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Associations between Serum 25-Hydroxyvitamin D Concentration and Physical Performance in Old-Old People Living in a Northern Area of Japan

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Abstract

Purpose: The present study aimed to investigate the relationship between serum 25-hydroxyvitamin D [25(OH) D] levels and physical performance, including muscle strength, balance, and gait speed, in older individuals living in a northern area of Japan (latitude approximately 43°north).

Subjects: This was a cross-sectional analysis of 273 community-based older individuals (160 women; mean age, 80.0 years), who participated in the "Population-based and Inspiring Potential Activity for Old-old Inhabitants (PIPAOI)"study.

Methods: We collected blood samples to determine serum 25(OH) D levels, and we assessed physical performance according to hand grip strength, knee extensor strength, static standing balance, hip walking distance, normal walking speed, and the results of the Timed-Up-and-Go (TUG) test. The other variables were fall experience in the year prior to the study, the Tokyo Metropolitan Institute of Gerontology Index of Competence (TMIGIC), frequency of going outdoors, sun exposure, and exercise habits. Correlations between serum 25(OH) D levels and physical performance as well as other variables were assessed using Pearson's and Spearman's correlation analyses. We performed an analysis of covariance (ANCOVA) controlled for age, sex, body mass index, sun exposure, and exercise habits to minimize the influence of confounders on physical performance.

Results: We found significant associations between serum 25(OH) D levels and sex (r_s=-0.19), bone density as measured by speed of sound in bone (r=0.16), grip strength (r=0.19), frequency of going outdoors (r_s=0.16), sun exposure (r_s=0.25), and TMIGIC (r_s=0.15). After controlling for age, sex, BMI, sun exposure, and exercise habits, total length of the center of gravity of participants with 25(OH)D insufficiency were significantly longer than those of participants with sufficient 25(OH)D levels (p<0.05).

Conclusion: Our results suggest that it is important for community-based older individuals to maintain sufficient 25(OH) D levels in order to avoid lowering physical performance.

Keywords: Vitamin D; 25(OH) D; Physical fitness; Northern area; Japanese

Introduction

Vitamin D plays a major role in the regulation of calcium homeostasis and bone metabolism [1]. It can be formed endogenously in the skin or ingested. Production of vitamin D in the skin is attributable to ultraviolet B conversion of 7-dehydrocholesterol to vitamin D_3. This is then hydroxylated in the liver and kidney to 1,25 dihydroxy-vitamin D_3[1,25(OH)D_3] under the control of endocrine factors, including parathyroid hormone (PTH), and the ionic effects of calcium and phosphate concentrations [2]. It regulates the blood levels of calcium and phosphorus by promoting their absorption from food in the intestine and calcium and phosphorus are essential for bone formation and mineralization and the development of a strong skeleton [3]. Vitamin D deficiency, which can result from inadequate exposure to sunlight coupled with inadequate dietary intake, plays an important role in the development of osteoporosis because it induces secondary hyperparathyroidism that leads to the mobilization of calcium from bone [3]. Some reports suggested that low levels of serum 25-hydroxyvitamin D [25(OH)D] are common amongst older populations, although the prevalence of vitamin D deficiency varies considerably depending on geographic location and season [4-7].

In older individuals, vitamin D deficiency leads to not only impaired bone mineralization but also muscular myopathy [8]. Multiple cross-sectional studies in older people have demonstrated an association between low levels of 25(OH)D and loss of muscle strength [2,9-11], sarcopenia [9], balance [12,13], functional disability, limitations [2,10,13,14], and falls [12,15,16]. Kwon et al. reported that low serum 25(OH)D and albumin may be associated with a decrease in the objective physical performance of community-based older individuals in Japan [17]. Suzuki et al. reported that low serum 25(OH)D may be associated with physical performance and fall experience [3]. In contrast, several studies that investigated the effects of serum 25(OH)D on physical performance found no evidence of these associations [18], and the relationship between vitamin D and physical performance remains controversial.

