

Older adults and vitamin D hip fracture connections-what is the 2022 research base indicating?

Abstract

Hip fractures among the older adult population remain highly prevalent oftentimes life-threatening events despite decades of efforts to study their causes and implement preventive endeavors. Even more concerning is the possible unabated prevalence of subsequent even more debilitating second or third hip fractures among primary hip fracture survivors. In an effort to explore if indeed there is current evidence of a key overlooked role for vitamin D as far as its probable benefits for preventing or mitigating hip fracture debility and speeding up the optimal recovery post hip fractures goes, this report examines most of the currently available peer reviewed articles listed on the PUBMED data base as of July 1 2021-July 10 2022 and some background material on this topic. It is concluded that while careful usage of vitamin D in cases of risk or deficiency may afford both preventive and optimal recovery opportunities towards reducing the persistent global age-associated hip fracture burden, as well as the burden of acquiring a second or third hip fracture, no current conclusive evidence prevails in this regard.

Keywords: bone health, hip fractures, older adults, prevention, supplementation, vitamin D

Volume 7 Issue 2 - 2022

Ray Marks

Department of Health and Behaviour Studies, Teachers college, Columbia University, United States

Correspondence: Marks Ray, Department of Health and Behaviour studies, Teachers college, Columbia University, Box 114, 525W, 120th Street, New York, NY 10027, United States, Tel +1-212-6783445, Email rm226@columbia.edu

Received: July 08, 2022 | **Published:** July 19, 2022

Introduction

Despite years of research and publication of over 50,000 articles since 1815 listed on PUBMED, the world's largest medically oriented repository, and despite some degree of orthopedic advancement in the pharmacologic and surgical realms in recent years, fractures of the hip, common among older adults remain highly prevalent and severely disabling in the event the hip fracture sufferers survive surgery.^{1,2} Also raising the risk for premature mortality, especially among those with comorbid illnesses,³ as well as future hip and other bone fractures, plus osteoarthritis of the hip, to date, preventive programs that mostly focus on obviating falls risk, including balance and strength training are clearly not sufficiently successful at preventing first or second hip fractures.^{4,5} Moreover, some current attempts at optimizing hip fracture recovery and the risk of future events fail to include any reference to vitamin D.⁶⁻⁸ As well, despite many years of study, potential benefits of efforts to help older adults to maintain adequate vitamin D levels, rather than employing falls-risk increasing drugs,^{9,10} may not only to help avert falls, but to foster underlying bone strength and bone protection even though its inherent impact on bone cells and others remain disputed or unsubstantiated. Given that the older adult population that is increasing in size as well as in actual years of life, may be expected to have more challenges than younger adults to maintain adequate vitamin D serum levels over time, and may arguably be quite prone to poor health, depression, and sleep challenges among other health and hip fracture risk attributes linked to vitamin D deficiency it appears research to date has tended to fail to provide adequate solutions in this regard. At the same time, the post COVID-19 era can be expected to have impacted the health of many older surviving adults, and has curtailed research in the geriatric realm as well.

Review aims

To examine if there are any advancements in this realm of hip fracture prevention, this mini review strove to examine the current degree of support for the idea that vitamin D is a possible highly

relevant factor that could not only help explain why some older adults are more at risk for a hip fracture than others, but if so, whether this finding may offer a means of hip fracture prevention among at least some vulnerable older adults. It also aimed thereby to establish whether a need exists for more research in this realm, and if so in what regard. Whether vitamin D, a collective term applied in this brief to represent a family of vitamins derived from sunlight as well as certain nutrients and that can be delivered via pharmacologic methods or injection will potentially reduce the rate of bone loss and foster healthy musculoskeletal functions that can mitigate against falls and hip fractures in the older adult was sought.

To obtain the desired data, a scan of available documents housed in the PUBMED and published in English between July 1 2021-July 10 2022 using the key terms Vitamin D and Hip Fractures was used. After scanning the available article listings those that addressed some aspect of the current topic of interest were downloaded and scrutinized in more depth by the author without regard to research design. After reviewing the available data, it was clear many postings were not directly relevant, and that no systematic overview of such a limited diverse data base was possible and would not be of sufficient value for definitively advancing current practice or research in the realm of hip fracture prevention and rehabilitation. Hence, while it is acknowledged that the present body of data may not be exhaustive-and that others have attempted meta-analyses or aggregate reviews on a similar theme, and no mention was made of former reports for the most part, it appeared that vitamin D while increasingly seen to be deficient in cases with a hip fracture, does not imply that its presence will prevent this injury or affect care practices.

