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ORIGINAL ARTICLE

Physical inactivity and vitamin D deficiency in hospitalized elderlies

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Abstract
Serum levels of 25(OH)D, which is known to correlate with systemic nutritional status, is used as an indicator of vitamin D sufficiency in the body. We studied the 25(OH)D status and its background factors including activity of daily living (ADL) in the elderlies hospitalized at the regional core hospital. We also examined whether or not vitamin D deficiency affects ADL among them. This study included newly hospitalized patients aged 65 years or over at Ohchi hospital April to August in 2015. At the time of admission, serum 25(OH)D concentration was measured, and ADL, instrumental ADL (IADL), cognitive function, blood test, nursing care certification were investigated as background factors. Among 209 patients, 25(OH)D was sufficient (> 30 ng/mL) only 14 cases (7%), insufficient (20–30 ng/mL) in 43 cases (20%), and deficient (< 20 ng/mL) in 152 cases (73%). Multivariate analysis showed that low ADL (OR 0.99, 95% CI 0.97–0.99) and low IADL (OR 0.88, 95% CI 0.78–0.99) were independent predictors of 25(OH)D deficiency in two models incorporating ADL and IADL, respectively. Furthermore, low 25(OH)D level was significantly associated with low ADL (OR 0.95, 95% CI 0.91–0.99) and low IADL (OR 0.93, 95% CI 0.88–0.97) scores, suggesting that vitamin D deficiency may affect physical activities. Most hospitalized elderly patients in Japan were deficient for vitamin D. In addition, physical inactivity is strongly associated with vitamin D deficiency.

Keywords 25-Hydroxy vitamin D · Activity of daily living (ADL) · Instrumental ADL (IADL) · Elderly

Introduction

Vitamin is an indispensable nutrient for keeping the body healthy, like carbohydrate, protein, fat, and mineral. Vitamin D, classified as a fat-soluble vitamin, has many roles in our body [1], and the blood concentration is reflected for the nutritional status of whole body. Vitamin D maintains calciumphosphorus metabolism and bone health. In addition, vitamin D is considered to affect cell proliferation and differentiation [2], skeletal muscle [3], and immune system [4].

Vitamin D is supplied to human from two pathways. One is biosynthesis in the skin by sunlight: 7-dehydrocholesterol is converted into cholecalciferol (Vitamin D) as a result of UV radiation. Another is an ingestion from meals (mainly fishes) and supplements. Vitamin D is hydroxylated in the liver into 25-hydroxyvitamin D [25(OH)D]. Then, 25(OH)D is hydroxylated in the kidneys into 1,25-dihydroxyvitamin D [$1,25(OH)_2D$], which is considered an active metabolite of vitamin D. However, serum concentration of $1,25(OH)_2D$ is not suitable to assess whole body vitamin D status, because it is affected by kidney function and hormonal and mineral status (e.g. parathyroid hormone, calcium, and phosphate), and because its half-life is considerably short. On the other hand, serum concentration of 25(OH)D is not directly influenced by such mechanisms and relatively stable, thus it is considered as a representative of the vitamin D status [5].

In Japan, 25(OH)D has been insurance listed since August 2016. Public institution and Japanese societies published

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"Assessment criteria for vitamin D deficiency/insufficiency in Japan", and defined deficiency of 25(OH)D < 20 ng/mL (50 nmol/L), insufficiency of 20–30 ng/mL (50–75 nmol/L), and sufficiency of 30 ng/mL (75 nmol/L) or more) [6]. It is consistent with global standard in the world [1].

According to previous studies, the rate of subjects with vitamin D deficiency was considered to be 19–58.8% [7–11], although it depends on the population. Moreover, sunshine hours, seasons, the latitude, and body mass index (BMI) have also been reported to affect vitamin D status [1, 2, 12–15]. In Japan, only short period has passed, since serum 25(OH)D level was commercially measurable. We assume that vitamin D deficiency highly presents in Japanese hospitalized elderlies, who are expected to be with low BMI and few opportunities to go outside. Additionally, from the fact that vitamin D relates to the maturation of the skeletal muscle, vitamin D deficiency may have an interrelation with their activities of daily living (ADL). Thus, we investigate the status of vitamin D deficiency in newly hospitalized patients and its background factors including ADL and instrumental ADL (IADL) at the core hospital (Ohchi Hospital) of the middle mountainous area of Japan.

