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The Role of Vitamin D₃ in Musculoskeletal Recovery: Implications for Bone, Muscle, and Tendon Healing Across Athletic Disciplines

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ABSTRACT

Background: Tissue repair, immunological control, skeletal muscle function, and calcium-phosphorus metabolism depend on vitamin D₃. Its deficiency is widespread among athletes and may impede musculoskeletal recovery. **Aim:** This review attempts to consolidate and critically analyze the most recent research on the role of vitamin D₃ in bone, muscle, and tendon healing in athletes. **Material and Methods:** Based on a thorough search of the PubMed/MEDLINE database for peer-reviewed publications released between 2010 and 2024, the authors conducted a narrative review. Twenty-three research were chosen based on their significance for sports medicine, methodological quality, and relevance. The review included original research, meta-analyses, and reviews on vitamin D₃ and its impact on athletes' musculoskeletal recovery. **Results:** Sufficient vitamin D₃ level correlates with improved muscle recovery and increased bone density. It is also beneficial for bone regeneration. Most of the findings originate from preclinical studies or animal models. Nevertheless, there are not many studies that evaluate vitamin D₃'s direct impact on athletes' tendon healing. Furthermore, there is considerable variation in study designs, dosage schedules, and evaluation techniques. **Conclusions:** Particularly for athletes with a known deficiency, customized vitamin D₃ supplements may aid in their recovery from injuries. To create evidence-based clinical protocols for vitamin D₃ used in sports injury recovery, however, strong randomized controlled trials are needed. Although incorporating vitamin D₃ testing and supplementation into multimodal rehabilitation plans may improve recovery, more study is required to determine the subgroups that stand to gain the most and optimize dosage.

Key words: Vitamin D₃, musculoskeletal regeneration, rehabilitation, sports medicine

1. INTRODUCTION

Cholecalciferol is primarily known for its essential role in bone metabolism. 1,25-dihydroxycholecalciferol, also known as calcitriol, is a biologically active form of cholecalciferol. Cholecalciferol is a secosteroid hormone, which means that one of the four aromatic rings is broken. Because of this, vitamin D3 has a more flexible chemical configuration compared to other "classic" steroids. What is worth underlining is information that cholecalciferol is something beyond a vitamin – in essence, it is a hormone. Cholecalciferol not only participates in mineral homeostasis but also has an impact on muscle function, the immune system, and tissue repair (Agoncillo et al., 2023).

Competitive athletes may be particularly vulnerable to vitamin D3 deficiency. Training schedules, wearing protective gear, increased metabolic demands, and, occasionally, dietary errors are some of the factors that affect the result (Todd et al., 2015). According to study findings, a vitamin D3 deficiency increases the risk of fractures, slows the healing process after injuries, and impairs muscle function (Barker et al., 2013; Close et al., 2013).

Numerous articles discuss the role of vitamin D, specifically cholecalciferol, in musculoskeletal health (Figure 1). However, the researchers did not focus their evaluation on how to apply vitamin D3 in the recovery of athletes with injuries. This review aims to present evidence of vitamin D3's impact on the regeneration of bones, muscles, tendons, and ligaments. Clinical implications and the lack of high-quality research regarding the use of the athlete population are also mentioned.

