

# Association of serum vitamin D with osteosarcopenic obesity: Korea National Health and Nutrition Examination Survey 2008–2010

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## Abstract

**Background** Serum vitamin D levels have been reported to be associated with individual components of body composition. However, the relationship between serum vitamin D and combined indices of adverse body composition is largely unknown. This cross-sectional study examined the association between serum vitamin D and osteosarcopenic obesity in a nationally representative sample of middle-aged and older adults.

**Methods** We analysed the Korea National Health and Nutrition Examination Surveys (IV and V) conducted in 2008–2010, consisting of 5908 (2485 men, 3423 women) aged  $\geq 50$  years. Serum vitamin D levels were determined by radioimmunoassay, and body composition was evaluated by dual-energy x-ray absorptiometry. The association between serum vitamin D levels and the number of abnormalities in body composition, including osteosarcopenic obesity, a low bone and muscle mass with concurrent high fat mass, was analysed by multinomial logistic regression adjusting for covariates.

**Results** In men, after controlling for covariates, higher vitamin D levels were associated with a significantly reduced likelihood of the number of phenotypes of adverse body composition ( $P$  for trend  $< 0.05$ ). Those in the highest tertile group of serum vitamin D levels, compared with those in the lowest tertile, were less likely to have adverse body composition, numbering one (odds ratio [OR] = 0.67, 95% confidence interval [CI]: 0.49, 0.92), two (OR = 0.49, 95% CI: 0.33, 0.73), and three (osteosarcopenic obesity; OR = 0.42, 95% CI: 0.26, 0.67). In women, those in the highest tertile group of serum vitamin D levels, compared with those in the lowest tertile, were less likely to have osteosarcopenic obesity (OR = 0.55, 95% CI: 0.33, 0.93). Vitamin D deficiency ( $< 20$  ng/mL) in men was significantly associated with an increased likelihood of a higher number of adverse body composition, especially for osteosarcopenic obesity (OR = 2.08, 95% CI: 1.42, 3.03). Vitamin D deficient women, compared with those having normal levels of serum vitamin D, were also more likely to demonstrate osteosarcopenic obesity (OR = 1.99, 95% CI: 1.30, 3.05).

**Conclusions** A high serum vitamin D level in mid- and late-life was associated with reduced odds of multiple adverse body composition, especially osteosarcopenic obesity, suggesting potential health benefits of maintaining adequate levels of vitamin D.

**Keywords** Vitamin D; Osteosarcopenic obesity; Osteoporosis; Sarcopenia; Obesity

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## Introduction

Ageing can lead to unfavourable changes in body composition, such as bone and muscle loss, and fat gain, raising the risk of osteoporosis, sarcopenia, and obesity in mid- and late-life.<sup>1–3</sup> Bone, muscle, and adipose tissues are interconnected.<sup>4</sup> The mechanical interactions between bone and muscle are well established, and a growing body of research suggests a potential cross-talk between bone and muscle.<sup>5</sup> The increase in adiposity also exacerbates the loss of bone and muscle mass.<sup>4</sup> A combination of adverse interrelationships in body composition is hypothesized to manifest in osteosarcopenic obesity, a term coined to depict a concurrent occurrence of the three phenotypes, osteopenia/osteoporosis, sarcopenia, and obesity.<sup>4</sup> Osteosarcopenic obesity may lead to functional impairment and increase the risk of falls, fractures, and morbidity.<sup>6</sup>

Vitamin D is known to be vital in sustaining musculoskeletal functions, with vitamin D deficiency causing muscle weakness and decreased bone mineral density.<sup>7</sup> Vitamin D also appears to have pleiotropic effects by inhibiting adipogenesis and modulating inflammatory response on adipose tissues, with accumulating evidence linking low levels of vitamin D to obesity.<sup>8</sup> Vitamin D inadequacy is highly prevalent, with vitamin D deficiency or insufficiency estimated to affect one billion people worldwide.<sup>7,9</sup>

