Vitamin D status, postural sway, and the incidence of falls in elderly community-dwelling Japanese women

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Abstract

Introduction There is little evidence of a preventive effect of vitamin D on falling in Japanese populations. The purpose of this study was to evaluate the effect of vitamin D status on postural sway, muscle strength, and the incidence of falls in elderly community-dwelling Japanese women. This study utilized a cross-sectional design for

postural sway and muscle strength as outcomes and a prospective design for the 1-year incidence of falls.

Methods Subjects included 633 ambulant elderly women 69 years of age and older who participated in the baseline examinations of the Muramatsu Study. Measurements of serum 25-hydroxyvitamin D (25[OH]D) and 1,25-dihydroxyvitamin D (1,25[OH]₂D) concentrations, intact parathyroid hormone (PTH), locus length (cm/s) of gravity-center sway, grip strength, body height, body weight, body mass index (BMI), and physical activity levels were recorded. Falls that occurred between May 2003 and early July 2004 were documented.

Results The average age and serum 25(OH)D concentration of the subjects was 74.3 years (SD 4.4) and 60.0 nmol/l (SD 17.9), respectively. The 1-year cumulative incidence of falls was 73/609 (12.0%). Multiple linear regression analysis showed that log-transformed locus length of the center of gravity was associated with age ($R^2=0.069$, $P<0.0001$) and BMI ($R^2=0.025$, $P<0.0001$) and that grip strength was associated with age ($R^2=0.141$, $P<0.0001$) and height ($R^2=0.100$, $P<0.0001$). A subgroup analysis revealed that log-transformed locus length was significantly associated with serum 25(OH)D concentrations ($R^2=0.075$, $P=0.0189$) in 75 subjects who had vitamin D insufficiency [serum 25(OH)D <40 nmol/l].

Conclusions The 1-year incidence of falls was associated with locus length of gravity-center sway. The present study failed to find associations between vitamin D status and gravity-center sway, grip strength, or the incidence of falls. This may be due to relatively high serum 25(OH)D level differences in this population. However, a significant association between vitamin D status and postural sway was found in the vitamin-D-insufficient subgroup, suggesting supplementation of vitamin D should be considered for those with vitamin D insufficiency.

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Introduction

Recent reviews have revealed that vitamin D deficiency impairs muscle function and increases risk of falls [1, 2]. Vitamin D receptors exist in muscle tissues [3, 4], which explains the molecular mechanisms of vitamin D action on muscle function. Low levels of vitamin D are reported to be associated with impaired muscle strength, decreased psychomotor function, and increased body sway [5–7]. Furthermore, supplementation of vitamin D has been reported to reduce body sway and number of falls in the elderly [8–10]. These findings suggest that vitamin D has the potential to prevent osteoporotic fractures that result from falls. Significant associations between vitamin D status and fall-related parameters have been observed in inactive elderly people with poor vitamin D status. Recent reports show, however, that such associations are also found in active elderly populations with better vitamin D status [11, 12]. The extant literature thus suggests that vitamin D may be effective in preventing falls in general elderly populations.

Previous studies have been conducted exclusively among Caucasian populations. In fact, no studies to date have been conducted with an Asian population. Some evidence suggests that elderly Japanese populations experience a lower occurrence of falls than Caucasian populations [13]. Recently, however, the incidence of osteoporotic fractures in Japan is steeply increasing [14]. In this context, it remains uncertain whether vitamin D has a preventive effect against falling in Japanese populations. The purpose of this study was to evaluate the effect of vitamin D status on postural sway, muscle strength, and the incidence of falls in elderly community-dwelling Japanese women.

Subjects and methods

Subjects

Subjects included 775 ambulant female volunteers 69 years of age and older who participated in baseline examinations of the Muramatsu Study, an epidemiologic study on osteoporotic fractures conducted between May and early July 2003. Letters were mailed to all households in the town of Muramatsu (female population ≥ 70 years old: 2,658) that invited all women 70 years of age or older as of 31 March 31 2004 to participate in the study [15]. The participation rate was 655/1,497 (43.8%) of women in their 70s, 117/920 (12.7%) of women in their 80s, and 3/241

(1.2%) of women in their 90s and older. Of the 775 participants, 19 women taking a minor tranquilizer and 123 women taking an alfacalcidol were excluded because of the potential effect on sense of balance. Consequently, 633 subjects were analyzed. Written informed consent was received from all subjects. This study was approved by the Ethics Committee of Niigata University School of Medicine.

