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ORIGINAL RESEARCH

SEASONAL VARIATION IN VITAMIN D STATUS AMONG FRAIL OLDER HOSPITALIZED PATIENTS

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Abstract: *Background and objectives:* Seasonal variation in 25-hydroxyvitamin D [25(OH)D] levels is the result of sunlight dependent skin synthesis of vitamin D. However, its presence is not studied in frail older hospitalized patients. We sought to investigate whether seasonal variation in 25(OH)D levels is evident among these patients. *Design and setting:* This study investigated older participants who were consecutively admitted between February 2015 and December 2016 to the geriatric acute care ward. Results of routine measurements of 25(OH)D at hospital admission were retrospectively analyzed and stratified according to months and seasons. Previous intake of vitamin D supplementation was derived from the patients' medical records. *Results:* The study group comprised 679 participants (mean age 82.1±8.2; 457 females), of which 78% had vitamin D deficiency. Older individuals not taking vitamin D supplements had a lower mean serum 25(OH)D than those receiving supplements. Of those patients with no vitamin D supplementation, 87.0% were vitamin D deficient and only 5% showing sufficient vitamin 25(OH)D. Further, there were neither monthly nor seasonal variations in vitamin 25(OH)D levels among these patients and their vitamin D levels stayed far below the recommended threshold of 20 ng/ml across the seasons. *Conclusion:* Vitamin D deficiency was very prevalent in the subgroup of older hospitalized patients without vitamin D supplementation, irrespective of season. Since no seasonal variations in mean 25(OH)D levels was observed, sunlight dependent skin synthesis is unlikely to contribute to vitamin D status in these patients. Supplementation seems to be necessary to maintain desirable vitamin D levels among this population throughout the year.

Key words: Vitamin D deficiency, seasonal variation, vitamin D supplementation, frailty.

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Introduction

Body stores of vitamin D as estimated by serum concentration of 25-hydroxyvitamin D [25(OH)D] are influenced by several factors such as seasonal variation of ultraviolet (UV) B exposure, time outdoor, clothing, the latitude upon the globe, nutritional vitamin D intake and supplementation (1, 2). It is estimated that more than 80% of human vitamin D is synthesized in the skin, depending on adequate UV radiation and only a very minor proportion is ingested with food in healthy subjects (3, 4). It is well recognized that in older individuals, average serum concentration of 25(OH)D is low due to multiple mechanisms which consist of insufficient sun exposure as a result of decreased mobility, reduced skin thickness and diseases (5). Beside these factors, malnutrition, changes of nutritional intake and avoidance of dairy products and fish may also contribute to suboptimal vitamin D status among this population. In older patients, vitamin D deficiency is a risk factor for neuromuscular decline and is associated with increased bone loss, falls and fractures (6, 7). In recent times, due to rising awareness about the adverse consequences of vitamin D deficiency on skeletal muscle strength and other health outcomes, need for recommendation of vitamin D intake has increased. Several previous cross-sectional studies have demonstrated that 25(OH) D levels vary by vitamin D intake in older people (8, 9). Further, meta-analysis of randomized controlled trials among older individuals has indicated that the risk of falls reduced by 14% (odds ratio, 0.86; 95% confidence interval, 0.77-0.96) in the group supplemented with vitamin D (10).

Epidemiological studies have indicated that within Europe, vitamin D deficiency is prevalent in the community dwelling older population irrespective of geographic location (11). The results of that study have demonstrated that among 824 older people aged >70 year from 11 European countries, 36% of males and 47% of females had serum 25(OH)D concentration <30 nmol/L during winter (11). The strength of solar radiation, as the main source of vitamin D, varies substantially over the year due to changing angle of the sun (12), reaching to the highest point in late summer and to the lowest point in late winter (2, 13). Although seasonal variations in 25(OH) D concentration have been addressed in several studies in older patients with or without disability and across different countries and latitude (14-19), this is not studied in a subgroup of population at increased risk for vitamin D deficiency such as frail older hospitalized patients. It would be worthwhile to understand the impact of sun radiation on 25(OH)D levels to extend our knowledge concerning the contribution of radiation-induced vitamin D synthesis in skin among this population.

Therefore, this study sought to investigate whether monthly

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and seasonal variation in serum concentration of 25(OH)D is evident among frail older hospitalized patients during 2 years, particularly in those not receiving vitamin D supplementation. We hypothesize the lack of seasonal variations in 25(OH)D levels in this patient group which would confirm the irrelevance of a radiation dependent skin synthesis and the need of oral intake among this population.

