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Severe vitamin D deficiency in Swiss hip fracture patients

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Abstract

Background: Most clinical guidelines for the prevention of hip fractures recommend 800 IU vitamin D per day. This dose shifted serum 25-hydroxyvitamin D levels (25(OH)D) in previous studies to between 60 and 100 nmol/l.
Aim: To measure 25(OH)D levels and prevalence of vitamin D supplementation in individuals age 65+ with acute hip fracture.
Methods: 222 consecutive hip fracture patients were investigated over a 12 month period. Mean age of patients was 86 years and 77% were women.
Results: Mean serum 25(OH)D levels were low among hip fracture patients admitted from home (34.6 nmol/l), from assisted living (27.7 nmol/l), and from nursing homes (24 nmol/l). Severe vitamin D deficiency below 30 nmol/l was present in 60%, 80% were below 50 nmol/l, and less than 4% reached desirable levels of at least 75 nmol/l. Consistently, only 10% of hip fracture patients had any vitamin D supplementation on admission to acute care with significantly higher 25(OH)D levels among individuals supplemented with 800–880 IU/day (63.5 nmol/l). Controlling for age and gender, vitamin D supplementation, type of dwelling, and season were independently and significantly associated with 25(OH)D levels.
Conclusion: These data provide evidence that current guidelines for the prevention of hip fractures need further effort to be translated into clinical practice.

Keywords: Hip fracture; 25-hydroxyvitamin D; Elderly; Guideline practice

Introduction

Fractures contribute significantly to morbidity and mortality of older individuals. Among individuals age 60 years and older, the mortality-adjusted residual lifetime risk of fracture has been estimated to be 44–65% for women and 25–42% for men [1]. After age 75, hip fractures are the most frequent fractures with up to 50% of older individuals having permanent functional disability, 15 to 25% requiring long-term nursing home care and up to 20% dying within the first year after the event [2–4]. The exponential increase in hip fractures after age 75 translates into an estimated 1 in 3 women, and 1 in 6 men who will have sustained a hip fracture by their 9th decade [5]. With the aging of the population a world-wide increase in hip fractures has been projected [6]. For Switzerland, a 33% increase in hip fractures has been estimated from 2000 to 2020 [7].

Given the high frequency of falls and fractures at older age plus future demographic changes with a significant increase of the older segment of the population, well tolerated and inexpensive prevention strategies are needed. For vitamin D, there is evidence today that with a daily intake of 800 IU vitamin D about one fourth of all first hip and any first non-vertebral fractures could be prevented [8]. In addition, addressing the primary risk factor of hip fractures, recent short- and long-term trials with vitamin D found a significant

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35–65% reduction in fall risk among community-dwelling and institutionalized individuals provided with a daily dose of 700–800 IU vitamin D [9–12].

These data are the basis of several guidelines recommending at least 800 IU vitamin D per day for the primary prevention of low-trauma fractures among older individuals. For fall and non-vertebral fracture prevention, the Swiss guidelines for the prevention of osteoporosis recommend 800 IU vitamin D among older individuals with limited sun exposure [13]. The National Osteoporosis Foundation (NOF) recommends 800–1000 IU vitamin D per day in adults starting at age 50 [14]. This recommendation was based on a quasi-consensus of vitamin D experts reviewing the evidence on bone health, fracture, and fall prevention with vitamin D [15]. Based on the available evidence, 5 out of the 6 experts proposed that if older men and women maintain serum levels of 25(OH)D that are higher than 75 nmol/l, they will be at lower risk of fracture [15]. The International Osteoporosis Foundation (IOF) supported this recommendation in 2006 under consideration of recent evidence [16]. Extending from bone health to fall prevention, function, dental health, and colo-rectal cancer prevention, a recent review on optimal serum 25(OH)D levels recommended a threshold of at least 75 nmol/l and suggested a minimal intake of 1000 IU vitamin D per day in all adults age 20 and older [17].

