International Journal of Research in Orthopaedics
Alexander B et al. Int J Res Orthop. 2026 May;12(3):837-847
http://www.ijoro.org

DOI: https://dx.doi.org/10.18203/issn.2455-4510.IntJResOrthop20261243

Review Article

Effect of vitamin D supplementation on bone healing in patients with avascular necrosis of the hip: a narrative review

Brytsko Alexander, Koshman Gennadiy, Naveen D. K. N. Direcksze*, Narendiran Yohanathan, D. M. N. P. K. Dassanayake

Department of Traumatology, Orthopaedics and Military Field Surgery, Grodno State Medical University, Grodno, Belarus

Received: 03 March 2026
Accepted: 08 April 2026

***Correspondence:**
Dr. Naveen D. K. N. Direcksze,
E-mail: ndkndis@gmail.com

ABSTRACT

Vitamin D has been widely known for its role in maintenance and repair of skeletal system, where vitamin D deficiency (VDD) led to hindered effect on bone healing after fractures, bone defects and osteon formation in implants. Some studies have shown that increasing serum Vitamin D levels requires a significant period of time after the application of vitamin D for VDD. In addition, VDD at the time of bone (mainly hip) fracture is associated with an inflammatory response after the fracture. Avascular necrosis (AVN) is a serious complication of defective bone healing. VDD may be a potential risk factor for this incidence; however, further studies are required to validate this aspect in orthopedics. The crucial role of vitamin D in upregulating vascular endothelial growth factor on the proliferation of type-H vessels connects osteogenesis and angiogenesis pathways, thereby providing insight into how to tackle AVN. The primary aim of this review is to highlight the importance of vitamin D supplementation in patients with AVN during the bone regeneration phase.

Keywords: Vitamin D, Bone mineral density, Bone healing, Avascular necrosis, Vitamin D receptors, Type-H blood vessels

INTRODUCTION

The interplay between nutrition and bone healing is a well-documented aspect of medical science, highlighting the crucial role of various components in the maintenance and repair of skeletal integrity.[1] While most of the literature on Vitamin D_3 supplementation in patients with fractures depicts the prevention of fractures, the effect of vitamin D_3 on bone healing is a much less studied and understood concept.[2] Vitamin D refers to a family of structurally related secosteroids. Among them, vitamin D_2 (ergocalciferol) obtained from plants and vitamin D_3 (cholecalciferol) synthesized in the skin under UVB exposure are the most relevant to humans. However, both D2 and D3 are biologically inactive precursors, which are hydroxylated first in the liver to 25(OH)D (calcidol) by the 25**α**-Hydroxylase enzyme and then by 1α-Hydroxylase to 1,25(OH)2D3 (calcitriol), the active form, in the kidneys.[3] Calcitriol binds the vitamin D receptor (VDR) to regulate gene expression. Other hydroxylated derivatives, such as 24,25(OH)2D3 and 1,24,25(OH)3D3, which are produced via other enzymes, also exhibit minor vitamin D receptor activity. Hydroxylated forms are absorbed better and raise serum 25(OH)D more efficiently, where vitamin D3 mostly increases circulating 25(OH)D with a longer half-life compared to D2, likely due to higher binding affinity for vitamin D-binding protein (DBP) and slower catabolism.[4]

The above flowchart (Figure 1) depicts vitamin D_3 metabolism and its classical function in the maintenance of calcium homeostasis and skeletal homeostasis. The ideal form of vitamin D_3 supplementation is calciferol, which is the most bioavailable form. Another study

revealed that the vehicle of oral vitamin D_3 supplementation has a huge impact on its bioavailability, where a comparison of three variants of products revealed that microencapsulated and oil-based vitamin D_3 were more effectively bioavailable than micellized vitamin D_3. Furthermore, the concentration of vitamin D_3 was checked in blood in the form of 25-hydroxyvitamin D (25(OH)D).[5]

VDD is a major global health issue, affecting approximately 1 billion children and adults.[6] This indicates that VDD cannot be undervalued because of its devastating consequences. One of the main challenges encountered in VDD is defective bone regeneration, which causes improper osteon matrix integration, leading to brittle bones and susceptibility to potential fractures.

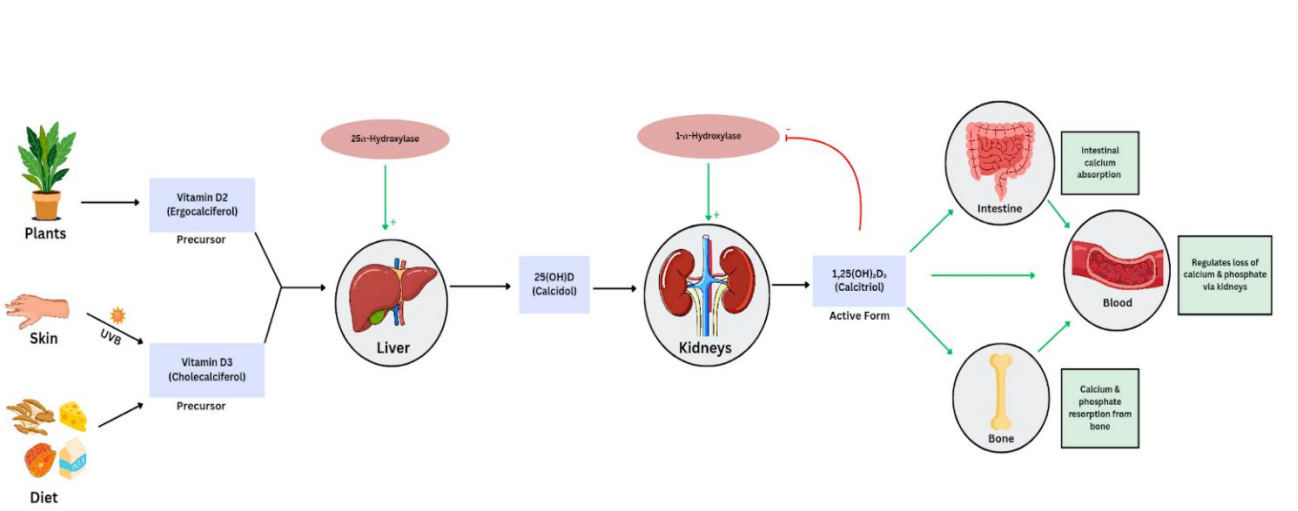

Figure 1: Flow chart of vitamin D metabolism and its classical function in the maintenance of calcium homeostasis and skeletal homeostasis.

Some consequences of VDD are osteomalacia in adults and rickets in children. Even mild chronic VDD can lead to chronic hypocalcemia and hyperparathyroidism, thus leading to an elevated risk of osteoporosis and an increased frequency of fractures following a fall, especially in the elderly population.