Results

General observations

As of July 10 2022, 70 directly relevant studies listed under the key words vitamin D and hip fractures published since July 1 2021 were examined. Among those articles of current interest articles that appeared pertinent to fulfilling the present review aims were duly accessed and carefully reviewed.

These data, although limited in number and design, and quite diverse as a whole on assessment tended to show that vitamin D status, if low, tends to be associated with an increased hip fracture risk and a poorer recovery among many in the older population. In addition, the presence of vitamin D at adequate serum concentrations appears to influence bone as well as muscle health in many cases with impaired health status as well as osteoporosis.

Thus, although disputed by some,¹⁰ it seems hard to refute a more general prevailing consensus that vitamin D is an important vitamin and co-factor for fostering bone mass, and may be an especially important nutrient to target in efforts directed towards preventing excess bone loss leading to hip fragility fractures in the elderly, thus offering clinicians a promising and low-cost strategy for reparative osteogenesis as well as falls prevention as summarized below.

Specific observations

As outlined briefly above, several diverse studies conducted over time have shown variations as to whether vitamin D is of high import in the realm of bone metabolism, as well playing a more established role in hip fracture prevention and recovery processes. However, as per Rizzoli et al.,¹¹ recommended general measures to counter fragility fractures include insuring the presence of vitamin D sufficiency. This idea appears reasonable given that as per Neale et al.,¹² even in a sunny country like Australia sufficient numbers of falls and hip fractures are attributable to a vitamin D deficiency in the affected older adults. Current research further reveals that vitamin D combined with calcium reduces the risk of hip fracture although on its own may not exhibit tangible effects but this could reflect the nature of available studies.¹³ Yet, a role for high-dose vitamin D after hip fracture is associated with lower declines of function and mortality associated with this fracture site, although the presence of cardiovascular disease reduces this protective effect.¹⁴ It has been noted that older adults presenting with incident hip fractures had vitamin D serum levels that were correlated with bone mineral density and bone content, as well as functional ability and balance. Those deemed deficient had a higher age adjusted hip fracture risk, especially for women.¹⁵

Another 2021 report found preoperative severe vitamin D deficiency to be a significant independent risk factor for poorer functional outcome and quality of life 6 months after surgery for fragility hip fractures.¹⁶ This was not surprising given that hip fractures are common in the elderly, and many of these patients may well have low vitamin D levels. This may be an important generalizable finding to some degree that indicates a possible need to routinely evaluate vitamin D levels among those older adults, especially those with any presiding severe vitamin D deficiency, and to do all that is possible to prevent a poorer recovery process than desirable¹⁶ and where up to 9% may have a severe vitamin D deficiency and 39%, a mild deficiency.

In another study, Lim et al.,¹⁷ who conducted a retrospective study designed to compare a vitamin D deficient group and a vitamin D sufficient group and assess the association of preoperative vitamin D deficiency and postoperative walking ability after hip fracture surgery found the mean postoperative validated KOVAL functional recovery score in the deficient group appeared to be significantly higher than in the vitamin D sufficient group. As well, vitamin D deficiency was significantly associated with a higher risk of delirium and pneumonia in the deficiency group. As such it was concluded that it appears necessary to evaluate the preoperative vitamin D level and recommend vitamin D supplementation in the older adult patient with a high probability of hip fracture.¹⁷

Thorpe et al.,¹⁸ concluded that without combined supplementation of both vitamin D and calcium, female vegans are at high risk of

hip fracture and this aspect of research warrants more study given that it does seem that low serum vitamin D levels in the older adult population are associated with an increase in the odds of incurring a hip fracture¹⁹ as well as poor post-operative outcomes²⁰ even if vitamin D deficiency is not associated with mortality, bacterial infection or delirium after hip fracture surgery.