Blood examinations

Vitamin D levels were assessed by measuring serum 25-hydroxyvitamin D (25[OH]D) and 1,25-dihydroxyvitamin D (1,25[OH]₂D) concentrations. Nonfasting blood specimens were drawn and stored at 4°C. Serum was obtained from the blood specimens within 12 h and immediately preserved at –20°C until biochemical analysis. Serum 25 (OH)D concentrations were determined by the Nichols Advantage chemiluminescent assay (Nichols Institute Diagnostics, San Clemente, CA, USA) with an interassay CV value of 2.4%. Serum 1,25(OH)₂D concentrations were determined by radioimmunoassay (IDS Ltd., Boldon, England, UK), with an interassay CV value of 6.0%. Serum intact parathyroid hormone (intact PTH) concentrations were measured to evaluate secondary hyperparathyroidism due to vitamin D insufficiency. Intact PTH concentrations were determined with a two-site immunoradiometric assay (Nichols Institute Diagnostics, San Clemente, CA, USA), with an interassay CV value of 8.4%.

Physical examinations

Postural sway was evaluated by measuring gravity-center sway. Subjects stood in the standard Romberg position [16] on a gravicorder (GS-10, Anima, Inc., Tokyo, Japan) [17]. Subjects stood for 30 s looking at a round mark (3 cm in diameter) placed 2 m in front of their eyes. Researchers ensured that the subjects looked at the mark during all measurements. The locus length (per second) of gravity-center sway was recorded. Grip strength was measured with a digital hand dynamometer (T.K.K.5401, Takei Scientific Instruments Co., Ltd., Niigata, Japan) once each for the right and left hands. The average value of both hands was recorded as the grip strength. Body height and weight were measured to the nearest 1 mm and 100 g, respectively, while the subjects wore only light underclothes, and body mass index (BMI) was calculated by weight (kg) divided by the square of height (m).

Other measurements

Demographic and lifestyle characteristics, disease history, and current medication were obtained through subject

interviews. Physical activity levels were assessed based on whether subjects regularly engaged in the following activities: (1) housework; (2) light exercise (such as gate ball or croquet), taking walks, traditional Japanese dancing; and (3) farm work, coded as 0 for “no” and 1 for “yes”. Calcium intake was estimated by a semiquantitative food frequency questionnaire [15].

Cumulative incidence of falls (1-year follow-up)

A fall was defined as “an event that results in a person coming to rest inadvertently on the ground or other lower level” [18]. Falls due to an intrinsic cause, such as syncope, or a clear extrinsic cause, such as a motor vehicle accident, were excluded from this study. The authors confirmed falls that occurred in the 1-year time period by one of two ways. Five hundred and twenty-seven subjects were reinterviewed when they participated in an annual health check-up program provided by the Muramatsu Town between May and early July 2004. Researchers also mailed or made telephone calls to the other 223 subjects who could not be interviewed and asked whether they had falls in the follow-up period. Ultimately, 609 (96.2%) subjects were questioned. A subject who fell at least once was coded as 1 and who did not was coded as 0.

Statistical analysis

Means and standard deviations were calculated for each variable. Because variables of serum 1,25(OH)₂D concentration, serum intact PTH concentration, and locus length of gravity-center sway were skewed to higher values, they were transformed logarithmically for the statistical tests. Simple linear regression analysis was conducted to evaluate linear associations between a continuous outcome variable (log-transformed locus length of gravity-center sway or grip strength) and other variables as predictors. The stepwise method of multiple linear regression analysis was used to determine independent variables predicting the continuous outcome variables. The relative risk for one or more falls compared with no falls was calculated for each variable. The PC-SAS (release 8.02, SAS Institute Inc., Cary, NC, USA) was used for computation. A *P* value less than 0.05 was judged to be statistically significant.

Results

Baseline characteristics of the subjects are shown in Table 1. Physical activity levels varied. Five hundred and sixty-three (89.1%) subjects did housework and 69 (10.9%) did not; 214 (33.9%) participated in light activity and 417 (66.1%) did not; and 325 (51.4%) engaged in farm work and 307

(48.6%) did not. The 1-year cumulative incidence of falls was 73/609 (12.0%).