In this study we aim to evaluate guideline practice in Zurich, Switzerland by assessing 25(OH)D status among consecutive patients age 65 and older admitted to one large hospital center with acute hip fracture. Provided guideline practice is in place, mean 25(OH)D levels of at least 50–60 nmol/l would be expected for a vitamin D intake between 400 and 800 IU per day [15,17–19].

Methods

Patients

From January 2005 to January 2006 consecutive patients age 65 and older admitted to one large hospital center in Switzerland (Zurich, Triemli Hospital) with acute hip fracture were assessed for their serum 25(OH)D levels. All patients were of Caucasian race/ethnicity. Assessment of 25(OH)D serum concentrations was approved by the ethics committee of the town hospitals as a quality control assessment in hip fracture care. There were no exclusion criteria other than age less than 65 years. We documented age, gender, month of serum 25(OH)D measurement, and type of dwelling prior to admission in all patients. In addition, on admission to acute care, we documented vitamin D intake and dose from the following sources: vitamin D supplement, combination with calcium, combination with bisphosphonates, multivitamin. In Switzerland dairy products or orange juice is not fortified with vitamin D as practiced in the US. A recent multi-center survey of 401 Swiss community-dwelling older individuals age 75–87 years documented a mean vitamin D intake of 99.6 IU (SD+58) per day based on a validated food frequency questionnaire [20]. Generally, supplements or multivitamins include cholecalciferol (D3) in Switzerland, while ergocalciferol (D2) is not commonly available. None of the hip fracture patients was on anti-epileptics, and diseases associated with malabsorption, such as Whipple, Crohn's disease, and colitis ulcerosa, were not noted in the medical reports of patients.

25(OH)D measurements

All blood tests for serum 25(OH)D measurement were taken during acute care within 2–6 days after the hip fracture event. Serum for 25(OH)D assessment was stored at −80 °C and all measurements were performed in one batch, in April 2006. 25(OH)D serum levels were measured with a radioimmuno assay (Diasorin/Inkstar RIA; sensitivity 1.5 μg/l; coefficient of variation 8.4%). All measurements were performed by the same technician in one batch at the laboratory of the University Hospital in Zurich.

Statistics

We present unadjusted means for 25(OH)D levels by type of dwelling, season, and vitamin D supplementation group according to the supplemental intake ranges documented (none, 200–440, 800–880) in Table 1. In addition, general linear models were used to calculate least square means (adjusted means) for serum 25(OH)D levels by subgroups while controlling for age, gender, type of dwelling (home, assisted living, and nursing home), season (spring, summer, fall, and winter), and vitamin D supplementation (none, 200–440 IU per day, 800–880 IU per day). Estimated serum 25(OH)D concentrations are based on the same model. SAS version 9.1 was used for all statistical analyses.

Results

Over the course of 12 months, we assessed 222 consecutive older individuals age 65 or older admitted to one large hospital center for their serum 25(OH)D concentrations. Mean age of individuals was 85.7 years and 63% were admitted from home, 22% from assisted living, and 15% from nursing homes.

Mean serum 25(OH)D levels were 31.5 nmol/l in the total group, 34.6 nmol/l in hip fracture patients admitted from home,

Table 1
Characteristics of patients with acute hip fracture and absolute 25(OH)D serum concentrations by subgroups

