



Vitamin D's Regulatory Role in Skeletal-Muscle Recovery Following Exercise-Induced Muscle Damage

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Abstract

Vitamin D is a key micronutrient with multiple roles in the body, including regulating the immune system and supporting muscular movement. However, vitamin D is a highly common deficiency in modern society. This high prevalence makes it important to clarify which health outcomes are affected by low vitamin D status. Maintaining adequate vitamin D levels may support musculoskeletal and immune health; however, the benefits for exercise recovery remain less certain. Athletic individuals may be at higher risk of low vitamin D status because of factors such as indoor training, seasonal variation, limited sun exposure, and inadequate intake. Although muscle-biopsy, rodent, and cell culture studies support a potential role for VDR signaling in skeletal muscle, direct human evidence linking vitamin D supplementation to post-EIMD recovery remains limited. Evidence suggests that correcting low vitamin-D status may support recovery related outcomes, whereas raising 25(OH)D (calcifediol) beyond sufficiency has not consistently improved muscle performance. Calcitriol-VDR signaling may influence myogenic progression and calcium related signaling, but this pathway has not been established in athletes. This review article addresses vitamin D's role in recovery from exercise-induced muscle damage (EIMD), more specifically vitamin D receptor's role in skeletal muscle as well as calcium handling, while evaluating the current evidence on the effectiveness of supplementation in athletic settings, and exploring the explanations for any potential benefits in recovery. Future research should involve placebo-controlled trials in low baseline 25(OH)D athlete populations, primarily evaluating functional recovery, with blood measurements and muscle biopsies to determine whether improving vitamin-D status leads to activation of VDR-related pathways that enhance recovery significantly.

Keywords

Exercise-induced muscle damage, VDR, Vitamin D3, Calcifediol, Vitamin D Deficiency, Calcitriol, Athletes, Supplementation

Metabolism and Intake of Vitamin D

Vitamin D can be obtained from sun exposure, diet, or supplements, but must be metabolized in the body before it can act as a hormone. There are two ways the body can obtain the precursor form of vitamin D called cholecalciferol (i.e., vitamin D3) (Giustina et al., 2024). In the first method, 7-dehydrocholesterol is converted into vitamin D3 in the skin by UVB exposure. Alternatively, vitamin D3 can be directly consumed through supplements or foods containing vitamin D3. Next, vitamin D3 is converted to 25(OH)D (also known as calcifediol) in the liver, before the enzyme 1 α -hydroxylase metabolizes calcifediol and metabolically activates it into calcitriol (or 1,25-dihydroxyvitamin D) in the kidney and other tissues. Finally, this active

hormonal form binds to the VDR and its effects can be expressed. Serum total 25(OH)D is the preferred biomarker used by researchers, since calcifediol is the principal circulating metabolite and has a longer half-life compared to calcitriol. Furthermore, calcifediol reflects vitamin D derived from cutaneous synthesis as well as dietary intake.

Using the National Academies/Institute of Medicine framework, deficiency is classified as concentrations below 30 nmol/L, while anything between 30 nmol/L and 50 nmol/L indicates insufficiency (Ross et al., 2011). Serum concentrations above 50 nmol/L are adequate for most individuals. Athlete-specific 25(OH)D targets have not been established, while ≥ 75 nmol/L is commonly used as a sufficiency cutoff in research, this number is not validated by randomized evidence as a threshold for performance or recovery (Langley et al., 2024).

Vitamin D's Link to Muscle Recovery: Existing Literature

Despite its importance, a 2023 global systematic review and meta-analysis composed of almost 8 million people concluded that an estimated 47.9% of the global population had vitamin D insufficiency (Cui et al., 2023). Vitamin D may be linked to skeletal-muscle recovery through several pathways, some of which overlap. The most direct question is whether vitamin D3 supplementation directly improves functional recovery following exercise-induced muscle damage (EIMD), particularly for individuals with low status. Existing human research has measured outcomes such as recovery of muscle torque, circulating muscle-damage markers, and post exercise phosphocreatine recovery. This includes a randomized, placebo-controlled trial in vitamin-D-insufficient men, where improved torque recovery after EIMD was reported after vitamin D3 supplementation (Owens et al., 2015). Among available human studies, Owens et al. provides direct evidence due to the measurement of peak torque as a functional outcome, rather than relying on circulating biomarkers. Similarly, vitamin D3 treatment in severely deficient adults was associated with faster phosphocreatine recovery alongside greater maximal oxidative phosphorylation (Sinha et al., 2013). Nevertheless, phosphocreatine recovery is a physiological marker of oxidative function, not a straightforward display of restored sport-specific strength. Both of these studies differ in baseline vitamin D status, intervention design, exercise protocol and sample size.