Previous studies have indicated a significant association between serum vitamin D and individual components of abnormal body composition, manifesting as osteoporosis, sarcopenia, and obesity.<sup>10–16</sup> Besides vitamin D having individual protective effects on either bone or muscle mass and modulating body fat accumulation,<sup>7,8,17–19</sup> vitamin D as a single factor displaying combined effects, such as on both bone and muscle mass, has been suggested.<sup>12</sup> However, few studies have examined the relationship between serum vitamin D with combined abnormalities in body composition.<sup>20–23</sup> Moreover, there is no study that has investigated its association with osteosarcopenic obesity.

The aim of this study was to examine the association of 25-hydroxyvitamin D (abbreviated 25(OH)D) level with a combined adverse body composition (bone, muscle, and fat) in a representative sample of middle-aged and older people living in the community.

## Subjects and methods

### Study population

Data are from the Fourth and Fifth Korea National Health and Nutrition Examination Survey (KNHANES IV–V) in 2008–2010, conducted by the Korea Centers for Disease Control and Prevention (KCDC). Details of the survey design are described

elsewhere.<sup>24</sup> KNHANES IV–V employs a multistage stratified cluster sampling for the selection of household units of non-institutionalized residents. The study protocols were approved by the Institutional Review Board of the KCDC. Written informed consent forms were obtained from all participants.

KNHANES IV–V consists of the health interview survey, health examination, and nutritional assessment. Among the 6056 aged  $\geq 50$  y who completed the three evaluations, those with implausibly high laboratory data ( $n = 2$ ) and low or high daily energy intake ( $< 800$  kcal/d or  $> 4000$  kcal/d for men,  $< 500$  kcal/d or  $> 3500$  kcal/d for women) (86 men and 60 women) were excluded. The sample used in the final analysis comprised of 2485 men and 3423 women.

### Measurements

To measure the serum 25(OH)D level, blood samples of individual subjects were collected during the survey after an overnight fast and analysed within 24 h after transport. A gamma counter (1470 WIZARD; Perkin-Elmer, Turku, Finland) with radioimmunoassay (DiaSorin; Stillwater, MN, USA) was used to assess serum 25(OH)D concentrations. Inter-assay coefficients of variation varied from 8.6% to 12.5%.<sup>25</sup> Subjects were classified by tertiles of serum vitamin D values. A serum 25(OH)D level less than 20 ng/mL was defined to indicate vitamin D deficiency.<sup>26</sup>

Body composition was measured with dual-energy x-ray absorptiometry (Discovery-W, Hologic Inc., Waltham, MA, USA). Based on the recommendations of the International Society for Clinical Densitometry in 2007,<sup>27</sup> bone mineral density measurements were performed. Low bone mass was defined to include both osteopenia ( $T$ -score between  $-1.0$  and  $-2.5$ ) and osteoporosis ( $T$ -score  $-2.5$  and below), using the World Health Organization criteria<sup>28</sup> calculated from the Asian reference data. Appendicular skeletal muscle mass (ASM), the sum of lean soft-tissue mass in both extremities,<sup>29</sup> was measured. Low muscle mass was defined as ASM more than 1 SD below the gender-specific mean of the young healthy reference group.<sup>30</sup> Obesity was defined as the upper 40% of body fat by gender.<sup>31</sup> The number of adverse body composition was categorized as 0 (normal; without low bone mass, low muscle mass, or obesity), 1 (having one of the components), 2 (having two of the components), and 3 (osteosarcopenic obesity; having all three components).