Characteristics	Home *N*=139 (63%)	AL *N*=50 (22%)	NH *N*=33 (15%)	Total *N*=222
Men: *N* (%)	26 (19%)	14 (28%)	12 (36%)	52 (23%)
25(OH)D nmol/l	34.3 (±20.7)	25.0 (±17.2)	27.9 (±20.2)	30.3 (±19.8)
Women: *N* (%)	113 (81%)	36 (72%)	21 (64%)	170 (77%)
25(OH)D nmol/l	34.7 (±22.9)	28.7 (±26.5)	21.8 (±19.0)	31.8 (±23.8)
Mean age years (±SD)	84.2 (±6.7)	89.1 (±6.3)	86.8 (±6.4)	85.7 (±6.9)
25(OH)D nmol/l	34.6 (±22.4)	27.7 (±24.2)	24.0 (±19.3)	31.5 (±22.7)
<30 nmol/l: *N* (%)	70 (50%)	36 (72%)	25 (76%)	131 (59%)
30–74 nmol/l: *N* (%)	64 (46%)	11 (22%)	7 (21%)	82 (37%)
75+ nmol/l: *N* (%)	5 (4%)	3 (6%)	1 (3%)	9 (4%)
25 (OH)D nmol/l by season				
Spring	26.8 (±17.4)	28.3 (±24.1)	9.5 (±1.9)	25.0 (±18.9)
Summer	36.8 (±21.6)	34.1 (±36.4)	28.9 (±24.4)	34.6 (±26.0)
Fall	42.4 (±24.9)	27.0 (±16.5)	24.8 (±17.6)	37.0 (±23.7)
Winter	31.2 (±21.7)	23.0 (±16.2)	25.4 (±17.6)	28.5 (±20.1)
Percent of individuals with severe 25(OH)D deficiency (<30 nmol/l) by season				
Spring	64%	70%	100%	70%
Summer	43%	62%	73%	54%
Fall	41%	67%	67%	49%
Winter	55%	83%	75%	64%
No vitamin D: *N* (%)	122 (88%)	47 (94%)	30 (91%)	199 (90%)
25(OH)D nmol/l	31.3 (±20.3)	25.5 (±22.6)	20.2 (±15.8)	28.2 (±20.6)
200–440 IU/d: *N* (%)	6 (4%)	2 (4%)	1 (3%)	9 (4%)
25(OH)D nmol/l	52.6 (±14.6)	50.1 (±18.2)	63.0 (±- -)	53.2 (±13.8)
800–880 IU/d: *N* (%)	11 (8%)	1 (2%)	2 (6%)	14 (6%)
25(OH)D nmol/l	61.7 (±26.3)	87.3 (±- -)	61.5 (±3.2)	63.5 (±24.1)

27.7 nmol/l in patients admitted from assisted living, and 24 nmol/l in patients admitted from nursing homes (see Table 1; ANOVA for type of dwelling: $p=0.02$). Severe vitamin D deficiency below 30 nmol/l was present in 50% of hip fracture patients admitted from home, in 72% from assisted living situations, and in 76% from nursing homes (see Table 1 and Fig. 1). 10% of hip fracture patients had any vitamin D supplementation on admission to acute care: 4% had 200–440 IU vitamin D, and 6% had 800–880 IU vitamin D per day (none of the 222 patients had vitamin D intakes between 441 and 799).

Table 2 shows the adjusted mean serum 25(OH)D levels among subgroups of individuals not supplemented and supplemented with vitamin D. Supplement users had significantly higher serum 25(OH)D levels while controlling for type of dwelling, season, age, and gender.

Fig. 2 shows mean serum 25(OH)D levels by month over 12 months. Despite a clear seasonal swing, mean 25(OH)D levels were far below desirable 25(OH)D concentrations of 75 nmol/l or higher, even during summer months (see Table 1; ANOVA by season: $p=0.03$). Comparing the most extreme seasons, spring versus summer season, 25(OH)D levels were 26% higher in the summer independent of other covariates (Table 2).

Fig. 3 illustrates the relative contribution of season and additional vitamin D supplementation of 800 to 880 IU vitamin D per day based on estimated serum 25(OH)D concentrations from the multivariate general linear model shown in Table 2.

Discussion

In this sample of 222 consecutive hip fracture patients age 65 and older admitted to acute care of one large hospital center between January 2005 and January 2006, 10% had any vitamin D supplementation, and 6% had the recommended dose of 800 IU per day according to guideline recommendations. Consequently, 25(OH)D serum concentrations were low in all subgroups with a high prevalence of severe vitamin D deficiency (<30 nmol/l) in 50% of individuals admitted from home, 72% of individuals admitted from assisted living, and 76% of individuals admitted from nursing homes. Our findings indicate that current guidelines on vitamin D supplementation for the prevention of hip fractures in older individuals are not sufficiently practiced.

