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Commentary

Hip Fractures and Vitamin D: 2021-2022

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Abstract

The elderly adult in all parts of the globe remains vulnerable to sustaining one or more hip fractures in their life time. Long considered to have a somewhat plausible, albeit unproven role in mitigating hip fracture injuries and debilitating outcomes, more recent reports shed new light on this possible adjunctive intervention where vitamin D levels are compromised. Reviewed are articles published between February 2021, and February 2022, where most imply an association of clinical relevance.

Introduction

Hip fractures, which are mostly injury derived, rather than pathologically derived pose an extremely serious and ongoing public health problem as well as excessive personal costs to the older adult, even if they survive surgery or the injury, in general [1,2]. As well as affecting various degrees of disability, and immense hardships for many, these negative hip fracture outcomes, along with persistent post hip fracture surgical mortality rates that remain high will probably continue to ensue for some time to come in light of the numbers of older adults living to higher ages [3], and especially in the face of COVID-19 social isolation impacts [4], and the fact that most patients who sustain a hip fracture will have significant co-morbid health conditions, and may also suffer from cognitive impairments to a high degree [2], and with excess peri-operative

complications and adverse outcomes in the presence of COVID-19 [5]. Moreover, those who survive surgery and incur excess disability may have a high risk of incurring a subsequent second or third hip fracture, especially if they have self-management challenges and others, such as following instructions or having to remain socially isolated in response to pandemic public health rulings. Indeed, factors contributing to the unrelenting numbers of older adults sustaining a hip fracture currently include but are not limited to osteoporosis, depression, and falls injuries that all imply there may be some approaches that can be harnessed readily to avert this highly deleterious crisis among the elderly [6], especially if there are persistent service restrictions. Of specific interest is thus regard, include approaches that might not only attenuate if not completely eliminate hip fracture risk and injury, but can also foster better bone health, cognitive health, immunity, falls injuries and sarcopenia [6,7]. To this end, this narrative overview highlights the most recent publications and their findings as regards vitamin D, a controversial realm of inquiry, but one with some observations that may yet prove clinically relevant.

The focus here on vitamin D, a fat soluble vitamin is not novel and has been pursued for some time, and is a one either absorbed into the skin in the presence of sunlight and converted to an active form thereafter, or ingested as a nutrient analogue. However, where its presence occurs at an insufficient level (25(OH)D < 50nmol/l (i.e., 20ng/mL)) or a deficient level (25(OH)D < 25nmol/l (i.e., 10ng/mL), the likelihood of fragility fractures is raised significantly and especially in those many elderly who sustain COVID-19 and/or one or more chronic health conditions. Thus even though the evidence on the effects of vitamin D deficiency and/or vitamin D supplementation on fracture healing and material osseointegration is still limited, and frequently discordant, it appears that vitamin D would be expected to have a positive influence on several physiological processes essential to bone and neuromuscular health, including its possible benefit on muscle strength, bone mass, balance and immune system functioning [8-10].

As well, in addition to evidence that COVID-19 is an independent risk factor for hip fracture mortality, mounting evidence shows taking a vitamin D supplement to maintain a serum concentration of 25(OH)D of at least 30ng/mL (preferred range 40-60ng/mL), can help reduce the risk of COVID-19 and its severe outcomes, including mortality [11]. In parallel research it is also evident that inadequate serum vitamin D levels are increasingly being linked to common chronic conditions that heighten hip fracture risk, such as depression, dementia, frailty, and poor cardiovascular health [9], thus providing more support than not for the importance of not neglecting to consider efforts to routinely assess prevailing levels of serum vitamin D among older adults at risk for hip fracture, as well as those who have sustained a hip fracture, and are recovering and intervening as indicated.

Methods

After searching the **PUBMED, GOOGLE SCHOLAR**, and **Web of Science Consolidated** databases to identify works published predominantly from February 1 2021-February 28 2022, items discussing either some relevant hip fracture statistic as well as articles related to Vitamin D and hip fractures and hip fracture determinants were sought and carefully examined.