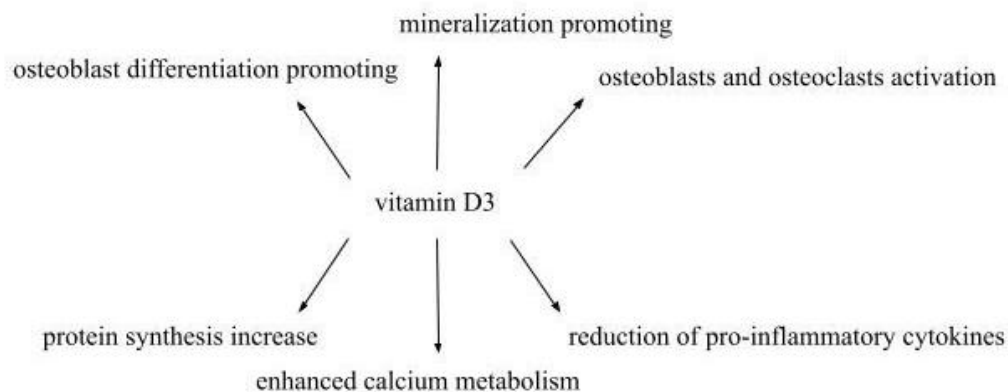


Figure 1 Mechanisms of vitamin D3 resulting in recovery of musculoskeletal system.

Mechanism of Vitamin D3 in Musculoskeletal Recovery

Bone Healing

Vitamin D Receptor (VDR) belongs to the nuclear receptor family of transcription factors. When an active form of vitamin D3 and the calcitriol receptor connect, VDR-mediated pathways are activated. It promotes osteoblast differentiation, bone mineralization, and the regulation of osteoclastogenesis. Adequate vitamin D3 supplementation significantly enhances bone formation and maturation in groups with Vitamin D3 deficiency, as preclinical studies have shown (Hussien et al., 2024). Some researchers are developing novel strategies for cholecalciferol supplementation. Polylactide-co-glycolide (PLGA) scaffolds saturated with vitamin D3 exhibit a high affinity for bone morphogenetic proteins (Park et al., 2024).

Park et al., (2024) examined the local presence of vitamin D3 and its impact on bone formation. Scaffolds integrated with 1,25-dihydroxycholecalciferol were tested for their impact on osteoblast differentiation and angiogenesis. Results showed improved bone tissue regeneration. Such a solution could enhance osteogenic potential; however, further research is needed on this topic. Athletes training in sports with high-impact forces, e.g., football, rugby, hockey, or track and field, are at high risk of stress fractures. In the aforementioned sports, athletes should pay particular attention to maintaining proper vitamin D3 levels to prevent bone damage and, if necessary, facilitate optimal healing (Brudecki et al., 2024).

Muscle regeneration

1,25-Dihydroxycholecalciferol affects muscle cells in various ways. Broadly, there are genomic and non-genomic effects. Genomic effects are expressed when vitamin D3 binds to the VDR. Then, a heterodimer 1,25D-VDR-RXR develops. This complex binds to nuclear receptors in order to activate or suppress specific transcription factors. The non-genomic pathway is represented when 1,25-

dihydroxycholecalciferol binds to the non-nuclear receptors. Protein kinases A (PKA), B (PKB), and C (PKC), and MAPK pathways are thought to be involved in the intracellular signaling of vitamin D. (Girgis et al., 2013). In animal models, mice with a knocked-out VDR receptor (VDRKO) exhibited decreased muscle strength and appeared to have worse endurance than those without VDRKO (Girgis et al., 2015).

Muscle cell regeneration plays a vital role in human organisms. It provides an efficient musculoskeletal system, which is crucial for maintaining homeostasis. Muscle regeneration is carried out by cells known as "satellite cells". Activated satellite cells proliferate and transform into committed myoblasts, which are essential for muscle regeneration and self-replenishment (Seale et al., 2000). Vitamin D enhances myocyte differentiation, myocyte hypertrophy, mitochondrial metabolism, angiogenesis, and muscle function, claim Agoncillo et al., (2023). The findings, as mentioned above, explain why sufficient 1,25-dihydroxycholecalciferol helps to reduce post-surgery healing times and the rate of revision rotator cuff surgeries (Agoncillo et al., 2023).

Moreover, vitamin D insufficiency correlates with increased muscle weakness, a higher risk of injury, and a prolonged rehabilitation process (Close et al., 2013; Todd et al., 2015). Barker et al. claim that not only can vitamin D-deficient people benefit from its supplementation, but also populations with "good" vitamin D levels would benefit from cholecalciferol supplementation (Barker et al., 2013).

