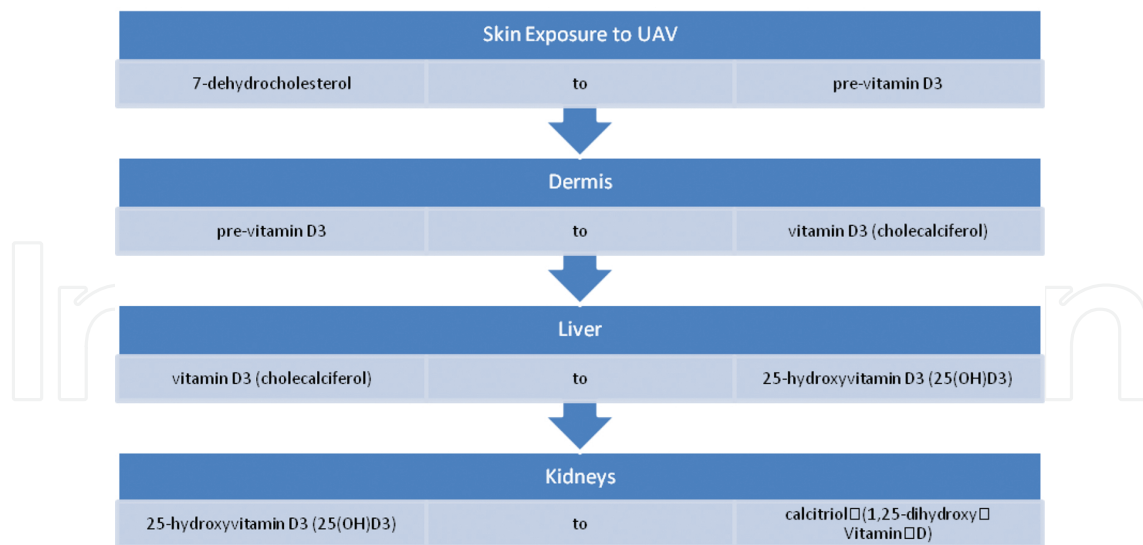
Skin Exposure to UAV		
7-dehydrocholesterol	to	pre-vitamin D3

Dermis		
pre-vitamin D3	to	vitamin D3 (cholecalciferol)

Liver		
vitamin D3 (cholecalciferol)	to	25-hydroxyvitamin D3 (25(OH)D3)

Kidneys		
25-hydroxyvitamin D3 (25(OH)D3)	to	calcitriol (1,25-dihydroxy Vitamin D)

Figure 1 Biochemical pathways of vitamin D production after exposure to UVB.

homeostasis in addition to its multiple effects in a plethora of tissues [3]. Indeed, vitamin D receptors (VDRs) are present in most tissues affecting the transcription of many genes [4–7]. Vitamin D is transported in the blood via vitamin D-binding protein [8, 9]. Vitamin D plays a role in the mineralization of type I collagen matrix in the skeleton [10]. Vitamin D and its nuclear receptor affect the expression of more than one thousand genes acting as a transcription factor [11]. Non-genomic effects of vitamin D have also been described [12–19].

2. Vitamin D deficiency

A surprisingly high prevalence of vitamin D insufficiency has been recently reported worldwide (**Table 1**) regardless of their insolation [20–23]. In Canada, 30–50 % of children and adults are vitamin D deficient and need vitamin D supplementation [24]. Similar data have been reported in Africa, Australia, Brazil, Middle East, Mongolia, and New Zealand documenting a high risk for vitamin D deficiency in adults and children [24–26]. Cross-sectional studies of vitamin D status in adolescents have found deficiency in 17–47 % with an increased risk in black and Hispanic teenagers [24–26]. It should be noted here that there are fewer reports regarding the prevalence of vitamin D in athletes. A high prevalence of vitamin D deficiency has been documented in athletes in both outdoor and indoor sports. For instance, it has been reported that more than 42 % of distance runners in Baton Rouge, Louisiana, were vitamin D insufficient or deficient [21]. Indeed, athletes may be more vulnerable to vitamin D deficiency than age-matched non-athletes even in regions with insolation. A recent meta-analysis pooling 23 studies composed of 2313 athletes found that 56 % of athletes had inadequate vitamin D [23]. In addition, a sizeable number of athletes do not meet the US dietary reference intake for vitamin D in addition to their inadequate endogenous synthesis when they train indoors [27]. In a recent study, Morton et al. [26] examined the prevalence of seasonal variation in vitamin D levels in 20 FA Premier League soccer players residing at a latitude of 53°N. Serum 25-

hydroxyvitamin D (25(OH)D) levels decreased in winter to insufficient levels in 65 % of the soccer players (<50 nmol/L). Koundourakis et al. [28] showed that professional Greek soccer players' training at a latitude of 35.9°N had insufficient vitamin D levels, while nearly identical levels were reported in American national football league players [29], in elite gymnasts in Australia [30], and in young Hawaiian skateboarders [31] and a variety of other athletes worldwide [32–35]. These findings were observed irrespective of sun exposure. In a recent study conducted in Israel in a favorable latitude (31.8°N) for insolation, 73 % of the athletes were vitamin D deficient. In Qatar, 84 % of soccer players were vitamin D insufficient. Furthermore, vitamin D deficiency in regions of high sunlight (high insolation) may be due to clothing, air pollution, and failure to meet the dietary reference intake for vitamin D in addition to their inadequate endogenous synthesis when they train indoors. Indeed, high prevalence of low vitamin D levels has been reported in the general population in the United Arab Emirates, India, and Egypt [36, 37].

Study	Population	Indoor/ outdoor	Season	Country, latitude	Vitamin D levels
Lovell [30]	18 female gymnasts, age = 13.6 ± 1.2 y	Indoor	Spring	Australia, 35.27°S	Insufficient 83.33 %, deficient 33.33 %
Constantini et al. [35]	98 Israeli male and female athletes and dancers, age = 14.7 ± 3.0 y	Outdoor/ indoor	Winter	Israel, 31°N	Insufficient 73 %, insufficiency was higher in dancers (94 %), basketball players (94 %), Tae Kwon Do fighters (67 %), athletes from indoor sports
Kopeć et al. [32]	24 Caucasian male Polish professional soccer players 26.24±3.41 y	Outdoor	Summer Winter	Poland, 51.10°N Cyprus, 30.11°N	Insufficient 37.5 %, deficient 12.5 % Insufficient 45.8 %, deficient 37.5 %
Morton et al. [26]	20 FA Premier League soccer players	Outdoor/ indoor	Winter	United Kingdom, 53°N	Insufficient 65 %
Galan et al. [40]	28 male soccer players, 26.7 ± 3.6 y	Outdoor/ indoor	Winter	Spain, 37°N	Deficient 64 %
Koundourakis et al. [28]	67 Caucasian male professional soccer players, age = 25.6 ± 6.2 y	Outdoor	Spring	Greece, 35.9° N	Insufficient 55.22 %
Halliday et al. [34]	93 male athletes (football, handball, shooting, squash, cycling, body building, martial arts), age = 21.3 ± 6.5 y	Outdoor/ indoor	Spring, summer	Middle East 29°N	Insufficient 91.39 %, deficient 8.60 %
Willis et al. [33]	19 male and female endurance-trained runners, age = 28.3 ± 3.4 y	Outdoor	N/A	United States, 30°N	Insufficient 42.10 %, deficient 10.52 %
Close et al. [211]	61 male athletes of soccer, rugby, jockeys, age = 24.3 ± 4.8 y	Outdoor/ indoor	Winter	United Kingdom, 50°N	Deficient 62 %
Close et al. [214]	30 male soccer and rugby athletes, age = 21.3 ± 1.3 y	Outdoor/ indoor	Winter	United Kingdom, 53°N	Deficient 57 %

Insufficient: vitamin D levels <30 ng/ml [75 nmol/L]; deficient: vitamin D levels < 20 ng/ml [50 nmol/L]; y = years.

Table 1. Vitamin D levels in various athletic populations.

Generally speaking, vitamin D insufficiency is defined (**Table 2**) as levels <30 ng/ml (80 nmol/L), whereas levels below 20 (50 nmol/L) and 10 ng/mL (25 nmol/L) represent deficiency and severe deficiency, respectively [7]. Levels between 40 and 60 ng/mL are the preferred range, while vitamin D intoxication usually does not occur until 25(OH)D3 reaches levels higher that 150 ng/ml [24].

Status	25-hydroxyvitamin D (ng/ml)	25-hydroxyvitamin D (nmol/L)
Severe deficiency	<10	<25
Deficiency	<20	<50
Insufficiency	20–30	50–75
Sufficiency	>30	>75
Toxicity	>150	>375

Table 2. Classification of vitamin D (25-hydroxyvitamin D) levels.