The search was limited however, by excluding studies prior to 2021 and those that currently did not directly address the present topic of interest. All forms of study that were deemed acceptable were classified as

representing basic information about hip fractures, vitamin D and its influence in the realm of hip fracture risk factors, and studies directly examining or reviewing vitamin D in the context of hip fractures directly.

Results

General

The current literature search revealed 87 **PUBMED** articles [of a possible 2572 discussing hip fractures and 5346 vitamin D related articles] using: Hip fracture and Vitamin D. However, almost half of the 87 articles listed on **PUBMED** for the years of February 2021-February 2022, and even among the 41 articles listed on **Web of Science** only some were relevant, while many were unrelated to this present discourse. Those listed on Google Scholar were generally represented in **PUBMED** or the **Web of Science**. As a whole, and despite any possible bias favoring the publication of articles with positive conclusions, most current reports that were deemed salient appeared to show persistently high rates of hip fracture mortality, and a linkage between this risk and the patient's pre fracture health status [12,13], as well as multiple post fracture factors that may implicate vitamin D [14]. See summary findings in below.

Hip Fractures

Among the salient articles published recently that pertain to hip fractures and their ongoing challenges are those listed in Table 1.

Table 1: *Snapshot of current relevant hip fracture investigations*

Gong *et al.* [15]	By 2050 the number of fractures in people older than 65 years in China is predicted to be 1.3 million
Galivanche *et al.* [5]	Hip fracture cases diagnosed as having COVID-19 have worse outcomes after hip fracture than COVID-19 negative patients
Kawaji *et al.* [16]	Hip fractures especially trochanteric fractures in super-aged females increased. 2006-2016
Lorentzon *et al.* [17]	Hip fragility fractures caused by osteoporosis raise the risk for increased morbidity and mortality
Meyer *et al.* [18]	Hip fracture incidence has declined across the Swedish population, but mortality after hip fracture remained high especially among men Hip fractures patients constitute a vulnerable population group with increasing comorbidity burden and high mortality risk Data obtained from 1987-Dec 2017 records
Park *et al.* [19]	Type 2 diabetes increases hip fracture risk
Schemitsch *et al.* [20]	Hip fracture predicts subsequent hip fractures
Shimizu *et al.* [21]	Frailty predicts adverse hip fracture outcomes
Zhang *et al.* [22]	Nationwide data indicate the prevalence of hip fractures in the elderly is generally on the rise

Vitamin D

Key findings indicate vitamin D is related to bone health, dementia, acute respiratory infections, fractures, frailty [23-27].

To optimize bone health among those older adults with poor sunlight exposure or access to vitamin D containing foods, use of a vitamin D supplement of 400-1000 IU/day should be considered [28].

Hip Fractures and Vitamin D

A summary of most of the current conclusions reached by authors as regards observations linking vitamin D to some aspect of hip fracture is shown in Table 2.

Table 2: *Showing a representative sample of recent hip fracture reports discussing vitamin D associations (2021-2022)*

Authors	Sample + Methodology	Key Finding
Bischoff Ferrari [29]	Review	Several randomized intervention trials, comparing 800-1000 IU vitamin D/day versus placebo or calcium, showed a significant reduction in falls and hip fractures in adults ≥65 years of age who had an increased risk of vitamin D deficiency and of falls or fractures
Arshad *et al.* [30]	Retrospective study of Pakistan hip fracture cases with low impact/past fractures-average age 73 yrs	Among those screened, all had low vitamin D levels, even if they previously took supplements
Chevalley *et al.* [10]	Narrative review	Vitamin D appears to benefit fracture healing
Li *et al.* [31]	Meta analysis and meta regression	Vitamin D_3 (700–800IU/d) plus calcium showed statistical significance in reducing the incidence of total, hip and non-vertebral fractures in the pairwise meta-analysis. Significant reductions were specifically identified in females in total and hip fractures
Ginsberg *et al.* [32]	Predictive study	The vitamin D metabolic ratio if low might predict low bone mass and fracture risk
Giordano *et al.* [33]	Comparative study of 180 hip or vertebral fracture patients	Patients of the same age with severe osteoporosis have a lowered vitamin D value when the fracture occurs at the hip and is recent
Hershkovitz *et al.* [34]	Retrospective study of 493 hip fracture cases	Routine screening for vitamin D post-acute hip fracture is essential