Once converted into its active form calcitriol, vitamin D_3 plays an important role in bone mineralization by increasing intestinal calcium and phosphate absorption. In VDD, calcium absorption decreases, leading to hypocalcemia and a compensatory increase in parathyroid hormone (PTH) levels. PTH reduces renal calcium loss and stimulates bone resorption. Thus, in the long run, serum calcium levels are maintained at the expense of bone, resulting in increased bone turnover and demineralization. In adults, this dysregulation manifests as osteomalacia, whereas in children, it presents as rickets. In both diseases, defective mineralization of the bone matrix, reduced skeletal strength, and increased bone fragility are observable.

Furthermore, with the progressive loss of bone density, the risk of osteoporosis, fragility fractures, and falls increases, especially in older adults. Clinically, VDD is also associated with muscle weakness, bone pain, myalgia, arthralgia, and neuromuscular irritability, including muscle cramps and spasms, which further increase fall risk.[6]

Prolonged and severe VDD can cause symptoms related to secondary hyperparathyroidism, including bone pain, myalgia, arthralgia, general weakness, and fasciculation (muscle twitching). Chronic VDD can also lead to fragility fractures, resulting in osteoporosis. VDD can be a growth inhibitor in children leading to a number of clinical symptoms such as developmental delays, lethargy, irritability and bones changes or sometimes fractures.[7] Furthermore, a randomized cross-sectional study showed decrease incidence rates of fractures in children after supplementation of vitamin D_3 to improve serum 25-hydroxyvitamin D. This is another area to be considered for low-energy pediatric trauma fractures.[8] Also, vitamin D_3 supplementation has shown to have positive effects on fracture management and bone healing, through its role of diminishing pain, facilitating recovery, occurrence of complications, thereby showing a standard fracture management protocol.[9]

Moreover, the general hypothesis between vitamin D_3 and AVN is depicted by the crucial role of vitamin D_3 in maintaining bone health, and its deficiency becomes an independent risk factor for AVN, especially in patients with sickle cell disease. Additionally, VDD is related to a significantly elevated risk of developing AVN (10 times more) due to its effect on bone turnover and potential vascular impairment by disruption of angiogenesis, immunomodulation and microvascular intergrity.[10]

PATHOPHYSIOLOGY

The underlying mechanisms of bone healing with vitamin D metabolism is a vicious cycle, where the interrelation between osteoblasts and osteoclasts is solely codependent on each other. Fracture healing activity is characterized by four stages: inflammation, soft callus formation, hard callus formation, and bone remodeling. Therefore, bone repair can be considered an independent comparison between anabolism or tissue formation in the early phases and catabolism or bone remodeling in the later phases.[11] According to normal physiology, bone healing after fractures is a complex biological process involving signaling molecules, growth factors, osteoprogenitor cells, and the extracellular bone matrix (ECBM). These requirements are controlled by genetic/molecular, physiological, and cellular factors. Moreover, vitamin D_3 receptors (VDR) play a major role in promoting bone remodeling and healing by mediating vitamin D to regulate calcium/phosphate absorption, thereby stimulating bone matrix mineralization. Therefore, low activity of VDR impairs these processes, leading to lower bone density and susceptibility for recurrent fractures.[12]

AVN is a condition primarily caused by a temporary or permanent compromise of the blood supply to the bone. As mentioned before, PTH-mediated bone resorption due to VDD results in reduced bone density, mineralization defects, and impaired bone microarchitecture. These changes are particularly detrimental to the femoral head, where structural strength is necessary for weight-bearing capabilities. Such changes can exacerbate underlying pathology and accelerate progression of the disease, suggesting that vitamin D3 may play not an etiological, but a contributory role by modulating the susceptibility and progression of AVN.

In a retrospective cohort study of 711 patients with sickle cell disease (SCD), those with VDD had a susceptibility to AVN that was almost 10 times higher than that of those without. This study found 17.9 % prevalence of AVN in the cohort and 42.3% prevalence of VDD, where it was significantly associated with AVN in both adults and children.[10]

In another study related to pediatric SLE, exploratory analyses found that subjects with AVN often had baseline VDD compared to those without AVN, which could suggest a potential link for further studies.[13]

Furthermore, vitamin D affects vascular endothelial cells through various mechanisms, such as modulating the activity of endothelial nitric oxide synthase (eNOS), enhancing the bioavailability of nitric oxide (NO), and counteracting oxidative stress, thereby aiding endothelial function and microcirculatory integrity.[14] Additionally, VDD has also been linked with the increased production of reactive oxygen species (ROS) and decreased antioxidant activity, increased expression of pro-inflammatory cytokines, and activation of nuclear factor-κB (NF-κB) in vascular tissue, which could all contribute to a compromise of microcirculatory perfusion while creating a state that predisposes bone tissue to ischemic injuries.[15]

Additionally, an important type of vessel, known as the type-H vessel, was found to elaborate the connection between angiogenesis and osteogenesis. These vessels are closely associated with osteogenic activity. In addition, the rate of bone metabolism in the femoral head is significantly higher than that in the distal femur, and the quantity of type-H vessels is more abundant in the femoral head than in the distal counterpart. However, further studies are required to verify this novel correlation.[16]

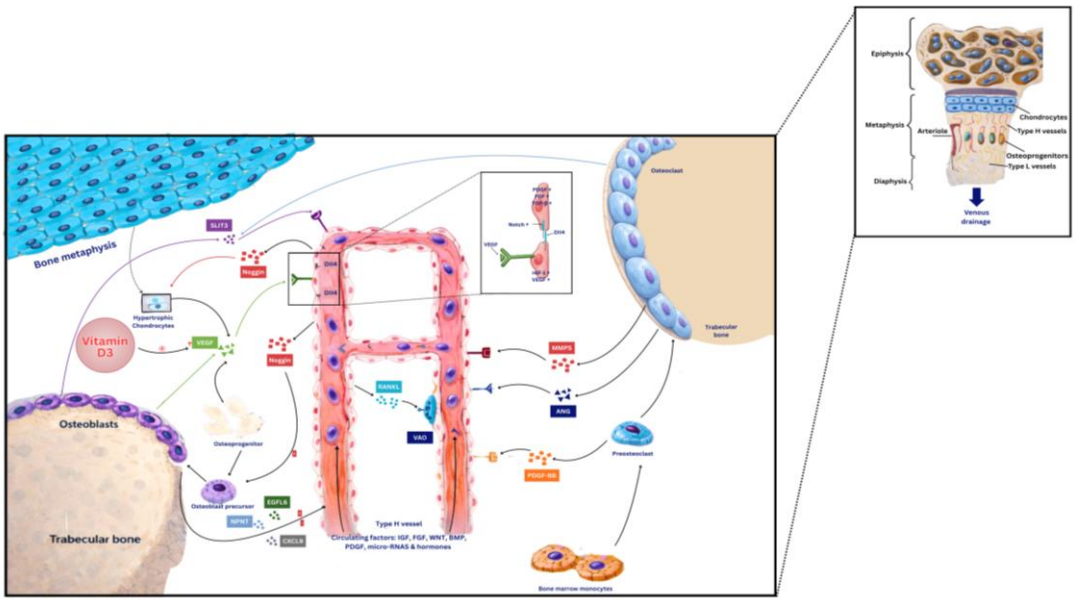

Figure 2: The pathophysiology of influence of vitamin D on type-H vessels during bone healing.