Simple and multiple regression analyses were conducted to explore factors associated with locus length of gravity-center sway. Simple linear regression analysis showed that log-transformed locus length was associated positively with age ($\beta=0.0226$, $R^2=0.069$, $P<0.0001$) and negatively with weight ($\beta=-0.00884$, $R^2=0.034$, $P<0.0001$) and BMI ($\beta=-0.0205$, $R^2=0.033$, $P<0.0001$) but not with serum 25(OH)D ($P=0.3410$), log-transformed 1,25(OH)₂D ($P=0.2807$), or log-transformed intact PTH ($P=0.5051$) concentrations. In the same manner, simple linear regression analysis showed that grip strength was associated positively with height ($\beta=0.326$, $R^2=0.169$, $P<0.0001$), weight ($\beta=0.144$, $R^2=0.064$, $P<0.0001$), and “doing housework” ($\beta=1.83$, $R^2=0.017$, $P=0.0013$) and negatively with age ($\beta=-0.382$, $P<0.0001$, $R^2=0.141$) but not with serum 25(OH)D ($P=0.5712$), log-transformed 1,25(OH)₂D ($P=0.2439$), or log-transformed intact PTH ($P=0.6480$) concentrations. Results of stepwise multiple logistic regression analyses are shown in Table 2. Multiple linear regression analysis showed that log-transformed locus length was associated independently with age and BMI and that grip strength was associated independently with age and height.

Similar analyses were conducted with a subgroup of 75 subjects who had serum levels of 25(OH)D <40 nmol/l. This serum level is the threshold value of 25(OH)D at which PTH begins to rise in this population [19]; therefore, the 75 subjects were considered to have vitamin D insufficiency. In this subgroup, log-transformed locus length was significantly associated with serum 25(OH)D concentrations ($\beta=-0.0190$, $R^2=0.075$, $P=0.0189$) (Fig. 1) but was not associated with other variables. Grip strength was not associated with serum 25(OH)D concentrations ($P=0.4576$).

Table 1 Baseline characteristics of the 633 subjects

	Mean	SD
Age (years)	74.3	4.4
Height (cm)	146.0	5.6
Weight (kg)	49.5	7.8
Body mass index (kg/m ²)	23.2	3.3
Locus length ^a (cm/sec)	2.1	0.9
Grip strength ^b (kg)	20.1	4.4
Calcium intake (mg/day)	581	249
Serum 25-hydroxyvitamin D ^c (nmol/l)	60.0	17.9
Serum 1,25-dihydroxyvitamin D (pmol/l)	144.4	47.0
Serum intact parathyroid hormone ^c (pmol/l)	3.8	1.8
Serum albumin (g/dl)	4.2	0.2

^a Three values missing

^b Eight values missing

^c One value missing

Table 2 Results of the stepwise method of multiple linear regression analysis

Outcome variable	Independent variable	Regression coefficient	Standard error	R ²	P value
Log-transformed locus length (cm)	Age	0.0214	0.0033	0.069	<0.0001
	Body mass index	−0.0180	0.0043	0.025	<0.0001
Grip strength (kg)	Age	−0.286	0.037	0.141	<0.0001
	Height	0.261	0.029	0.100	<0.0001

Relative risks for falls according to levels of possible risk factors are shown in Table 3. The third quartile (≥ 145.8 , < 149.8 cm) of height had significantly higher risk than the fourth quartile (reference). The second (≥ 1.5 , < 1.9 cm/s) and fourth quartiles (≥ 2.5 cm/s) of locus length of gravity-center sway had significantly higher risk than the first quartile (< 1.5 cm/s). No other variable had a statistically significant relative risk.

Discussion

The present study failed to demonstrate an association between vitamin D status and postural sway, muscle strength, or the 1-year incidence of falls in ambulant elderly Japanese women. This result is inconsistent with a number of studies that showed an association between vitamin D and balance as well as incidence of falls in the elderly. A previous metaanalysis demonstrated that vitamin D supplementation reduces risk of falls in the elderly by more than 20% [9]. Also, a large cross-sectional study recently showed that 25(OH)D concentrations between 40 and 94 nmol/l were associated with better musculoskeletal function in the lower extremities than concentrations

