

## Original Article

# Serum 25-hydroxyvitamin D levels are not associated with impaired postural sway in community-dwelling older women: a 6-year follow-up study

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## Abstract

**Objectives:** A positive association between levels of blood 25-hydroxyvitamin D (25[OH]D), an index of vitamin D status, and physical balance has been reported from cross-sectional studies, but longitudinal studies are rare. The present study aimed to test the hypothesis that low serum 25(OH)D levels are longitudinally associated with impaired postural sway over a 6-year follow-up period in older women. **Methods:** The present cohort consisted of 392 community-dwelling Japanese women aged  $\geq 69$  years. Baseline examinations included serum 25(OH)D and physical performance tests, including postural sway velocity. Standing postural sway was evaluated by measuring gravity-center sway velocity. Follow-up physical performance tests were conducted 6 years later. **Results:** Mean subject age and serum 25(OH)D levels were 73.3 years (SD 3.7) and 61.0 nmol/L (SD 16.9), respectively. No significant association was found between 25(OH)D levels and changes in postural sway velocity (adjusted P for trend=0.72). Women with 25(OH)D  $< 30$  nmol/L tended to have lower  $\Delta$ postural sway velocity than those with 25(OH)D  $\geq 30$  nmol/L (mean, -0.59 vs 0.37 cm/s, respectively; adjusted P=0.13). **Conclusions:** Vitamin D levels are not longitudinally associated with impaired postural sway in older women. Further longitudinal studies are needed to corroborate the results of this study.

**Keywords:** 25-Hydroxyvitamin D, Longitudinal Study, Older Women, Postural Sway, Vitamin D

## Introduction

Vitamin D and parathyroid hormone play an essential role in the maintenance of physical function. As vitamin D acts through vitamin D receptors in skeletal muscle tissue<sup>1</sup> and the central nervous system<sup>2</sup>, vitamin D deficiency can cause neuromuscular dysfunction<sup>3,4</sup> and may be detrimental to physical performance in older people, who are prone to vitamin D deficiency. Secondary

hyperparathyroidism due to insufficient vitamin D may also have a direct adverse effect on skeletal muscle and the nervous system<sup>3,5</sup>. Moreover, low vitamin D levels are reported to be associated with inflammation markers<sup>6,7</sup>, which potentially cause functional decline<sup>8</sup>.

Impaired body balance is an important risk factor for falls and fractures in older people<sup>9,10</sup>. Observational studies have shown that levels of serum 25-hydroxyvitamin D (25[OH]D), an established biomarker of vitamin D status, are associated with better postural sway in older adults<sup>11-13</sup>. Elevated parathyroid hormone (PTH) levels among older persons are associated with impaired postural stability and balance<sup>14,15</sup>. However, all of these previous studies were cross-sectional in design, and longitudinal studies are required to examine causality<sup>14</sup>. Vitamin D supplementation has been found to be effective in improving postural stability<sup>16</sup>. However, results from recently conducted randomized controlled trials (RCTs) suggest that vitamin D supplementation does not impact balance<sup>17-19</sup>, and thus causality in the relationship between

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vitamin D and physical balance remains inconclusive.

We previously conducted a longitudinal study to measure the effects of vitamin D levels on 6-year changes in musculoskeletal parameters (primarily bone mineral density and occurrence of fragility fractures) in Japanese women<sup>20,21</sup>. Within the framework of that study, we analyzed the effect of vitamin D levels on changes in postural balance. The present study aimed to test the hypothesis that serum 25(OH)D levels can predict impaired postural sway during a 6-year follow-up period in older women.

## Methods

### Subjects

The present study used a longitudinal design with a 6-year follow-up. We targeted 774 community-dwelling women aged  $\geq 69$  years who participated in baseline medical and physical examinations of the Muramatsu study conducted in 2003<sup>22</sup>. Among these 774 women, 392 who participated in the follow-up examination 6 years later were analyzed in the present study. Written informed consent was obtained from all subjects. The study protocol was approved by the Ethics Committee of Niigata University School of Medicine.