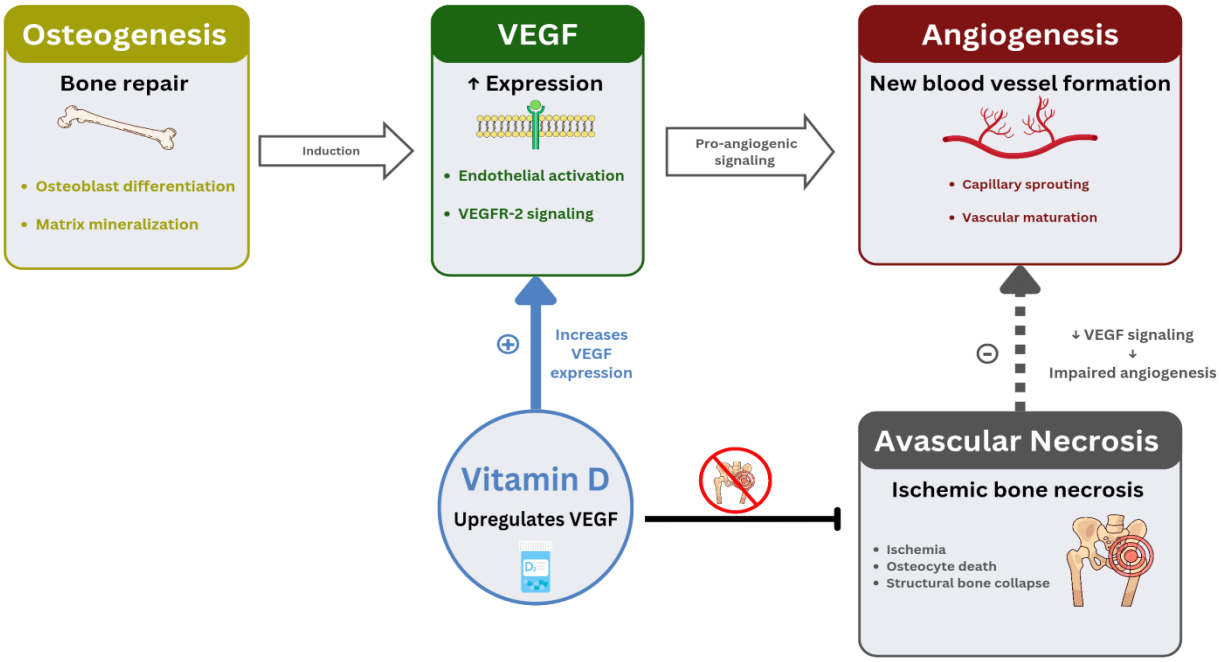

Figure 3: The pathophysiology of influence of vitamin D in bone healing during avascular necrosis.

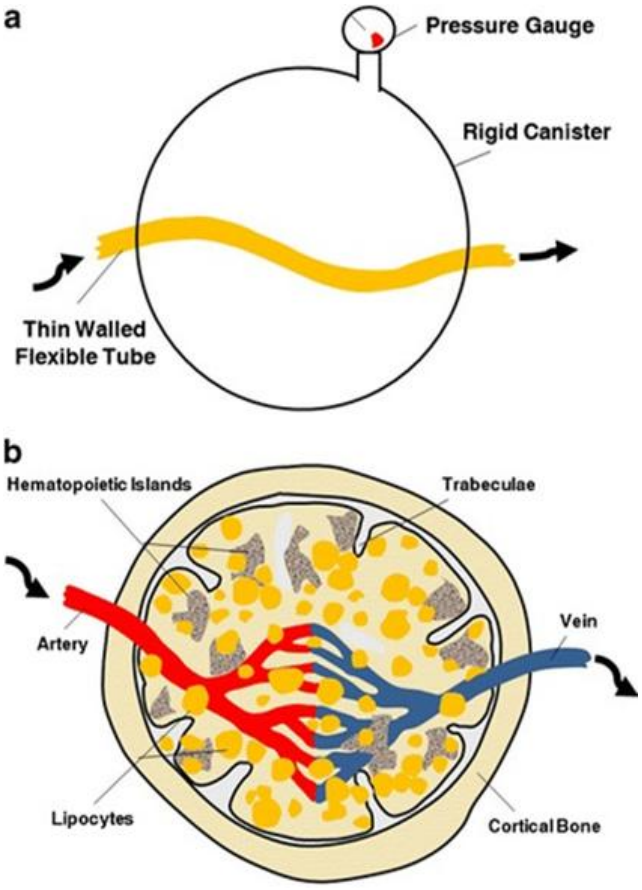

Figure 4: Concept of the starling resistor as applied to bone microcirculation. A-Raising the pressure in a rigid-walled chamber can decrease fluid flow in a flexible-walled tube passing through the chamber. B-In the case of bone, the intraosseous extravascular compartment may function like a rigid-walled chamber. Intraosseous hypertension or space-occupying tissue may sufficiently restrict microcirculatory blood flow to produce ischemia.[19]

Additionally, an important type of vessel, known as the Type-H vessel, was found to elaborate the connection between angiogenesis and osteogenesis. These vessels are closely associated with osteogenic activity. In addition, the rate of bone metabolism in the femoral head is significantly higher than that in the distal femur, and the quantity of type-H vessels is more abundant in the femoral head than in distal counterpart. However, further studies are required to verify this novel correlation (Figure 2).[16]

Pathophysiology of this correlation is often misunderstood; however, this review may help elucidate correlation between AVN and vitamin D supplementation during bone regeneration phase (Figure 3).