Methods

Participants

This cross-sectional study retrospectively analyzed the results of routine measurements of serum 25(OH)D of 679 older patients who were consecutively hospitalized between February 2015 and December 2016 to a geriatric acute care ward at Marien-Hospital, Herne, Germany. Serum vitamin 25(OH) D concentrations in each month and outcomes of the routine geriatric assessment were obtained from the local patient database. The study protocol had been approved by the ethical committee of Ruhr-University Bochum.

Serum vitamin 25(OH)D concentrations

The measurements were performed at time of hospital admission with an electro-chemiluminescence immunoassay (ECLIA) on Cobas 8000 (e602), Roche, Mannheim, Germany. The patients were classified into three diagnostic categories according to their serum vitamin 25(OH)D concentrations suggested by Endocrine Society (20): deficiency (levels <20 ng/ml), insufficiency (levels 20 to 29.99 ng/ml) and desirable (levels of 30 ng/ml or higher). In addition, seasons were determined according to meteorological seasons (21): spring (March, April and May), summer (June, July and August), autumn (September, October and November) and winter (December, January and February). Further, previous intake of vitamin D supplementation was derived from the patients' medical records.

Geriatric Assessment

Full results of the geriatric assessment were available in a subgroup of 358 older patients. Mini Nutritional Assessment Short Form (MNA-SF) (22) was used to identify nutritional status and subjects were stratified as malnourished (0-7 points), at risk of malnutrition (8-11 points) and having normal nutritional status (12-14 points). The range of the German version of the Barthel-Index is 0-100 pts., with 100 pts. indicating independency in all activities of daily living (23, 24). Mini Mental State Examination (MMSE) (25) and the 15 item Geriatric Depression Scale (GDS-15) (26) were assessed as described in the literature. All assessments were performed soon after hospital admission.

Data analysis

The statistical analysis was performed with SPSS statistical software (SPSS Statistics for Windows, IBM Corp, Version 23.0, Armonk, NY, USA). Continuous variables are reported by their means and standard deviations (SDs) for normally distributed variables and median values with interquartile ranges (IQR) were expressed for non-normally distributed data. Categorical variables are expressed as absolute numbers and relative frequencies (%). A group comparison was performed using the t-test for continuous data with normal distribution, the Mann-Whitney U test for continuous variables with non-normal distribution and Pearson Chi-square test for categorical variables. Comparison of mean vitamin 25(OH) D concentrations within consecutive months and within each season was performed by using one-way ANOVA Tukey's post hoc test. A *P*-value of <0.05 was considered as the limit of significance.

Results

Baseline characteristics of study participants stratified by different serum vitamin 25(OH)D concentrations are described in Table 1. The study group comprised 679 participants, predominantly females (67.3%), with a mean age of 82.1 ± 8.2 (age range between 61 and 99 years). Median Barthel-Index and MMSE were 40 pts. and 24 pts., respectively, representing frail older hospitalized patients. According to MNA-SF, 48.9% of patients were considered to be at risk of malnutrition and 48.6% were malnourished. In total, the average 25(OH)D serum level was 12.4 ng/ml (range, 0-70 ng/ml). The proportion of vitamin D deficiency, insufficiency and desirable were 78.0, 10.0 and 12.0%, respectively.

The highest value of vitamin 25(OH)D level was in May (15.1 ± 10.8 ng/ml) and the lowest value in October (10.5 ± 10.5 ng/ml). However, the difference was not statistically significant (P=0.730) and even changes in vitamin 25(OH) D levels in the other months showed much less variation. In addition, the overall vitamin D deficiency according to seasonal categorization were 76.0, 81.0, 78.0 and 77.0% in spring, summer, autumn and winter, respectively. There were no seasonal (P=0.649) and monthly (P=0.874) variations in mean serum levels of vitamin 25(OH)D in total population (data not shown).

Figure 1
Serum 25-hydroxyvitamin D [25(OH)D] concentration according to vitamin D supplementation in total population (n=679). The solid line is the regression line