Mechanistic evidence suggests several plausible explanations for vitamin D related recovery effects. Human muscle-cell studies suggest that direct calcitriol exposure may influence mitochondrial oxygen consumption, ATP production and myogenic progression (Ryan et al., 2016; Montenegro et al., 2019). VDR expression has been reported in human muscle-biopsy studies, while experimental work in rodent and cell culture models have examined regulation pertaining to myoblast differentiation, muscle remodelling, and satellite cell behaviour (Bischoff et al., 2001; Olsson et al., 2016; Hassan-Smith et al., 2017).

In a rodent regeneration model, intramuscular calcitriol did not improve satellite cell differentiation or regenerating fiber formation at a physiological dose, despite VDR expression being identified (Srikuea & Hirunsai, 2016). Overall, VDR-mediated regulation of myoblast differentiation and satellite cell biology is well-established. Other areas that have been comprehensively explored include mitochondrial function and muscle repair, with research spanning cell culture studies and animal models. The relevance of these studies is ultimately

determined by whether they translate into an athlete's ability to restore performance session to session following EIMD.

Supplementing Vitamin D May Improve Ability to Restore Baseline Performance

During periods of intense exercise, especially heavy eccentric-loading contractions, skeletal-muscle can accumulate EIMD (Peake et al., 2016). According to an article in the *Journal of Applied Physiology*, recovery refers to the restoration of baseline performance (Markus et al., 2021). In practice, recovery can be assessed by whether an athlete can reproduce previous strength or sport-specific performance in a later session. If recovery remains impaired after major factors such as sleep, total energy and protein intake, and hydration are addressed, low vitamin D status may be an additional factor worth investigating. For example, a study measuring single-leg peak isometric force (PIF) before and after exercise found that higher pre-exercise serum 25(OH)D levels were associated with smaller immediate, 48-hour and 72-hour deficits in PIF after exercise, although this association was not statistically significant after 24 hours (Barker et al., 2013). This association between higher pre-exercise 25(OH)D concentrations and smaller reductions in peak isometric force helps to establish vitamin D status as a potential recovery-related factor.

Evidence from human skeletal-muscle precursor cells suggests that vitamin D signaling through VDR may influence skeletal-muscle-related processes relevant to repair and development, with one example being myogenic differentiation (Olsson et al., 2016). Athletes experience a high prevalence of low 25(OH)D, and may be at increased risk of low vitamin D status due to limited sun exposure from indoor training and inadequate intake. A 2022 review cited a meta-analysis that found 56% of athletes had insufficiency status and 65.4% of power sport athletes showed inadequacy (Ip et al., 2022). Current evidence suggests that vitamin D primarily functions as a threshold nutrient for skeletal muscle rather than ergogenic aid. A recent double-blind, placebo-controlled study in 31 physically active, vitamin D-sufficient young adults concluded that increasing 25(OH)D to 123 nmol/L through high dose supplementation did not result in additional muscle or performance benefits relative to placebo (Montenegro et al., 2020).

Conversely, limited data suggest that improving low vitamin D status may influence certain responses to eccentric EIMD (Pilch et al., 2020). In one randomized, controlled trial, young men with baseline 25(OH)D ≤ 30 ng/mL (roughly 75 nmol/L) received individualized vitamin D3 supplementation or placebo for three months. Both groups completed downhill running eccentric exercise, and researchers found lower post-exercise myoglobin after supplementation. Myoglobin is a protein released into the bloodstream when skeletal-muscle fibers are disrupted, these results may indicate less muscle-cell membrane disruption. Furthermore, IL-1 β (a pro-inflammatory cytokine that plays a central role in tissue healing and adaptive immune response) levels decreased, which suggests supplementation may have had an anti-inflammatory effect, but since serum concentrations also increased in placebo participants, these effects cannot be confidently attributed to supplementation. Blood levels of creatine kinase (CK) did not differ between groups, and functional recovery markers such as restored strength, subsequent exercise performance and soreness were not measured. Therefore, these blood biomarkers should be taken as preliminary evidence of a possible physiological response to EIMD. Moreover, this study has a small sample size ($n=60$), and was also conducted during

summer months with sunlight, which makes attributing the results of the test specifically to vitamin D3 supplementation more challenging. Collectively, supplementation benefits lie in correcting inadequate status rather than universal performance enhancement beyond physiological sufficiency, which applies particularly to athletes. Although the link between vitamin D status and recovery outcomes remains preliminary, a proposed basis for these effects is calcitriol signaling through the vitamin D receptor (VDR) in skeletal muscle.