3. Seasonal variation of vitamin D levels

Seasonal variation of vitamin D is a well-documented phenomenon [38]. In the winter months, endogenous vitamin D production is drastically reduced, as a result of reduced exposure to UVB radiation, while in summer exposure to UVB radiation is adequate for vitamin D synthesis by the skin [5]. Similar variations have been reported for athletes. In soccer players, the levels of 25(OH)D3 are normal in 50 % of the athletes, while this number drops to 16.7 % in winter [32]. A study performed in a high latitude (Laramie, WY 41.3°N) revealed vitamin D insufficiency of 63 % in winter compared to only 12 % in autumn and 20 % in spring in both indoor and outdoor athletes [38]. Similar findings were reported in a study conducted at higher latitudes (Ellensburg, WA 46.9°N), using exclusively outdoor athletes. The authors reported that a percentage of 25–30 % of the athletes were vitamin D insufficient from fall to winter [39]. Morton et al. [26] also reported a significant drop of serum levels of 25(OH)D3 in a group of professional soccer players of the English Premier League at the latitude of 53°N between summer and winter. In agreement with these data were findings in professional soccer players in Spain that have been training at a latitude of 37°N showing a statistically significant reduction in serum levels of 25(OH)D3 between October and February [40].

Seasonal variation of athletic performance has been found to parallel that of the seasonal fluctuation of vitamin D levels. Indeed, athletic performance peaks when vitamin D levels are the highest, i.e., during summer [41]. Koch and Raschka [42] reviewed the German literature on the seasonality of physical performance. They reported that early studies indicated that strength and maximal oxygen uptake peaks (VO_{2max}) in late summer. Comparable findings have been reported by Erikssen and Rodahl [43]. More specifically, in a population of 1835 Norwegian men, physical performance exhibited seasonal variability peaking in summer. Similar data were reported for the Swedish national track and field teams where VO_{2max} was observed in summer [44].

Most authors explain the enhanced athletic performance in summer to the higher vitamin D levels. However, other authors disagree [41]. According to Moran et al. [26], the higher physical performance in summer is a consequence of outdoor physical activity in the warmer weather which also results in exposure of athletes to UAV, i.e., these authors see the two phenomena as parallel but independent. Athletes participating in athletic events such as track and field competitions have to be in their best conditioning in the summer since most major competitions take place at this time period. As a consequence, enhanced training and competition in summer would result in both better athletic performance and higher vitamin D levels [1, 45]. In contrast, participants in other sports such as soccer, American football, or basketball attain their best performance in winter while in summer recuperate resulting in a reduction and/or cessation of their training and to a deterioration of exercise performance and capacity [28]. Nevertheless, even when controlling for seasonal fluctuations in time spent exercising, variation in wrist flexor strength and muscle trainability still correlated with seasonal variations of vitamin 25(OH)D levels [41].

4. Effects of vitamin D in calcium absorption and bone physiology

Vitamin D plays an essential role in calcium homeostasis and the mineralization of bones [46, 47]. In the small intestine, vitamin D augments calcium uptake via an energy-dependent transcellular pathway and by a passive paracellular pathway through tight junctions [24, 48].

Insufficient levels of circulating vitamin D cause an increase of serum parathyroid hormone (PTH) due to secondary hyperparathyroidism, i.e., in a desperate effort of the body to keep circulating levels of calcium normal borrowing them from bones via an increase of bone turnover and increased bone resorption [26]. In chronic vitamin D-deficient states, individuals are susceptible to osteopenia, osteoporosis, and increased incidence of bone fractures [49, 50]. Administration of vitamin D is recommended as a first-line strategy reducing the incidence of osteoporotic fractures [51]. Indeed, low 25(OH)D levels in women could be viewed as a general marker of impaired health as the Malmö study has documented correlating with increased overall mortality [52].

Furthermore, low serum vitamin D is associated with cortical bone porosity indicative of increased bone fragility [53]. Vitamin D also enhances the activity of insulin-like growth factor 1 (IGF-1) via an induction the expression of its receptor, an affect crucial in bone formation both in vitro and in vivo [54].

4.1. Implications of these data on physical activity and exercise performance

Low vitamin D levels are related with osteoporosis and the risk of fractures in elderly individuals. Data from cross-sectional and longitudinal studies report that vitamin D insufficiency impairs bone health [4, 7]. As a result of this deterioration in bone health, the increased incident of falls in the elderly can easily result to bone fractures. However, recent evidence indicates that this is also evident in young physically active individuals. A study on Finish military recruits reported that those with insufficient vitamin D levels (<30 ng/mL) were susceptible

with a significant risk of developing stress fracture [55]. Similar findings have been reported in a number of other studies [56] including athletes [57, 58]. Deterioration in bone strength could be a problem apart from non-athletes, also in athletic populations. Hypothetically, athletes with low bone mineral density are predisposed to skeletal injury especially in contact individual and/or team sports [4, 7]. The latter could have several implications for the athletic performance especially in professional athletes. Notably the association between the incident of fractures and low vitamin D levels in athletes has not yet been determined, and there are also a number of studies in nonathletic populations that failed to support the hypothesis that high adequate vitamin D levels protect against stress fractures [4].

5. Effects of vitamin D on the skeletal muscle

The potential association between vitamin D and muscle function was also based on early clinical descriptions that myopathy was strongly associated with severe vitamin D deficiency [59]. Currently, vitamin D has been shown to be a potent modulator of skeletal muscle physiology [5]. Although the expression of the vitamin D receptors in the skeletal muscle tissue was questioned [60], recent data strongly indicate that they are also expressed in the skeletal muscle [61]. As we mentioned earlier, $1,25(OH)_2D$ by binding to its nuclear receptor augments the transcription of key muscular proteins [5–7]. It should be noted here that both genomic and non-genomic effects of vitamin D are crucial for muscular performance. Indeed, vitamin D affects muscular calcium and phosphate transport across cell membranes, phospholipid metabolism, and muscle cell proliferation and differentiation [62]. In addition, vitamin D downregulates the expression of myostatin (a negative regulator of muscle mass) and upregulates the expression of follistatin and insulin-like growth factor 2 (IGF-2) [5–7, 63]. Exposure of skeletal muscles to 1,25-dihydroxyvitamin D3 induces the expression of several myogenic markers and transcription factors [63]. A 10-day incubation of muscle cells with 1,25-dihydroxyvitamin D3 induces myosin heavy chain (MHC) type II, a late myogenic marker, while the mean diameter and width of muscular fibers increase compared to parallel controls. Indeed, vitamin D increases the size of MHC type II-positive myotubes [61, 64] and the cross-sectional area (CSA) of skeletal muscle fibers [65]. Vitamin D signaling has been also reported to alter the expression of C2C12 myotube size [5, 61], indicating a direct positive effect on the contractile filaments and thus muscle strength. In addition, it affects the diameter and number of type II muscle fibers [5–7] and in particular type IIa fibers [61]. In severe vitamin D deficiency, a proximal myopathy is observed characterized by type II (fast twitch) muscle fiber atrophy [5, 61]. A recent vitamin D supplementation study showed that in young male populations, a significant increase in the percentage of type IIa fibers was evident in the vitamin D group compared to the placebo group, demonstrating a positive effect on the muscle fiber type morphology, calcium transport, and regulation of intracellular calcium [61].

5.1. Implications of these data on physical activity and exercise performance

The data presented above suggest that vitamin D exerts beneficial effects on skeletal muscles and thus may improve physical performance capacity in both physically nonathletic individ-

uals and athletes. The documented vitamin D-mediated induction of muscle protein synthesis and myogenesis could result in muscles of higher quality and quantity. This could be in turn translated into increased muscle strength since it is well documented that there is a strong linear associations between muscle mass and strength [66]. In addition the association between vitamin D levels and muscle anabolism could also be related with another positive effect, which is particularly important for athletic populations in that it could accelerate muscle recovery from the stress of intense exercise [26]. This hypothetically could be of major importance in periods of continues competitions since it could enable them to maintain their performance capacity at a better level. In the elderly on the other hand, low vitamin D levels could cause a reduced muscular anabolism, sarcopenia, and thus negatively altered muscle mass which in turn leads to a negative effects in the sense of balance, strength, and stability. In addition, in vitamin D-insufficient states, active individuals may not have adequate energy provisions to sustain a moderate- to high-intensity muscular effort. Lastly, hypertrophy of type II muscle fibers could result in enhanced neuromuscular performance [4, 66]. These types of fibers are a major determinant of the explosive type of human movements resulting in high-power output. It is well documented that type II muscle fibers display a markedly faster muscle contraction velocity and thus higher force than type I muscle fibers [67]. Therefore the anaerobic maximal-intensity short-burst activities, such as jumping, sprinting, acceleration, deceleration, and change of direction, which are of crucial importance for the majority of the athletic events, are highly related with the type II muscle fibers. Interestingly, apart from athletes the importance of type II muscle fibers is highlighted also on the elderly. Reversal of type II fiber atrophy as a result of vitamin D supplementation is thought to account for approximately 20 % lower risk of falling [68]. Vitamin D deficiency apart from the atrophy of type II fibers in these individuals enables fat infiltration and consequently fibrosis (fibrosis is observed in different tissues including the muscle due to excess fat accumulation) which are important factors underpinning muscle quality and also may be a predictor of muscle function in older adult [69]. In closing, based on the available literature, we propose that vitamin D is beneficial for individuals since it increases muscle protein synthesis, adenosine triphosphate (ATP) concentration, strength, jump height, jumping and sprinting velocity and power, and aerobic and anaerobic exercise capacity. Physical performance could be significantly enhanced and/or preserved with adequate vitamin D. Vitamin D also prevents muscular degeneration and reverses myalgia [68, 70].