Materials and methods

Subjects

From May 13 to August 23 in 2015, consecutive newly hospitalized patients with 65 years or older, who admitted to the department of general internal medicine at Ohchi hospital, were enrolled. Excluded cases were as follows: transported to advanced medical institutions, hospitalization because of just follow-up or examination, lack of data, and the consent was not obtained.

Method

Serum concentration of 25(OH)D was measured at the time of admission by the LIAISON 25-OH Vitamin D TOTAL assay (DiaSorin USA, Stillwater, Minn). In addition, age, sex, and the following items were evaluated. Then, we performed statistical analysis for the difference between vitamin D deficient group [25(OH)D < 20 ng/mL] and vitamin D non-deficient group [25(OH)D ≥ 20 ng/mL].

ADL

ADL of each patient was evaluated using Barthel index [16]. We revised the sentences in Japanese to make it easy to understand, and asked the patient, family, or caregiver using questionnaire. The higher the score, the better ADL. Hundred points represents a perfect score.

IADL

IADL was evaluated by Lowton and Brody criteria [17]. We revised the sentences to make it easier to understand in Japanese, and asked the patient, family, or caregiver using questionnaire. In the original criteria, the scoring method differs between men and women. In this study, the original female scoring system was adapted to both males and females, considering modernity in which men and women participate in housework almost equally. The higher the score, the better IADL. Eight points represents a perfect score.

Observation list for early signs of dementia (OLD)

To evaluate the cognitive function before the onset of acute illness, OLD, which is an observational cognitive evaluation, was adopted [18]. A family member or a caregiver was asked these questions. A case where it did not correspond to an item was regarded as 1 point, and the higher the score, the better OLD. Twelve points represents a perfect score.

Laboratory data

Serum levels of blood urea nitrogen (BUN), C-reactive protein (CRP), and Creatine phosphokinase (CPK) on admission were measured using an automatic analyzer.

Care certification

Each case was investigated whether Japanese care certification was present or not.

Statistical analysis

We compared the vitamin D deficient group with the non-deficient group using statistical software R3.0.3 (2014.03.06). Fisher's Exact Test is used for nominal variables. For continuous variables, those not showing normal distribution in Shapiro–Wilk normality test were adopted to Wilcoxon rank sum test. Those showing normal distribution, were further evaluated for equal variance by Levine's test. For equal variance samples, 2 samples *t* test was adopted, while for non-equal variance samples, Welch *t* test was adopted. Simple liner regression and multiple liner regression analysis was performed

with 25(OH)D level as a continuous variable. A p value of less than 0.05 was considered to indicate statistical significance.

Ethics

Written informed consent was obtained from each participant. The study protocol was approved by the local ethics committee of Ohchi Hospital (#2015–2).

Results

A total of 209 patients were included in the analysis (Fig. 1). The baseline characteristics of patients are shown (Table 1). After admission, these patients were diagnosed as pneumonia in 38 cases, urinal tract infection in 22 cases, gastrointestinal diseases in 47 cases, bone fractures in 7 cases, and the others in 95 cases.

Only 14 cases (7%) were sufficient with vitamin D (30 ng/mL or more), 43 cases (20%) were insufficient (20–30 ng/mL), 152 cases (73%) were deficient (< 20 ng/mL).