Known causes of vitamin D deficiency include reduced synthesis of vitamin D in the skin, lower gastrointestinal absorption of vitamin D, obesity, and reduced synthesis of 25(OH)D [19]. Synthesis of vitamin

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D in the skin is influenced by the season, time of the day, latitudinal position, skin pigmentation, use of sunscreen, and the synthesis of pre vitamin D3. Only 2 studies have investigated the association between serum 25(OH) D and physical performance in older Japanese individuals up to date [3,17]. Both were conducted in Tokyo, Japan, at a latitudinal position of 37°north. However, similar studies have not yet been conducted in other areas of Japan, especially in northern area. Furthermore, the present study aimed to enroll old-old individuals who are prone to experience lowering of serum 25(OH) D levels. Very few studies have investigated the role of 25(OH) D in the physical performance of these individuals.

Hence, the purpose of the present study was to investigate the relationship between serum 25(OH)D and physical performance, including muscle strength, balance, and gait speed, in older people living in a northern area of Japan, at a latitude of approximately 43° north.

Materials and Methods

Participants

The study was conducted as a cross-sectional study in November 2012 with the participation of community-based older individuals (≥ 75 years of age) residing in a nursing home and residential dwellings as a part of the first round of the "Population-based and Inspiring Potential Activity for Old-old Inhabitants (PIPAOI)" project. The Ethics Committee of the Sapporo Medical University Hospital approved the study protocol, and the study was conducted in accordance with the Declaration of Helsinki. Written informed consent is obtained from all participants. A total of 1312 individuals were invited with an introductory letter to participate in the study. Out of the 316 confirmed, 275 individuals actually participated in the study and all of them were living in residential dwellings. Participants were excluded if they were hospitalized for >1 week because of high blood pressure, stroke, cardiovascular disease, respiratory disease, diabetes, joint pain and osteoporosis in the 3 months before the commencement of the study. Participants with diagnosis of dementia, depression, or schizophrenia were also excluded.

Methods

Functional measures: We assessed physical performance of older people considering the handgrip strength, knee extensor strength, static standing balance, hip walking distance, normal walking speed, and the results of the Timed-Up-and-Go (TUG) test. The handgrip strength of a participant's dominant hand which is regarded as a valid indicator of general health status when measured using a Smedley-type handheld dynamometer (Matsumiya Ika SeikiMfg. Ltd., Tokyo, Japan) [20] was measured twice, and the best result was used for analysis. Isometric knee extension strength was tested once using a dynamometer (μTas F-1; Anima Corp., Tokyo, Japan). Knee extension was measured whilst a participant was sitting on a chair and the knee flexed at 90°. A testing pad was attached to the front lower leg of the participant and strapped to the leg of the chair [21]. The participants were instructed to push the pad with maximum strength (N) and isometric knee extensor torque (Nm/kg) was normalized against arm moment (m) and body mass (kg) in the data analysis. To assess balance (postural stability), postural sway during quiet standing was measured using a force plate (ECG-1500A, KYOWA, Japan). Signals were sampled at 50 Hz and registered for period of 20 seconds. Subjects were instructed to keep their eyes open and to stand as symmetrically as possible. Center-of-pressure (COP) oscillation was analyzed using the total length indicating the amount of COP [22,23]. Hip walking distance was based on the results of a hip walking exercise, which is an exercise used to train the muscles of the trunk [24]. For the hip walking distance test, participants were asked to sit with outstretched legs, to cross their arms over their chests, and then to move forward on their buttocks as fast as possible. Trunk rotation with lifting of the ischium was permitted during this test. The distance that participants could move forward within a 10-second period was recorded. The position of the participant's right lateral malleoli at the start of the exercise and after 10 seconds of hip walking was taken as the starting and ending point for distance measurements.

To assess normal walking speed, we used the mean of 5 test results. The walking analysis test was conducted at a normal walking speed using sheets with foot pressure sensors (Walk Way MW - 1000; Anima, Tokyo, Japan) [25]. Walking speed was measured over a distance of 2.4 m, and measurements were performed between 2 and 4.4 m from the start of the walkway. Participants were instructed to continue to walk for an additional 2 m to ensure that the walking pace was consistent throughout the task. The TUG test was conducted according to the ordinary method by measuring the time required to rise from a chair, to walk 3 m, to turn, and then to return to a sitting position [26]. Participants were instructed to complete this task at their maximal walking pace [27].