6. Effects of vitamin D on the cardiovascular system

Vitamin D receptors are expressed in human myocardium as well as in vascular smooth muscles and the endothelium [5, 6]. The activated form of vitamin D, i.e., 1,25(OH)2D, participates in the structural remodeling of cardiac muscles and vascular tissues [71] and results in improvements in flow-mediated dilation and blood pressure [72]. Improved cardiac muscle function has been reported in patients with severe vitamin D deficiency following treatment [71]. In addition, animal studies have demonstrated that $1,25(OH)_2D$ directly alters

myocyte contractility with accelerated relaxation, which is crucial in the normal cardiac diastolic function [6]. Vitamin D has been also found to regulate the function of calcium channels in cardiac myocytes, providing a rapid influx of calcium into cells promoting myocyte contractility [73]. Data from both animal and human studies show that vitamin D can act as a negative regulator of the renin-angiotensin-aldosterone system (RAAS) [6]. It is well documented that the RAAS maintains vascular resistance since it is a strong vasoconstrictor agent, due to angiotensin II synthesis, blood pressure, electrolyte, and intravascular fluid volume homeostasis. Vitamin D has the ability to decrease RAA activity by suppressing renin gene expression resulting to the downregulation of the RAA system [6, 45]. This is a vital mechanism that is regulated by vitamin D since it has been observed that the elevation in renin synthesis is highly related with left ventricular hypertrophy and the development of hypertension [45]. Another mechanism via which vitamin D insufficiency may induce left ventricular hypertrophy is by affecting and in particular elevating PTH levels. Observational studies have suggested that apart from hypertension, elevated PHT levels also result to left ventricular hypertrophy [74]. Vitamin D insufficiency has been found to be related with increased arterial stiffness and endothelial dysfunction in the conductance and resistance blood vessels in humans [75, 76]. Vitamin D has also some antiatherogenic functions by promoting HDL transport and inhibiting cholesterol uptake by the macrophages and the formation of foam cells [77], while its deficiency stimulates systemic and vascular inflammation, enabling atherogenesis [78]. In contrast, vitamin D has been shown to suppress inflammation via several pathways, such as inhibition of prostaglandin and cyclooxygenase pathways, upregulation of anti-inflammatory cytokines, decrease of cytokine-induced expression of adhesion molecules, reduction of matrix metalloproteinase, and downregulation of the RAA [45].

The presence of vitamin D receptors in the vascular wall suggests that it plays a role in vascular physiology and pathophysiology [74]. Among individuals with peripheral arterial disease, low vitamin D status has been associated with a faster decline of functional performance [79]. Severe vitamin D deficiency results in a disrupted adaptive immune response and an inflammatory milieu, promoting vascular dysfunction, insulin resistance, and arteriosclerosis [45, 80].

In addition, recent evidences indicate that severe vitamin D deficiency is strongly associated with sudden cardiac death [81, 82]. Furthermore, Vitamin D has been found to be a useful biomarker for the prediction of mortality when obtained at admission for chest pain [83]. The mechanisms via which vitamin D exert beneficial effects on human myocardium are as follows: vitamin D inhibits the proliferation of cardiomyoblasts by promoting cell-cycle arrest and enhances the formation of cardiomyotubes without inducing apoptosis. Vitamin D also attenuates left ventricular dysfunction in animal models and humans [84]. However, a group of researchers were unable to find any association between vitamin levels and risk of cardiovascular disease [85]. It should be noted though that analyzed data from more than 13,000 adults in the Third National Health and Nutrition Examination Survey (NHANES III) found a strong association between low vitamin D levels and key cardiovascular risk factors (i.e., hypertension, diabetes, overweight, and hypertriglyceridemia, but not hypercholesterolemia) after adjustment for multiple variables [86].

6.1. Implications of these data on physical activity and exercise performance

As per the available literature presented above, vitamin D plays an important role in the cardiovascular system [75]. Vitamin D affects several aspects of vascular health, including arterial stiffness and endothelial function which are crucial components of aerobic and anaerobic exercise performance and even the ability to perform daily activities. It should be noted that there is a linear association between vascular health and arterial stiffness to endurance capacity [80]. In addition, it is well documented that the most accurate measurement of aerobic capacity, i.e., that of VO_{2max}, is regulated by cardiac output, arterial oxygen content, shunting of blood to active muscle, and extraction of oxygen by muscles. Since low serum vitamin D levels may result in pathological myocardial hypertrophy, increased blood pressure, and endothelial dysfunction [87], these converging lines of evidence could support the idea that inadequate vitamin D levels could negatively influence cardiorespiratory fitness and the ability to perform efficiently during exercise. Thus, vitamin D affects aerobic capacity and VO_{2max}, cardiac output, vascular tone, and supply of oxygen and nutrients to the exercising muscles.

7. Effects of vitamin D on the nervous system

Vitamin D affects the central and peripheral nervous systems. Vitamin D receptors are present throughout the brain including the primary motor cortex, the region coordinating movement [88–91]. Specifically, VDRs have been identified in neuronal and glial cells in several brain areas including the cortex, deep gray matter, cerebellum, brainstem nuclei, spinal cord, and the ventricular system [90]. Furthermore, the enzyme 1α-hydroxylase, the activator of vitamin D precursors, is also present in the brain [89–93]. Vitamin D levels are associated with the conductance velocity of motor neurons and neurotransmission mediated by dopamine, serotonin, acetylcholine, GABA, and the catecholamines [92, 93]. Vitamin D also affects neuronal differentiation, maturation, and growth, its levels correlating to the levels of several neurotrophic factors including nerve growth factors (NGF) and that of neurotrophins, which play crucial roles in the maintenance and growth of neurons [94, 95]. In addition, vitamin D exerts direct neuroprotective effects via the synthesis of proteins binding calcium (Ca^{2+}) ions which are important in neuronal function including transmission. Proper levels of neuronal calcium are critical since their excess may result in the formation of reactive oxygen species (ROS) which lead to neuronal damage. Indeed, vitamin D levels are inversely associated with oxidative stress which damages the brain leading to neuronal apoptosis or necrosis [96]. Vitamin D also affects neuroplasticity, a process via which neural synapses and pathways are adapted to the needs of environmental and behavioral demands adjusting the brain to noxious stimuli diseases or environmental cues [90, 97, 98]. The VDRs in glial cells play in the uptake and release of neurotransmitters, including that of GABA neurotransmission within the motor cortex [99]. GABAergic function is the principal "brake" within the brain affecting muscle relaxation via the corticospinal neurons [100].

7.1. Implications of these data on physical activity and exercise performance

The data described above suggest that vitamin D exerts major effects on several aspects of brain function. The effects of vitamin D on GABAergic tone and on serotonin and dopamine are crucial for muscular coordination and avoidance of central fatigue, a condition associated with the synaptic concentration of several neurotransmitters [101]. A high ratio of serotonin to dopamine affects exercise performance because of its effect on the general feeling of tiredness and the perceptions of effort [102].

Another mechanism via which vitamin D affects the brain and athletic performance may involve the nocireceptors or nociceptors, i.e., the sensory nerve cell that responds to noxious stimuli by sending signals to the spinal cord and brain. The nociceptors are replete in VDRs and 1α-hydroxylase [103, 104]. When these receptors transfer pain signals to the brain, an inhibitory physical response takes place [104]. The relevance of this mechanism and vitamin D and physical activity/performance is based on the recent findings in animal studies that vitamin D depletion could result in nociceptive hyperinnervation and hypersensitivity within deep muscle tissue and a loss of balance without affecting muscle strength or the cutaneous nociceptive response [103]. Based on this finding, we could speculate that nociceptive hyper-innervation and hypersensitivity within deep muscle tissue could result to a false onset of myalgia during physical activity which in vitamin D-deficient individuals could result to a reduction in performance. The beneficial effects of vitamin D-mediated effects of the nervous system on physical activity and exercise performance are further supported by the findings of Dhesi et al. [105]. Reaction times deteriorate with age [105] and play an important role in neuroprotective responses [106]. In cross-sectional work, we identified a correlation between vitamin D status and reaction times, suggesting a neuroprotective role of this vitamin [105]. However, it is still unknown whether the latter mechanisms could be attributed also to young healthy individuals or athletic population.