### Baseline examination

Baseline examinations conducted in May and June 2003 included blood tests, physical performance tests, and an interview. Standing postural sway was evaluated by measuring gravity-center sway. Subjects stood in the Romberg position on a gravicorder (GS-10, Anima, Inc., Tokyo, Japan) for 30 seconds, and the velocity (cm/s) of locus of gravity-center sway (postural sway) was recorded. Higher velocity indicates poorer postural sway. Grip strength was measured once for both hands with a digital hand dynamometer (T.K. K.5401, Takei Scientific Instruments Co., Ltd., Niigata, Japan), and the average strength between the hands was calculated. Body height and weight were measured, and body mass index (BMI) was calculated.

A non-fasting blood specimen was provided by the subjects and serum was obtained. Serum 25(OH)D levels were determined by the Nichols Advantage chemiluminescent assay (Nichols Institute Diagnostics, San Clemente, CA, USA), with an inter-assay CV of 2.4%. Serum intact PTH (iPTH) levels were determined with a two-site immunoradiometric assay (Nichols Institute Diagnostics, San Clemente, CA, USA), with an inter-assay CV of 8.4%. The reference value of iPTH was 1.1–6.9 pmol/L<sup>23</sup>. For the purposes of the present study, we defined serum 25(OH)D  $< 30$  nmol/L as “severe vitamin D deficiency”, and iPTH  $\geq 6.9$  as “high PTH” or “mild hyperparathyroidism”.

Demographic and lifestyle information was obtained through interviews. Regarding physical activity, total amounts of time spent gardening or performing other leisure activities during the previous week were recorded separately, with each classified as low (no activity), medium (lower half),

and high (upper half), i.e., 0, 1–17.74, and  $\geq 17.75$  hrs/week, respectively, for gardening, and 0, 1–3.4, and  $\geq 3.5$  hrs/week, respectively, for leisure activities<sup>24</sup>. Calcium intake was estimated using a validated semiquantitative food frequency questionnaire. Smoking (1, non-smoker; 2, ex-smoker; 3, occasional smoker; and 4, daily smoker) and drinking (1, non-drinker; 2, occasional drinker; and 3, daily drinker) statuses were also recorded. Details on the medical and physical examination procedures were described previously<sup>22,24</sup>.

### Follow-up survey

The follow-up postural sway and grip strength tests were conducted in June and July 2009 in the same manner and setting as the 2003 baseline examination.

### Statistical methods

All continuous variables were assessed for normality, and means and standard deviations were calculated. iPTH levels and postural sway velocity were skewed to higher values and underwent log transformation before statistical analysis. Linear associations between 25(OH)D/iPTH levels (groups) and postural sway velocity/grip strength were evaluated with P-for-trend values calculated by simple and multiple linear regression analyses. Multiple linear regression analysis was used to determine whether differences in postural sway velocity and grip strength were dependent on the presence or absence of severe vitamin D deficiency/mild hyperparathyroidism. In the multivariate analysis, age, BMI, gardening, leisure activity, calcium intake, smoking, drinking, and baseline postural sway velocity or grip strength were included as covariates. For example, when assessing the association between 25(OH)D levels (predictor) and changes in postural sway velocity (outcome), age, BMI, gardening, leisure activity, calcium intake, smoking, drinking, and baseline postural sway velocity were set as covariates. Graphical associations between 25(OH)D/iPTH levels and postural sway velocity/grip strength were drawn by the cubic spline model with 5 knots. Statistical analyses were performed with SAS software (release 9.4, SAS Institute Inc., Cary, NC, USA).  $P < 0.05$  was considered statistically significant.