Ingstad *et al*. [35]	Registry review followed by logistic regression	Low vitamin D at admission for hip fracture increased delirium risk, a new fracture, and medical readmissions Those receiving 1000.000 IU of vitamin D in a single dose had fewer 30 day surgical complications
Jamal *et al*. [36]	Cross sectional study of men and women with inter trochanteric fracture	There is a strong correlation between the degree of vitamin D deficiency and type of inter trochanteric fracture
Lim *et al*. [37]	Prospective study of elderly hip fracture patients	Pre-operative vitamin D deficiency increased hospital length of stay and reduced functional recovery
Mahmood *et al*. [38]	Multicentre observational study of 1633 hip fracture cases	There was a potential association of decreasing vitamin D levels and increasing mortality rates for COVID-19 positive patients who had higher mortality rates than non COVID-19 cases
Scragg *et al*. [39]	Meta analysis of 4 vitamin D fortification trials	Vitamin D supplementation may have beneficial effects on intermediate outcomes such as spine bone mineral density and hips in vitamin D deficient cases
Sim *et al*. [40]	Retrospective analysis of 664 hip fractures 2012-2016	Severe preoperative vitamin D deficiency was an independent risk factor for poorer functional recovery and life quality after hip fracture surgery
Seshadri *et al*. [41]	Long-term prospective observational study of calcium and vitamin D supplementation	Regular supplementation reduced fracture risk, as well as mortality
Skuladottir *et al*. [8]	Prospective analysis of hospital records	Deficient versus sufficient serum vitamin D yielded higher hip fracture risk
Thorpe *et al*. [41]	Retrospective study of survey data	Almost 8% of hospitalizations for hip fracture were linked to low vitamin D levels
Valle *et al*. [42]	Cross sectional observational fracture oriented study	Fracture injuries were commonly found to be associated with low vitamin D levels
Yu *et al*. [43]	Retrospective analysis of 268 hip fragility fracture patients	Vitamin D deficiency was common, especially among the female patients
Zhao *et al*. [44]	Cross-sectional study of 90 older women with hip fractures	Compared to a control group, vitamin D was shown to be a key factor predicting hip fracture

As outlined in the above highlighted and current body of research, and which represents a high percentage of available publications listed on **PUBMED** and the additionally reviewed electronic data bases over the time periods February 2021-2022 these tend to imply vitamin D is a potentially relevant and possibly noteworthy factor in explaining hip fracture incidence, severity, and outcomes. It also appears there is some support for considering vitamin D supplementation among vulnerable older adults, in the event food associated vitamin D intake or sunlight exposure produces insufficient serum vitamin D levels, especially in the realm of: 1) primary and secondary fracture prevention efforts [29,45,46], 2) minimizing post-operative hip fracture surgery mortality risk, while maximizing recovery efforts, especially intermediate outcomes such as hip bone mineral density in vitamin D deficient cases [39] and walking or functional ability [47], fewer surgical complications, new fractures, or medical readmissions [35] and life quality [40] given the possible direct impact on either severe preoperative vitamin D deficiency [40] and/or the reactive depletion of prevailing vitamin D levels due to the inflammation caused by the fracture and/or surgical intervention [33]. Moreover, even though disputed in a meta analysis conducted by Chakhtoura *et al*. [48], these authors point to other evidence showing that vitamin D does appear to play a critical role in musculoskeletal health [48] and its common deficiency in older adults is a strong hip fracture correlate [49] that increases the length of hospital stays and reduces functional recovery [37]. Accordingly, a meta analysis by Bischoff-Ferrari concluded that in the realm of the geriatric 'at risk' older adult suffering from a vitamin D deficiency, implementing vitamin D supplementation of 800-1000IU per day is yet strongly recommended for purposes of minimizing falls and hip fracture risk and injury [29]. The current impact of low vitamin D serum levels and COVID-19 risk, an independent hip fracture mortality correlate as well as a potent fracture risk factor also warrants attention [8,38,41,44].