8. Effects of vitamin D on pulmonary function

Vitamin D affects pulmonary function and health. Vitamin D insufficiency has been associated with impaired pulmonary function, asthma, and chronic obstructive pulmonary disease (COPD) [107, 108]. It should be noted that vitamin D deficiency may harm the lungs not only via its well-known immune effects. The Third National Health and Nutrition Examination Survey (NHANES III) reported a strong positive association between serum 25(OH)D and forced expiratory volume (FEV1) and forced vital capacity (FVC). These effects of vitamin D may be mediated through surfactant, a substance maintaining alveolar structural integrity [109], lung compliance, and oxygen exchange. It should be stressed that lung compliance, FEV1, FVC, and cardiopulmonary oxygen transfer are linearly related with physical perform-ance [110]. Indeed, vitamin D induces the synthesis of alveolar surfactant and plays a critical role in epithelial-mesenchymal interactions during lung growth [111]. Vitamin D plays a role in COPD and more specifically in smooth muscle proliferation in the airways [112, 113]. Zosky et al. [114] have provided evidence supporting a direct role of vitamin D on lung growth in

vivo, while vitamin D deficiency results in lung volume deficits [115]. Finally, vitamin D insufficiency correlates with multiple indices of compromised lung function and increased airway reactivity [115].

8.1. Implication of these data on physical activity and exercise performance

The data described above provide evidence implicating vitamin D in alveolar structural integrity, lung compliance, vital capacity, cardiopulmonary oxygen transfer, airway smooth muscle proliferation, and lung remodeling. Regarding athletes, exercise performance and aerobic capacity (VO_{2max}) depend on all these lung functions [28]. Adequate VO_{2max} levels are needed in all sporting disciplines. Vitamin D appears to affect all components of VO_{2max} adequacy.

9. Effects of vitamin D on immunity

Vitamin D affects the innate and adaptive immunity via VDRs [116–118]. Vitamin D enhances monocyte/macrophage activity. Vitamin D directly activates the transcription of several antimicrobial substances including defensin β2 (DEFB) and cathelicidin [118, 119]. Human cathelicidin (hCAP18) causes destabilization of microbial membranes [120]. In college athletes vitamin D insufficiency is associated with higher frequency of illnesses including common colds, influenza, and gastroenteritis [27]. Furthermore, vitamin D affects both T and B cells [121]. Under resting conditions the expressions of VDRs are low in both T and B cells, but they are upregulated in infectious diseases, suggesting a crucial role in adaptive immunity [122–125]. Indeed, vitamin D affects B-cell function, including inhibition of memory- and plasma-cell generation and apoptosis.

It is also known for years that immune cells can activate vitamin D to $1,25(OH)_2D$ via 1α-hydroxylase, an effect resulting in several beneficial paracrine effects including modulation of T-cell function [126]. Vitamin D upregulates the expression of several antimicrobial peptides (AMP) while at the same time downregulates the expression of inflammatory cytokines including that of tumor necrosis factor α (TNFα) and interleukin (IL) 6 [126]. Low levels of vitamin D in the general population and in athletes (especially following intense exercise) result in IL6 and TNFα increase. Vitamin D ameliorates this inflammatory response.

Several studies have also documented a negative association between vitamin D levels and upper respiratory tract infections (URTIs) in young and elderly adults [127–129]. In athletes, the incidence of respiratory illnesses is higher (especially at the elite level) because of the high dements on the lungs during prolonged exercise [130]. This could lead to increased exposure to viral and bacterial pathogens from the external environment, increasing the risk of URTIs. Li and Gleeson [131] have suggested that low vitamin D levels may exaggerate the vulnerability of athletes to URTIs, while individuals with higher vitamin D levels exhibit a lower propensity to URTI [132, 133]. It has been suggested that vitamin D prevents the development of URTIs by affecting the activation of toll-like receptors (TLRs) [134]. Vitamin D interferes with the activation of TLR signaling by microbial antigens via cathelicidin and β-defensin

[134]. Cathelicidin enhances the microbicidal capability of monocytes/macrophages by increasing the oxidative burst of these phagocytic cells, an effect also depended on vitamin D [134].

9.1. Implications of these data on physical activity and exercise performance

It is reasonable to suggest that the well-documented association between optimal vitamin D levels and the well-being and the proper function of the immune system combined with the anti-inflammatory effects of this vitamin D may improve athletic performance. The observation that low vitamin D levels may result in increased pro-inflammatory cytokine levels, such as TNFα and IL6, following periods of intense exercise training may suggest that this pro-inflammatory period may be ameliorated by vitamin D [68]. This effect may accelerate the recovery phase from the stress of intense exercise. High IL6 and TNFα levels may partially explain age-related skeletal and muscular failings in vitamin D-deficient older individuals. Reduction of TNFα levels following vitamin D supplementation may be crucial to combat the "overtraining syndrome" in athletes [135]. Furthermore, the cytokines IL-10 and IL-13 have been shown to promote muscle regeneration and prevent skeletal muscle damage [136, 137]. Regarding the effects of vitamin D on the URTIs, its negative association with URTIs has been addressed by He et al. [138] who reported a higher proportion of subjects who experienced one or more URTI episodes in the vitamin D-deficient state during the 4-month study period than the optimal vitamin D group [138]. In closing, since vitamin D has been shown to affect the inflammatory response and prevent URTIs, its use may be of practical significance in the athletes.

10. Effects of vitamin D on the adipose tissue

Vitamin D plays a crucial role in the physiology of adipocytes. VDRs and the 25-hydroxyvitamin D 1α-hydroxylase (CYP27B1) genes are all expressed in human adipocytes [139]. Vitamin D levels are inversely related to obesity including body fat percentage (BFP), body mass index (BMI), and waist circumference [140, 141]. Vitamin D supplementation for 16 weeks reduces visceral fat in overweight and obese adults [142]. Drincic et al. [143] identified body weight as the single strongest predictor of 25OHD levels followed by fat mass. The loss of weight results in an elevation of vitamin D levels [144]. Epidemiologically, vitamin D levels are negatively associated with BFP in non-athletes [19, 145, 146]. Interestingly, a high BFP in winter months has been found correlating with indoor athletic activities and low vitamin D levels [146].

10.1. Implications for physical activity/exercise performance

The close association between vitamin D levels and adiposity could affect athletic performance. It should be noted that neuromuscular performance capacity including sprinting ability, jumping performance, agility, acceleration, aerobic capacity, and deceleration is inversely

associated with BFP [147]. These data suggest that high BFP in conjunction with low vitamin D levels exerts a detrimental effect on exercise performance in athletes as well as in the general population. It should be noted that increased BFP is associated with the development of a systemic chronic low-grade inflammation and insulin resistance, a characteristic of obesity, which also negatively affect exercise performance [148].

11. Effects of vitamin D on the electron transport system

Vitamin D has been also suggested to be related with the production of adenosine triphosphate (ATP) via the aerobic pathway. In particular, this speculation has been based on the observations that vitamin D appears to affect electron transport. Vitamin D receptors are present within mitochondria. Silencing of vitamin D receptors in several cell lines results in growth inhibition accompanied by an increase in mitochondrial membrane potential sensitizing cells to oxidative stress [149]. Vitamin D plays a role on mitochondrial respiratory chain activity acting as a facilitator of the diversion of acetyl-CoA from the energy-producing TCA cycle toward biosynthetic pathways that are essential for cellular proliferation. These effects of vitamin D on aerobic energy production during exercise are needless to say crucial for exercise performance.

12. Insolation and vitamin D on athletic performance

Early studies on collegiate athletes and students showed that cardiovascular fitness, muscle endurance, and speed were enhanced following exposure to ultraviolet radiation [150–152]. In particular, in 1938 Russian authors [151] reported that a course of ultraviolet irradiation improved speed in the 100 m dash in four students compared with matched controls. The authors observed that the experimental group (i.e., under UAV treatment) had a 7.4 % increase in 100 m dash times compared to only 1.7 % of the control group. Notably both groups were undergoing the same training schedule throughout the study. Supportive evidence came from a study by German researchers in 1944 [152]. A treatment under UV irradiation twice a week for a period of 6 weeks resulted in a 13 % improvement in performance on a bike ergometer. No alteration was evident in the control group. Enhanced performance parameters were also reported by Allen and Cureton [150] as a result to UAV treatment in college students. The authors observed that a period of 10 weeks under UV treatment resulted in improvements in both cardiovascular fitness and muscular endurance. UV increased cardiovascular fitness by 19.2 % compared to only 1.5 % improvement in the controls. In 1956, Sigmund [153] examined the effects of UV radiation on reaction times on adolescents and adult individuals. UV treatment improved by 17 % the reaction time compared to controls. In another study in the late 1960s, a single dose of UV irradiation beneficially affected the strength, speed, and endurance of college women [154]. Interestingly, the beneficial effect was evident in white participants but not in African American females, suggesting a different skin response to UV. A follow-up study from the same team [155] observed that the same amount of UV managed

to improve aerobic performance in the same population. Enhanced performance was also observed by another study in a 30-yard dash of 15 college women after 6-minute exposure in UV light [156].