Tendon and ligament repair

Preclinical research shows promise. However, there are still issues with translating the results to clinical models (e.g., local vs. systemic delivery). Emerging research emphasizes the role of vitamin D3 in the healing of the tendon-bone connection. Vitamin D3 applied locally demonstrates biological characteristics. Particularly, it increases the synthesis of tendon-associated proteins and has pro-proliferative and anti-apoptotic effects on tenocytes.

It also results in inhibition of the p38 and ERK pathways and decreased expression of NF- κ B. Consequently, there is an increase in tendon regeneration (Kim et al., 2022; Jiang et al., 2024). According to epidemiological evidence, tendinopathy and poor tendon healing are associated with vitamin D deficiency (Tarantino et al., 2024). In the matter of ligaments, the clinical studies are nonconcurrent. The majority of publications, including Shafiee et al., (2020) research, conclude that low serum levels of vitamin D3 are associated with ACL injury.

2. REVIEW METHODS

A narrative review was formulated to combine current data on the impact of vitamin D3 on musculoskeletal recovery. The regeneration of bones, muscles, tendons and ligaments of the athletic population is the main topic of this narrative review. A literature search was undertaken in the PubMed database, with adjustment for 2000–2024 (Figure 2).

Search strategy

The search terms and combinations consisted of: "vitamin D3", "cholecalciferol", "bone healing", "muscle regeneration", "tendon repair", "ligament", "sports", "athletes", "musculoskeletal recovery", and "sports injuries". All studies were included if they were published in English or had an English abstract, even if it was translated. Studies were included if they involved either humans or animal models that were sufficiently relevant. The inclusion and exclusion criteria are outlined in Table 1.

The inclusion criteria for articles were as follows:

- Studies investigating the effects of vitamin D3 on bone, muscle, tendon, or ligament healing
- Studies involving physically active groups, e.g., athletes or appropriate animal models
- Studies that were original research articles, reviews, or meta-analyses. Only peer-reviewed articles were included for analysis.

The exclusion criteria for articles were as follows:

- Case reports
- Letters to the editors
- Conference abstracts
- Studies that did not address musculoskeletal recovery
- Studies where only geriatric or pediatric groups were assessed