Vitamin D Supplementation May Increase Intramuscular Calcitriol and Enhance VDR Signaling in Skeletal Muscle

In order for vitamin D to act directly on the muscle, this requires the presence of its receptor. Early immunohistochemical studies used anti-VDR antibodies to stain the frozen tissue, and intranuclear VDR immunostaining was reported in all sampled specimens in biopsies collected from 20 female orthopedic surgery patients (Bischoff et al., 2001). A subsequent human biopsy study from the same research group also reported similar outcomes (Bischoff-Ferrari et al., 2004). No correlation between serum 25(OH)D concentrations and level of VDR expression was found. This supports the premise that VDR is expressed in human skeletal-muscle tissue. In contrast, an alternate detection method did not identify VDR in mature skeletal, cardiac, and smooth muscle, primarily in mouse tissue (Wang & DeLuca, 2011).

However, muscle biopsies contain more than just samples of mature muscle cells; they include satellite cells, myogenic precursor cells and others. Although direct *in vivo* evidence localizing VDR to different human muscle fiber cells remains limited, rodent injury models provide a plausible explanation for this discrepancy. VDR expression was much lower in uninjured muscle compared to actively regenerating fibers and satellite cells (Srikuea et al., 2012). One possible explanation is that these satellite cells and myogenic precursor populations are activated from muscle injury. This may elucidate why studies using mature, uninjured muscle tissue have reported undetectable VDR expression, while an increased presence in regeneration is shown by raised VDR detection in whole-muscle samples. In an alternate study measuring VDR mRNA expression instead of immunostaining, VDR mRNA was detected in biopsies from 80 healthy human vastus lateralis muscle, which supports the presence of VDR gene expression in adult human skeletal muscle (Hassan-Smith et al., 2017). Vastus lateralis muscles are often selected for biopsies since they are large, superficial and relatively accessible to obtain from the thigh. This allows for highly safe and practical repeated sampling. Furthermore, its context in mobility makes it highly relevant for sport and exercise recovery studies. Nonetheless, a biopsy only represents a small region of muscle, which limits its ability to be generalized to whole body skeletal-muscle recovery. Taken together, current evidence suggests that VDR expression in skeletal muscle is context-dependent and may be more detectable in regenerating tissue or muscle-associated cell populations than in mature resting muscle alone.

Mechanistic evidence implies that human skeletal-muscle cells can directly respond to calcitriol-VDR signaling (Pojednic et al., 2015). In primary myoblasts, VDR expression was increased by calcitriol in a dose-dependent manner. Additionally, 16 weeks of vitamin D3 oral supplementation increased VDR mRNA in the muscle. Because the study population was small (n=20) and consisted of older women aged >60 years, these findings may not directly generalize to young athletes recovering from damaging exercise. In addition, a randomized controlled trial

involving patients with low 25(OH)D found that vitamin D supplementation led to higher levels of intramuscular calcitriol (Trummer et al., 2017). This suggests that increased dietary intake of vitamin D3 could increase calcitriol levels in skeletal muscle, in turn increasing VDR expression.

Calcitriol and VDR May Impact Hypertrophic Outcomes

Interestingly, in cultured skeletal-muscle cells, calcitriol activated both ERK1/ERK2 MAP kinase signaling, an intracellular signaling pathway relevant to muscle-cell growth and remodeling (Morelli et al., 2001). While this experiment is well designed as a cell culture study, it may not reflect post-exercise recovery in humans. Also independent of the aforementioned immunostaining debate, later work concluded that VDR mRNA in human skeletal muscle differs with adaptations from resistance training, and is associated with hypertrophy (Bass et al., 2020). While recovery includes immediate restoration of performance, its long term process also overlaps with hypertrophic adaptations. For example, both include the production of protein; one to restore muscle damage and one to build additional muscle. If recovery is incomplete, repeated reductions in force output could reduce training quality and may interfere with long-term adaptation. Decreased force output would lower mechanical tension experienced, the main driver of hypertrophy (Van Every et al., 2025). Resistance training can induce EIMD, due to its high volume while training close to task failure with high eccentric loading. In the 20 week human training study by Bass et al. (2020), greater VDR mRNA induction significantly correlated with greater hypertrophy after long-term resistance training. Interpreted differently, with repeated loading, higher VDR expression was associated with the muscle growth response.