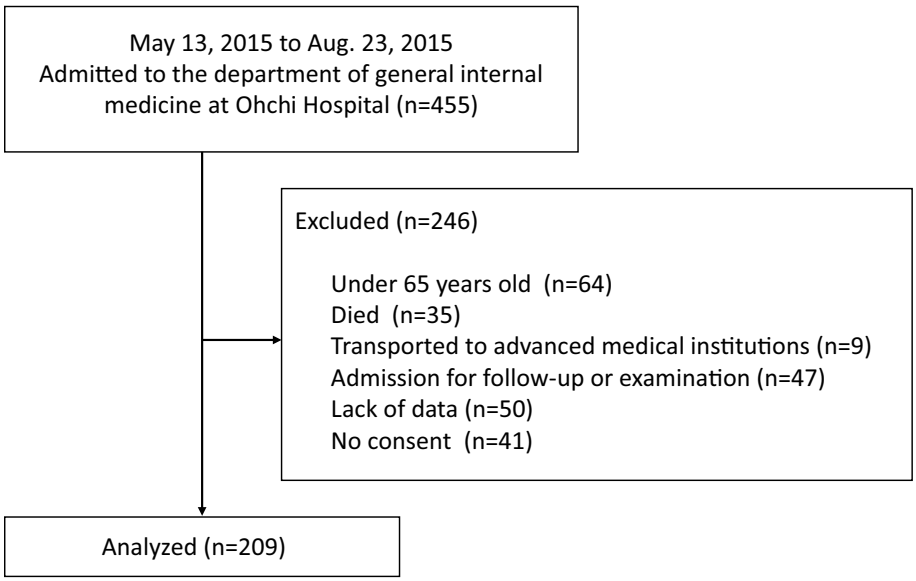

Fig. 1 Patient disposition

Table 1 Baseline characteristics of subjects along with the comparison by 25(OH)D levels

		All	25(OH)D		p
			< 20	20 ≤	
		$N=209$	$N=152$	$N=57$	
Age	Median (IQR)	85 (78, 91)	86 (79, 91)	80 (74, 91)	0.06
Gender (male)	N (%)	91 (44)	61 (40)	30 (52)	0.10
Admission from home	N (%)	157 (76)	101 (66)	46 (82)	0.02
Hight	Mean ± SD	150.2 ± 10.6	149.5 ± 10.4	152.1 ± 11.0	0.10
Weight	Mean ± SD	45.9 ± 10.4	44.7 ± 9.9	49.2 ± 11.3	< 0.01
BMI	Mean ± SD	20.3 ± 3.5	19.9 ± 3.4	21.1 ± 3.6	< 0.01
ADL (Barthel)	Mean ± SD	66.0 ± 33.0	61.4 ± 33.7	78.1 ± 32.0	< 0.01
IADL	Mean ± SD	3.42 ± 3.30	2.99 ± 3.16	4.56 ± 3.40	< 0.01
OLD	Mean ± SD	7.04 ± 4.38	6.78 ± 4.42	7.74 ± 4.21	0.30
BUN	Mean ± SD	22.4 ± 14.1	21.9 ± 14.6	23.6 ± 12.8	0.13
Cre	Mean ± SD	0.99 ± 0.63	0.96 ± 0.51	1.07 ± 0.87	0.37
CPK	Mean ± SD	134 ± 301	172 ± 347	105 ± 81	0.78
logCRP	Mean ± SD	0.11 ± 0.82	0.18 ± 0.81	− 0.06 ± 0.83	0.07
Care+	N (%)	97 (47)	78 (52)	19 (33)	0.01

ADL activity of daily living, *Care+* presence of care certification, *IADL* instrumental activity of daily living, *IQR* interquartile range, *OLD* observation list for early signs of dementia, *SD* standard deviation

Univariate analysis was performed after classification of the subjects into two groups of vitamin D status: 152 cases (73%) in deficient group and 57 cases (27%) in non-deficient group. As a result, BMI, ADL, and IADL were significantly lower in the vitamin D deficient group respectively, compared to those in the non-deficient group.

The care certification rate and the number of hospitalized patients from facilities other than home were significantly higher in the vitamin D deficient group. In other words, it can be said that elder people with vitamin D deficiency have higher degree of dependence on long-term care and higher probability of living in facilities but not at home.

On the other hand, there was no difference in sex and cognitive function. The vitamin D deficient group tended to be higher in age, although the significant difference was not identified. In the blood tests, there was no significant difference, except CRP, which tended to be higher in the vitamin D deficient group.