13. Vitamin D deficiency in athletes versus non-athletes

It is increasingly apparent that athletes need higher levels of vitamin D because of the higher demands of the daily strenuous training exercise which they undergo [157]. Indeed, experimental findings suggest a major role of vitamin D in muscle mass, strength, and function. Vitamin D affects significantly the athletic ergometrics [158]. Furthermore, athletic performance appears to show a seasonal variability peaking when vitamin D levels peak and declining as they decline reaching nadir when vitamin D levels are at their lowest. It should be noted that vitamin D administration improves athletic performance in vitamin D-deficient athletes [41].

14. Vitamin D in non-athletes

Overwhelming evidence demonstrates the association between vitamin D levels and the ability of non-athletes to perform their daily physical activities and/or exercise (**Table 3**). Early on, myopathy and muscle weakness were attributed to the most obvious consequence of vitamin D deficiency, i.e., that of rickets and osteomalacia [159]. To date, several cross-sectional observations and longitudinal studies have reported a close association between vitamin D and several parameters of physical performance. The majority of the studies have been performed on elderly subjects although similar data have been reported in adults below the age of 65 years [160] and in young individuals [161, 162].

Author	Participants	Physical performance parameters tested	Results
Ward et al. [161]	99 adolescent girls, 12–14 y	Jump power, countermovement jump(CMJ) height, and velocity, Esslinger Fitness Index, force	Positive relationship between vitamin D levels and jump velocity, jump height, power, Esslinger Fitness Index, and force
Foo et al. [162]	301 healthy Chinese adolescent girls, age 15.0 ± 04 y	Handgrip strength, physical activity levels	Adequate vitamin D status had greater handgrip muscle strength than deficient
Gerdhem et al. 155	1044 elderly women, 75 y old (range 75.0–75.9 y old)	30 m gait, knee extension, knee flexion, Romberg balance, self-estimated activity level	Positive relationship between vitamin D levels and gait speed, Romberg balance

Author	Participants	Physical performance parameters tested	Results
			test, self-estimated activity level, and thigh muscle strength
Houston et al. [166]	988 elderly males and females, age 85.2 ± 3.6 y	SPPB test (standing balance, repeated chair stands, 3 m walk [gait speed]), grip and knee extensor strength	Significantly poorer SPPB in deficient individuals versus those in sufficient state. No relationship between vitamin D levels and absolute grip and knee extensor strength. Older adults with deficient 25(OH)D levels had significantly lower muscle strength indicating poorer muscle quality
Visser et al. [167]	1260 elderly males and females >65 y old	Physical activity (30, 30–59, or 60 min/day), timed walking test, and a repeated chair stand test	Vitamin D-deficient and vitamin D-insufficient individuals had poorer physical performance in all tests
Bischoff-Ferrari et al. [168]	4100 elderly males and females >60 y old	8-foot walk test and sit-to-stand test	Vitamin D levels between 40 and 94 nmol/L were associated with better musculoskeletal function in the lower extremities than concentrations of 40 nmol/L. Significant positive association between vitamin D levels and the 8-foot walk test, the sit-to-stand test
Tieland et al. [169]	127 pre-frail and frail elderly people, ≥65 y old	Short physical performance battery (SPPB) test, maximum strength (one repetition maximum)	Significant positive associations were observed between vitamin D levels and gait speed and chair rise
Houston et al. [174]	1155 elderly individuals, aged 65–102 y old	Short physical performance battery (SPPB), handgrip strength	Significant positive associations were observed between vitamin D levels and SPPB score in men and handgrip strength in men and women
Wicherts et al. [177]	1234 elderly men and women, age 79.8 ± 5.9 y	Time taken to walk 3 m, turn 180°, and walk back (walking test); time taken to rise five times from a kitchen chair with arms folded in front of the chest (chair stands); the ability to stand with the heel of the one foot directly in front of, and touching the toes of, the other foot for at least 10 s (tandem stand)	Vitamin D levels were associated with physical performance which was poorer in participants with levels < 10 ng/ml and levels of 10–20 ng/ml
Mastaglia et al. [178]	44 postmenopausal women, age 71 ± 4 y	Walking-speed test, standing balance, and sit-to-stand tests.	Women with vitamin D levels ≥ 20 ng/ml scored higher on the muscle function

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Author	Participants	Physical performance parameters tested	Results
		Lower extremity muscle strength was determined using a manual dynamometer	tests and had stronger knee extensor and hip abductor muscles
Ceglia et al. [181]	1219 males, age 4.9 ± 12.8 y	Timed walking test, chair stand test, grip strength	No association was evident between any physical performance test and vitamin D levels
Matheï et al. [182]	367 elderly males and females, age 84.7 ± 3.6 y old	Balance, grip strength, and gait speed	No significant relation between vitamin D levels and balance, gait speed and grip strength, and serum

y, years

Table 3. Vitamin D levels and physical performance in non-athletes.

In the elderly vitamin D deficiency has been associated with myopathy, reduced muscle mass and strength, low exercise performance, and an increased risk of falling [163]. The rise of vitamin D levels has been associated to improved balance [164], reduced frailty and disability [165, 166], independence [167], and better mobility [168, 169]. Improved balance and mobility independent of muscle function may partly explain the association of vitamin D with the reduced risk of falls in older adults. It is well documented that the maintenance of muscle strength and power in this population is also related with the ability to perform all types of physical activities and therefore well-being and functional performance. In the elderly, mobility limitations have been defined as the self-reported inability to walk a mile, climb stairs, or perform heavy housework [170]. This is dependent on multiple components such as muscles, bones, and the cardiovascular system, and vitamin D has been found to play a crucial role in the functionality of these tissues. The impairment in any of these tissues could lead to reduced mobility that in turn could cause accelerated functional decline and disability. Given that both muscle strength and power are related to the functional activities in older adults [161, 171], it could be argued that assessing the potential parameters that could affect muscle strength or power and even muscle quality would identify ways to avoid impaired mobility and functional performance. In addition, proper cardiovascular function is essential to perform adequately all types of activities. In this context, it could be suggested that vitamin D is involved in the regulation of strength and power (as a product of strength) and affects the proper cardiovascular function and also the quality of the muscles (fat infiltration in vitamin D-deficient state). The latter is related with vitamin D since in the deficient state, it has been reported that there is increased fat infiltration in the muscle. This physiological mechanism is associated with lower levels of muscle strength and physical performance, independent of muscle mass [172]. To date, a number of organizations recognize that vitamin D is directly related with the falls in the elderly, including the International Osteoporosis Foundation, the Endocrine Society, and the US Preventive Services Task Force [173]. In accordance are the observations of Gerdhem et al. [164]. The authors evaluated the association between 25-

hydroxyvitamin D levels (25OHD), fall-associated variables (including tests of functional performance), and fracture in ambulatory women. A low 25OHD was associated with lower physical activity, gait speed, and balance. Vitamin D levels below 20 ng/ml have been associated with an increased risk of fractures. It has been suggested that the minimum level of 25OHD required to maximize the reduction of falls and fractures appears to be in the order of 60 nmol/L. Any increases above this do not appear to have any additional beneficial effect in lowering the risk of falling [173].

Regarding physical performance per se, several cross-sectional studies indicate a positive association between physical performance and serum vitamin D in the elderly. In the In-CHIANTI study, a representative sample of 976 persons aged 65 years or older at study baseline was examined [174]. Physical performance was assessed. A significant association between low levels of vitamin D and poor physical performance as assessed by the handgrip strength test and a short physical performance battery (SPPB) test (which included ability to stand from a chair and ability to maintain balance in progressively more challenging positions) was documented. It was found that individuals with serum vitamin D levels < 25 nmol/L performed worse than those with levels above 25 nmol/L. Muscle strength using a handgrip test was also significantly greater in subjects with vitamin D levels higher than 50 nmol/L than those with lower levels [174]. The use of grip strength as a tool is relatively straightforward to stratify adults at risk of impaired mobility. It has been shown in elderly individuals that higher levels of vitamin D correlated with better lower extremity muscle performance compared to age-matched individuals with lower levels [169]. Similar data have been shown in the Rancho Bernardo Study cohort [175]. Likewise in a longitudinal survey of community-dwelling Japanese, older women showed that those with higher levels of vitamin D responded better in a 3-month exercise program than those with lower vitamin D levels [176].

Wicherts et al. [177] examined the association of serum 25-hydroxyvitamin D levels to physical performance and its decline with age. The authors reported that after adjustment for age, gender, chronic diseases, degree of urbanization, body mass index, and alcohol consumption, a relationship was evident between vitamin D levels and physical performance indices. Physical performance was inferior in individuals with low vitamin D compared to age-matched individuals with serum 25OHD levels higher than 30 ng/ml. Thus 25OHD levels below 20 ng/ml appear to be associated with poorer physical performance and a greater decline in physical performance in older men and women.