EPIDEMIOLOGY AND PREDISPOSITION

AVN is most frequent in the hip but can also be seen in the humerus, knee, and talus and is rarely seen in the carpal bones of the wrist, such as the scaphoid and lunate. While the jaw is also affected, this review focuses on the more common forms of hip AVN presented during examination by a traumatologist.[17] AVN typically affects adults aged between 30-65, with a higher incidence in males (in the ratio of 5:1), thus showing male dominance and accounting for approximately 10% of cases recorded in the USA.

The major predisposing of AVN of hip AVN include corticosteroid use, excessive alcohol consumption, bilateral trauma, and medical conditions such as systemic lupus erythematosus (SLE), sickle cell disease (SCD), HIV infection, dyslipidemia, and hypercoagulable states.[18] Other predisposing factors for AVN include vascular interruption in the bone matrix, which is observed in intracapsular fractures of the femoral neck, causing direct trauma to the blood vessels that supply the subchondral bone; intravascular occlusion, which is observed in SCD, lipid thrombi, or clots; and intraosseous extravascular compression, as seen in the concept of Starling resistors on the femoral head (Figure 4 A and B). Overall, AVN is predominant in males; however, certain autoimmune conditions, such as SLE, affect women, shifting the significance of AVN to the female population.[20] A retrospective cohort study reported a higher incidence of AVN in patients with SCD with VDD; 301 out of 711 patients with SCD were affected by VDD (42.3%), and 127(17.9%) suffered from AVN. This indicates that VDD is an independent risk factor for AVN in patients with SCD.[11]

CLASSIFICATION OF AVN OF THE FEMORAL HEAD

The staging strategy for managing AVN allows for treatments that have been tailored to its evolving nature, thereby enhancing results and maintaining joint functionality. Various classification systems have been proposed, each with distinct advantages and drawbacks. The most widely used include the Ficat and Arlet, Steinberg, Association Research Circulation Osseous (ARCO), Japanese Investigation Committee (JIC), Kerboul angle, and Beijing classification.[21]

Classification systems of AVN of the femoral head

ARCO classification (1993, revised 2019)

The ARCO classification integrates clinical, radiographic, MRI, and histopathological data.

Stage I: Normal radiography, MRI positive.

Stage II: Radiographic changes (sclerosis and cysts) without collapse.

Stage IIIA: Early subchondral collapse (<2 mm).

Stage IIIB: Advanced collapse (>2 mm).

Stage IV: Osteoarthritis with joint destruction.

Thus, the advantages of this study emphasize the application of magnetic resonance imaging (MRI) while moving away from reliance on traditional radiographic standards and detailed assessment of lesion extent

On the contrary, the limitations include dependency on advanced imaging as it relies heavily on MRI, No interobserver reliability and variability and limited range of staging as limited clinical context.[22]

The classification of AVN is essential for prognosis and treatment planning purposes. Although the Ficat and Arlet system remains widely used, modern classifications such as ARCO and Steinberg offer improved lesion characterization. Future research should focus on refining these classifications for precise assessment of disease progression and aids in identifying the most appropriate treatment strategies.[23]

The ARCO classification is a popular staging system for AVN that utilizes radiographic and MRI findings to explain how the disease progresses from pre-collapse to advanced osteoarthritis. In the revised 2019 ARCO system, Stage I shows normal X-rays but abnormal MRI/bone scan findings, Stage II demonstrates radiographic bone changes without subchondral fracture, Stage III includes subchondral fracture with femoral head depression, and Stage IV shows secondary osteoarthritis with joint destruction.[24] This kind of classification is more clinically significant because it helps differentiate pre-collapse disease, where preservation of the joint is still feasible, from post-collapse disease where joint replacement may prove more effective than joint preservation.

Treatment depending on arco includes,

Stage I and II: Femoral head structurally intact. → procedures such as core decompression, (with or without

bone marrow or biological adjuncts), are commonly used to reduce intraosseous pressure thus promoting revascularization.

Stage III: Onset of subchondral fractures reduces likelihood of efficient joint preservation → treatment may shift towards osteotomy or arthroplasty methods.

Stage IV: Femoral head loses its spherical shape and secondary osteoarthritic changes are observed → total hip replacement [25,26,27]

INTERVENTIONAL STRATEGIES (PHARMACO-THERAPY AND SURGICAL INTERVENTION)

The management of hip osteonecrosis encompasses both nonsurgical and surgical approaches, depending on the stage of the disease and the extent of the bone involvement.

Pharmacological interventions

Bisphosphonates

Inhibit osteoclast-mediated bone resorption, potentially preventing collapse of the femoral head. However, their efficacy is still under investigation and they are not universally recommended. Alendronate relieves pain, enhances functional capacity, and slows the progression of AVN if initiated before the collapse stage. A well-documented side effect of oral preparations is esophageal or gastric irritation, along with the concerns for osteonecrosis of the jaw (ONJ) as well as the subtrochanteric fractures.[28]

Anticoagulants

In cases where thrombosis contributes to reduced blood flow to the femoral head, anticoagulants may be used to improve circulation by reducing intraosseous pressure and reduce disease progression

Lipid-lowering agents

Statins may provide protection against osteonecrosis in patients requiring steroid therapy.[29]

ACTH

It has offered some protection against osteonecrosis of the femoral head in patients under steroids.[30]

Iloprost

A vasodilator, has shown improved clinical outcomes when associated with bone marrow edema.[31]

Extracorporeal shock wave therapy (ESWT)

ESWT has been explored as a treatment option for early-stage osteonecrosis of the femoral head. A study conducted on rabbits showed that shock wave treatment increased VEGF levels, which correlated with neovascularization.[32] ESWT may aid in preventing the advancement of AVN and managing pain in patients with ARCO stages I and II.[33] It also improved hip function in long term follow up where x-rays and MRI showed regression of lesions.[34]

Pulsed electromagnetic therapy

While it is considered advantageous as it protects articular cartilage from the detrimental impacts of inflammation and subchondral bone-marrow edema in the short term and enhances osteogenic activity in the necrotic region in the long term, reducing the risk of trabecular fractures and subchondral bone collapse, some authors suggest further exploration.[29,35]

Hyperbaric oxygen therapy

It is said to have an effect in promoting angiogenesis and improving microcirculation.[36] A study demonstrated the effectiveness of using hyperbaric oxygen therapy (HBO) to treat Steinberg stage I AVN of the femoral head.[37] Another small prospective study in patients with unilateral FHN Ficat stage II demonstrated significant improvements in pain and range of motion after several HBO treatments.[38] However, the high cost of this method poses a significant constraint.[39]

Surgical treatment

For ONFH in the pre-collapse stage, surgical interventions typically focus on hip-preserving techniques, such as core decompression and various bone grafting methods (vascularized or non-vascularized), whereas total hip arthroplasty is typically considered only in cases of advanced collapse and significant arthritic changes.[36]