## Results

Mean age and serum 25(OH)D level among the 392 subjects were 73.3 years (SD 3.7) and 61.0 nmol/L (SD 16.9), respectively. Baseline characteristics according to serum 25(OH)D and iPTH levels are shown in Table 1. Serum 25(OH)D levels were inversely associated with iPTH levels ( $P$  for trend  $< 0.01$ ), and positively associated with the proportion of current drinkers ( $P$  for trend = 0.01). Among the 774 women who participated in the baseline examination, those who completed the follow-up survey were younger (mean age, 73.3 vs 75.8 years,  $P < 0.01$ ), and had lower postural sway velocity (2.01 vs 2.16 cm/s,  $P = 0.02$ ) and higher grip

**Table 1.** Baseline characteristics according to quintiles of serum 25-hydroxyvitamin D (25[OH]D) and intact parathyroid hormone (iPTH) levels.

	Serum 25(OH)D (nmol/L)					P for trend	Serum iPTH (pmol/L)					P for trend
	<30	30-49	50-69	70-89	≥90		<3.0	3.0-4.9	5.0-6.9	7.0-8.9	≥9.0	
	N=5	N=101	N=177	N=90	N=19		N=165	N=171	N=41	N=9	N=5	
Age (years)	73.2 (5.3)	73.8 (4.1)	73.1 (3.3)	73.1 (3.8)	73.6 (3.5)	0.35	73.9 (3.8)	72.6 (3.3)	73.3 (3.8)	73.2 (3.7)	76.6 (4.6)	0.40
BMI (kg/m <sup>2</sup> )	21.4 (4.4)	22.5 (3.3)	23.4 (2.9)	22.8 (2.9)	23.4 (2.4)	0.24	22.9 (3.0)	23.2 (3.1)	22.4 (3.2)	23.1 (2.8)	24.0 (1.6)	0.80
Ca intake (mg/day)	432 (246)	652 (299)	597 (245)	588 (257)	556 (319)	0.16	614 (266)	618 (281)	516 (199)	622 (285)	605 (235)	0.28
25(OH)D (nmol/L)	27.7 (1.5)	42.3 (5.2)	59.5 (5.8)	78.2 (5.5)	101.6 (9.2)	<0.01	62.3 (16.5)	61.5 (16.7)	57.7 (17.8)	47.8 (17.7)	48.4 (19.0)	<0.01
iPTH (pmol/L)	7.6 (4.3)	3.9 (1.9)	3.4 (1.4)	3.4 (1.5)	3.1 (1.1)	<0.01	2.3 (0.4)	3.8 (0.5)	5.7 (0.5)	7.7 (0.6)	12.1 (2.3)	<0.01
Engaged in gardening (%)	0.0	45.5	43.5	62.2	47.4	0.02	50.6	46.2	51.2	11.1	60.0	0.34
Engaged in leisure-time activity (%)	40.0	39.6	33.9	32.2	31.6	0.27	34.9	36.3	26.8	66.7	0.0	0.71
Current smoker (%)	0.0	2.0	1.7	2.2	0.0	0.89	1.8	2.3	0.0	0.0	0.0	0.53
Current drinker (%)	20.0	4.0	11.3	20.0	10.5	0.01	14.5	8.8	7.3	22.2	20.0	0.51

BMI, Body mass index; Ca, Calcium. Values are expressed as mean (SD) or percent.

**Table 2.** Baseline and 6-year changes ( $\Delta$ ) in postural sway velocity and grip strength according to quintiles of baseline 25-hydroxyvitamin D (25[OH]D) levels.