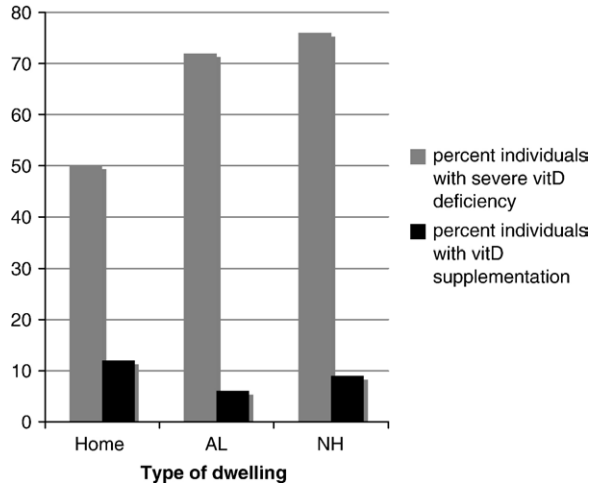

Fig. 1. Percent of hip fracture patients with severe vitamin D deficiency and percent of hip fracture patients with any vitamin D supplementation on admission to acute care. Illustrates the documented high prevalence of severe vitamin D deficiency (25(OH)D<30 nmol/l) in older patients admitted for acute hip fracture care. Consistent with these findings is the very low prevalence of any vitamin D supplementation in these patients documented on admission to acute care independent of type of dwelling.

Table 2
Independent predictors of 25(OH)D serum concentrations in patients with acute hip fracture

Independent predictors	Adjusted means (+SE)	Adjusted percent difference from reference (*p*-value)
Vitamin D supplementation		
None (reference)	25.8 (1.7)	Reference
200–440 IU/day	48.3 (7.0)	+87% (0.002)
400–880 IU/day	60.6 (5.6)	+135% (<0.0001)
Type of dwelling		
Nursing home (reference)	39.1 (4.5)	Reference
Assisted living	45.5 (4.1)	+17% (0.16)
Home	50.1 (3.2)	+28% (0.006)
Season		
Spring (reference)	39.7 (4.5)	Reference
Summer	50.0 (4.1)	+26% (0.02)
Fall	48.7 (3.7)	+23% (0.04)
Winter	41.2 (3.7)	+4% (0.7)

Adjusted means are calculated from least square means derived from a general linear model controlling for age, gender, vitamin D supplementation, type of dwelling, and season. Age and gender did not significantly predict serum 25(OH)D concentrations.

Based on intervention studies, mean serum 25(OH)D levels in a vitamin D supplemented older population would be expected to be at least 50–60 nmol/l with a daily dose of 400 to 800 IU vitamin D3 [17]. This rise is likely to be less with vitamin D2 [21–23], which is, however, not commonly available in Switzerland. In this sample of consecutive hip fracture patients mean 25(OH)D levels were about half the minimum mean expected if guideline practice was in place and findings were similar among individuals admitted from home, assisted living or nursing homes. On the other hand, the small percentage of individuals supplemented with vitamin D upon admission to acute care reached the expected minimum mean of 50.1 nmol/l in all subgroups if supplementation was 200–440 IU vitamin D per day, or a minimum mean of at least 61.5 nmol/l with 800–880 IU vitamin D per day.

Adjusted means for 25(OH)D levels were 87% higher with supplementation between 200 and 440 IU vitamin D per day and 135% higher with supplementation between 800 and 880 IU vitamin D per day. Regression analyses suggested that 800 IU vitamin D per day may shift hip fracture patients to between 52 and 62 nmol/l in the spring (seasonal low), and to between 63 and 74 in the summer depending on type of dwelling.