Table 2 Multivariate logistic regression analysis for vitamin D deficiency in 209 subjects

	OR	95% CI	*p*
Model 1			
Age	0.990	0.947–1.033	0.64
Gender (male)	0.643	0.319–1.288	0.21
BMI	0.930	0.836–1.031	0.17
ADL	0.986	0.973–0.998	0.02
LogCRP	1.025	0.970–1.092	0.40
Model 2			
Age	0.989	0.943–1.034	0.62
Gender (male)	0.642	0.316–1.294	0.22
BMI	0.928	0.833–1.032	0.17
IADL	0.880	0.784–0.985	0.03
LogCRP	1.023	0.968–1.089	0.45

ADL activity of daily living, *CI* confidence intervals, *IADL* instrumental activity of daily living, *OR* odds ratio

In a multivariate logistic regression analysis (Table 2) in two models incorporating ADL and IADL respectively, each of low ADL (OR 0.99, 95% CI 0.97–0.99) and low IADL (OR 0.88, 95% CI 0.78–0.99) was shown to be an independent predictor of vitamin D deficiency. When this analysis was performed in only the hospitalized patients from home, the same association between ADL/IADL score and vitamin D deficiency was observed (OR 0.98, 95% CI 0.96–0.99, $p = 0.04$, and OR 0.86, 95% CI 0.75–0.99, $p = 0.04$, respectively).

In a simple regression analysis with continuous variables (Table 3), ADL, IADL, BMI, and OLD showed a positive correlation with 25(OH)D value whereas age and CRP showed inverse correlation with 25(OH)D value. In addition, multiple linear regression analysis (Table 3) in two models incorporating ADL and IADL, respectively, showed that ADL as well as IADL had a significant positive correlation with 25(OH)D. This is consistent with the results of the multivariate logistic regression analysis described above.

We also examined whether or not vitamin D deficiency affects ADL or IADL. In a multivariate logistic regression analysis, low 25(OH)D level was significantly associated with low ADL defined as Barthel index < 70 (OR 0.95, 95% CI 0.91–0.99) and low IADL defined as IADL < 4 (OR 0.93, 95% CI 0.88–0.97) (Table 4).

Discussion

There is no doubt that vitamin D controls Ca balance, bone metabolism, and skeletal development in the human body. Vitamin D deficiency promotes osteopenia, osteoporosis, and rickets/osteomalacia. Prevention or treatment by vitamin D replacement is already common. However, it has also been pointed out that vitamin D deficiency is related to falls [19, 20], cardiovascular disease [1, 21, 22], dementia [1, 11, 23, 24], malignancy [1, 25, 26], autoimmune diseases [1, 4, 27], and all-cause mortality [28]. Moreover,

Table 3 Simple and multiple liner regression analysis for 25(OH)D levels in 209 subjects

	r	*p*	Standard β	SE	*p*	Standard β	SE	*p*
ADL	0.326	< 0.01	0.046	0.020	0.02			
IADL	0.328	< 0.01				0.610	0.218	< 0.01
age	− 0.214	< 0.01	− 0.096	0.063	0.13	− 0.072	0.064	0.26
BMI	0.282	< 0.01	0.170	0.163	0.3	0.203	0.157	0.2
BUN	0.006	0.42						
CPK	0.029	0.69						
Cre	0.046	0.51						
LogCRP	− 0.138	0.05	− 0.770	0.608	0.21	− 0.625	0.608	0.31
OLD	0.189	< 0.01	− 0.010	0.148	0.95	− 0.083	0.155	0.59

ADL activity of daily living, *IADL* instrumental activity of daily living, *OLD* observation list for early signs of dementia, *SE* standard error

Table 4 Multivariate logistic regression analysis for ADL and IADL scores

	ADL (BI < 70)			IADL (< 4)		
	OR	95% CI	*p*	OR	95% CI	*p*
Age	1.072	1.032–1.115	< 0.01	1.098	1.056–1.145	< 0.01
Gender (male)	1.227	0.653–2.332	0.53	1.173	0.608–2.301	0.64
BMI	0.907	0.822–0.997	0.04	0.924	0.836–1.018	0.11
LogCRP	1.011	0.992–1.055	0.44	1.010	0.990–1.059	0.54
25OHD	0.951	0.906–0.996	0.03	0.925	0.879–0.971	< 0.01

ADL activity of daily living, *BI* Barthel index, *CI* confidence intervals, *IADL* instrumental activity of daily living, *OLD* observation list for early signs of dementia, *OR* odds ratio

vitamin D deficiency was observed in 93% of patients with bone or muscle pain, who were admitted to the hospital after being diagnosed with fibromyalgia, chronic fatigue syndrome, and depression [29]. Although the action in the human body has not been elucidated yet, we can mention at least that vitamin D deficiency or low concentration of 25(OH)D in the blood has negative effects on the human body.