The joint-preserving surgical options consisting of following techniques,

Core decompression

A prospective study with 36 patients to compare the effectiveness between conservative treatment and core decompression for cases of ONFH produced more favorable outcomes were seen with core decompression compared to conservative management in the initial phases of ON.[40] A study focusing on long-term results of core decompression as the sole treatment for Ficat stages I, II and III ischemic necrosis of 128 femoral heads in 90 patients concluded that Core decompression has been shown to delay the necessity for total hip replacement in young patients suffering from ischaemic necrosis.[41] A study states using modern techniques of core decompression is safe and effective for early stage ONFH, while another study focused on comparing the efficacy of multiple drilling vs standard core decompression concluded that decompressive techniques yield poorer

outcomes for larger lesions and those located laterally, even during the precollapse phase.[42,43] While multiple drilling is considered safer and less invasive than single coring for patients with SCD, outcomes and complication rates remain statistically similar between the two procedures when addressing AVN of the femoral head ANFH.[44] A study conducted in steroid treated rabbits for ONFH concluded that there was gradual normalization of femoral head blood flow after decompression.[45]

Mesenchymal stem cells implantation

Applying osteogenic or angiogenic precursor cells with or without growth factors at the necrotic lesion site can improve regeneration.[36] Several angiogenic growth factors, such as VEGF, G-CSF, Hepatocyte growth factor (HGF), contribute to angiogenesis, albeit to varying extents.[46] Mesenchymal stem cells may be introduced as either mononuclear cells obtained from bone marrow concentrate or as bone marrow-derived stem cells that have been expanded through ex vivo culture.[36] By incorporating ancillary growth factors, these procedures not only effectively minimize donor site morbidity and restore femoral head integrity but also have the potential to delay joint arthroplasty in carefully selected patients.[46,47] In a study analyzing the number of circulating endothelial progenitor cells (EPCs), decreased numbers and functional status of EPCs were identified; hence, supplementation of these would be beneficial.[48] In the prospective cohort study pioneered by Hernigou et al where patients classified according to the Harris hip score underwent core decompression with bone graft prior to bone collapse (Stages I and II), a total of nine hip replacements were performed out of 145 hips. Conversely, among the 44 hips treated after collapse (Stages III and IV), total hip replacement was required for 25 hips, which concluded great outcomes.[49] Liu et al conducted a retrospective study examining the outcomes of combining CD with hydroxyapatite/polyamide implantation, with or without the addition of bone marrow-derived mesenchymal stem cells (MSCs). After two years, the results indicated superior clinical outcomes (measured by HHS and pain scores) and radiographic enhancements in the group receiving stem cells. Specifically, 21.4% (6 out of 28) of hips with osteonecrosis in the bone marrow cohort experienced collapse, in contrast to 59.3% (16 out of 27) in the CD group.[50] Between May 2004 and July 2006, 100 patients with 104 hips diagnosed with ONFH were included in the study. The patients were randomly assigned to two treatment groups: one group received CD (50 patients with 51 hips), and the other received BMMSC (50 patients with 53 hips). Follow-up assessments were performed at 6, 12, 24, and 60 months postoperatively. These findings indicate that autologous implantation of cultured BMMSCs into the femoral head is a safe and effective treatment for early stage ONFH. Compared with CD treatment, BMMSC transplantation led to significant improvements in the clinical outcomes related to osteonecrosis, while also delaying or preventing the progression of the disease to more severe stages or the collapse of the femoral head, potentially avoiding the need for further surgical procedures such as total hip replacement.[51] In a recent randomized controlled trial involving 51 hips classified as ARCO Stage I and II ON, Sen et al 84 compared the effects of CD with the instillation of bone marrow mononuclear cells. Their findings revealed a significant enhancement in pain reduction, deformity correction, and hip survival in the group receiving bone marrow concentrate ($p<0.05$) after a follow-up period of two years.[52] Gagala et al study utilized cartilage regenerative technique autologous osteochondral transfer in ONFH of 20 patients with 21 hips with a higher rate of hip survival in osteo articular transfer system (OATS) group- 85.71% after 4 years in 7 patients compared with 61.54% in OATS/allograft group after 3 years and reported it as time buying procedure for young patients with ONFH.[36] But because it is a highly surgical demanding and more invasive procedure, commenting on its efficacy is controversial.[53]

Nonvascularized bone graft

This procedure is performed when CD fails in Ficat stages I and II ONFH and is successful in the pre-collapse and early post-collapse stages with viable cartilage.[54] Osteochondral grafting on the femoral head using a diamond bone-cutting system (DBCS) has been shown to be technically viable for restoring the articular surface. However, this procedure yielded unsatisfactory outcomes in four out of five patients.[55] This retrospective analysis assessed the long-term efficacy of core decompression combined with non-vascularized bone grafting for the treatment of ONFH. A study by Keizer et al involved 80 hips from 65 patients with a mean age of 36 years. Among the evaluated hips, a variety of stages of the disease were recorded preoperatively. The findings revealed that 44% of hips required revision after an average of four years, with a five-year survival rate of 59% when assessed clinically. Notably, a significant survival advantage was identified for tibial autografts compared to fibular allografts, attributed to the superior quality and volume of the tibial bone.[56]

Porous tantalum implant

Compared with a historical cohort undergoing vascularized fibular grafting, porous tantalum implants showed significantly better results across all measured parameters ($p<0.00001$). Most surviving implants (86%) yielded favorable clinical outcomes. Kaplan-Meier analysis at 39 months revealed implant survival rates of 86% and 67% for the plate and fibular grafts, respectively ($p=0.21$). These early results suggest that porous tantalum implants are a safe and promising approach for preserving the femoral head, although further long-term follow-up is needed to fully assess their effectiveness.[57] However the results of Floerkemeier et al states m-core decompression with the placement of a tantalum osteonecrosis intervention implant did not demonstrate improved outcomes compared to core decompression alone.[58]

Vascularized bone graft

A study reported the effectiveness of free vascularized fibular grafts in treating ONFH in 56 hips of 48 patients, starting in October 2000. With an average follow-up of approximately 16 months, Harris hip scores improved across all stages of the disease.[59] Marciniak et al stated that in certain patients experiencing ONFH, vascularized fibular grafting could potentially enable normal hip function over the intermediate to long term.[60] However, Yoo et al indicated that free vascularized fibular grafting effectively preserved joint function and postponed the necessity for hip replacement. Graft survival was linked to patient age, lesion size, and location, and not related to the cause or stage of osteonecrosis.[61]