< 40 nmol/l in ambulatory elderly persons [11]. The association between vitamin D status and the incidence of falls seems significant in vitamin-D-depleted populations. Stein et al. [20] and Flicker et al. [21] demonstrated that low serum 25(OH)D concentrations were associated with falls in ambulant elderly populations (median 25[OH]D concentrations, 27 and 35 nmol/l, respectively). However, one prospective study did not show low serum vitamin D to predict new disability or loss of muscle strength in older disabled women (mean 25[OH]D, 53 nmol/l) [22]. Accordingly, the lack of association between vitamin D status, balance, and the incidence of falls in the subjects found in this study may be due to relatively high levels of serum 25(OH)D (mean, 60 nmol/l). This study was conducted in late spring to early summer, and the mean serum 25(OH)D concentration of 60 nmol/l is as high as that of another Japanese study conducted in the same season [23], suggesting serum 25(OH)D levels in this study sample were not exceptionally high. Even in winter, active elderly Japanese are known to have high levels of serum 25(OH)D [24].

Dhesi et al. [7] reported that subclinical vitamin D deficiency results in impairment of postural stability, with subjects who had 25(OH)D < 30 nmol/l being most affected. Applying the cutoff point of 30 nmol/l of serum 25(OH)D concentration to this study, subjects with 25(OH)D < 30 nmol/l have shorter locus length of gravity-center sway ($P=0.2286$), weaker grip strength ($P=0.1840$), and higher incidence of falls ($RR=1.85$, 95% CI:0.83–4.13) than those with 25OHD ≥ 30 nmol/l (data not shown in “Results” section). Moreover, a negative linear relationship was found between the serum 25(OH)D concentration and locus length of the gravity-center sway only in the vitamin-D-insufficient subgroup (25[OH]D < 40 nmol/l). These findings also support the hypothesis that the lack of overall association between serum 25(OH)D concentration and postural sway in this study is considered to be the result of relatively good vitamin D status.

This study can be compared with the Swedish cohort study [the Osteoporosis Prospective Risk Assessment (OPRA) study] of 986 elderly ambulatory women 75 years of age [12]. The mean serum 25(OH)D concentration of the subjects in the OPRA study was relatively high at, 95 nmol/l, and the serum 25(OH)D concentration < 75 nmol/l was associated with inferior muscle strength and postural

Fig. 1 Scatterplot of serum 25-hydroxyvitamin D (25[OH]D) concentration and locus length of gravity-center sway. Serum 25(OH)D concentration was negatively associated with log-transformed locus length ($\beta=-0.0190$, $R^2=0.075$, $P=0.0189$)

Table 3 Relative risk of falls according to levels of possible risk factors

	Relative risk	(95% CI)	Trend <i>P</i> value
Age (years)			
<75	1 (reference)		0.2404
≥75, <80	1.23	(0.75–2.02)	
≥80	1.48	(0.82–2.64)	
Height (cm)			
Q1 (<142.3)	0.94	(0.55–1.63)	0.3695
Q2 (≥142.3, <145.8)	0.82	(0.46–1.43)	
Q3 (≥145.8, <149.8)	0.43*	(0.21–0.88)	
Q4 (≥149.8)	1 (reference)		
Weight (kg)			
Q1 (<43.5)	1.16	(0.62–2.18)	0.6089
Q2 (≥43.5, <48.6)	1.10	(0.58–2.07)	
Q3 (≥48.6, <54.0)	1.23	(0.67–2.29)	
Q4 (≥54.0)	1 (reference)		
Body mass index (kg/m ²)			
Q1 (<20.8)	0.68	(0.37–1.27)	0.3381
Q2 (≥20.8, <22.9)	0.96	(0.55–1.68)	
Q3 (≥22.9, <25.2)	0.74	(0.40–1.37)	
Q4 (≥25.2)	1 (reference)		
Locus length of the center of gravity (cm/s)			
Q1 (<1.5)	1 (reference)		0.1335
Q2 (≥1.5, <1.9)	1.97*	(1.05–3.71)	
Q3 (≥1.9, <2.5)	0.75	(0.34–1.67)	
Q4 (≥2.5)	1.95*	(1.04–3.66)	
Grip strength (kg)			
Q1 (<17.4)	1.44	(0.83–2.52)	0.6016
Q2 (≥17.4, <20.3)	0.78	(0.40–1.53)	
Q3 (≥20.3, <22.9)	0.91	(0.48–1.72)	
Q4 (≥22.9)	1 (reference)		
Serum 25-hydroxyvitamin D (nmol/l)			
Q1 (<47.7)	1.12	(0.63–2.00)	0.9156
Q2 (≥47.7, <59.4)	0.78	(0.41–1.49)	
Q3 (≥59.4, <71.1)	0.91	(0.50–1.67)	
Q4 (≥71.1)	1 (reference)		
Serum 1,25-dihydroxyvitamin D (pmol/l)			
Q1 (<112.8)	0.92	(0.50–1.69)	0.7894
Q2 (≥112.8, <134.4)	1.04	(0.59–1.84)	
Q3 (≥134.4, <165.6)	0.72	(0.37–1.38)	
Q4 (≥165.6)	1 (reference)		
Serum intact parathyroid hormone (pmol/l)			
Q1 (<2.44)	1 (reference)		0.6126
Q2 (≥2.44, <3.29)	0.64	(0.33–1.24)	
Q3 (≥3.29, <4.24)	1.34	(0.77–2.34)	
Q4 (≥4.24)	0.87	(0.48–1.58)	
Serum albumin (g/dl)			
Q1 (<4.0)	0.83	(0.43–1.60)	0.3089
Q2 (≥4.0, <4.2)	0.65	(0.36–1.15)	
Q3 (≥4.2, <4.3)	1.11	(0.62–1.97)	
Q4 (≥4.3)	1 (reference)		
Do housework			
Yes	1 (reference)		–
No	0.86	(0.41–1.79)	
Engage in light exercise			
Yes	1 (reference)		–
No	1.33	(0.82–2.16)	