### Covariates

Sociodemographic characteristics included age, education level (elementary school or lower vs. higher than elementary school), and equivalent household income (monthly household income divided by the square root of the number of

household members by gender and 5-year age group). Smoking status was classified as none, past, or current. Alcohol consumption was dichotomized as  $\leq 1$  drink/d vs.  $> 1$  drink/d. Physical activity assessed participation in recommended levels ( $\geq 150$  min/week of moderate-intensity and/or  $\geq 75$  min/week of vigorous-intensity) of aerobic physical activity.<sup>32</sup> Sunlight exposure ( $< 5$  h/d vs.  $\geq 5$  h/d) and dietary supplement use were also obtained by self-report. For women, menopausal status was reported. Laboratory data included systolic blood pressure (SBP), diastolic BP (DBP), fasting blood sugar (FBS), total cholesterol, high density lipoprotein cholesterol (HDL-C), triglyceride, aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine, and parathyroid hormone (PTH). Homeostasis model assessment of insulin resistance (HOMA-IR) was defined as fasting plasma glucose (mg/dL) multiplied by fasting insulin (microIU/mL) divided by 22.5.<sup>33</sup> The 24-h dietary recall and food frequency questionnaire were applied to measure dietary intakes. Frequency of food group consumption (meats, egg, fish, mushrooms, and milk) and nutrient intake (energy, protein, and calcium) was derived from dietary intakes.

### Statistical analyses

The characteristics of the study sample were presented as mean and standard deviation (SD), or percentages. The

relationship between sample characteristics and the number of adverse body composition was analysed using the analysis of variance (ANOVA) and chi-square tests. Potential laboratory confounders with  $P < 0.20$  in their associations with both serum vitamin D and body composition in the bivariate analyses were adjusted in the final model. Using multinomial logistic regression analysis, risks of adverse body composition, with tertiles or deficiency of serum vitamin D levels, were shown as odds ratios (OR) and 95% confidence intervals (CI), adjusting for covariates. All analyses were conducted separately by gender, using IBM SPSS Statistics 22.0 (SPSS, International Business Machines Corp., Armonk, NY). The complex sampling weights were applied in all analyses.

## Results

Among men, for the number of adverse body composition, 26.3% had none, 38.9% had one, 21.4% had two, and 13.5% had all three (osteosarcopenic obesity). In women, it was 10.2%, 46.0%, 18.8%, and 25.0%, respectively. The prevalence of vitamin D deficiency was 45.5% in men and 63.4% in women.

The sample characteristics are shown in *Table 1*. The mean age was higher in women than men. The education levels, rates of current smoking, alcohol consumption, participation in recommended levels of physical activity, and sunlight

**Table 1** Characteristics of study subjects<sup>a</sup>

	Men (n = 2485)	Women (n = 3423)		Men (n = 2485)	Women (n = 3423)
General characteristics			Laboratory data <sup>d</sup>		
Age (y)	60.7 ± 8.4	61.7 ± 8.9	SBP (mmHg)	123.8 ± 17.1	125.1 ± 18.1
Education level			DBP (mmHg)	77.8 ± 10.7	76.5 ± 10.1
≤Elementary school	31.0	60.0	FBS (mg/dL)	105.3 ± 27.7	101.3 ± 24.3
>Elementary school	69.0	40.0	HOMA-IR	2.6 ± 1.7	2.7 ± 2.2
Quartiles of equivalent income <sup>b</sup>			Total cholesterol (mg/dL)	187.7 ± 37.0	201.3 ± 36.2
1 (lowest)	23.1	23.8	HDL-C (mg/dL)	44.6 ± 10.6	48.4 ± 10.9
2	25.9	23.6	Triglyceride (mg/dL)	162.0 ± 119.5	138.2 ± 86.7
3	24.0	26.4	AST (IU/L)	26.0 ± 15.4	22.9 ± 9.2
4 (highest)	27.0	26.2	ALT (IU/L)	24.6 ± 14.6	20.2 ± 11.9
Smoking			Creatinine (mg/dL)	1.0 ± 0.2	0.7 ± 0.2
Nonsmoker	16.4	92.0	PTH (pg/mL)	65.0 ± 25.2	67.9 ± 30.6
Past smoker	48.7	3.5	25(OH)D (ng/mL)	21.5 ± 7.3	18.6 ± 7.0
Current smoker	34.9	4.5	Frequency of food group consumption		
Alcohol consumption			Meats (times/wk)	1.5 ± 1.3	1.2 ± 1.5
≤1 drink/d	79.1	96.2	Egg (times/wk)	1.9 ± 1.9	1.7 ± 1.9
>1 drinks/d	20.9	3.8	Fish (times/wk)	4.6 ± 3.9	4.4 ± 4.0
Recommended level of exercise <sup>c</sup>	45.0	37.5	Mushrooms (times/wk)	1.2 ± 1.6	1.1 ± 1.5
Sunlight exposure			Milk (times/wk)	1.7 ± 2.5	2.1 ± 3.0
<5 h/d	64.0	78.5	Nutrient intake		
≥5 h/d	36.0	21.5	Energy (kcal/d)	2111.1 ± 639.9	1570.3 ± 537.0
Dietary supplement use (yes)	33.0	48.3	Protein (g/d)	74.0 ± 30.6	53.0 ± 24.9
Menopause (yes)		91.6	Calcium (mg/d)	556.4 ± 344.3	435.3 ± 399.7