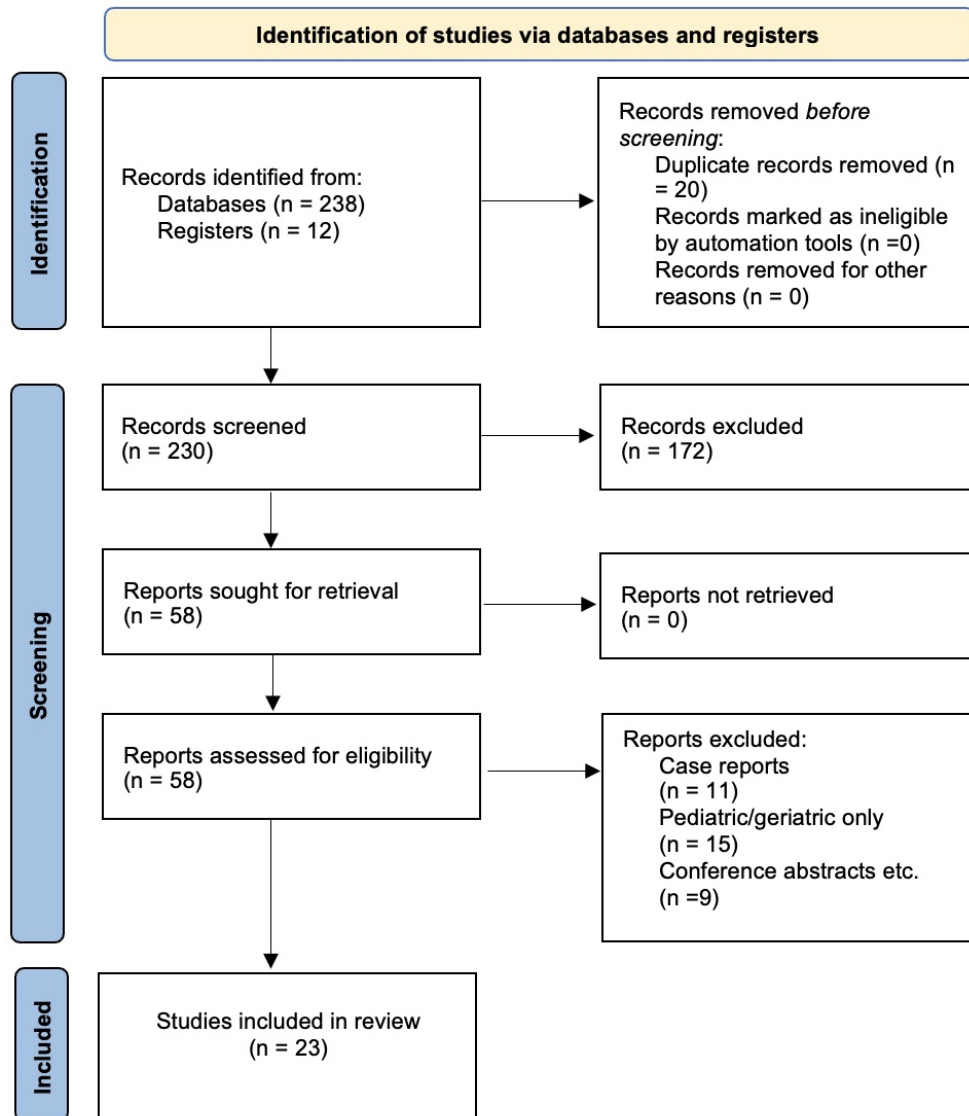


Figure 2. PRISMA chart

Table 1. Summary of inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Effects of vitamin D3 on bone, muscle, tendon, or ligament healing were investigated.	No musculoskeletal recovery is covered.
Physically active groups e.g., athletes or appropriate animal models.	Assessment of solely geriatric and/or pediatric groups.
Original research articles, reviews, or meta-analyses. Only peer-reviewed articles were included.	Case reports, letters to the editors, or conference abstracts.

Study selection and data extraction

The titles and abstracts of the chosen studies were independently checked for relevance by three researchers. Full texts were screened for appropriate studies. References within chosen articles were identified, reviewed, and cited if eligible. The pivotal data included the

study design, characteristics of the population, cholecalciferol interventions or their status assessment, measured results, and finally, the main findings on musculoskeletal healing.

Data synthesis

Since heterogeneity existed among the included articles, particularly in terms of populations, interventions, and outcomes, a narrative synthesis was conducted. This article presents results according to the type of tissue: bone, muscle, and tendon/ligament. A discussion on mechanistic observations and clinical outcomes that are potentially valuable for sports medicine was presented.

Use of Artificial Intelligence (AI)

AI's contribution to this article was limited to refining the academic language used in the manuscript, ensuring uniformity, lucidity, and the long-term viability of scientific writing standards. The authors interpreted the data and came to their conclusions.

3. RESULTS AND DISCUSSION

Multiple studies indicate a connection between improved musculoskeletal outcomes and adequate vitamin D3 (Table 2):

- Hussien et al., (2024) demonstrated accelerated bone regeneration with vitamin D3-loaded hydrogels in rabbits.
- Barker et al., (2013) found that sufficient vitamin D3 was associated with increased recovery of muscle strength after eccentric exercise-induced injury.
- Brudecki et al., (2024) linked adequate vitamin D3 levels to improved bone density markers in athletes.
- Jiang et al., (2024) provided preclinical evidence that vitamin D3 plays a role in bone and tendon healing.

RCTs concentrating on athletes' post-injury recovery are desperately needed, as the majority of the data is derived from preclinical or observational studies.