This study is limited to Japanese elderly inpatients. Among them, the ratio of vitamin D deficiency shows 73%, which is higher than 19–58.8% already reported from other countries [7–11]. Because of the skin activation mechanism, concentration of 25(OH)D in the blood is related to sun exposure [1, 2, 12–14]. The similar findings have been confirmed in Japanese, where the lower Vitamin D levels were shown in the winter, most probably due to short sunshine hours [30]. This study was performed from spring to summer, which is relatively long sunshine hours. Thus, the rate of patients with low vitamin D level should be relatively low. In spite of this situation, the results showed markedly high rate of vitamin D deficiency (73%).

However, this does not mean that our study population has special characteristics. Previous Japanese studies showed that the rate of vitamin D deficiency is considered to be 49–75% [31–34], which is not much different from our study. In other words, vitamin D insufficiency seems to be very common in Japanese. One of the reasons for this is that little vitamin D is added to commercial foods or drinks in Japan, as compared to Western countries.

Because Japanese are yellow race and have eaten a lot of fishes and shellfishes since ancient times, we have presumably had few problems with rickets/osteoporosis. Thus, there was no need to add vitamin D to foods. However, the change in our dietary habits accompanying internationalization that especially means decreased intake of fishes, may develop and promote vitamin D deficiency in Japanese [35]. In addition, compared with Western countries where rickets/osteoporosis had been a critical issue, the fact that sunbathing has not become a habit (rather, avoiding sunlight and preferring indoor in today's Japanese culture) can also be considered as one of the causes.

In this study, low ADL and low IADL are independent factors predicting Vitamin D deficiency. This is also consistent with the results of a previous study [36]. The concentration of 25(OH)D in the blood, an indicator of whole-body content of vitamin D, is affected by exposure to sunlight. Since patients with low ADL and low IADL, that means physical inactivity, have few chances of going outside, sunlight exposure time would decrease. Therefore, biosynthesis of vitamin D in the skin decreases, leading to vitamin D deficiency or insufficiency. On the contrary, considering vitamin D affects skeletal muscle function [3], it is possible that vitamin D deficiency lower ADL and IADL. From this viewpoint, vitamin D supplementation against vitamin D deficiency or insufficiency may improve physical activity or prevent the further deterioration. As mentioned above, vitamin D has various functions besides bone and skeletal muscle, thus, supplementing vitamin D may benefit the human body.

Actually, it has been reported that the risks for hip fracture and non-vertebral fracture decrease with supplementation of vitamin D [37, 38], and the risk for fall itself also decreases [19, 20]. Since the present study suggests that most of subjects with low ADL and IADL are considered to have vitamin D deficiency, care should be taken with conscious of an increase in sun exposure. Above all, educational activities on vitamin D deficiency and its harm would be important. It is needless to say that hypercalcemia (nausea, dehydration, constipation), hypercalciuria (polyuria), and kidney stone are recognized as complications due to vitamin D supplementation [39]. Appropriate serum concentration of vitamin D is 30 ng/mL or more, whereas it has been reported that intoxication is observed at 150 ng/mL or more [40].

Our study has some limitations. Because of a cross-sectional study, causal relation is unclear, which is discussed above. Because we obtained information using questionnaire from the patient, family, or caregiver, standards are not unified. We did not evaluate patient's food intake, vitamin D supplementation, sunlight exposure time, and calcium-phosphorus metabolism (such as serum PTH, Ca, P). Thus, further prospective study is necessary to clarify these issues. Additionally, it is somewhat difficult to evaluate the long-term

influence of laboratory data such as CRP, because these data were collected in the acute or active phase of illness.

In summary, most newly hospitalized elderly patients in Japan were deficient or insufficient for vitamin D. Physical inactivity is strongly associated with vitamin D deficiency.

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Author contributions Conceived and designed the experiments: ST SY, collected the data: ST, analyzed the data: ST, supervised: SM AN, wrote the manuscript: ST, and edited the manuscript: SY.

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Compliance with ethical standards

Conflict of interest All authors have no conflicts of interest.

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