Indeed, most prevailing 2021-2022 published articles remain favorable to the idea that a sufficient vitamin D level is beneficial to the health status of older adults, and by analogy to a lower risk of fragility or osteoporotic hip fractures in post menopausal women [45]. Hence, in addition to its possible wide ranging health benefits, vitamin D supplementation is strongly recommended for protecting older vulnerable adults during this persistent pandemic period of social isolation by those wishing to mitigate fragility fractures, infections and pulmonary dysfunction [50], while reducing hip fracture mortality outcomes as well as hip fracture risk [51]. Other evidence suggests attention to resolving this current lack of consistent vitamin D associated impacts despite years of study should still assume a high research priority for purposes of advancing geriatric well-being and care, as well as for delineating sound evidence based clinical and post surgical hip fracture initiatives and practices. This is because, apart from the persistent risk of fragility fractures, and their high mortality rates observed among older hip fractures patients, many who survive may yet develop an additional or secondary fragility fracture [52].

Discussion

One of the most pervasive problematic health issues facing older adults is the fact they are often highly prone to falls and falls injuries, bone mass deficits, muscle weakness, and cognitive challenges that can threaten their very existence. However, according to Zhao *et al*. [44] vitamin D along with femoral neck bone mineral density and height are significantly associated with the occurrence of hip fractures in elderly women even after adjustment for confounding factors. Other evidence implies exposure to vitamin D-in sufficient quantities may greatly help to mitigate one or more hip fracture determinants such as low bone

mineral density or mass or both, thus possibly limiting the extent of low energy fractures that commonly produce adverse outcomes [10]. As well, the post-surgical use of vitamin D supplements, although not discussed by Kim *et al*. [1], but where indicated, appears to offer the possibility of more favorable bone repair than its absence [10]. Accordingly, these latter authors called for routine assays of vitamin D in the context of bone fracture services, a call supported by Lim *et al*. [37] in both the post and pre surgical contexts, even if not concluded by Chakhtoura *et al*. [49].

Factors that might impact the presence of vitamin D negatively include:

- Malnutrition
- Poor nutrition [42,53]
- Lack of sunlight exposure
- No supplement usage/irregular usage
- Limited calcium usage/presence [49]

At the same time, a failure to routinely test for and remediate lower vitamin D levels in a timely manner may be an additional hip fracture determinant, especially if a present deficiency is reversible and is affecting bone as well as muscle function in some way [54]. However, since confusion still reigns in this regard, it seems reasonable to proceed with caution and to only advocate vitamin D supplementation if this is clearly indicated.

To advance this line of inquiry, it is possible that efforts to collate data from all available historic records, studies employing multiple research designs, diverse samples, and vitamin D status definitions will be helpful.

Until then, despite the lack of any solid consensus, it appears the most up to date literature on vitamin D shows its deficiency can have enormous ramifications for the older adult and may predictably result in immense excess personal as well as societal health costs and increases in hospitalization rates due to excess ground level falls incurred by the elderly [54], as well as osteoporotic fractures [12]. For example, by starting to simply target older adults and their families and health providers, and especially identifying older adults at high risk for vitamin D deficits early on in adult life, including those who have previously suffered from hip fractures, it appears that when all factors are considered the delivery of vitamin D to recovering hip fracture patients may impact both mortality, as well as desired functional outcomes favorably [46], and may provide benefits as far as fostering bone mineral density through its timely and appropriately targeted fortification [39] and its apparent ability to boost the Alendronate tail effect on bone density in osteoporotic women [55]. This includes those suffering from multiple co-morbid health conditions, and providing these adults all necessary resources to offset any vitamin D deficiency in the future [10]. In particular, as discussed by Downey *et al*. [56], since the number of fragility hip fractures in adults 60 years of age or older is estimated to triple or quadruple by 2050, with an estimated global cost of hip fractures in the year 2050 of $ 130 billion [57], the possible favorable role of vitamin D supplements in mitigating this to some degree, as indicated, must surely warrant widespread consideration.