In another study on elderly females aged over 65 years, the authors examined the association between vitamin D levels and muscle function and strength. Performance was evaluated by a walking-speed test, standing balance, and a sit-to-stand test [178]. It was observed that vitamin D levels above 50 nmol/L were related with higher levels of muscle strength. The authors also reported that the individuals with the lowest 25OHD levels (i.e., below 20 nmol/L) had the poorest values in strength. Stockton et al. [179], based on the observations from their meta-analysis, concluded that vitamin D had no significant effect on lower extremity muscle strength except in individuals with starting serum 25OHD levels <25 nmol/L. In support to this suggestion are the findings of Pramyothin et al. [180]. In a study performed in older Hawaiian women of Japanese ancestry, which are known for its very low rate of falls, a high dietary intake

in vitamin D, and a large exposure to sunlight, their mean vitamin D level was 80 nmol/L, while no individuals were in a vitamin D-deficient state. The authors failed to observe any association between vitamin D levels and all the measured performance parameters, i.e., physical strength test (except for the quadriceps), falls, and daily activities. It was concluded that the absence of a relationship was due to the very high level of vitamin D that these women had at baseline. Mastaglia et al. [178] suggest that there is a limit below which vitamin D insufficiency may affect physical performance. In agreement to this hypothesis are the findings of a recent study [181]. The authors reported that in a population-based sample of adult men with a broad age range (mean age is 47 years), there was no association between serum 25(OH)D concentration and lean body mass, muscle strength, and physical function after controlling for multiple lifestyle factors. However, only 20 % of the subjects had a vitamin D level below 50 nmol/L. This observation is giving further support to the cause-effect hypotheses of "sufficient" or "insufficient" vitamin D levels on several indices on human physiology including physical function and athletic performance. However confusing findings have been reported by Matheï et al. [182] in elderly individuals (>80 years) with an 80 % prevalence of vitamin D insufficiency where no correlation was evident between vitamin D levels and physical performance, as assessed by gait speed, handgrip test, and a static balance test. The authors suggest that this absence of association could be at least partly due to age-related downregulation of the VDR in muscles [182]. On the other hand, Ward et al. [161] reported that in vitamin D-insufficient young adolescent girls, there was a correlation between vitamin D levels and muscle power, force, velocity, and jump height. Similarly, Foo et al. [162] found a positive association between vitamin D serum levels and handgrip strength in a population of 301 vitamin D-sufficient adolescent girls. However, studies in young women failed to verify any association between vitamin D status and muscle performance, handgrip strength [183], or any other physical performance parameter [184]. These discrepancies may be partially explained by differences in the experimental protocols, accuracy of vitamin D serum measurements, age of the participants, muscle fitness, health state, gender, and other variables. In summary, most published data suggest an association of vitamin D levels greater than 50 nmol/L with muscle fitness. Vitamin D-associated improvement of balance and mobility are independent variables form muscle function and may partially explain the beneficial effect of vitamin D supplementation on the rate of falls in older individuals [185].

15. Vitamin supplementation in non-athletes

Vitamin D levels in the blood are increasingly recognized as an important factor in muscular well-being and functional performance. As a consequence, it was speculated that vitamin D3 supplementation may exert beneficial effects on physical activity. Indeed, several major trials have demonstrated that vitamin D supplementation lower the risk of falling (**Table 4**). Prince et al. [186] in a randomized, controlled trial in Australia evaluated women with at least one fall in a 12-month period and with a plasma 25-hydroxyvitamin D level <24.0 ng/mL. The authors suggested that elderly with a history of falling and vitamin D insufficiency living in sunny climates benefit from ergocalciferol supplementation resulting in a 19 % reduction in

the relative risk of falling, mostly in winter. Pfeifer et al. [187] demonstrated a reduction in falls of 27–39 % in community-dwelling seniors supplemented with 800 IU vitamin D and calcium daily versus calcium alone. This drop in falls was correlated with an improvement in quadriceps strength and in the timed up and go (TUG) test. Similarly, Zhu et al. [188] reported an enhanced muscular strength and TUG test in the individuals within the lowest vitamin D quartile. These results are consistent with another study that showed a 49 % reduction of falls in elderly women from a geriatric ward supplemented with 800 IU per day of vitamin D [189]. Bischoff-Ferrari et al. [189] evaluated several studies involving men and women with an average age of 70 that vitamin D supplementation resulted in a significant 22 % decrease in fall risk.

Study	Quality	Participants	Intervention	Parameters measured	Results
Prince et al. [186]	Double-blind, randomized controlled trial	302 community-dwelling ambulant older women, aged 70–90 y old	1000 mg/day of calcium for 1 year combined with 1000 IU/day of ergocalciferol or identical	Risk of falling	Ergocalciferol supplementation resulted in a 19 % reduction in the relative risk of falling
Zhu et al. [188]	Randomized controlled trial	302 community-dwelling ambulant elderly women; mean age: 76.9 ± 4.5 y	1000 IU/day of vitamin D2 or identical placebo; calcium citrate (1 g calcium/day) in both groups for 1 y	Timed up and go (TUG) test, ankle dorsiflexion, knee flexor, knee extensor, hip abductor, hip flexor, hip extensor, and hip adductor strength were assessed	Significant ↑ in knee flexor strength and all hip muscle strength and TUG in both groups. Ankle dorsiflexion strength significantly ↓ in both groups, no change in knee extensor strength after 12 months
Bunout et al. [191]	Randomized double-blind controlled trial	96 healthy elderly subjects aged > 70 y	Participants were randomized to a resistance training or control group. Trained and control groups were further randomized to receive vitamin D 400 IU plus 800 mg of calcium per day or calcium alone for 9 months	Handgrip strength, Isometric quadriceps maximum voluntary strength, endurance, general physical fitness, measuring the timed up and go (TUG), short physical performance battery (SPPB)	Timed up and go ↑ more in trained subjects supplemented with vitamin D. At the end of the follow-up, gait speed was ↑ among subjects supplemented with vitamin D (whether trained or not)
Bischoff et al.	Randomized double-blind controlled	122 elderly women, mean age = 85.15 ±	Calcium 1200 mg and 800 IU/day vitamin D	TUG test, grip a strength, knee flexor strength, knee	↓Risk of falls and in 62 women with complete for all strength test,

Study	Quality	Participants	Intervention	Parameters measured	Results
[192]	trial	6.8 y	versus calcium 1200 mg/day for 12 weeks	extensor strength, risk of falls	there was significant ↑ in all measured parameters
Moreira-Pfrimer et al. [193]	Randomized double-blind controlled trial	46 individuals (11 males and 35 females), age = 77.6 8 ± 8.2 y	6-month period: daily calcium + monthly placebo or daily calcium + oral cholecalciferol (150,000 IU once/month the first 2 months, 90,000 IU once/month until the end)	Maximum isometric strength of hip flexors (SHF) and knee extensors (SKE)	SHF ↑ in the calcium/vitamin D group by 16.4 % and SKE ↑ by 24.6 %
Pfeifer et al. [194]	Randomized double-blind controlled trial	242 community-dwelling elderly women and men, mean age 77 ± 4 y	1000 mg of Ca or 1000 mg of Ca plus 800 IU of vitamin D per day for 12 months, followed by an 8-month treatment-free observation period	Timed up and go (TUG) test, maximum isometric leg extensor strength	Vitamin D resulted in a significant ↓ falls of 27 % at month 12 and 39 % at month 20 and in significant ↑ and ↓in quadriceps strength and time to perform the TUG test, respectively
Janssen et al. [196]	Randomized double-blind placebo-controlled trial	70 female geriatric patients >65 y old	400 IU/day of cholecalciferol + 500 mg/day of Ca or a placebo +500 mg/day of Ca for 6 months	Handgrip strength, leg extension power, get up and go (GUT) test, modified Cooper test	No significant improvements in strength and physical activity measures
Brunner et al. [197]	Randomized, double-blind, placebo-controlled trial	33,067 women aged 50–79 y old	1000 mg calcium carbonate plus 400 IU vitamin D-3 or matching placebo in a regimen of two pills per day	Grip strength, chair stand test, timed walk test, physical activity status, physical function (self-report), physical activity (self-report)	No evidence of treatment effects on measures of any kind of physical functioning, activity, and strength were observed
Gupta et al. [200]	Randomized, double-blind, placebo-controlled trial	40 healthy males and females, age 31.5 ± 5.0 y	60,000 IU of vitamin D3/w for 8 weeks followed by 60,000 IU/m for 4 months with 1 g of Ca daily or dual placebos for 6 months	Handgrip and gastro-soleus dynamometry, pinch-grip strength, respiratory pressures, 6 min walk test	All measured physical performance parameters ↑ significantly in the treatment group

Study	Quality	Participants	Intervention	Parameters measured	Results
Owens et al. [201]	Placebo-controlled trial	29 male participants, mean age = 22.7 ± 3 y	Oral dose of 10,000 IU/day vitamin D3 or a visually identical placebo for 3 months	Lower limb muscle function, isokinetic torque, percutaneous isometric electromyostimulation	No significant changes in any of the measured performance indices

y, years; ↑, increase; ↓, decrease

Table 4. Vitamin supplementation in nonathletic population.