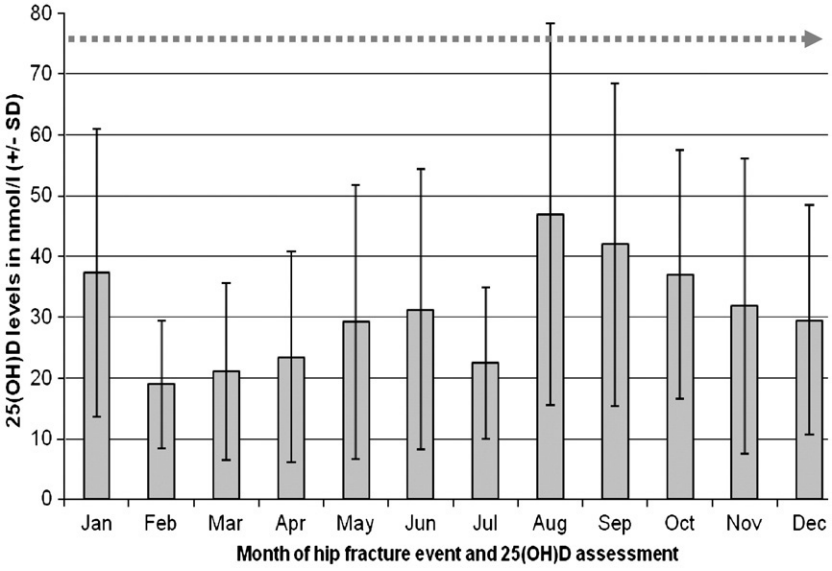

Fig. 2. Absolute 25(OH)D serum concentrations by month of measurement. Shows absolute mean 25(OH)D serum concentrations by month of measurement suggesting a seasonal swing with highest levels achieved in late summer and fall whereas lowest levels are achieved in spring months. Both, mean 25(OH)D levels of summer months (June, July, August: p-value=0.02), and fall months (September, October, November: p-value=0.01) differed significantly from spring levels (March, April, May). The arrow indicates the threshold for adequate vitamin D status at 75 nmol/l. Mean 25(OH)D levels measured for each month were far below adequate 25(OH)D status. See Table 1 for the percent of individuals with severe vitamin D deficiency by season and type of dwelling.

In this study, winter time declines, spring lows, and end summer highs in 25(OH)D levels were present in all subgroups of hip fracture patients. This seasonal pattern has been observed in previous studies of healthy older individuals in Switzerland [24,25], Boston [26], and Stockholm [27], as well as nursing home residents in Canada [28]. In regard to hip fracture patients, our data contradict earlier findings from one Australian study, where a seasonal swing of 25(OH)D levels was not documented in hip fracture patients admitted from nursing homes, while healthy older adults did show a seasonal swing of 25(OH)D levels in the same study [29].

Previously, among Swiss community-dwelling older individuals (mean age 76) without a hip fracture, prevalence of severe deficiency was 15% and 30% had desirable 25(OH)D levels of at least 75 nmol/l during summer season [25], while in our study, prevalence of severe deficiency was 43% and desirable