Laboratory analyses: Serum 25(OH) D concentrations in blood samples, which were collected between 9 am and 3 pm from participants in a non-fasting state were measured. A total of 273 serum samples were collected and all were analyzed for 25(OH)D in the same laboratory (Ikagaku Co. Ltd., Kyoto, Japan). These were measured using as a competitive protein-binding assay (CPBA) (Ikagaku Co. Ltd.). Intra-assay variation and inter-assay variation were less than 10% for 25(OH) D levels. Vitamin D insufficiency was defined as a 25(OH) D level of <20 ng/ml, in accordance with previous studies performed in the Japan and the United States [3,19].

Questionnaire: For the present study, we used self-reported questionnaires to assess functional capacity, such as fall experience over the previous year, the Tokyo Metropolitan Institute of Gerontology Index of Competence (TMIGIC), frequency of going outdoors, sun exposure, and exercise habits. We posed the following question to assess fall experience: "In the past 1 year, have you had any falls including a slip or a trip in which you lost your balance and landed on the floor or ground or a lower level?" [28]. And used the 13-item TMIGIC to measure the high-level functional capacity of our participants. The validity and reliability of this index have been previously verified, and widely accepted in Japan as a tool to assess functional capacity [29]. To estimate mobility outside the home, participants were asked how often they went outdoors within a week, and the responses were recorded in an 8-point scale, with 7 indicating 7 days per week, and 0 indicating less than once per week. Exposure to sunlight was assessed by an index related to the time of daily exposure using five categories as mentioned: 1=<1 h; 2=1–2 h; 3=2–3 h; 4=3–4 h; and 5=>4 h [30]. Exercise habits were assessed according to stages of change for exercise behavior using the 5-item Japanese questionnaire developed by Oka et al. [31]. The stages included were "precontemplation," "contemplation," "preparation," "action," and "maintenance." Participants were considered to have an exercise habit if they indicated stages of "action" or "maintenance" and no exercise habit if they indicated stages of "precontemplation," "contemplation" and "preparation."

Other covariates: To assess bone status, the bone mineral density of the right calcaneus was assessed using an ultrasound densitometer (AOS-100, Hitachi Aloka Medical Ltd., Tokyo, Japan). It measures the Speed of Sound (SOS, in m/sec) in bone, which is correlated to Bone Marrow Density (BMD) as measured by dual-energy X-ray absorptiometry and is commonly used to assess bone status [32].

Body fat content was determined using Bioelectrical Impedance Analysis (BIA). A specially calibrated Maltron BIA analyzer with a handheld device was used (BioScan 920, MP JAPAN CO., Tokyo, Japan) [33].

For anthropometric measurements, participants were dressed in light clothing without shoes. Height (to the nearest 0.1 cm) and body mass (to the nearest 0.1 kg) were recorded. The body mass index (BMI) was calculated using the standard formula: weight (kg)/[height (m)^2].

Statistical analysis: Data were analyzed using SPSS statistical software (version 17.0, IBM Japan Ltd., Tokyo, Japan). The level of significance was set at 5%. Differences between men and women were assessed using t-tests, Mann-Whitney U-tests, and χ^2 analyses for continuous, ordinal, and categorical variables, respectively. In addition, we assessed differences in serum 25(OH) D levels in the 2 age groups (aged 75–79 years and ≥ 80 years) in both sexes using t-tests. Relationships between serum 25(OH) D levels and parameters of physical performance as well as other variables were examined using Pearson's correlation analysis for continuous variables and Spearman's correlation analysis for ordinal and categorical variables. Furthermore, comparisons between physical performance and fall experiences according to 25 (OH) D levels were performed using t-tests and χ^2 analyses for continuous and categorical variables, respectively. We assessed the association between physical performance and 25(OH) D levels using an analysis of covariance (ANCOVA) after controlling for age, sex, BMI, sun exposure, and exercise habits.

Results

Table 1 shows the characteristics of study participants. A quantitative vitamin D analysis was available for 273 participants (112 men and 161 women). The mean age of the entire group was 80.0 ± 4.1 years and no individuals with primary hyperparathyroidism were reported. We found no statistically significant associations between men and women with regards to mean age, BMI, hip walking distances, TMIGIC, and participants with vitamin D insufficiency. However, there were significant differences between men and women with regards to physical performance such as grip strength (p<0.01), knee extensor strength (p<0.01), total length (p<0.05), normal walking speed (p<0.05), and TUG results (p<0.01). In addition, fall experience, exercise habits, sun exposure, and the frequency of going outdoors differed significantly between the sexes (p<0.01). The mean 25(OH) D concentrations in men and women were 24.7 ± 6.8 and 22.2 ± 6.3, respectively (p<0.01). In each sex, the 25 (OH) D concentrations of the 2 age groups (75–79 years and ≥ 80 years) did not differ significantly.