While it is important to acknowledge that this correlation does not definitively prove that VDR caused the response in humans, rodent models conducted in the same study demonstrated that when VDR was experimentally increased, this resulted in greater total protein and RNA content, greater mTor-related signaling and rates of protein synthesis, increased satellite cell content, increased markers of ribosomal biogenesis, and perhaps most significantly, larger myofiber cross-sectional area, one of the main markers when measuring muscular hypertrophy. Since VDR expression was directly manipulated by the researchers beforehand, a causal claim that VDR expression was sufficient to stimulate muscle hypertrophy in rats can be considered. This explores the possibility of VDR's role in anabolic remodelling related pathways. However, this short-term rodent overexpression model did not involve EIMD and does not show that vitamin D3 supplementation reproduces similar effects in humans.

This also proposes the question of whether reducing VDR expression would result in the opposite phenotype (impaired muscle maintenance and atrophy). In a further study, transient VDR knockdown was induced in rat tibialis anterior muscles and skeletal-muscle cells in vitro (Bass et al., 2021). Reducing VDR expression decreased muscle protein content and myofiber cross-sectional area, was associated with increased autophagy-related signaling, and disrupted myogenic processes. In contrast to the anabolic effect of overexpression, muscle atrophy was triggered. Pairing both studies together gives convincing converging evidence that point toward VDR's regulatory role in muscle mass and remodeling, although this causal evidence is derived primarily from rodent in vivo and cell culture models. Importantly, evidence that VDR regulates muscle remodeling does not automatically mean that increasing vitamin D intake or serum 25(OH)D will produce the same effect in humans.

Calcitriol May Influence Calcium-related Signaling

Calcitriol-bound VDR can regulate gene transcription. It may also contribute to intracellular signaling in skeletal-muscle cells, therefore increases in VDR signaling could plausibly influence regulatory pathways of intracellular calcium. Calcium has two distinct yet related functions in skeletal muscle. Calcium ions initiate muscle through the excitation-contraction coupling mechanism, while also acting as an intracellular signaling molecule influencing gene expression and muscle remodelling. During excitation-contraction coupling, Ca^{2+} is released from the sarcoplasmic reticulum (SR), binding to troponin C and permitting cross-bridge cycling. This leads to force production, after which calcium ions are returned to the SR to enable relaxation (Calderon et al., 2014). Apart from initiating muscular contraction, intracellular calcium also acts as a cell signaling molecule. In cultured skeletal-muscle cells, rapid changes in intracellular calcium metabolism were reported after the cells were directly exposed to calcitriol, with a larger response in myotubes than myoblasts (Capiati et al., 2000). A later study noticed that calcitriol stimulated MAP kinase through pathways containing protein kinase C and calcium (Morelli et al., 2001). In human skeletal muscle, Ca^{2+} dependent protein kinase II (CaMKII) was activated rapidly during continuous exercise, with greater activation observed during high-intensity exercise where there are high levels of intracellular calcium. (Rose et al., 2006).

CaMKII is one calcium kinase responsible for converting transient increases in intracellular calcium into gene regulatory signals involved in muscle remodelling. This includes satellite cell activation, proliferation, and differentiation, processes required to repair damaged muscle cells (Tu et al., 2016). Although vitamin D supplementation has not been conclusively proven to improve EIMD through CaMKII, this evidence suggests the biological plausibility of calcitriol's involvement as a cell signaling molecule, rather than simply a long-term regulator of gene transcription through nuclear VDR. However, these cell studies did not measure SR Ca^{2+} release/reuptake or EIMD recovery, and therefore cannot prove that vitamin D3 supplementation can systemically enhance the excitation-contraction coupling mechanism. Since current research is limited, calcitriol's role in skeletal-muscle calcium can only be justified as a mechanistic hypothesis supported primarily by cell culture evidence. A strong mechanistic conclusion would have to involve a complete causal sequence, starting with correction of low vitamin D status. Then, evidence of altered intramuscular calcitriol must be demonstrated alongside proof of altered calcium-handling physiology. Finally, improved functional recovery outcomes must also be shown. While each component of this sequence is presently supported by separate cell culture, animal, and a few human studies, the full pathway has not been demonstrated in a single athlete recovery trial. Such a trial would clarify whether improving vitamin D status directly improves functional recovery outcomes and could be used to guide the design of individualized sport-nutrition strategies or even provide a model for investigating alternative micronutrients in athletic populations.