Muscle pedicle bone graft

Baksi et al studied 61 patients (68 osteonecrotic femoral heads, average age 36) who underwent surgery involving muscle pedicle bone grafting. Over a 3-12-year follow-up period, pain relief and improved joint mobility were observed. Outcomes were better for post-traumatic or idiopathic necrosis than for cortisone-induced cases.[62]

Vascularized iliac crest graft

Eisenschenk et al assessed ONFH treated with vascular pedicled iliac crest transplant using Harris hip scores. In the postoperative follow-up averaging 5 years, clinical evaluations and imaging showed 86.6% of patients achieved favorable clinical results and radiographic stability was observed in 56.1% during follow-up.[63] Sudhir et al concluded that of 31 patients in ARCO stage 2 and 3 who underwent core decompression and vascular pedicle bone grafting, only one required joint replacement due to disease progression.[64]

Vascularized fibular graft (VGF)

The results of Urbaniak et al prospective study of 103 consecutive hips (89 patients) that had been treated with free vascularized fibular grafting because of symptomatic osteonecrosis of the femoral head with a follow-up of 5 years concluded that Harris hip scores improved along with the overall improvement in functionality without the need for arthroplasty in the majority of the patients.[65] Taolin et al stated that VFG is a reasonable approach to prevent collapse and delay or avoid hip replacement in ONFH, particularly in Steinberg stages I-III.[66] A study stated that VFG in pre-collapse osteonecrosis of the femoral head (ONFH) often results in hip preservation for over 10 years, with pain control and functionality.[67]

Proximal femoral osteotomy

Ito et al concluded that conventional varus half-wedge osteotomy yields good long-term outcomes when less than two-thirds of the medial femoral head is necrotic and the superolateral bone is healthy, although leg shortening is a potential complication.[68]

Jacobs et al studied 22 intertrochanteric osteotomies for ONFH, followed for an average of 63 months, 16 achieved good or excellent results which had an inverse relationship to size.[69]

Maistrelli et al review of 106 intertrochanteric osteotomies for ONFH (average age 47.5 years) showed 71% satisfactory results at 2 years and 58% excellent/good results at 8.2-year follow-up. 24 hips required subsequent replacement or arthrodesis. He suggested that intertrochanteric osteotomy should be considered for younger adults without metabolic bone disease or advanced joint destruction.[10]

CONCLUSION

AVN of the hip is a pathological debilitating condition, with a higher incidence of stress fractures presenting in elderly patients and trauma in young patients due to independent causes such as VDD. However, the beneficial effect of vitamin D_3 supplementation on the upregulation of VEGF produced by osteoblasts, osteoclasts, and osteoprogenitors for proliferation-type-H vessels links osteogenesis with angiogenesis, which plays a major role in promoting bone remodeling and fracture healing.

This concept is seldom discussed in the current literature, and this article helps to illustrate the relationship between AVN and vitamin D_3 supplementation during bone healing. However, further studies are required to validate this correlation in this section of literature.

Recommendations

This narrative review aims to fill the gap in the current literature on vitamin D_3 supplementation in patients with AVN during bone healing. Therefore, vitamin D_3 is a common supplement prescribed by orthopedic surgeons to address the underlying deficiency, improve bone health, and manage bone pain. Moreover, it is strongly recommended to correct low vitamin D levels to treat VDD, since VDD is known to be an independent risk factor for AVN. The recommended dose is approximately 4000 IU daily to manage AVN. However, this dose should be corrected to the patient's serum levels, since 4000 IU is considered the higher upper safe administration of vitamin D_3 for adults. The safe dose of vitamin D_3 administration prevents toxicity. The timing of vitamin D_3 administration is crucial for improving clinical outcomes; thus, when coupled with calcium supplementation, it results in improved bone density, particularly after hip surgery. Certain studies have shown that the administration of vitamin D_3 as a first-line treatment prior to prescribing antibiotics for planned surgeries demonstrated beneficial effects on bone healing in patients with AVN. Additionally, a case report highlighted the significance of