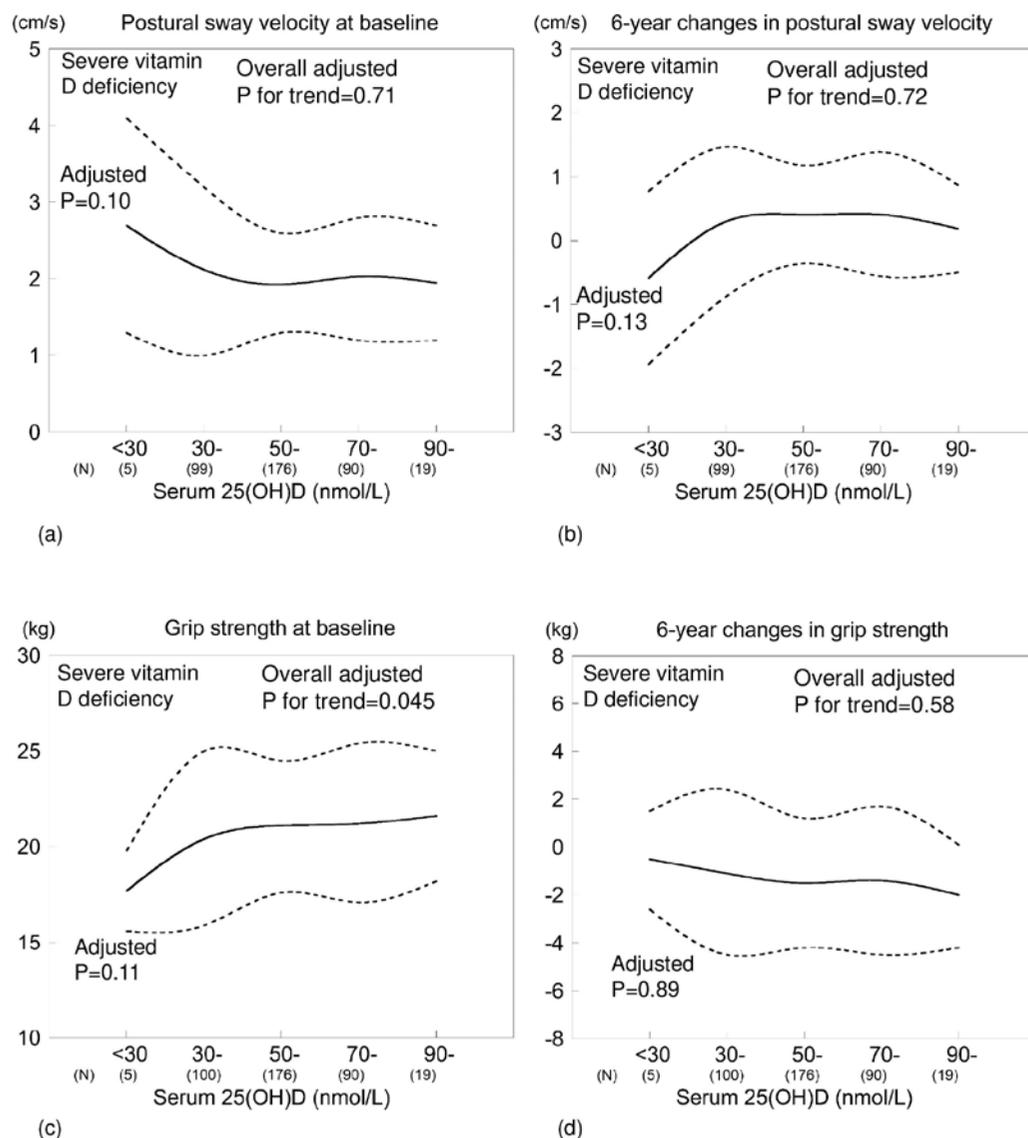
	Serum 25(OH)D (nmol/L)					Unadjusted P for trend	Adjusted P for trend
	<30	30-49	50-69	70-89	≥90		
	N=5	N=101	N=177	N=90	N=19		
<b>Baseline</b>							
Postural sway velocity (cm/s)	2.70 (1.36)	2.12 <sup>a</sup> (1.10)	1.93 (0.66)	2.03 (0.80)	1.95 (0.74)	0.46	0.71 <sup>b</sup>
Grip strength (kg)	17.7 (2.1)	20.4 (4.6)	21.1 (3.4)	21.2 (4.1)	21.6 (3.4)	0.04	0.045 <sup>b</sup>
<b>6-year change</b>							
$\Delta$ Postural sway velocity (cm/s)	-0.59 (1.36)	0.30 <sup>a</sup> (1.17)	0.41 (0.77)	0.41 (0.98)	0.19 (0.68)	0.39	0.72 <sup>c</sup>
$\Delta$ Grip strength (kg)	-0.5 (2.1)	-1.1 (3.4)	-1.5 (2.7)	-1.4 (3.1)	-2.0 (2.2)	0.20	0.58 <sup>c</sup>