Discussion

Existing direct recovery studies are heavily limited by small sample size, short time frame, lack of an exercise model, or incomplete functional outcomes. CK, myoglobin, and cytokines alone cannot establish functional recovery. Functional recovery outcomes like repeat session performance should be the primary factor assessed, since it directly addresses whether an athlete can return to baseline performance. Depending on the specific sport, different functional

outcomes would be more logical. For example, maximal voluntary torque and peak isometric force could be measured in the context of resistance training, while sprint/jump performance may be more reasonable for track and field. Additionally, soreness should also be assessed, although soreness and perceived readiness is more subjective and could therefore act to complement the functional outcomes. Characteristics of participants should also be considered, since the degree as well as time course of the EIMD experienced can vary with age, sex, training status, and body composition. Both male and female athletes should be included where possible. There are few adequately powered trials testing EIMD, and much of this direct EIMD work is in men or non-athletic populations. For this, populations such as women, endurance and power athletes, and indoor/outdoor athletes must also be tested. Regarding VDR, there is no direct VDR to recovery evidence. While VDR biology is supported by muscle biopsies, cell culture models and rodent models, this is not directly connected to athletic recovery. Further research in this area could include muscle biopsy samples before and after eccentric exercise in order to relate it to EIMD. Moreover, the link between serum concentrations of 25(OH)D and intramuscular calcitriol has to be made clearer. Whether or not raising serum concentrations through supplementation or dietary intake has a direct effect on altering calcitriol and VDR signaling in skeletal muscle, and whether this leads to improved recovery outcomes, still remains to be proven. Lastly, present literature concerning calcitriol's role in calcium handling mostly stems from cell culture models or assessment of gene expression. Physiological calcium measurements such as SR Ca^{2+} release/reuptake are needed.

A useful experiment to test this paper's topic would be a randomized, double-blind, placebo-controlled trial of the effects of vitamin D3 supplementation in vitamin D insufficient athletes who regularly perform eccentric loading exercise. This would involve both male and female athletes with serum concentrations below 50 nmol/L, excluding participants with disorders that could affect calcium metabolism. Factors such as protein and energy intake, sleep, sun-exposure and training must be tracked and standardized. Participants would be randomly split into the treatment group or placebo group for 8-12 weeks, using an individualized dosage designed to rectify low status without reaching excessively high serum concentrations. Serum 25(OH)D measurements should be taken regularly throughout this 8-12 week duration. Optionally, another group of vitamin D sufficient athletes can be monitored for comparison. After the intervention period, these athletes would go through damaging exercises relevant to their sport, for example downhill running for endurance athletes. Assess before and after recovery outcomes repeatedly, for at least one week. Preferably, an unexercised control limb could be included when feasible, since EIMD is specific to the recruited muscle. This could be carried out in a similar fashion to Barker et al's (2013) single leg peak isometric force model for resistance training athletes.

A secondary mechanistic biopsy can also be conducted within the same experiment. A smaller subgroup could provide vastus lateralis biopsies before EIMD and at various recovery time points post-exercise. Markers including VDR mRNA, satellite cell markers (like Pax7), protein synthesis rate, and calcium-handling proteins can all be measured. VDR localization across myofibers and satellite cells can also be observed. Measuring SR calcium release-reuptake would be highly valuable but technically demanding. Unlike routine blood biomarkers, direct assessment of SR Ca^{2+} measurements require freshly biopsied muscle fibers and specialized lab procedures. In summary, current research supports the biological plausibility of vitamin D as



a modifier of skeletal-muscle repair and remodeling, particularly for individuals with corrected low vitamin D status. However, human evidence linking vitamin D3 supplementation to meaningful post-EIMD recovery remains limited. The proposed explanation of the VDR-calcium signaling pathway relies heavily on cell and animal studies rather than direct measurements in athletes. Future research should prioritize placebo-controlled trials in low baseline 25(OH)D athlete populations, and primarily evaluate functional recovery, while also incorporating repeated blood and muscle measurements to determine whether alterations in vitamin-D status leads to activation of VDR-related pathways that improve recovery to a significant degree.

Correcting low vitamin-D status with vitamin D3 supplementation may improve functional recovery after exercise-induced muscle damage through increasing calcitriol-VDR signaling in skeletal muscle. This signaling may influence muscle repair and calcium related pathways. For athletes with low 25(OH)D concentrations, particularly those who train indoors and have limited sun exposure, identifying and correcting this low status should be prioritized in order to support recovery and performance. In the context of sport medicine, current studies do not justify that levels beyond sufficiency will further improve or accelerate recovery, therefore unsupported high-dose supplementation claims should be avoided.

Conflict of Interest

There is no conflict of interest, financial or personal relationships declared.

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and feedback on organizing resources. All information was independently read and verified, and original scholarly sources are cited. I take full responsibility for this paper's final arguments, analysis, citations, and conclusions.