From another perspective, a report by Ginsberg et al.,²¹ recently showed the vitamin D metabolite ratio is associated with changes in bone density and fracture risk in older adults. Moreover, in future research the incorporation of this vitamin D measure may reveal previously unidentified or obscured associations as far as fractures and bone loss goes. This conclusion was based on evidence that among a diverse cohort of community-dwelling older adults, a lower vitamin D ratio measure was more strongly associated with both the loss of bone mineral density as well as fracture risk. However, a completely contrary possibly unexpected observation was that a study conducted over three years showed the highest 3-year survival and the lowest mortality in the studied cohort appeared in those cases with pre-fracture serum 25-hydroxyvitamin D levels of 50-74 nmol/L. This result thus differed from similar studies and is lower than the recommended level of 25-hydroxyvitamin D among hip fracture patients.²² The authors suggested these results should be examined in future research with a larger data set.

Vaculik et al.,²³ have shown that baseline serum levels of vitamin D or calcitriol levels tended to be lower than those of total hip arthroplasty cases undergoing similar surgeries. Moreover, after seven weeks, these levels decreased significantly in those with hip fractures. Seven weeks after sustaining a hip fracture, a significant positive relationship was observed between the change in calcitriol-a man made form of vitamin D and serum vitamin D concentrations and free vitamin D, such that a decrease in calcitriol during recovery was associated with the presence of a low availability of free vitamin D. The implications of these observations were not totally clear though. However, it seems reasonable to suggest that some forms of hip fracture in older populations that are often not treated for possible osteoporotic risk²⁴ may derive some independent or collective benefit from vitamin D supplementation as far as reducing hip fracture incidence rates as well as mortality rates or further fractures post hip fracture surgery in vulnerable older adults.²⁴⁻²⁸

In combination with silicon a recent basic study has revealed some degree of vitamin D influence on bone structure restoration and improved calcium absorption that appears to offer a possible avenue for enhancing bone related regeneration and that may prove valuable to examine further in the realm of hip fracture prevention and that is supported by human clinical evidence,²⁹⁻³² even though its presence may not impact number of falls or injurious falls that often lead to hip fractures.³³ However, there are multiple contrary study findings as well as multiple design problems that remain in this body of research, even though more favorable potentially relevant clinical findings prevail than not.^{34, 36-40}

Discussion

Hip fractures, which remain a high priority concern to avert and treat successfully, have been the subject of research for several decades. Often associated with an elevated risk of multi morbidity, possible subsequent hip and other bone fractures, pain, loss of independence and enormous medical and social costs, the slow recovery rates in survivors as well as the possible increase in hip fracture prevalence among frail elders of high ages, demand this line of inquiry be continued. Indeed, over time, not only have minimal preventive advancements been advanced to any meaningful widespread degree,

but among other controversies related to vitamin D in this regard, has produced inconsistent results at best.

This current status of discord is often surprising to encounter because although not conclusive, it appears that a deficient vitamin D intake, sunlight exposure, and related vitamin D deficiency or lack of availability can be shown to have a discernable impact on bone health, as well as on muscle function and health in general, yet was shown to have more favorable outcomes when subnormal in a cohort of hip fractures followed prospectively.

As well, osteoporosis and falls injuries found to often accompany hip fracture injuries in the absence of adequate vitamin D are not uncommon,³⁴ and appear to impact bone health in the frail or obese older adult to a high degree, especially in those cases already vitamin D compromised.³⁶ This injury is especially problematic and essential to prevent because of those primary hip fracture cases that survive, the majority will become seriously impaired functionally and a fair percentage remain at risk for second hip fractures.

By contrast, efforts to limit or prevent osteoporosis and improve muscle function attributable to vitamin D,⁴⁰ while raising vitamin D levels to physiologically beneficial levels through supplementation where needed, which has been observed to be safe for cases who are deficient is now possibly more important than ever, because the prevalence of this debilitating injury rises exponentially with age, a state associated with declining bone mineral density and content levels that may be injurious in their own right and fail to afford protection against even minimal forms of perturbation.²⁶ At the same time, some studies recently reviewed imply that depression, an established falls risk factor, might be mitigated in some cases by supplementation combined with physical activity to provide effective results, and that supplementation is less effective than vitamin D supply from food sources that may need to be acknowledged,⁴¹ while another shows a high deficiency rate of 75 percent in recent hip fracture cases.²⁶ As in the bulk of the literature on this topic, it was observed that studies reviewed were conducted in diverse populations and followed various doses and intervals of administration, so the results may be incomparable. Jeopardized too may be the rehabilitation process, as well as the ability to avert secondary bone fracture injuries, especially if the sufferer is malnourished and in great pain.