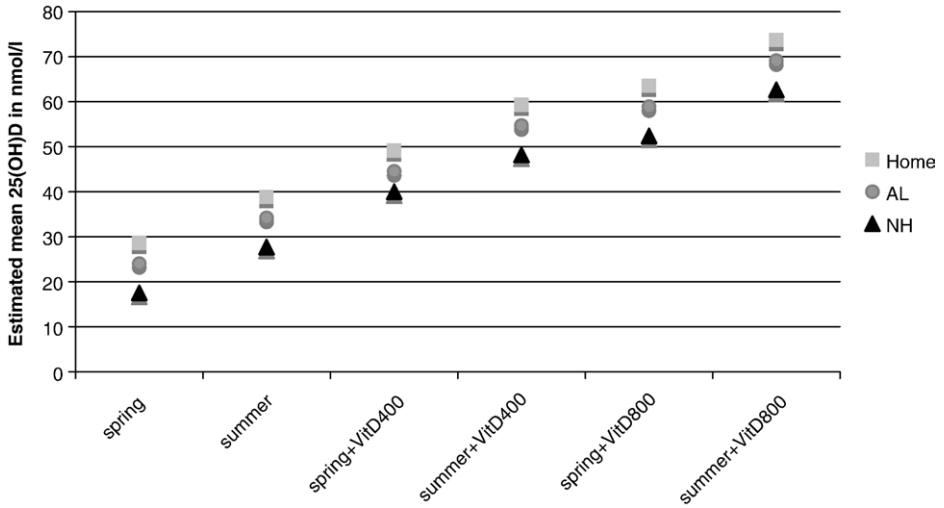

Fig. 3. Estimated 25(OH)D levels in extreme seasons with and without additional vitamin D supplementation. Estimated 25(OH)D levels are based on a general linear regression model illustrated in Table 2. Season, vitamin D supplementation, and type of dwelling were independent and significant predictors for 25(OH)D serum concentrations while controlling for age and gender. Fig. 2 shows the strong additional benefit of vitamin D supplementation on estimated serum 25(OH)D concentrations in older individuals with acute hip fracture. Independent of type of dwelling, summer sunshine exposure is insufficient to raise 25(OH)D levels into a desirable range of 75 nmol/l or higher among hip fracture prone older individuals. 800 IU vitamin D per day during the seasonal high (summer) may shift estimated mean levels into the desirable range of at least 75 nmol/l. Low dose vitamin D (200–440 IU per day) may be insufficient in rising 25(OH)D levels into the desirable range even during the summer season.

25(OH)D levels were documented among 4% of community-dwelling individuals admitted with an acute hip fracture in the same season. This difference may be explained in part by older age in the hip fracture patients, as cutaneous vitamin D production declines with age [30]. Additionally, individuals at risk for a hip fracture are generally frailer and less mobile, and thus may have spent less time outside [31]. However, it is important to note that even in the healthier population studied previously only 30% of community-dwelling older individuals reached desirable 25(OH)D levels during summer time [25].

A 1999 landmark publication in the Journal of the American Medical Association (JAMA) by LeBoff et al. documented a 50% prevalence of severe vitamin D deficiency among postmenopausal women admitted with acute hip fracture (serum 25(OH)D levels <30 nmol/l) [32]. The authors suggested in 1999 that heightened awareness is necessary to ensure adequate vitamin D nutrition, especially as vitamin D deficiency is preventable. The high prevalence of severe vitamin D deficiency among hip fracture patients has been confirmed in the early and late nineties by several studies from Europe [33–41]. According to our data collected in 2005–2006, the prevalence of severe 25(OH)D deficiency is still significant and basically unchanged compared to earlier data [17–26].

A limitation of this analysis is its cross-sectional design. On the other hand, consecutive patients of the largest center hospital in Zurich, have been studied. The urban setting would add to a bias for better care. Thus, the presented results may be conservative. A strength of the study is the assessment of seasonality plus living situation as additional important determinants of 25(OH)D status in hip fracture patients. Adding to a conservative estimate, vitamin D for the prevention of hip fractures is primarily prescribed by physicians and covered by insurance companies in Switzerland, which should improve guideline practice compared to countries where vitamin D supplementation is primarily sold over the counter, such as in the US. On the other hand, nursing homes in Zurich have a per day medication cost limitation, which may contribute to the low prescription rate of vitamin D in individuals admitted from nursing homes, although the cost for vitamin D is low. Finally, we chose the most widely used vitamin D assay (Diasorin Assay) allowing for direct comparison with studies from the literature, where the serum 25(OH)D threshold of at least 75 nmol/l has been suggested with respect to function [42], bone density [43], and fracture risk [8] among older individuals.

In summary, our study indicates that further efforts are needed to improve guideline practice for the prevention of hip fractures in Switzerland. A 10% prevalence of vitamin D supplementation in hip fracture patients is insufficient and consistent with the documented 59% rate of severe vitamin D deficiency. In this frail population, 25(OH)D levels were low throughout the year despite a seasonal swing with somewhat higher levels at the end of the summer season. Thus, year-long vitamin D supplementation is warranted in individuals at risk for hip fracture. According to our analyses, desirable serum 25 (OH)D concentrations of at least 75 nmol/l among older individuals at risk for hip fracture may only be achieved during the summer season with additional 800 IU vitamin D per day. In the winter season, 800 IU vitamin D may not be sufficient to raise serum 25(OH)D levels into the desirable range.

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