We also investigated associations between serum 25(OH) D and parameters of physical performance as well as other variables (Table 2). Sex, SOS, grip strength, physical activity, frequency of going outdoors, and TMIGIC were significantly associated with the serum 25(OH) D (sex: r_s=-0.19, p<0.01; SOS: r=0.16, p<0.01; grip strength: r=0.19, p<0.01; frequency of going outdoors: r_s=0.16, p<0.01; sun exposure: r_s=0.25, p<0.01; TMIGIC: r_s=0.15, p<0.05).

Participants with 25 (OH) D insufficiencies (<20 ng/ml) were compared with those who had sufficient 25(OH) D levels (≥ 20 ng/ml) (Table 3). Participants with 25 (OH) D insufficiencies had significantly lower grip strength than that of participants with normal 25(OH) D

	All (n=273)	Male (n=112)	Female (n=161)	
age (years)[a)]	80.0 ± 4.1	80.1 ± 3.4	79.9 ± 4.5	n.s.
height (cm)[a)]	152.4 ± 9.2	160.8 ± 5.8	146.5 ± 6.0	**
weight (kg)[a)]	56.4 ± 10	63.1 ± 8.8	51.7 ± 8.0	**
BMI (kg/m^2)[a)]	23.9 ± 3.0	24.1 ± 2.9	23.7 ± 3.1	n.s.
body fat (%)[a)]	31.0 ± 8.0	25.0 ± 5.2	35.4 ± 6.8	**
SOS (m/s)[a)]	1528.3 ± 25.7	1542.2 ± 27.8	1518.5 ± 18.9	**
grip strength (kg)[a)]	25.1 ± 7.9	31.8 ± 6.5	20.4 ± 4.7	**
Knee extensor strength (Nm/kg)[a)]	1.0 ± 0.4	1.2 ± 0.4	0.9 ± 0.3	**
total length of center of gravity with eyes open (mm)[a)]	700.4 ± 189.5	734.2 ± 235.3	676.7 ± 145.7	*
hip walking distance (cm)[a)]	66.7 ± 30.7	69.2 ± 30.8	65.0 ± 30.7	n.s.
normal walking speed (m/s)[a)]	1.2 ± 0.3	1.3 ± 0.3	1.2 ± 0.3	*
TUG (sec)[a)]	7.1 ± 2.5	6.4 ± 1.8	7.5 ± 2.8	**
frequency of going outdoors (days/week)[b)]	4 [2–6]	5 [3–7]	3 [2–5]	**
sun exposure (1–5)[b)]	2 [1 - 3]	2 [1 - 4]	2 [1 -3]	**
TMIGIC (points)[b)]	12 [11–13]	12 [11–13]	12 [11–13]	
exercise habits (yes)[c)]	111 (40.7)	54 (48.2)	47 (29.2)	**
fall experience over the previous year (yes)[c)]	91 (33.3)	27 (24.1)	64 (39.8)	**
serum 25(OH)D (ng/ml)[a)]	23.2 ± 6.6	24.7 ± 6.8	22.2 ± 6.3	**
Age Group[d)]				
75–79	23.9 ± 6.8	25.9 ± 7.1 } n.s.	22.7 ± 6.3 } n.s.	
80+	22.4 ± 6.3	23.5 ± 6.4	21.5 ± 6.2	
Insufficient (< 20ng/ml)[c)]	90(33.0)	34(30.4)	56(34.8)	n.s.

SOS: speed of sound
TUG: Timed-Up-and-Gotest
TMIGIC: Tokyo Metropolitan Institute of Gerontology index of competence
[a)] means ± SD. Student'st-test for continuous variables between men and women.
[b)] median [interquartile range]. Mann - Whitney's U test for ordinal variables between men and women.
[c)] numbers (%). Chi-squared test for categorical variables between men and women.
[d)] Student's t-test in both men and women.
*: p< 0.05, **: p< 0.01

Table 1: Characteristics of study participants.