As a result, and until more careful study to explain competing and conflicting results begins to emerge and that are not duly compromised by suboptimal research design flaws, it is our view that the importance of continued vigilance against preventable hip fractures, both primary and secondary, which may include the need for vitamin D supplementation should not be neglected, or overlooked in the context of the delivery of evidence driven care. In this regard, it appears that alone or in combination with physical activity, the presence of adequate vitamin D may yet limit the degree of age-associated bone attrition, muscle weakness and limited mobility or falls risk as well as high mortality rates that can additively produce one or more devastating osteoporotic hip fractures. Indeed, a recent anatomically oriented hip fracture study⁴² led the researchers to stress the view that subjects with hip fractures should not only receive careful education and medication as indicated, but should be carefully monitored, as there are differences according to anatomical location of the fracture that could impact treatment desirability and recovery of subjects presenting with first time hip fractures.

Unfortunately, despite the need, very few studies have emerged of late to advance this field, or that could be defined as meeting desired 'gold' standards for supporting or rejecting any vitamin D-hip fracture hypothesis. Even though these issues have been raised for some

time, a sizeable number of currently available studies continue to be fragmentary at best and employ flawed, or no controls, or adequate size well defined samples. In addition, varied modes of defining vitamin D, interpreting and assessing vitamin D presence and efficacy, unknown effects of health and co-morbidity status, body mass measures, other interventions, variations in fracture type, diets, food availability, and fracture severity commonly persist. Thus, as has been documented in the past, the quest to provide solid quantifiable directives that could be uniformly harnessed for reducing the immense suffering of the older adult who incurs and survives an incident hip fracture remains unfulfilled.

As such, and in light of the burgeoning aging populations, with older adults many living to high ages, it appears evident there is arguably a great need to pursue all lines of inquiry in this regard methodically and comprehensively without any undue delay, if one seeks the best evidence science can provide to guide cogent and valid objective directives for medical practice and public health purposes that can then be delivered and evaluated on a global scale.

In the interim, since mechanistic studies are largely indicative of multiple and important bone associated vitamin D linkages, as, as are increasing numbers of studies showing an association between muscle attributes and vitamin D presence, the evaluation and supplementation of vitamin D as indicated appears strongly warranted in primary and post hip fracture preventive efforts, as implied by several current authors,^{26,44,45} although discounted by some.^{9,43} As well, since it seems this body of clinical research that has emerged from the knowledge base to date is more promising than not, even if this is only due to publication bias. it also appears that more might be done to translate what is shown into practice on an individualized basis in the context of post fracture preventive efforts in light of the immense importance of reducing the prevalence of second or third hip fractures,⁴⁶ and mortality rates⁴⁷ along with higher rates of disability than those cases experiencing single hip fractures, which alone is substantive.⁴⁸

Needed in terms of research however, are both consortia as well as funders willing to support the desired magnitude and scope of effort required to ensure success, including the use of some agreed upon standard procedures, sampling strategies, and outcome measures, plus long term follow up studies of well defined samples of hip fracture subgroups of various ages, and of various degrees of health, located in diverse geographic, institutional, community and cultural venues and locations. Until then, and in light of the growing number of older adults worldwide, and the fact that many already suffer from multiple health issues and frailty as well as obesity and bone fragility, hip fracture prevalence rates are yet more likely to rise, rather than fall over time, even though pharmacologic strategies have yielded some protective benefits for some time.

As well, it appears plausible to hypothesize that until some consensus is reached in general about how to prevent hip fractures, public health and social costs will escalate along with immense suffering for many. In contrast, and subject to careful well designed study with emphasis on what is measured, and for how long in varied samples, researchers could yet be able to rule out currently competing conclusions and feel more confident to intervene in the hip fracture disability cycle in a timely way, thus offering a practical passageway to reducing current and anticipated human as well as public health related costs.

Meantime, and based on what we do know, it appears reasonable to encourage hip fracture preventive program organizers and those who work with the older adult not to overlook the utility of ensuring their vulnerable elderly clients are able to obtain foods that foster

the presence of consistently adequate vitamin D serum levels, and/or make these or supplements available, if necessary. Educators and care givers of the elderly can be especially helpful in this often neglected realm in this regard in our view by carefully expounding upon the importance of maintaining adequate vitamin D serum levels since these may be implicated in numerous essential physiological processes, including bone and muscle maintenance, and directing these older adults accordingly. The possible utility of combining a number of other bone building elements and vitamin D in the context of hip fracture prevention, such as walking in the sunlight for brief periods, should also be discussed further, along with implications of vitamin D presence as far as the interaction of poor neuromuscular and cognitive functions goes as well as its role in calcium absorption and bone metabolism that can clearly mediate or exacerbate the risk of incurring one or more hip fractures as envisioned in Figure 1.