preventing secondary hyperparathyroidism with Vitamin D_3 supplementation for a better prognosis.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Slobogean GP, Bzovsky S, O'Hara NN, Marchand LS, Hannan ZD, Demyanovich HK, et al. Effect of Vitamin D_3 Supplementation on Acute Fracture Healing: A Phase II Screening Randomized Double Blind Controlled Trial. JBMR Plus. 2023;7(1):e10705.
2. Gatt T, Grech A, Arshad H. The effect of vitamin D supplementation for bone healing in fracture patients: a systematic review. Adv Orthop. 2023;2023:6236045.
3. Na SY, Kim KB, Lim YJ, Song HJ. Vitamin D and Colorectal Cancer: Current Perspectives and Future Directions. J Cancer Prevent. 2022;27(3):147-56.
4. Dominguez LJ, Farruggia M, Veronese N, Barbagallo M. Vitamin D Sources, Metabolism, and Deficiency: Available Compounds and Guidelines for Its Treatment. Metabolites. 2021;11(4):255.
5. Šimoliūnas E, Rinkūnaitė I, Bukelskienė Ž, Bukelskienė V. Bioavailability of different vitamin D oral supplements in laboratory animal model. Medicina. 2019;55(6):265.
6. Holick MF. The vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention. Rev Endocrine Metabol Disorders. 2017;18(2):153-65.
7. Sizar O, Khare S, Goyal A, Givler A. Vitamin D deficiency. StatPearls. StatPearls Publishing, Treasure Island (FL). 2018.
8. Herdea A, Ionescu A, Dragomirescu MC, Ulici A. Vitamin D-A Risk factor for bone fractures in children: A population-based prospective case–control randomized cross-sectional study. Int J Environ Res Publ Health. 2023;20(4):3300.
9. Singh TM, Kumar CV. The Effect Of Vitamin D Supplementation On Bone Healing After Fracture: An Observational Study. Int J Acad Med Pharm. 2024;6(2):629-33.
10. Tammas AJ, Albehlal LB, Alabbas F, Albehlal L. Vitamin D Deficiency and Avascular Necrosis in Patients With Sickle Cell Disease: A Retrospective Cohort Study. Cureus. 2024;16:10.
11. Schindeler A, McDonald MM, Bokko P, Little DG. Bone remodeling during fracture repair: the cellular picture. Semin Cell Dev Biol. 2008;19.
12. Markopoulos G, Lepetsos P, Perrea DN, Iliopoulos DC, Nikolaou VS, Perrea DN. Possible roles of vitamin D in bone grafting. Cureus. 2021;13:4.
13. Gurion R, Tangpricha V, Yow E, Schanberg LE, Mccomsey GA, Robinson AB. Avascular necrosis in pediatric systemic lupus erythematosus: a brief report and review of the literature. Pediat Rheumatol Online J. 2015;13:22.
14. Kim DH, Meza CA, Clarke H, Kim JS, Hickner RC. Vitamin D and Endothelial Function. Nutrients. 2020;12(2):575.
15. Ayoub G. Vitamins, Vascular Health and Disease. Nutrients. 2025;17:18.
16. Liu X, Zhang P, Gu Y, Guo Q, Liu Y. Type H vessels: functions in bone development and diseases. Front Cell Develop Biol. 2023;11:1236545.
17. Matthews AH, Davis DD, Fish MJ, Stitson D. Vascular necrosis. In StatPearls. StatPearls Publishing. 2023.
18. Prasad P, Sandhu PS. An epidemiological study of diagnosed avascular necrosis of hip joint (AVN hip) cases and exploring the etiology and treatment offered in patients coming to Dr. Hardas Singh Orthopedic Hospital and Superspeciality Research Centre, Circular Road, Amritsar, Punjab. Sch Acad J Biosci. 2020;8:344-9.
19. Shah KN, Racine J, Jones LC, Aaron RK. Pathophysiology and risk factors for osteonecrosis. Curr Rev Musculoskeletal Med. 2015;8:201-9.
20. Lespasio MJ, Sodhi N, Mont MA. Osteonecrosis of the Hip: A Primer. Perm J. 2019;23:18-100.
21. Sugano N, Atsumi T, Ohzono K, Kubo T, Hotokebuchi T, Takaoka K. The 2001 revised criteria for diagnosis, classification, and staging of idiopathic osteonecrosis of the femoral head. J Orthop Sci. 2002;7(5):601-5.
22. Schmitt-Sody M, Kirchhoff C, Mayer W, Goebel M, Jansson V. Avascular necrosis of the femoral head: inter-and intraobserver variations of Ficat and ARCO classifications. Internat Orthop. 2008;32:283-7.
23. Atilla B, Bakırcıoğlu S, Shope AJ, Parvizi J. Joint-preserving procedures for osteonecrosis of the femoral head. EFORT open Rev. 2019;4(12):647-58.
24. Cui Q, Jo WL, Koo KH, Cheng EY, Drescher W, Goodman SB, et al. ARCO consensus on the pathogenesis of non-traumatic osteonecrosis of the femoral head. J Kor Med Sci. 2021;36(10):e65.
25. Theopold J, Armonies S, Pieroh P, Hepp P, Roth A. Nontraumatic avascular necrosis of the femoral head: Arthroscopic and navigation-supported core decompression. Operat Orthop Traumatol. 2020;32(2):107-15.
26. Yue JA, Guo X, Wang R, Li B, Sun Q, Liu W, et al. Reliability and repeatability of 2021 ARCO classification and its guiding significance in treatment of nontraumatic osteonecrosis of the femoral head. BMC Musculosk Disord. 2023;24(1):469.
27. Hines JT, Jo WL, Cui Q, Mont MA, Koo KH, Cheng EY, et al. Osteonecrosis of the femoral head: an updated review of ARCO on pathogenesis, staging and treatment. J Kor Med Sci. 2021;36(24):e177.
28. Chen CH, Wang GJ. Alendronate in the prevention of collapse of the femoral head in nontraumatic osteonecrosis. In Osteonecrosis. Berlin, Heidelberg: Springer Berlin Heidelberg. 2014;265-71.

29. Pritchett JW. Statin therapy decreases the risk of osteonecrosis in patients receiving steroids. Clin Orthop Related Res. 2001;386:173-8.
30. Zaidi M, Sun L, Robinson LJ, Tourkova IL, Liu L, Wang Y, et al. ACTH protects against glucocorticoid-induced osteonecrosis of bone. Proceedings National Academy of Sci. 2010;107(19):8782-7.
31. Disch AC, Matziolis G, Perka C. The management of necrosis-associated and idiopathic bone-marrow oedema of the proximal femur by intravenous iloprost. J Bone Joint Surg Brit. 2005;87(4):560-4.
32. Ma HZ, Zeng BF, Li XL. Upregulation of VEGF in subchondral bone of necrotic femoral heads in rabbits with use of extracorporeal shock waves. Calcified Tissue Int. 2007;81(2):124-31.
33. Vulpiani MC, Vetrano M, Trischitta D, Scarcello L, Chizzi F, Argento G, et al. Extracorporeal shock wave therapy in early osteonecrosis of the femoral head: prospective clinical study with long-term follow-up. Arch Orthop Trauma surg. 2012;132:499-508.
34. Wang CJ, Huang CC, Wang JW, Wong T, Yang YJ. Long-term results of extracorporeal shockwave therapy and core decompression in osteonecrosis of the femoral head with eight-to nine-year follow-up. Biomed J. 2012;35(6):481-5.
35. Eftekhar NS, Schink-Ascani MM, Mitchell SN, Bassett CA. Osteonecrosis of the femoral head treated by pulsed electromagnetic fields (PEMFs): a preliminary report. The Hip. 1983;306-30.
36. Tripathy SK, Goyal T, Sen RK. Management of femoral head osteonecrosis: Current concepts. Indian J Orthop. 2015;49:28-45.
37. Reis ND, Schwartz O, Militianu D, Ramon Y, Levin D, Norman D, et al. Hyperbaric oxygen therapy as a treatment for stage-I avascular necrosis of the femoral head. J Bone Joint Surg Brit Vol. 2003;85(3):371-5.
38. Camporesi EM, Vezzani G, Bosco G, Mangar D, Bernasek TL. Hyperbaric oxygen therapy in femoral head necrosis. J Arthroplasty. 2010;25(6):118-23.
39. Zhang S, Wang C, Shi L, Xue Q. Beware of steroid-induced avascular necrosis of the femoral head in the treatment of COVID-19-Experience and lessons from the SARS epidemic. Drug Des Devel Ther. 2021;15:983-95.
40. Stulberg BN. Osteonecrosis of the femoral head: a prospective randomized treatment protocol. Clin Orthop Related Res. 1991;268:140-51.
41. Fairbank AC. Long-term results of core decompression for ischaemic necrosis of the femoral head. J Bone Joint Surg Brit Vol. 1995;77(1):42-9.
42. Marker DR. Do modern techniques improve core decompression outcomes for hip osteonecrosis? Clin Orthop Rel Res. 2008;466:1093-103.
43. Kim SY. Multiple drilling compared with standard core decompression for the treatment of osteonecrosis of the femoral head. Orthop Proceedings. 2004;86:2.
44. Al Omran, Abdullah. Multiple drilling compared with standard core decompression for avascular necrosis of the femoral head in sickle cell disease patients. Arch Orthop Trauma Surg. 2013;133:609-13.
45. Wang GJ. The effect of core decompression on femoral head blood flow in steroid-induced avascular necrosis of the femoral head. JBJS. 1985;67(1):121-4.
46. Rackwitz L, Lars E, Stephan R, Johannes CR, Franz J, Heike W, et al. Stem cell-and growth factor-based regenerative therapies for avascular necrosis of the femoral head. Stem Cell Res Therapy. 2012;3(1):1-9.
47. Feng Y, Shu-Hua Y, Bao-Jun X, Wei-Hua X, Shu-Nan Y, Tian X, et al. Decreased in the number and function of circulation endothelial progenitor cells in patients with avascular necrosis of the femoral head. Bone. 2010;46(1):32-40.
48. Hernigou P, Beaujean F. Treatment of Osteonecrosis With Autologous Bone Marrow Grafting. Clin Orthop Rel Res. 2002;405:14-23.
49. Liu Y, Shubin L, Xiuyun S. Core decompression and implantation of bone marrow mononuclear cells with porous hydroxylapatite composite filler for the treatment of osteonecrosis of the femoral head. Arch Orthop Trauma Surg. 2013;133(1):125-33.
50. Zhao D, Daping C, Benjie W, Fengde T, Lin G, Lei Y, et al. Treatment of early stage osteonecrosis of the femoral head with autologous implantation of bone marrow-derived and cultured mesenchymal stem cells. Bone. 2012;50(1):325-30.
51. Sen RK, Sujit KT, Sameer A, Neelam M, Ratti RS, Niranjan K. Early results of core decompression and autologous bone marrow mononuclear cells instillation in femoral head osteonecrosis: a randomized control study. J Arthroplasty. 2012;27(5):679-86.
52. Gagala J, Tarczyńska M, Gawęda K. Clinical and radiological outcomes of treatment of avascular necrosis of the femoral head using autologous osteochondral transfer (mosaicplasty): preliminary report. Int Orthop. 2013;37(7):1239-44.
53. Leah F, Natalie S, Kristen HL, Todd D, Kelly RE. A scoping review of simulation modeling in built environment and physical activity research: current status, gaps, and future directions for improving translation. Elsevier. 2019;28.
54. Rittmeister M, Hochmuth K, Kriener S, Richolt J. Five-year results following autogenous osteochondral transplantation to the femoral head. Der Orthopäde. 2005;34(4):320-6.
55. Keizer SB, Kock NB, Dijkstra PDS, Taminiau AHM, Nelissen RGHH. Treatment of avascular necrosis of the hip by a non-vascularised cortical graft. J Bone Joint Surg Brit Volume. 2006;88(4):460-6.
56. Shuler MS, Michael DR, James RR. Porous tantalum implant in early osteonecrosis of the hip: preliminary report on operative, survival, and outcomes results. J Arthroplasty. 2007;22(1):26-31.
57. Floerkemeier T, Fritz T, Dorothea D, Matthias L, Phillip K, Henning W, et al. Clinical and radiological outcome of the treatment of osteonecrosis of the femoral head using the osteonecrosis intervention implant. Int Orthopaed. 2011;35:489-95.
58. Zhang C, Bingfang Z, Zhengyu X, Wenqi S, Lei S, Dongxu J, et al. Treatment of femoral head necrosis