Values are expressed as mean (SD) or percent. <sup>a</sup>Two values missing. <sup>b</sup>Adjusted for age, BMI, gardening, leisure activity, calcium intake, smoking, drinking, and iPTH. <sup>c</sup>Adjusted for age, BMI, gardening, leisure activity, calcium intake, smoking, drinking, iPTH, and baseline values for postural sway or grip strength.

**Table 3.** Baseline and 6-year changes ( $\Delta$ ) in postural sway and grip strength according to quintiles of serum intact parathyroid hormone (iPTH) levels.

	Quintiles of serum iPTH (pmol/L)					Unadjusted P for trend	Adjusted P for trend
	<3.0	3.0-4.9	5.0-6.9	7.0-8.9	≥9.0		
	N=165	N=171	N=41	N=9	N=5		
<b>Baseline</b>							
Postural sway velocity (cm/s)	2.03 <sup>a</sup> (0.80)	2.00 (0.89)	1.88 (0.61)	2.30 (1.31)	2.55 <sup>a</sup> (1.20)	0.99	0.63 <sup>b</sup>
Grip strength (kg)	20.9 (3.8)	21.1 (3.9)	20.0 (4.4)	21.6 (4.5)	22.0 (4.0)	0.84	0.93 <sup>b</sup>
<b>6-Year change</b>							
$\Delta$ Postural sway velocity (cm/s)	0.38 <sup>a</sup> (0.97)	0.33 (0.94)	0.54 (0.89)	-0.06 (0.62)	-0.48 <sup>a</sup> (0.87)	0.35	0.40 <sup>c</sup>
$\Delta$ Grip strength (kg)	-1.8 (2.7)	-1.3 (3.1)	-0.1 (3.6)	-0.6 (2.3)	-3.3 (1.3)	0.04	0.04 <sup>c</sup>

Values are expressed as mean (SD) or percent. <sup>a</sup>A value missing. <sup>b</sup>Adjusted for age, BMI, gardening, leisure activities, calcium intake, smoking, drinking, and 25(OH)D. <sup>c</sup>Adjusted for age, BMI, gardening, leisure activities, calcium intake, smoking, drinking, 25(OH)D, and baseline values for postural sway or grip strength.



**Figure 1.** Cubic spline curves showing associations between serum 25-hydroxyvitamin D (25[OH]D) and (a) baseline postural sway velocity, (b) 6-year changes in postural sway velocity, (c) baseline grip strength, and (d) 6-year changes in grip strength. Solid and dashed lines represent mean values and standard deviations, respectively. Statistical robustness of the overall association between 25(OH)D and physical performance levels is indicated by an “adjusted P for trend” value, with the statistical difference in physical performance levels between women with 25(OH)D <30 nmol/L and  $\geq$ 30 nmol/L indicated by an adjusted P value.