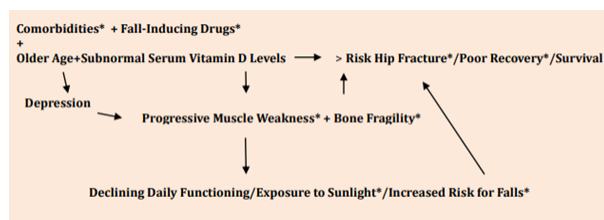


Figure 1 Points at which vitamin D or a lack thereof may influence the hip fracture risk cycle [Key reference sources: 3, 6, 11, 12, 16, 17].

Conclusion

Based on an in depth examination of the research published over the last year, it is clear:

- 1) Hip fractures, which produce high levels of mortality and morbidity remain a major challenge to treat, and prevent despite multiple laudable programs to address this issue, most commonly by targeting multiple factors considered to heighten hip fracture risk.
- 2) Despite much attention to the role of bone quality in this regard, efforts to safely promote bone mineral density remain limited.
- 3) Although, the current 2021-2022 literature fails to provide convincing evidence as whether vitamin D can uniquely foster a favorable protective role against excess bone attrition in the vulnerable older adult, especially those suffering from bone fragility and poor balance or those who have recently incurred a hip fractures and undergone surgery.
- 4) Even if not considered by some to be relevant in efforts to address hip fracture risk and recovery, vitamin D research, which remains largely limited, has possible merit that warrants further careful study.

Indeed, since no single ‘magic bullet’ or ‘cure’ has been developed to counter hip fracture disability to any meaningful degree in more than 30 years or more, it is possible that some advancement can yet be made among those older adults at risk for frailty and osteoporosis, as well as second hip fractures by exploring all avenues of vitamin D and its osteogenic potential.

Acknowledgements

None.

Conflicts of interest

The authors declare they have no conflicts of interest that are directly or indirectly related to the research.

Funding

None.

References

1. Emmerson BR, Varacallo M, Inman D. Hip Fracture Overview. In: StatPearlsTreasure Island (FL): Stat Pearls Publishing. 2022.
2. Ferris H, Brent L, Sorensen J. Cost of hospitalisation for hip fracture-findings from the Irish hip fracture database. *Osteoporos Int.* 2022;11:1–9.
3. Liow MHL, Ganesan G, Chen JDY, et al. Excess mortality after hip fracture: fracture or pre-fall comorbidity? *Osteoporos Int.* 2021;32(12):2485–2492.
4. Fu TS, Huang TS, Sun CC, et al. Impact of bisphosphonates and comorbidities on initial hip fracture prognosis. *Bone.* 2022;154:116239.
5. McCarthy CJ, Kelly MA, Kenny PJ. Assessment of previous fracture and anti-osteoporotic medication prescription in hip fracture patients. *Ir J Med Sci.* 2022;191(1):247–252.
6. Ravensbergen WM, Blom JW, Kingston A, et al. TULIPS consortium. Declining daily functioning as a prelude to a hip fracture in older persons—an individual patient data meta-analysis. *Age and Ageing.* 2022;51(1):afab253.
7. Fischer H, Maleitzke T, Eder C, et al. Management of proximal femur fractures in the elderly: current concepts and treatment options. *Eur J Med Res.* 2021;26(1):86.
8. Iuliano S, Poon S, Robbins J, et al. Effect of dietary sources of calcium and protein on hip fractures and falls in older adults in residential care: cluster randomised controlled trial. *BMJ.* 2021;375:2364.
9. Montero Odasso MM, Kamkar N, Pieruccini-Faria F, et al. Task Force on Global Guidelines for Falls in Older Adults. Evaluation of clinical practice guidelines on fall prevention and management for older adults: a systematic review. *JAMA Netw Open.* 2021;4(12):e2138911.
10. Lai SW. Risk factors for hip fracture. *Osteoporos Int.* 2021;32(12):2599.
11. Rizzoli R, Biver E, Brennan-Speranza TC. Nutritional intake and bone health. *Lancet Diabetes Endocrinol.* 2021;9(9):606–621.
12. Neale RE, Wilson LF, Black LJ, et al. Hospitalisations for falls and hip fractures attributable to vitamin D deficiency in older Australians. *Br J Nutr.* 2021;126(11):1682–1686.
13. Chakhtoura M, Bacha DS, Gharios C, et al. Vitamin D supplementation and fractures in adults: a systematic umbrella review of meta-analyses of controlled trials. *J Clin Endocrinol Metab.* 2022;107(3):882–898.
14. Koutalos AA, Chalatsis GI, Varsanis G, et al. The effect of zoledronic acid and high-dose vitamin D on function after hip fractures. *A prospective cohort study Eur J Orthop Surg Traumatol.* 2021;10.
15. Skuladottir SS, Ramel A, Eymundsdottir H, et al. Serum 25-hydroxy-vitamin D status and incident hip fractures in elderly adults: looking beyond bone mineral density. *J Bone Miner Res.* 2021;36(12):2351–2360.
16. Sim DS, Tay K, Howe TS, et al. Preoperative severe vitamin D deficiency is a significant independent risk factor for poorer functional outcome and quality of life 6 months after surgery for fragility hip fractures. *Osteoporos Int.* 2021;32(11):2217–2224.
17. Lim C, Roh YH, Kim S, et al. Preoperative vitamin D deficiency is associated with postoperative functional recovery and complications after hip fracture surgery. *J Bone Metab.* 2021;28(4):333–338.