In this regard, individuals living in the community and who might benefit most are-

- Those who are sedentary with mobility problems
- Those with multiple co-morbid health conditions
- **Previous fallers/those who previously fractures a hip** [30]
- Those who live alone/and don't venture out of doors
- Frail adults older than 80 years of age [58]
- Those who are **depressed**
- Those who are weak and deemed to have fragile bones [30]

To this end, carefully tailored prevention programs are strongly indicated, even if these are only able to produce modest bone building benefits, as well as possible reductions in COVID-19 infection rates, fragility fractures, and lower post surgical complications [See Figure 1].

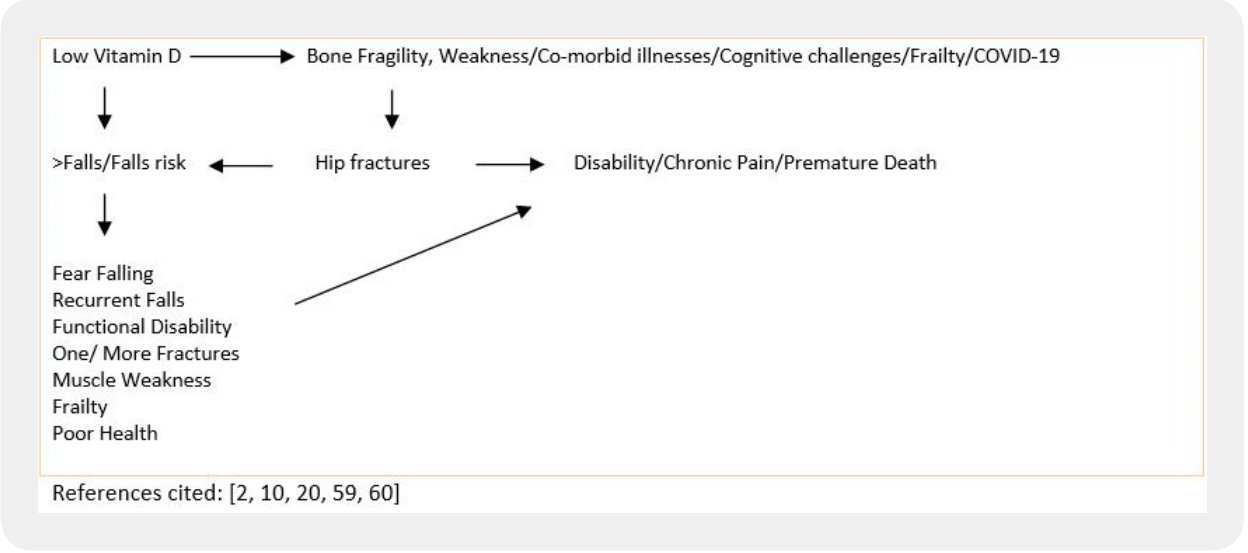

Figure 1: *Hypothetical interactions of vitamin D, in the context of the risk of hip fractures among older community dwelling adults and in face of the persistent COVID-19 pandemic*

In sum, despite obvious limitations to the above discourse such as its focus solely on data for the past year derived from various observational studies and others, and the fact the quality of the evidence may be lower than desired, and may not include a broad enough spectrum of adults who have suffered hip fractures during the pandemic period, vitamin D and its association with hip fracture risk and recovery clearly warrants further study.

In particular, a clear exploration of the role of sunlight, diet, and exercise and vitamin D serum levels on bone health and bone healing across the lifespan is highly recommended and may yield far reaching benefits.

Conclusions

On the basis of this snapshot of the past years' hip fracture/vitamin D publications we conclude:

- Many hip fracture cases are found to have deficient serum vitamin D levels.
- Early screening and possible vitamin D supplementation should be considered for at risk older adults living in the community.
- Restoring or helping hip fracture patients to maintain a sufficient vitamin D level is likely to be beneficial in multiple ways.
- More research to examine this issue remains desirable.

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