Recent studies on elderly populations support the data regarding the beneficial effect of vitamin D supplementation on neuromuscular performance improving strength [9] and force production [190]. Furthermore, a significant linear association between vitamin D levels and muscular strength, body sway, and physical performance is evident [106, 191, 192]. In addition, Moreira-Pfrimer et al. [193] reported that vitamin D supplementation results in improved isometric muscle strength following a 6-month supplementation of daily cholecalciferol resulting in an increase of strength of hip flexors (SHF) and strength of knee extensors (SKE).

In addition to the strength of lower extremities, upper extremity strength also benefits from vitamin D supplementation. However, regarding grip strength, a tool that is relatively straightforward to stratify adults at risk of impaired mobility, the results are confusing. In a recent review of the literature, it was reported that grip strength does not seem to respond to vitamin D supplementation in males [194]. The failure to observe any association between grip strength in the male population is in agreement with others. Effects of vitamin D treatment on handgrip strength have been evaluated in several studies, none of them showing significant effects in contrast to women [191, 194–197]. This could be related with the gender of the participants in the studies. A recent research suggests that there are gender differences in the vitamin D that affect functional performance [198].

In an attempt to examine the effects of vitamin D supplementation concomitantly with resistance training, Agergaard et al. [61] performed a study in young and elderly untrained males. The participants of this study were randomized to a daily supplementation of vitamin D plus calcium or just calcium for a period of 16 weeks. The study took place during a period and at latitude of low sunlight (December–April, 56°N). All individuals followed a progressive resistance training program of the quadriceps muscle during the last 12 weeks of the study. Measurements of muscle hypertrophy (defined as changes in CSA) and quadriceps isometric strength levels were performed. Muscle biopsies were analyzed for fiber type morphology, expression of VDR, and Myostatin [61]. The authors failed to observe any difference between the groups in quadriceps CSA and isometric strength despite the observed increase in strength that was evident in both groups compared to baseline. Vitamin D intake and strength training increased both strength and CSA in elderly individuals compared to the young group. In the young vitamin D group, the authors observed that the experimental period resulted in an increase in fiber type IIa percentage and a lower Myostatin mRNA expression compared to the control group. No additive effect of vitamin D intake during 12 weeks of resistance training

could be detected on either whole muscle hypertrophy or muscle strength. The authors attributed this lack of response to vitamin D supplementation to the fact that the participants in their study were vitamin D sufficient, compared to the findings of studies that have observed enhanced performance to vitamin D supplementation that have employed individuals in a deficient state [191–193, 196, 199, 200]. They suggest that the muscular performance benefits may be relevant only for individuals with vitamin D deficiency. However, a recent study using insufficient young males failed to report improvements to performance via vitamin D treatment [201]. The authors observed that despite the elevation in vitamin D levels (>120 nmol/L), no effect was observed in performance parameters (muscle strength evaluated by isokinetic dynamometry and percutaneous isometric electromyostimulation). The latter study suggests that other parameters apart from vitamin D levels are responsible for the effect on performance such as age, type of vitamin D that was given, period of supplementation, and amount of supplementation.

A recent review of the literature which included controlled and randomized controlled trials that have measured muscle strength and serum vitamin concentration in 18–40-year-old participants reported that the outcome of the available evidence is that vitamin D supplementation increases upper and lower limb strength in young and healthy individuals [200, 200, 202]. However, this increase seems to be dependent on the supplementation treatment employed. According to Tomlinson et al. [202], studies that have reported individual significant increases in muscle strength employed a total dosage of between 60,000 and 14,000 IU vitamin D/week over 6–4 months. Another study prescribed a daily dose of 2000 IU vitamin D as per previously published systematic reviews which suggested that daily dosages are more beneficial than larger, staggered doses. However, adding to the contradiction, Gupta et al. [200], who also reported significant results, used a large, weekly dose of vitamin D, 60,000 IU D3/week for the first 8 weeks followed by 60,000 IU/month for 4 months. The findings of these studies contradict previous evidence that suggested larger weekly, monthly, or one-off doses of vitamin D are not as effective in producing an improvement in muscular strength. According to Tomlinson et al. [202], the inconsistencies in the literature are partly the result of different dosages of vitamin D and different treatment regimens.

16. Vitamin D levels, Athletes, and exercise performance

The first evidence regarding the possible association between vitamin D and performance comes from early studies [41]. It have been reported that cardiovascular fitness, muscle endurance, and speed were enhanced after exposure to ultraviolet radiation [41].

To date there is a growing number of evidence (**Table 5**) to support the association between this secosteroid and exercise performance indices in athletic and physically active populations. A recent study from our laboratory [28] reported a linear relationship between vitamin D levels and muscle strength as evaluated by squat jump (SJ) and countermovement jump (CMJ), sprinting ability (10 m and 20 m), and VO_{2max} in non-supplemented professional soccer players. Our results are comparable with others showing that vitamin D levels are related with

neuromuscular performance capacity and aerobic endurance in young physically active individuals and athletes [202–205]. However, these findings are not universal. Others have failed to find an association between exercise performance and vitamin D levels [206]. Vitamin D status was not associated with grip strength or swimming performance in adolescent swimmers [207] nor with isokinetic peak torque during knee flexion and extension after adjusting for total body mass and lean mass in Qatar soccer players [208]. Hamilton et al. [208] reported that vitamin D levels were not related with lower limb isokinetic muscle function in soccer players. According to the authors, the lack of an association was most probably a result of the different modes of exercise used in their study. They hypothesized that vitamin D could preferentially affect muscle groups that were not evaluated in the study. In this study, soccer players with vitamin D levels <50 nmol/L exhibited significantly lower torque in hamstring and quadriceps muscle groups, suggesting that low vitamin D levels are associated with impaired muscular function during exercise. However, no association was observed between performance and vitamin D levels in hockey players [206]. Indeed, low explosive strength during jumping was not associated with vitamin D levels neither status nor power production during the Wingate anaerobic test [206].

Study	No. of participants	Sport	Study location/period	Parameters measured	Results
Koundourakis et al. [28]	67 male professional players, age 25.6 ± 6.2 y	Soccer	6-week off-season transition period, June–July, 35.9°N latitude	Squat jump (SJ), countermovement jump (CMJ), 10m sprint, 20 m sprint, maximal oxygen consumption (VO_{2max})	Significant associations between vitamin D levels and all the measured performance indices
Fitzgerald et al. [206]	53 junior and collegiate male ice hockey players, age 20.1 ± 1.5 y	Hockey	Off-season period, 44.9°N latitude	Grip strength, Wingate anaerobic test, squat jump (SJ)	Significant associations between vitamin D levels and grip strength, time to half peak force but not Wingate test and SJ
Forney et al. [205]	39 males and females, physically active individuals, age 23.26 ± 0.7 y	Various types of physical activity	July and September, 30.46°N latitude	Maximal oxygen consumption (VO_{2max}), Wingate test, vertical and horizontal jump, sit and reach test, maximum muscle strength of bench press, leg curl, leg extension, upright row, bicep curl, triceps pushdown	Significant positive associations between vitamin D levels and VO_{2max}, but not for any measures of strength and power
Dubnov-Raz et al. [207]	80 competitive adolescent swimmers from both sexes, age 14 ± 1.6 y	Swimming	Israel, located between latitudes 32.40°N and 31.55°N	Grip strength, balance, and swimming performance at several speeds	No significant associations between vitamin D levels and any measures of performance

y, years

Table 5. Vitamin D levels and athletes.

Regarding VO_{2max} and aerobic capacity, evidence from large epidemiologic cross-sectional investigations indicate that 25(OH)D concentration is associated with cardiovascular fitness. Mowry et al. [204] found a positive correlation between baseline cardiorespiratory fitness VO_{2max} and serum 25(OH)D levels in 16- to 24-year-old healthy women. Similarly, Ardestani et al. [209] reported that there was evident a strong association between 25(OH)D levels and VO_{2max} in men and women (20–73 years old) over a broad range of 25(OH)D levels (10–82 ng/mL). Interestingly, this correlation was also evident in subjects with low levels of physical activity after adjusting for age, gender, BMI, and moderate to vigorous physical activity. Early studies have shown that exposed to sun athletes showed improved aerobic fitness compared to controls [28]. A recent study in professional soccer players reported that VO_{2max} was significantly related to vitamin D status [28]. Similar findings were reported in young physically active individuals [205]. The authors also reported that the individuals who had 25OHD levels above the recommended limit of 35 ng/mL, which was used as a cut-off value indicating vitamin D sufficiently in their study, were found to have significantly higher VO_{2max} values (20 %) than individuals below this cut-off point. On the contrary, it was reported that vitamin D status was not associated with neither the VO_{2peak}, as a measure of cardiorespiratory fitness, nor the end stage completed during a skating treadmill GXT in junior and collegiate male hockey players [206]. The authors suggested that these findings could be the result of the fact that none of their players were vitamin D deficient. According to Wilson et al. [210], worsening in aerobic capacity could result only as in vitamin D-deficient individuals. In the study by Fitzgerald et al. [206], the authors reported that although 37.7 % of their athletes had insufficient 25(OH)D levels, levels at the deficiency range are necessary for a compromise of cardiovascular fitness to ensue.