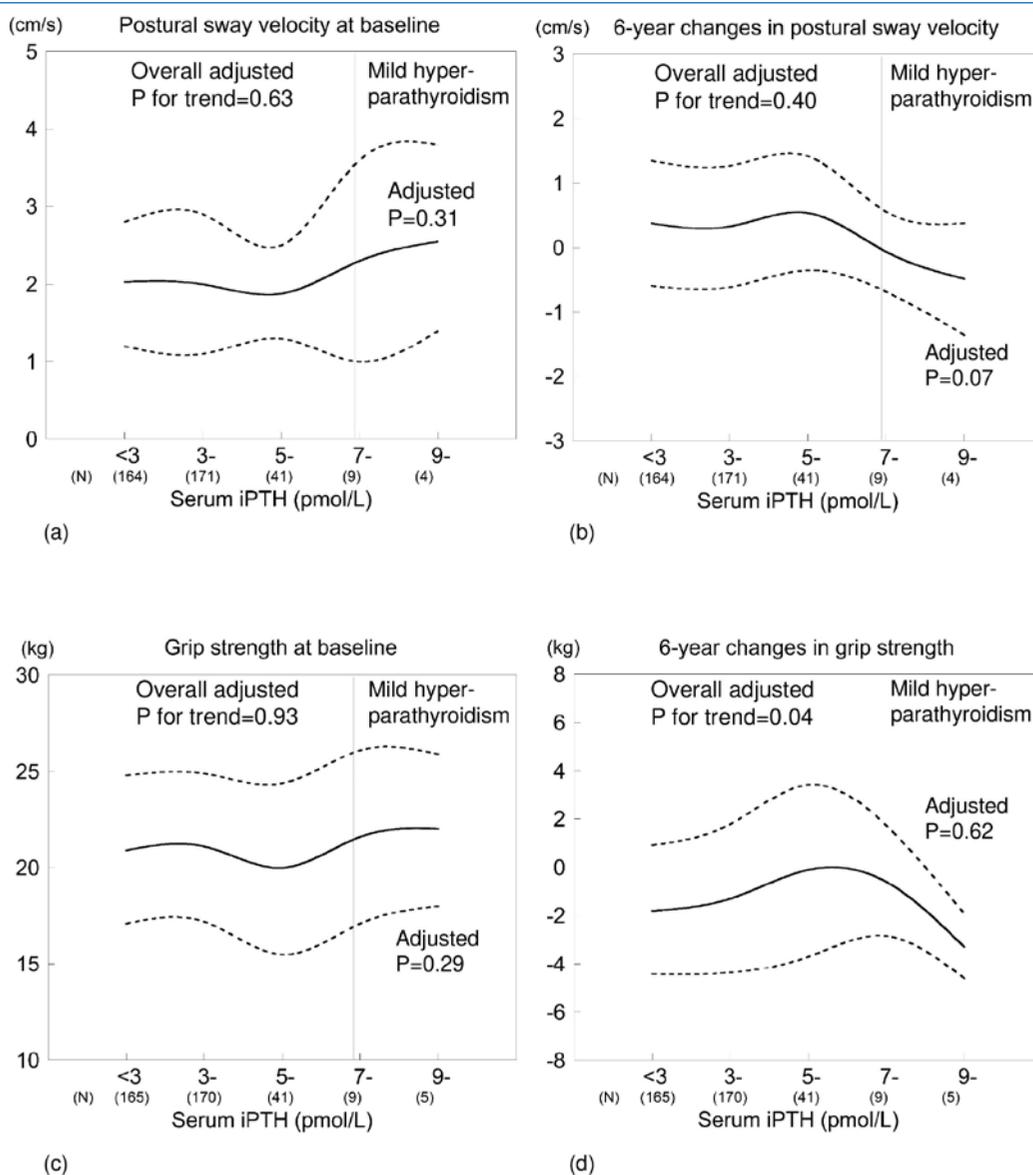
strength (20.9 vs 19.0 kg,  $P < 0.01$ ) than those who did not. Serum 25(OH)D (61.0 vs 58.9 nmol/L,  $P = 0.10$ ) and iPTH (3.6 vs 3.7 pmol/L,  $P = 0.57$ ) levels did not differ significantly between these two groups.