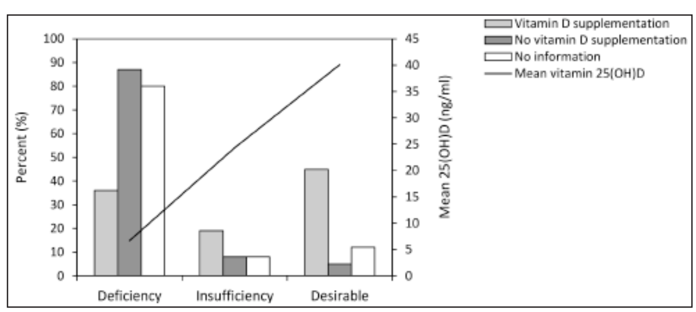


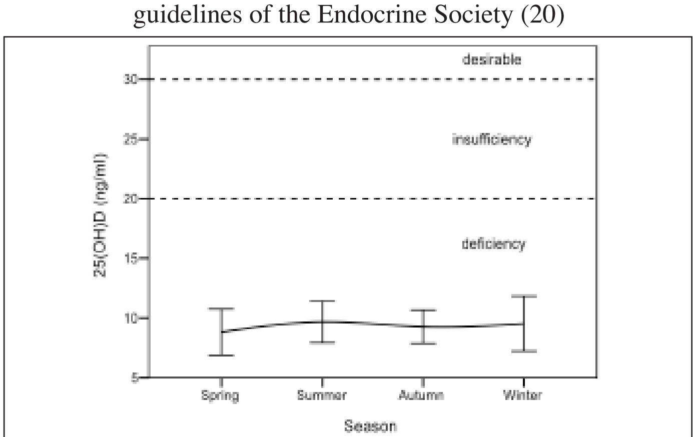
Table 1
Characteristics of study participants stratified according to different serum 25(OH)D levels

	All	Deficiency (<20 ng/ml)	Insufficiency (20 - 29.99 ng/ml)	Desirable (≥30 ng/ml)	P value
Total, N (%)	679 (100)	531 (78.0)	66 (10.0)	82 (12.0)	
Female, N (%)	457 (67.0)	343 (75.0)	50 (11.0)	64 (14.0)	0.072
Male, N (%)	222 (33.0)	188 (85.0)	16 (7.0)	18 (8.0)	
Age, years	82.1 ± 8.2	81.8 ± 8.2	82.8 ± 6.9	83.1 ± 8.7	0.308
Weight, kg	70.5 ± 17.6	71.7 ± 17.6	66.6 ± 15.1	66.4 ± 14.4	0.011
Vitamin 25(OH)D, ng/ml	12.4 ± 13.0	6.7 ± 5.4	24.3 ± 3.1	40.1 ± 9.8	<0.001
25(OH)D supplementation +, N (%)	115 (16.9)	42 (36.0)	22 (19.0)	51 (45.0)	
25(OH)D supplementation -, N (%)	503 (74.1)	440 (87.0)	39 (8.0)	24 (5.0)	<0.001
No information, N (%)	61 (9.0)	49 (80.0)	5 (8.0)	7 (12.0)	
Barthel-Index, pts.	40 (30-50)	40 (30-50)	45 (35-50)	40 (30-50)	0.598
MMSE, pts.	24 (20-27)	24 (20-27)	25 (22-27)	23 (20-26)	0.109
GDS-15, pts.	3 (2-3)	3 (2-3)	3 (1-4)	2 (0-3)	0.233
MNA-SF, pts.	8 (6-9)	8 (6-9)	8 (6-10)	9 (5-9)	0.159

25(OH)D supplementation +, previous 25(OH) supplementation; 25(OH)D supplementation -, no previous 25(OH) supplementation; MMSE, Mini-Mental-State-Examination; GDS-15, 15-item geriatric depression scale; MNA-SF, Mini-Nutritional-Assessment short form; Values are given as number (%), mean ± SD or median (interquartile range). Weight was measured in a subgroup of 586 patients and MMSE, GDS, MNA-SF and Barthel-Index were measured in a subgroup of 358 patients.

Compared with the patients not receiving supplementation, those on supplementation had significantly higher serum vitamin 25(OH)D concentrations (26.8 ± 15.4 ng/ml vs 9.3 ± 10.1 ng/ml, P<0.001; Figure 1). In addition, of the older patients who reported not taking vitamin D supplement and of those who reported taking supplement, 87.0% and 36.5% had vitamin D deficiency, respectively (P<0.001; Fig.1). However, duration of vitamin D supplementation was unspecified in the latter group.

Figure 2
Distribution of seasonal mean serum concentrations of 25-hydroxyvitamin D [25(OH)D] among a subgroup of patients not taking supplementation (n=503). 95% confidence intervals (CI) are shown by error bars. Dotted lines reflect the threshold of vitamin 25(OH)D deficiency (<20 ng/ml), insufficiency (20 to 29.99 ng/ml) and desirable (≥30 ng/ml), according to the guidelines of the Endocrine Society (20)



To compare the results of mean vitamin 25(OH)D production in response to sunlight exposure, we also analyzed the data by comparing the seasonal vitamin D levels among a subgroup of 503 patients not taking vitamin D supplement. As shown in Figure 2, the values found in any given season did not differ significantly from the values in any other season (P=0.933). In addition, there were also no statistically significant differences in vitamin 25(OH)D concentrations when comparing consecutive months among this group (P=0.641).