	25(OH) D	
	Correlation coefficient	p
Age[a)]	–0.05	0.46
Sex[b)]	–0.19	< 0.01
BMI[a)]	0.08	0.26
SOS[a)]	0.16	< 0.01
grip strength[a)]	0.19	< 0.01
knee extensor strength[a)]	0.09	0.13
total length of center of gravity with eyes open[a)]	–0.09	0.16
hip walking distance[a)]	0.04	0.51
normal walking speed[a)]	0.10	0.10
TUG[a)]	–0.12	0.05
frequency of going outdoors[b)]	0.16	< 0.01
sun exposure[b)]	0.25	< 0.01
TMIGIC[b)]	0.15	0.02
exercise habits[b)]	0.04	0.53
fall experience over the previous year[b)]	0.06	0.32

SOS: speed of sound
TUG: Timed-Up-and-Go test
TMIGIC: Tokyo Metropolitan Institute of Gerontology index of competence
[a)] Pearson's correlation coefficient (r)
[b)] Spearman's correlation coefficient (r_s)

Table 2: Relationships between 25(OH)D and other variables.

	Insufficiency (< 20 ng/ml) (n = 90)	Normal (≥20 ng/ml) (n = 183)	Unadjusted	Age, sex controlled ANCOVA	Age, sex, BMI, sun exposure, exercise habit, controlled ANCOVA
age[a)]	79.8 ± 3.7	80.0 ± 4.2	n.s.		
sex (female)[b)]	59(52.7)	102(63.4)	n.s.		
BMI[a)]	24.1 ± 3.5	24.3 ± 3.1	n.s.		
grip strength[a)]	23.7 ± 8.1	25.9 ± 7.7	*	n.s.	n.s.
knee extensor strength[a)]	1.0 ± 0.4	1.0 ± 0.4	n.s.	n.s.	n.s.
total length of center of gravity with eyes open[a)]	730.0 ± 226.2	685.5 ± 166.8	n.s.	*	*
hip walking distance[a)]	66.2 ± 31.3	67.0 ± 30.5	n.s.	n.s.	n.s.
normal walking speed[a)]	117.1 ± 29.9	122.8 ± 26.4	n.s.	n.s.	n.s.
TUG[a)]	7.3 ± 2.8	7.0 ± 2.3	n.s.	n.s.	n.s.
fall experienceover the previous year (yes)[b)]	25 (22.3)	66 (41.0)	n.s.		

TUG: timed up and go test
[a)] means ± SD. Student's t-test for continuos variables between 25(OH) D insufficiency and normal.
[b)] numbers (%). Chi - Square test categorical variables between 25(OH) D insufficiency and normal.
*: p< 0.05, **: p< 0.01

Table 3: Serum 25(OH) D level and characteristics for insufficiency and normal.

levels (unadjusted model, p<0.05). Furthermore, in an age- and sex-controlled model, participants with 25(OH) D insufficiency had a significantly longer total length of center of gravity (tested with open eyes) than those with normal 25(OH) D levels (p<0.05). After controlling for age, sex, BMI, sun exposure, and exercise habits, total length of center of gravity were significantly longer in participants with 25(OH) D insufficiency than in those with normal 25(OH)D levels (p<0.05).

Discussion

The present study investigated the relationship between serum 25(OH) D levels and physical performance, including muscle strength, balance, and gait speed, in older people living in an area located in northern Japan. We found significant associations between serum 25(OH) D levels and gender, bone density as measured by SOS in bone, grip strength, frequency of going outdoors, sun exposure, and TMIGIC. Further, the participants in our study with 25(OH)D insufficiency had significantly longer total length of center of gravity(tested with open eyes) than those with sufficient 25(OH)D levels after adjusting for age, sex, BMI, sun exposure, and exercise habits. Our findings therefore support the notion that serum 25(OH)D levels are related to the bone mineral density [19] and that low serum 25(OH)D in older individuals can lead to impairments in daily living activities during periods of limited sun exposure [4].