Baseline and 6-year changes ( $\Delta$ ) in postural sway velocity and grip strength are shown in Table 2 according to baseline 25(OH)D levels. We found no significant association between 25(OH)D levels and baseline postural sway velocity (adjusted P for trend=0.71),  $\Delta$ postural sway velocity (adjusted P for trend=0.72), or  $\Delta$ grip strength (adjusted P for trend=0.58). However, there was a positive association between 25(OH)D

levels and baseline grip strength (adjusted P for trend=0.045).

Baseline and 6-year changes in postural sway velocity and grip strength according to baseline iPTH levels are shown in Table 3. iPTH levels were not significantly associated with baseline postural sway velocity (adjusted P for trend=0.63), baseline grip strength (adjusted P for trend=0.93), or  $\Delta$ postural sway velocity (adjusted P for trend=0.40), but were positively associated with higher  $\Delta$ grip strength (adjusted P for trend=0.04).

Graphical associations between baseline 25(OH)D levels and physical performance levels by the cubic spline model



**Figure 2.** Cubic spline curves showing associations between intact PTH (iPTH) and (a) baseline postural sway velocity, (b) 6-year changes in postural sway velocity, (c) baseline grip strength, and (d) 6-year changes in grip strength. Solid and dashed lines represent mean values and standard deviations, respectively. Statistical robustness of the overall association between iPTH and physical performance levels is indicated by an “adjusted P for trend” value, with the statistical difference in physical performance levels between women with iPTH <6.9 pmol/L and  $\geq$ 6.9 pmol/L indicated by an adjusted P value.

are shown in Figure 1. Women with 25(OH)D <30 nmol/L tended to have higher baseline postural sway velocity (mean, 2.70 cm/s; adjusted P=0.10) compared to those with 25(OH)D  $\geq$ 30 nmol/L (mean, 2.00 cm/s) (Figure 1a). In contrast, women with 25(OH)D <30 nmol/L tended to have lower  $\Delta$ postural sway velocity (mean, -0.59 vs 0.37 cm/s, respectively; adjusted P=0.13) (Figure 1b). Regarding grip strength, women with 25(OH)D <30 nmol/L tended to have lower baseline grip strength (mean, 17.7 kg; adjusted P=0.11) than those with 25(OH)D  $\geq$ 30 nmol/L (mean, 21.0 kg; Figure 1c). However, there were no significant differences in  $\Delta$ grip

strength between women with 25(OH)D <30 nmol/L and  $\geq$ 30 nmol/L (adjusted P=0.89) (Figure 1d).

Graphical associations between baseline iPTH levels and physical performance levels by the cubic spline model are illustrated in Figure 2. We found no significant differences in baseline postural sway velocity between women with iPTH <6.9 pmol/L and  $\geq$ 6.9 pmol/L (adjusted P=0.31) (Figure 2a). However, women with iPTH  $\geq$ 6.9 pmol/L tended to have lower  $\Delta$ postural sway velocity (mean, -0.19 cm/s; adjusted P=0.07) than those with iPTH <6.9 pmol/L (mean, 0.38 cm/s) (Figure 2b). Regarding grip strength, there were no significant

differences in baseline and  $\Delta$ grip strength between women with iPTH <6.9 pmol/L and  $\geq$ 6.9 pmol/L (adjusted  $P=0.29$  and  $0.62$ , respectively) (Figures 2c, 2d).

## Discussion

This is the first longitudinal study to examine the association between serum 25(OH)D/PTH levels and changes in postural sway/grip strength in community-dwelling older women. Main findings of the present study include: 1) overall, physical performance parameters were not positively associated with serum 25(OH)D levels and not inversely associated with PTH levels, 2) women with severe vitamin D deficiency did not exhibit more marked changes in postural balance decline or grip strength relative to those without vitamin D deficiency; in fact, they seemed to exhibit less change in balance and grip strength than those without vitamin D deficiency. This was the case for women with high PTH levels as well.