18. Thorpe DL, Beeson WL, Knutsen R, et al. Dietary patterns and hip fracture in the Adventist Health Study 2: combined vitamin D and calcium supplementation mitigate increased hip fracture risk among vegans. *Am J Clin Nutr*. 2021;114(2):488–495.
19. Habibi Ghahfarokhi S, Mohammadian Hafshejani A, Sherwin CMT, et al. Relationship between serum vitamin D and hip fracture in the elderly: a systematic review and meta-analysis. *J Bone Miner Metab*. 2022;40(4):541–553.
20. Dauny V, Thietart S, Cohen-Bittan J, et al. Association between Vitamin D deficiency and prognosis after hip fracture surgery in older patients in a dedicated orthogeriatric care pathway. *J Nutr Health Aging*. 2022;26(4):324–331.
21. Ginsberg C, Hoofnagle AN, Katz R, et al. The vitamin D metabolite ratio is associated with changes in bone density and fracture risk in older adults. *J Bone Miner Res*. 2021;36(12):2343–2350.
22. Nurmi Lũthje I, Tihihonen R, Paattiniemi EL, et al. Relatively low and moderate pre-fracture serum 25-hydroxyvitamin D levels associated with the highest survival in elderly hip fracture patients in Finland: a minimum 3-year follow-up. *Osteoporos Int*. 2022;33(3):611–621.
23. Vaculik J, Wenchich L, Bobelyak M, et al. Decrease in serum calcitriol (but not free 25-hydroxyvitamin D) concentration in hip fracture healing. *J Endocrinol Invest*. 2021;44(9):1847–1855.
24. Bugeja M, Curmi A, Desira D, et al. Hip fractures in Malta: are we missing an opportunity? *Surg J (N Y)*. 2021;7(3):184–190.
25. Valle CARD, Pedri LAF, Pires GB, et al. Influence of hypovitaminosis D on the occurrence of fractures. *Rev Bras Ortop (Sao Paulo)*. 2021;56(6):784–789.
26. Or O, Fisher Negev T, Hadad V, et al. Fracture Liaison Service for hip fractures: is it a game changer? *Isr Med Assoc J*. 2021;23(8):490–493.
27. Guerra MTE, Wagner M, Vargas A, et al. Low serum levels of vitamin D significantly increase the risk of death in older adults with hip fractures: a prospective cohort. *Rev Col Bras Cir*. 2022;49:e20223054.
28. Chevalley T, Brandi ML, Cavalier E, et al. How can the orthopedic surgeon ensure optimal vitamin D status in patients operated for an osteoporotic fracture? *Osteoporos Int*. 2021;32(10):1921–1935.
29. Bychkov A, Koptev V, Zaharova V, et al. Experimental testing of the action of vitamin D and Silicon Chelates in bone fracture healing and bone turnover in mice and rats. *Nutrients*. 2022;14(10):1992.
30. Borojević A, Jauković A, Kukulj T, et al. Vitamin D3 stimulates proliferation capacity, expression of pluripotency markers, and osteogenesis of human bone marrow mesenchymal stromal/stem cells, partly through SIRT1 Signaling. *Biomolecules*. 2022;12(2):323.
31. Reid IR. Bone-friendly lifestyle and the role of calcium or vitamin D supplementation. *Climacteric*. 2022;25(1):37–42.
32. Bouillon R, Manousaki D, Rosen C, et al. The health effects of vitamin D supplementation: Evidence from human studies. *Nature Rev Endocrinol*. 2022;18(2):96–110.