17. Vitamin D supplementation and athletes

Few published studies have reported that vitamin D supplementation benefits neuromuscular and aerobic performance capacity (**Table 6**). Indeed, a randomized placebo-controlled study examined the effects of vitamin D3 supplementation (5000 IU per day) for 8 weeks on musculoskeletal performance [211] in highly trained male professional soccer players. Approximately 62 % of the athletes on supplementation and 73 % of the controls exhibited serum total 25(OH)D < prior to treatment at 50 nmol/L. Vitamin D supplementation increased serum total 25(OH)D from a mean baseline of 29–103 nmol/L, whereas the placebo group showed no significant change. The authors found that vitamin D supplementation increased 10 m sprint time and vertical jump compared to the placebo group. Similar data were found in another study where athletes living at northerly latitudes (the United Kingdom = 53°N) had low vitamin D levels (<50 nmol/L). Additionally these data suggest that inadequate vitamin D levels are detrimental to musculoskeletal performance in athletes, while supplementation may increase both sprinting capacity and jumping ability of the soccer players. In support to these findings, Wyon et al. [212] reported enhanced neuromuscular performance in a different type of athletic population, i.e., in elite classical ballet dancers in a study which employed a 4-month oral supplementation of vitamin D3. Isometric muscular strength and vertical jump height

were measured pre- and post intervention. A significant increase of isometric strength (18.7 %) and vertical jump (7.1 %) was observed. The intervention group also sustained significantly less injuries than the controls during the study period. In agreement with these data are the findings of another study from the same group [213]. The authors examined the acute effects of vitamin D supplementation on muscle function using isokinetic dynamometry. White adult male national-level judoka athletes who were involved in full-time training participated in the study and were randomly allocated to the treatment (150,000 IU vitamin D3) or placebo and given blinded supplements by an independent researcher. Participants were tested twice, 8 days apart, on a Monday morning before the start of judo training and after 2 days of rest. A 5–7 mL of blood sample was collected followed by isokinetic concentric quadriceps and hamstring. The treatment group had a significant increase in serum 25(OH)D3 levels (34 %) and muscle strength (13 %). However, other studies were unable to document any benefit following vitamin D supplementation in athletes with adequate or moderately deficient levels of vitamin D prior to supplementation. Close et al. [214] examined the effects of vitamin D3 supplementation on serum 25[OH]D concentrations and on several exercise performance indices in club-level athletes. Participants were randomized into those receiving placebo, 20,000 or 40,000 IU per week of oral vitamin D3 for a 12-week period. At baseline 57 % of the participants were found to be almost vitamin D deficient (mean 51 nmol/L). In the two supplementation groups, the following 6-week and 12-week period either with 20,000 IU vitamin D levels increased to 79 and 85 nmol/l, respectively, or with 40,000 IU vitamin D3 to 98 and 91 nmol/l, respectively. Despite the different supplementation dosages, all individuals managed to reach levels greater than the suggested deficiency limit of 50 nmol/l. However, despite the observed increase in vitamin D serum levels, neither group exhibited an improvement of their exercise performance compared to controls [214]. The inability of the authors to document any beneficial effect of vitamin D on athletic performance may be due the fact that the participants of their study were not vitamin D deficient. It has been shown that the beneficial effects of vitamin D supplementation take place in individuals with significant vitamin D deficiency [158]. The lack of any beneficial effect of vitamin D supplementation was also reported in another study involving football players [215]. A placebo group and one receiving 5000 IU/day of vitamin D were examined. Both groups followed the same high-intensity training regime and had total work, sprint performance (5, 10, 20, 30 m), and jumping ability (squat jump and countermovement jump) measured. No significant differences were evident at baseline between the two groups for any of the measured parameters. The authors reported that although all examined performance indices, apart from the 30 m sprint value, were significantly higher as a result of the high-intensity interval training regime, the mean change scores (obtained values at the end of the study minus those of baseline) did not differ significantly between the two groups, an outcome suggesting that vitamin D supplementation did not had any beneficial effect. It should be noted here that the baseline vitamin D levels of the majority soccer players in this study were deficient. Therefore the proposed mechanism by Dahlquist et al. [158] was not applicable in this study. The authors suggest that other factors apart of vitamin D levels play a pivotal role including their initial training status. It is true though that the studies evaluating the effects of vitamin D supplementation on aerobic capacity in athletes are few and between. Jastrzebski et al. [216] have examined the effects of vitamin

D supplementation on VO_{2max}. The treatment group was composed of 14 elite lightweight rowers having sufficient 25(OH)D concentrations (>30 ng/mL). They were put under vitamin D supplementation of 6000 IU per day for an 8-week period. The authors found a significant increase in VO_{2max} following vitamin D supplementation. Thus, it was concluded that 8 weeks of vitamin D supplementation during the training cycle of the same period of time resulted in enhanced aerobic metabolism in this type of athletes. However, since this is the only study that has examined vitamin D supplementation in athletes, these results cannot be generalized to all sporting disciplines. Furthermore, the low sample size of the study is another limiting factor regarding these findings.

Study	Quality	Sports	Participants	Intervention	Parameters measured	Results
Close et al. [211]	Placebo-controlled trial	Soccer	11 male soccer players, age = 18 ± 5 y	8 weeks, supplementation of 5000 IU/day of vitamin D3 or a cellulose placebo	1RM bench press and back squat, 10 m and 30m sprint, Illinois agility test, vertical jump	Significant ↑ in vertical jump height, 10m sprint times, and a trend for ↑ bench press and back squat 1RM
Wyon et al. [212]	Controlled trial	Ballet	24 elite male and female classical ballet dancers, age 28 ± 3.85 y	4-month supplementation of vitamin D3 (2000 IU per day)	Isometric muscular strength and vertical jump height	Significant ↑ in isometric muscular strength and vertical jump height
Wyon et al. [213]	Randomized controlled double-blind trial	Judoka	22 white male national-level judoka athletes. 27.5± 4 y	Acute effects, 1 week, one single dose of 150 000 IU vitamin D3 or placebo	Isokinetic concentric quadriceps, hamstring muscle strength	Significant ↑ in all measured strength-related indices
Close et al. [214]	Randomized controlled trial	Various sports	30 club-level athletes	Three groups receiving a placebo (PLB) either 20,000 or 40,000 IU/week of oral vitamin D3 for 12 weeks	RM bench press, leg press, vertical jump height	Neither dose given for 12 weeks improved the examined measures of physical performance
Jastrzebski, [216]	Randomized controlled trial	Rowing	14 elite lightweight rowers	8 weeks of 6000 IU/day of vitamin D3 in sufficient athletes (>30 ng/mL)	Maximal oxygen consumption (VO_{2max})	Significant ↑ in VO_{2max}
Jastrzębska et al. [215]	Controlled trial	Soccer	36 young soccer players, age: 17.5 ± 0.6 y	Treatment: around 5000 IU/day placebo— sunflower oil	Wingate test. 5, 10, 20, and 30 m sprint, squat jump (SJ), countermovement jump (CMJ)	No significant difference in any of the measured exercise performance parameters

y, years; ↑, increase

Table 6. Vitamin D supplementation and athletes.

18. Conclusion

This chapter describes the role of vitamin D in athletic performance. It describes the effect of vitamin D in several systems involved in exercise performance and physical activity in both athletes and non-athletes.

Vitamin D undoubtedly has a key role in the osseous health of both athletes and non-athletes. A growing body of evidence suggests that vitamin D is strongly related with the cardiovascular, immune, and neuromuscular systems. It is now clear that vitamin D plays an important role in the ability to perform efficiently during the normal daily activities, while its deficiency may result in poorer exercise performance. It should be mentioned that the vast majority form the evidence regarding vitamin D and exercise come from non-athletes. A growing number of studies have suggested that vitamin D exerts a beneficial effect on exercise performance, particularly in older adults and those with lower levels of circulating vitamin D. Regarding the optimum levels of vitamin D, the current evidence suggests that value levels above 30 ng/mL are needed. The majority of the vitamin D supplementation studies indicate that it may beneficially affect physical activity, frailty, muscular tone, stability, mobility in the elderly, and performance in physically active individuals or athletes only when pretreatment levels are within the insufficiency range (<30 ng/ml). Specifically for athletes, although the results of performance trials are not yet convincing enough to support vitamin D as a direct performance enhancer, obtaining optimal 25(OH)D levels can reduce the risk of debilitating musculoskeletal injury, and due to the active role in muscle, resolution of vitamin D insufficiency has the potential to impact performance.

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