Table 2. Summary of evidence by tissue type

Tissue Type	Key Findings	Limitations
Bone	Vitamin D ₃ -loaded scaffolds accelerate bone formation; higher serum levels linked to improved bone density in athletes (Brudecki et al., 2024, Hussien et al., 2024, Park et al., 2024)	Mainly animal models or observational studies; no RCTs confirming faster healing in athletes.
Muscle	Faster muscle strength recovery post-injury; reduced inflammation and enhanced protein synthesis (Barker et al., 2013, Ceglia et al., 2013, Close et al., 2013, Todd et al., 2015, Agoncillo et al., 2023).	Limited intervention trials; a possible ceiling effect may be observed in vitamin D-sufficient individuals.
Tendon	Improved tendon-bone integration and reduced cytokine activity in animal models (Jiang et al., 2024, Xu et al., 2024).	There are no human trials; current evidence is based on scaffolds or local delivery systems.

Vitamin D3 in Bone Healing and Implications for Athletes

There is currently no concrete proof from randomized controlled trials (RCTs) that vitamin D3 has any beneficial effects on bone healing mechanisms in athletes, despite promising preclinical research on the subject (Hussien et al., 2024). For example, Brudecki et al., (2024) observed improved bone density markers in athletes; however, this does not necessarily mean faster fracture healing. Thus, one should be careful when using these results as proof that this group has increased bone regeneration. This is a critical topic in sports medicine because athletes who play high-impact sports often get stress fractures and other bone injuries. Athletes with sufficient serum

vitamin D3 levels have more bone density and stiffer heel bones, which can prevent them from microstructural injuries, according to Brudecki et al., (2024). Nevertheless, there is no concrete proof that vitamin D3 supplementation promotes fracture healing in athletes, even in spite of these favorable correlations. Future RCTs should focus on specific types of fractures, such as stress fractures of the tibia in runners, and clearly defined recovery results.

Vitamin D3 and Muscle Function in Injury and Recovery

At the same time, the links between vitamin D3 status and muscle strength recovery after injury are well established (Stockton et al., 2011; Barker et al., 2013). It is essential to consider the potential ceiling effects of supplementation. In particular, the benefits of supplementation may be particularly evident in individuals with a baseline vitamin D3 deficiency (Ceglia et al., 2013). Therefore, the amount of improvement in muscle strength by vitamin D3 supplementation in athletes with sufficient vitamin D3 remains unclear.

Additionally, observational research on athletes has linked low vitamin D3 levels to a higher risk of injuries, such as strained muscles (Close et al., 2013; Todd et al., 2015). Despite these links, only a few intervention studies have assessed whether increasing vitamin D3 deficiency accelerates muscle recovery from injury or return to play. Barker et al., (2013) found that anti-inflammatory cytokine profiles improved after supplementation, suggesting a role for the immune system in muscle recovery. This area requires further research, particularly in a sports context, where rapid muscle recovery is crucial for performance and injury prevention (Miyake et al., 2014).

Emerging Role in Tendon and Ligament Repair

Vitamin D3 shows a promising role in regulating the inflammatory microenvironment during tendon healing (Jiang et al., 2024), but care should be taken when applying these results in clinical practice. The techniques employed, such as vitamin D3-integrated scaffolds (Xu et al., 2024), differ significantly from the oral supplementation typically taken by people. Thus, human population clinical trials are necessary before definitive clinical applications can be made.

After all, there is no human research involving the application of vitamin D3 supplementation as an adjunct to rehabilitation for tendons or ligaments after an injury. This calls for comprehensive clinical research, as the clinical applicability must still be determined.

Integrating Vitamin D3 Into Rehabilitation Protocols for Athletes

Given the information presented here, a justified evidence base would indicate keeping vitamin D3 levels sufficient, not only for health reasons, but as a potential adjunct for injury rehabilitation. Wyon et al., (2014) demonstrated that winter supplementation of vitamin D3 for ballet dancers resulted in a reduction in the incidence of injuries and improved muscle function. However, in most of the studies published, the focus was on injury prevention rather than injury healing.