with free vascularized fibula grafting: a preliminary report. Microsurgery. 2005;25(4):305-9.
59. Marciniak D, Furey C, Shaffer JW. Osteonecrosis of the Femoral Head: A Study of 101 Hips Treated with Vascularized Fibular Grafting. J Bone Joint Surg. 2005;87(4):742-7.
60. Yoo M-C, Kang-Il K, Chung-Soo H, Javad P. Long-term followup of vascularized fibular grafting for femoral head necrosis. Clin Orthop Rel Res. 2008;466(5):1133-40.
61. Baksi DP. Treatment of osteonecrosis of the femoral head by drilling and muscle-pedicle bone grafting. J Bone Joint Surg Brit Vol. 1991;73(2):241-5.
62. Eisenschenk A, Lautenbach M, Schwetlick G, Weber U. Treatment of Femoral Head Necrosis With Vascularized Iliac Crest Transplants. Clini Orthop Rel Res. 2001;386:100-5.
63. Babhulkar S. Osteonecrosis of femoral head: treatment by core decompression and vascular pedicle grafting. Indian J Orthop. 2009;43(1):27.
64. Urbaniak JR, Coogan PG, Gunneson EB, Nunley JA. Treatment of osteonecrosis of the femoral head with free vascularized fibular grafting. A long-term follow-up study of one hundred and three hips. JBJS. 1995;77(5):681-94.
65. Fang T, Elizabeth WZ, Frederick CS, Robert AMcG, William CL, Feng Z. Vascularized fibular grafts in patients with avascular necrosis of femoral head: a systematic review and meta-analysis. Arch Orthop Trauma Surg. 2013;133(1):1-10.
66. Eward WC, Craig AR, James RU, Marc JR, David SR. The vascularized fibular graft in precollapse osteonecrosis: is long-term hip preservation possible? Clin Orthop Rel Res. 2012;470(10):2819-26.
67. Ito H, Tanino H, Yamanaka Y, Nakamura T, Takahashi D, Minami A. Long-term results of conventional varus half-wedge proximal femoral osteotomy for the treatment of osteonecrosis of the femoral head. J Bone Joint Surg Brit Vol. 2012;94(3):308-14.
68. Jacobs MA, David SH, Krackow KA. Intertrochanteric osteotomy for avascular necrosis of the femoral head. J Bone Joint Surg Brit Vol. 1989;71(2):200-4.
69. Maistrelli G, Fusco U, Avai A, Bombelli R. Osteonecrosis of the hip treated by intertrochanteric osteotomy. A four-to 15-year follow-up. J Bone Joint Surg Brit Vol. 1988;70(5):761-6.
70. Diaconu C, Cipăian RC, Iliescu MG, Ciortea VM, Irsay L, Ungur RA, et al. Medical management and rehabilitation in a patient with avascular necrosis of the femoral head in the context of vitamin D deficiency and secondary hyperparathyroidism-case report. Balneo PRM Res J. 2023;14(2):547.
71. Baker RJ, Mark PB, Patel RK, Stevens KK, Palmer N. Renal association clinical practice guideline in post-operative care in the kidney transplant recipient. BMC Nephrol. 2017;18:1-41.

Cite this article as: Alexander B, Gennadiy K, Direcksze NDKN, Yohanathan N, Dassanayake DMNPK. Effect of vitamin D supplementation on bone healing in patients with avascular necrosis of the hip: a narrative review. Int J Res Orthop 2026;12:837-47.