Discussion

In the present study, we found that 78% of frail older hospitalized patients demonstrated vitamin D deficiency and only 12% showed sufficient vitamin 25(OH)D levels, which suggests that vitamin D deficiency is clinically underdiagnosed in this population. In addition, older persons taking vitamin D supplements had a higher mean serum 25(OH)D concentrations than those not receiving supplements. However, in a supplemented group, just 45% showing adequate vitamin D status which might reflect the insufficient dosage or duration of vitamin D therapy. Our findings are consistent with a study among 123 Portuguese hospitalized patients in Internal Medicine (mean age 71 years), in which 92.7% had vitamin D deficiency and only 7.3% demonstrated levels >20 ng/ml (27). Further, a previous study in older females acute medical admissions (aged 65> years) indicated that despite the recommended vitamin D supplementation, majority of patients remained deficient (28).

Seasonal variations in 25(OH)D concentration have been well addressed in several prior studies in community-dwelling and homebound older patients and across different countries and latitude (14-19). However, to the best of our knowledge, this is the first study to report the seasonal variation in mean 25(OH)D levels among frail older hospitalized patients. In this group, we found no evidence of monthly or seasonal variability in mean 25(OH)D levels among a subgroup of patients not consuming supplement whereas their vitamin D levels stayed far below the threshold of 20 ng/ml across the season. Our findings may put the role of radiation dependent skin synthesis of vitamin D into perspective among this population. The results of our study are in agreement with the findings of a study in 143 community dwelling middle age and older females (mean age of 61 years) with no subscribed vitamin D supplementation which demonstrated only 4% had desirable vitamin D status over the time of year and no statistically significant seasonal variation in 25(OH)D levels was noted (29).

Undetectable 25(OH)D seasonality and higher prevalence of vitamin D deficiency observed in our study cohort is presumably associated with less exposure to sunlight as a result of decreased mobility. Since, in our study, according to walking ability as described by the Barthel-Index in a subgroup of 358 patients, 83.5% complained of mobility limitation (mobility scores of ≤5; data not shown). On the other hand, there were no significant differences in mobility limitation between the groups with and without vitamin D deficiency (P=0.644). In addition, beside of aging skin, elderly people are prone for reducing skin thickness due to medications as a result of many underlying comorbidities. Therefore, the efficiency of the skin to synthesize vitamin D is significantly decreased (30, 31) which might further confirm our hypothesis concerning the irrelevance of a radiation dependent skin synthesis in this population.

The findings of this study are in contrary with several previous published studies that addressed the seasonality of vitamin D status in geriatric population (3, 32). A cross-sectional study of 1,418 community-dwelling older individuals (aged ≥65 years) not receiving vitamin D supplementation (3) and another study of 596 older female patients with osteoporosis (mean age 65.3 ± 9.4 years) (32) showed strong seasonal variations in 25(OH)D levels. However, similar to our results, a large number of elderly patients in both studies had 25(OH)D concentrations far below the recommendation. Accordingly, it is absolutely not possible to reach an optimal vitamin D concentration only through sun exposure for majority of older patients and would need supplementation throughout the year. Therefore, assessment of vitamin D status might be trivialized if vitamin D deficiency can be recognized in almost every elderly patient without vitamin D supplementation.

Some limitations of the current study should be discussed. First, it is the retrospective design and we did not assess some factors such as BMI, dietary habits of the patients or direct measure of sun exposure that might influence seasonal variation in 25(OH)D concentrations. Second, there is no consensus on the desirable serum concentrations of 25(OH)D. Similar to the reports of others, we applied the recommended threshold suggested by Endocrine Society (20). Third, we have no information regarding duration of previous vitamin D supplementation and therefore we did not also control for doses of supplementation. Since, the data were derived from the patients' medical records, it cannot be excluded that some subjects had previous vitamin D supplementation without respective information in the record. Finally, frailty evaluation was not defined by exact frailty criteria, but the outcomes of the geriatric assessment and our experience with these patients confirm an entirely frail cohort.

Conclusion

This retrospective study has elucidated that vitamin D deficiency is very prevalent in frail older hospitalized patients, irrespective of season. No seasonal variability in mean 25(OH) D levels was observed reflecting that radiation dependent skin synthesis of vitamin D does not play a role in this population.

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Conflicts of interest: The authors declare no conflict of interest.
Ethical standard: The authors declare that the study procedures comply with current ethical standards for research involving human participants in Germany. The study protocol had been approved by the ethical committee of Ruhr-University Bochum.
Author contributions: The study designed and obtaining data were performed by MP and RW. Statistical analysis was performed by MP. MP and RW prepared the manuscript.

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