<sup>a</sup>Values are mean ± SD, or percentage.

<sup>b</sup>Monthly household income/ $\sqrt$ number of household members according to sex and 5 year age group.

<sup>c</sup> $\geq 150$  min/wk moderate-intensity and/or  $\geq 75$  min/wk vigorous-intensity aerobic physical activity.

<sup>d</sup>ALT, alanine aminotransferase; AST, aspartate aminotransferase; DBP, diastolic blood pressure; FBS, fasting blood sugar; HDL-C, high density lipoprotein cholesterol; HOMA-IR, insulin resistance assessed by homeostasis model assessment; PTH, parathyroid hormone; SBP, systolic blood pressure; 25(OH)D, 25-hydroxyvitamin D.

exposure were higher among men than women. Compared with men, more women used dietary supplements and most of the women were post-menopause. The laboratory data, frequency of food group consumption, and nutrient intakes were higher in men, but PTH levels and frequency of milk consumption were higher in women.

In men, those having a higher number of adverse body composition tended to be older, less educated, and less likely to consume alcohol, participate in recommended levels of physical activity, and to have shorter exposure to daily sunlight. Laboratory data were significantly associated with the number of adverse body composition, with those having a higher number of adverse body composition exhibiting lower nutrient intakes (Table 2). In women, with an increasing number of adverse body composition, participants tended to be older, less educated, current smokers, and to report less frequent alcohol consumption, lower amounts of physical activity, shorter duration of daily sunlight exposure, and no

dietary supplement use, with a higher percentage in post-menopause. Laboratory data were significantly associated with the number of adverse body composition, and there was a tendency of less frequent consumption of fish, mushrooms, milk, energy, and protein for those with more adverse body composition (Table 3).

The association between 25(OH)D levels and the number of adverse body composition is displayed in Table 4. In men, vitamin D serum levels were inversely associated with higher number of adverse body composition. After controlling for covariates, men in the higher tertiles of serum vitamin D levels, compared with those in the lowest tertile, had a significantly reduced likelihood of multiple adverse body composition (*P* for trend < 0.05 for those with one, two, or three simultaneous adverse components). Those in the highest tertile exhibited a 58% reduced odds of osteosarcopenic obesity (OR = 0.42, 95% CI: 0.26, 0.67). In women, those in the highest tertile of serum 25(OH)D levels,

**Table 2** Relationship between the number of adverse body composition<sup>a</sup> and subject characteristics in men<sup>b</sup>