Previous cross-sectional studies conducted in community settings showed that blood 25(OH)D levels were positively, and PTH levels were inversely, associated with better postural balance. Boersma et al.<sup>11</sup> reported that serum 25(OH)D levels <30 nmol/L were associated with postural instability in 145 older adults, and Bird et al.<sup>13</sup> reported that lower serum 25(OH)D levels were associated with poorer balance performance in 119 women aged 47–80 years. Also, de França et al.<sup>14</sup> showed that higher serum PTH levels were associated with more marked instability in static balance in 127 older adults, and Bislev et al.<sup>15</sup> found that elevated PTH levels are associated with poor performance in body sway in 104 older women with low 25(OH)D levels (<50 nmol/L). Regarding grip strength, Kocak et al.<sup>25</sup> showed that low vitamin D levels are associated with low grip strength in Turkish men aged >50 years, and Kitsu et al.<sup>26</sup> showed that low serum 25(OH)D levels (<50 nmol/L) are associated with low grip strength in 492 older Japanese. However, Kitsu et al.<sup>26</sup> also reviewed several comparable studies that examined the association between blood 25(OH)D levels and grip strength, noting mixed results. A few studies have found that high PTH levels are associated with low grip strength<sup>27,28</sup> and muscle strength in the lower extremities<sup>15</sup>. These findings are consistent with our cross-sectional results showing that women with severe vitamin D deficiency and high PTH levels tended to exhibit poor physical performance.

We were unable to find previous observational studies reporting an association between 25(OH)D/PTH levels and changes in postural balance. However, several intervention studies have evaluated the effects of vitamin D supplementation. Muir et al.<sup>16</sup> concluded that vitamin D supplementation improves balance and strength in older adults. However, recently conducted RCTs have not supported this conclusion<sup>17–19</sup>. In addition, a recently published meta-analysis of RCTs found no significant effect of vitamin D supplementation on fall occurrence<sup>29</sup>. Collectively, these studies may indicate that vitamin D may have only a

small effect, if any, on postural balance. The lack of a positive association between blood 25(OH)D levels and improvements in postural balance in the present study are consistent with this view.

Our study findings revealed that women with severe vitamin D deficiency tended to have lower  $\Delta$ postural sway velocity, i.e., postural sway is less impaired, although the subjects tended to have poor postural sway at baseline. This could indicate that, while women with severe vitamin D deficiency have poor postural balance, it does not worsen. Although it is difficult to explain this finding, we speculate that there is reverse causality, which is often observed in cross-sectional analysis, such that impaired physical performance decreases vitamin D levels. The exact mechanism should be explored in future studies.

Ethnic differences in the association between vitamin D levels and musculoskeletal parameters have been reported. For example, one study found a positive association between vitamin D levels and bone mineral density in Caucasians, but not in African and Asian groups<sup>30</sup>. Because the present study population included only East Asian older women, this could have influenced the association between vitamin D levels and postural balance.

This study has some limitations worth noting. First, participation in the follow-up examination was not high (50.6%), and thus follow-up data on physical performance may have been influenced by selection bias. Follow-up participants were younger and had better physical performance than non-participants, and thus follow-up results may have been skewed to reflect data of healthier women. In addition, as the present study targeted older women, the results may not be generalizable to older men.

## Conclusions

In conclusion, the present study found that vitamin D and PTH levels are not longitudinally associated with impaired postural sway or grip strength in older women. Further longitudinal studies are needed to confirm these results.

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### Authors' contributions

*Kazutoshi Nakamura: Conceptualization, Methodology, Investigation, Formal analysis, Writing (Original draft preparation). Toshiko Saito: Investigation. Akemi Takahashi: Methodology. Ryosaku Kobayashi: Investigation. Rieko Oshiki: Investigation. Kaori Kitamura: Writing (Reviewing and Editing). and Yumi Watanabe: Writing (Reviewing and Editing).*

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