33. Bischoff Ferrari HA, Freystätter G, Vellas B, et al. Effects of vitamin D, Omega-3 fatty acids, and a simple home strength exercise program on fall prevention: the DO-HEALTH randomized clinical trial. *Am J Clin Nutr*. 2022;115(5):1311–1321.
34. Kong SH, Jang HN, Kim JH, et al. Effect of Vitamin D supplementation on risk of fractures and falls according to dosage and interval: a meta-analysis. *Endocrinol Metab (Seoul)*. 2022;37(2):344–358.
35. Pilz S, Trummer C, Theiler-Schwetz V, et al. Critical appraisal of large vitamin D randomized controlled trials. *Nutrients*. 2022;14(2):303.
36. Amphansap T, Wongthanakitcharoen P, Stitkitti N, et al. Prevalence and risk factors of vitamin d inadequacy among thai elderly patients with osteoporotic hip fracture. *J Southeast Asian Med Res*. 2022;6:e0110.
37. Liu H, Wang G, Wu T, et al. Efficacy and safety of Eldecacitol for osteoporosis: a meta-analysis of randomized controlled trials. *Front Endocrinol (Lausanne)*. 2022;13:854439.
38. Abe S, Kashii M, Shimada T, Suzuki K, et al. Relationship between distal radius fracture severity and 25-hydroxyvitamin-D level among perimenopausal and postmenopausal women. *Bone Jt Open*. 2022;3(3):261–267.
39. Helynen N, Rantanen L, Lehenkari P, et al. Predisposing factors for a second fragile hip fracture in a population of 1130 patients with hip fractures, treated at Oulu University Hospital in 2013-2016: a retrospective study. *Arch Orthop Trauma Surg*. 2022.
40. Yoo JI, Chung HJ, Kim BG, et al. Comparative analysis of the association between various serum vitamin D biomarkers and sarcopenia. *J Clin Lab Anal*. 2021;35(9):e23946.
41. Guzek D, Kolota A, Lachowicz K, et al. Association between Vitamin D supplementation and mental health in healthy adults: a systematic review. *J Clin Med*. 2021;10(21):5156.
42. Dinamarca Montecinos JL, Vásquez Leiva A, Durán Agüero S, et al. Vitamin d and its relation with the anatomical location of hip fracture in chilean older adults hospitalized. *Nutr Hosp*. 2015;32(6):2777–82.
43. Yao P, Bennett D, Mafham M, et al. Vitamin D and calcium for the prevention of fracture: a systematic review and meta-analysis. *JAMA Netw Open*. 2019;2(12):e1917789.
44. Chang CB, Yang RS, Chang LY, et al. One-year outcomes of an osteoporosis liaison services program initiated within a healthcare system. *Osteoporos Int*. 2022;32(11):2163–2172.
45. Bouillon R, Manousaki D, Rosen C, et al. The health effects of vitamin D supplementation: Evidence from human studies. *Nature Rev Endocrinol*. 2022;18(2):96–110.
46. Schemitsch E, Adachi JD, Brown JP, et al. Hip fracture predicts subsequent hip fracture: a retrospective observational study to support a call to early hip fracture prevention efforts in post-fracture patients. *Osteoporos Int*. 2021.
47. Hjelholt TJ, Johnsen SP, Brynningsen PK, et al. Development and validation of a model for predicting mortality in patients with hip fracture. *Age and Ageing*. 2022;51(1):afab233.
48. Barry ML, Maday KR. Reviewing acute hip fractures in adults. *J Am Acad PAs*. 2021;34(9):1–0.