The relationship between serum 25(OH)D levels and physical performance is controversial, because some studies have found associations between low serum 25(OH)D levels and low physical performance [2,3,9-14] whilst others have found no such correlations [18,34]. Vitamin D fulfills an important role in muscle function because it regulates calcium transport, uptake of inorganic phosphate for the production of energy-rich phosphate compounds, and protein synthesis in muscles [35]. Muscle strength also appears to be influenced by the vitamin D receptor (VDR) genotype in muscle cells. VDR appears to be expressed in skeletal muscles, and the active form of 25(OH)D [1,25(OH)$_2$D] is thought to modulate muscle function via this receptor by regulating gene transcription and promoting *de-novo* protein synthesis [36].

Our results suggest that it is important for community-based older people to maintain a good 25(OH) D status in order to avoid lowering in physical performance. Although we found an association between serum 25 (OH) D levels and the total length of center of gravity after adjusting for age, sex, BMI, sun exposure, and exercise habits, the associations between serum 25(OH) D and grip strength, knee extensor strength, hip walking distance, normal walking speed, and TUG were not significant. Serum 25(OH) D levels and physical performance were lowly correlated (Table 2). Mathei et al. also found that serum 25(OH) D levels were not associated with the physical performance of elderly individuals (mean age, 84.7 years) [18]. The authors of that study concluded that the expression of VDR in human muscle tissue decreases with age and that decreased VDR expression might reduce the functional response of the muscle cells to 1,25$(OH)_2$D. In contrast, Kwon et al. reported an association between serum 25(OH) D levels and the physical performance of older men and women with a mean age of 74.5 and 75.4 years, respectively [17]. In the present study, there was a low association between serum 25 (OH) D levels and the physical performance of older individuals with a mean age of 80.0 years. The mean age of our study participants can be considered mid-way between the mean age of the study participants included in the studies by Mathei et al. and Suzuki et al. [3,18]. Annweilar et al. also found that low serum 25(OH) D levels are lowly correlated with weak upper and lower muscle strength in older individuals with mean ages of 80.1 and 79.8 years [34,37]. The lowness of an association between serum 25(OH) D level and physical performance might be the result of an age-related decrease in the expression of the VDR in muscle tissue [38].

The men and women in our study had serum 25(OH) D concentrations of 24.7 ng/ml and 22.2 ng/ml, respectively, whereas serum 25(OH) D levels measured in October/November in Japanese men and women ≥75 years of age were 28.5 ng/ml and 23.8 ng/ml, respectively [3]. The latitudinal position of that study and our study differed; this may explain the variations in the 25(OH) D levels of participants in these studies. In addition, the physical performance and psychosocial factors of participants differed between our study and the study by Suzuki et al. [3]. This likely explains the discrepancies, with regards to the associations between serum 25(OH) D and physical performance, between our findings and those reported by Suzuki et al. [3].

Older people are prone to vitamin D deficiency; therefore, it is important to evaluate their 25(OH) D levels. In addition, living at latitude that does not allow for ample sun exposure may contribute to a lower vitamin D status. Therefore, it is also important to evaluate 25(OH) D levels in older people living in northern areas in Japan.

A limitation of the present study was its cross-sectional design. This study design does not enable the identification of a cause-and-effect relationship between serum 25(OH) D and physical performance. Serum 25(OH)D levels can be affected by season, latitude, and skin pigmentation [19]; therefore, serum 25(OH)D levels of all our participants were measured in November to avoid any potential effects of seasonal variation. This has an important meaning when we examine longitudinal follow-up study. In the future, a follow-up study is necessary to clarify the relationship between serum 25 (OH) D levels and physical performance. PTH and 1, 25$(OH)_2$ D were not measured in the present study. High PTH levels were associated with an increased risk of sarcopenia [9] and high 1,25$(OH)_2$D was associated with high physical performances [39,40]. In the present study, these relationships were unknown, and in future studies these indexes will be considered depending on the necessity.

In conclusion, our results show that older individuals with insufficient 25(OH) D had lower physical performances, including total length of center of gravity, than those with sufficient 25(OH) D. The partial association between serum 25(OH) D levels and physical performance might be the result of an age-related decrease in the expression of VDR in muscle tissue. Nevertheless, the results of the present study suggest that it is important for community-based older individuals to maintain a good 25(OH) D status in order to avoid lowering physical performance. A longitudinal study is necessary to further clarify the relationship between serum 25(OH) D and physical performance.

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