Vitamin D3 supplementation should be part of a broader approach involving physiotherapy, nutritional strategies, and sport-specific training (Agoncillo et al., 2023). It is important to acknowledge the need for customized supplementation protocols (Table 3) due to individual variability in response to supplementation. It is influenced by genetic polymorphisms that have an impact on vitamin D3 metabolism (Desmarchelier et al., 2016; Bahrami et al., 2019; Ammar et al., 2023).

Table 3. Influence of genetic polymorphism on Vitamin D3 metabolism

Article on genetic polymorphism affecting Vitamin D3 metabolism	
A genetic variation in cytochrome determines response to vitamin D supplementation P450 family 2 subfamily R member 1. (Bahrami et al., 2019)	Interindividual variability in cholecalciferol bioavailability in healthy men Is associated with a mix of Single-Nucleotide Polymorphisms (SNPs)
Variability in healthy adults' reactions to vitamin D supplementation based on gene polymorphisms related to vitamin D metabolism (Ammar et al., 2023)	Variants in DBP-rs4588, CYP2R1-rs10766197, and rs12794714 are linked to changes in serum 25(OH)D concentrations and the effectiveness of an adult's response to vitamin D3 supplementation.
A Combination of Single-Nucleotide Polymorphisms is associated with interindividual variability in cholecalciferol bioavailability in healthy men (Desmarchelier et al., 2016)	In healthy men, there is a high interindividual variability in cholecalciferol bioavailability that is associated with a combination of SNPs located in or near genes involved in both vitamin D3 and lipid metabolism.

Limitations

This narrative review shares some intriguing findings but lacks a quantitative synthesis, such as a meta-analysis of bone density values or muscle strength values. The conclusions are based primarily on observational research and preclinical research that was conducted prior to any clinical trials. The strength of evidence is variable in different tissues. For example, the conclusions on tendons and ligaments were mostly based on preclinical animal studies (Jiang et al., 2024; Xu et al., 2024) while the sections on bone and muscle were more focused on human clinical research (Barker et al., 2013; Wyon et al., 2014; Brudecki et al., 2024). Further research would significantly enhance our current understanding.

Research Deficits and Future Directions

Several significant gaps were found in this review:

- Lack of RCTs that examined the effect of vitamin D3 supplementation on athletic performance metrics, tissue-specific healing, and time to injury resolution.
- Absence of stratified analyses by sport type, injury severity, and individual vitamin D3 metabolism profiles.
- There is a need for mechanistic studies to elucidate the role of vitamin D3 in human tendon healing. Few RCTs have tested vitamin D3 in Anterior Cruciate Ligament (ACL) rehabilitation despite a high incidence of such injuries in athletes.

Future research should prioritize:

- RCTs in athletes' post-fracture or muscle/tendon injury.
- Dosing studies define optimal vitamin D3 regimens for rehabilitation.
- Explore the potential synergistic effects of vitamin D3 with other factors, such as nutritional/therapeutic treatments.

4. CONCLUSION

The literature demonstrates that vitamin D3 has several roles in the regeneration of bone, muscle, and tendon/ligament tissue (including implications for both acute injury prevention and more prompt recovery). Therefore, the evidence is clear regarding its anabolic properties in bone repair, its muscle regenerative properties, and its novel role in integrating tendons with bone. While we are starting to provide some evidence to support this novel dimension, there are few solid clinical studies involving athlete populations. The future of athlete rehabilitation may require personalizing supplementation doses to achieve adequate Vitamin D3 levels, which could also be incorporated into rehabilitation protocols. It remains to be seen how the wide-ranging implications of such findings can be formalized into applied practice with sufficient quality research.

Author's Contributions

Conceptualization: Brzyska Agata, Kucharski Tomasz, Kowalczyk Oliwia

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Writing review and editing: Kopala Justyna, Pawlak Magdalena, Mikołaj Wiśniewski, Maciejowski Michał

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Informed consent

Not applicable.

Ethical approval

Not applicable.

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Conflict of interest

The authors declare that there is no conflict of interest.

Data and materials availability

All data associated with this work are present in the paper.

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