Table 3 (continued)

	Relative risk	(95% CI)	Trend <i>P</i> value
Engage in moderate activity			
Yes	1 (reference)		–
No	1.04	(0.67–1.60)	

A level that is hypothesized to have the lowest risk of falls is set as a reference group for each variable.

Q1 first quartile, *Q2* second quartile, *Q3* third quartile, *Q4* fourth quartile

**P*<0.05

stability. The mean serum 25(OH)D concentration of subjects in the OPRA study is higher than in this study (60 nmol/l). It should be noted that considerable interassay and interlaboratory variations for the 25(OH)D determination potentially exist [25]. The interassay difference is negligible because both the present study as well as the OPRA study used the same 25(OH)D assay (the Nichols Advantage^R chemiluminescent assay). However, there is possibly an interlaboratory variation leading to an overestimation of the difference (35 nmol/l) in serum 25(OH)D concentration between the two studies. In any case, the mean serum 25(OH)D concentrations of subjects in both the OPRA study and the present study are relatively high, and yet significant associations between serum 25(OH)D concentrations and muscle balance and strength were found only in the OPRA study. Though the discrepancy between the results of this study and the OPRA study cannot be fully explained, it is hypothesized that the disparity between the two studies is due to the different ethnicities of study populations, given that the threshold value of serum 25(OH)D concentration for vitamin D insufficiency in elderly Japanese is lower than in elderly Caucasians.

The 1-year fall incidence of 12% in this study appeared to be lower than that in many previous studies, which reported around 30–40% in community-dwelling elderly in Europe and North America [26]. One reason explaining this discrepancy may be that the subjects were volunteers who were physically healthier than the general population, which includes the frail elderly. Another explanation may be ethnic differences. The 1-year incidence of falls previously reported in the community-dwelling elderly in Japan ranged from 10–20% [27], which is generally lower than the incidence in Europe or North America. The lower incidence of falls in elderly Japanese may be due to relatively good vitamin D status, as discussed earlier, as well as other important risk factors for falls, including genetic issues.

This study has some limitations. First, there may be a misclassification bias in recalling falls, which could lead an association between vitamin D status and fall occurrence toward the null. Second, the participation rate of this study was not high, especially regarding women in their 80s and older. This may have led to selection bias based on the assumption that very elderly participants were probably

healthier than nonparticipants. Finally, participants were healthy female persons living in a community whereas frail and/or disabled elderly persons were not included. Therefore, generalization of the results should be made with caution.

In conclusion, the present study failed to find an association between vitamin D status and postural sway, muscle strength, or the 1-year incidence of falls in elderly community-dwelling Japanese women. This may be due to relatively high serum 25(OH)D levels. Therefore, vitamin D status may not be an important factor for the prevention of falls in ambulant elderly Japanese women. However, a significant association between vitamin D status and postural sway was found in the vitamin-D-insufficient subgroup, suggesting supplementation of vitamin D should be considered for those with vitamin D insufficiency.

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