	Men (n = 2485)				<i>P</i> <sup>c</sup>
	0	1	2	3	
<b>General characteristics</b>					
Age (y)	58.0 ± 6.7	60.9 ± 8.5	61.6 ± 8.4	63.9 ± 9.4	<0.001
Education level (> elementary school)	75.5	64.6	70.7	66.1	0.002
Quartiles of equivalent income <sup>d</sup> (highest)	31.0	24.9	28.6	22.5	0.37
Current smoker	39.3	35.5	30.5	31.7	0.13
Alcohol consumption (> 1 drinks/d)	19.6	23.7	20.9	14.9	0.04
Recommended level of exercise <sup>e</sup> (yes)	52.4	46.1	42.1	31.6	<0.001
Sunlight exposure (≥ 5 h/d)	37.9	39.4	34.1	25.5	0.003
Dietary supplement use (yes)	32.7	32.1	37.8	28.3	0.11
<b>Laboratory data<sup>f</sup></b>					
SBP (mmHg)	122.3 ± 17.4	123.1 ± 17.4	125.1 ± 16.0	126.5 ± 17.0	0.002
DBP (mmHg)	77.7 ± 10.8	77.4 ± 11.0	78.8 ± 10.2	77.7 ± 10.3	0.30
FBS (mg/dL)	106.4 ± 29.9	101.9 ± 24.8	108.6 ± 30.8	108.0 ± 24.6	<0.001
HOMA-IR	2.4 ± 1.3	2.3 ± 1.5	3.1 ± 2.2	3.1 ± 2.0	<0.001
Total cholesterol (mg/dL)	189.0 ± 36.9	185.8 ± 36.6	189.1 ± 38.3	188.3 ± 35.8	0.40
HDL-C (mg/dL)	45.3 ± 10.7	45.9 ± 10.8	42.8 ± 9.8	42.2 ± 10.0	<0.001
Triglyceride (mg/dL)	153.7 ± 117.2	150.8 ± 112.0	184.4 ± 125.8	175.0 ± 128.2	<0.001
AST (IU/L)	25.0 ± 12.5	26.4 ± 16.1	27.2 ± 19.8	25.2 ± 9.3	0.07
ALT (IU/L)	23.5 ± 12.8	23.5 ± 13.5	27.8 ± 18.1	24.9 ± 14.3	<0.001
Creatinine (mg/dL)	1.0 ± 0.2	0.9 ± 0.1	1.0 ± 0.2	1.0 ± 0.3	<0.001
PTH (pg/mL)	62.6 ± 22.7	63.4 ± 23.6	68.8 ± 28.4	68.7 ± 27.3	<0.001
<b>Frequency of food group consumption</b>					
Meats (times/wk)	1.6 ± 1.3	1.5 ± 1.3	1.7 ± 1.5	1.4 ± 1.2	0.13
Egg (times/wk)	2.1 ± 2.0	1.8 ± 1.8	2.0 ± 2.1	1.9 ± 1.9	0.12
Fish (times/wk)	4.5 ± 3.8	4.7 ± 4.0	4.7 ± 3.7	4.1 ± 3.9	0.15
Mushrooms (times/wk)	1.3 ± 1.5	1.3 ± 1.7	1.2 ± 1.4	1.1 ± 1.3	0.40
Milk (times/wk)	1.8 ± 2.5	1.7 ± 2.7	1.5 ± 2.4	1.4 ± 2.5	0.15
<b>Nutrient intake</b>					
Energy (kcal/d)	2235.6 ± 653.1	2102.9 ± 627.2	2067.5 ± 649.3	1961.4 ± 589.6	<0.001
Protein (g/d)	79.0 ± 30.3	72.4 ± 29.7	73.5 ± 31.6	69.6 ± 31.0	0.001
Calcium (mg/d)	600.0 ± 370.3	555.8 ± 332.7	540.0 ± 309.8	499.3 ± 365.5	0.006

<sup>a</sup>Multiple adverse body composition: number of osteopenia/osteoporosis, muscle mass loss, or obesity.

<sup>b</sup>Values are mean ± SD, or percentage.

<sup>c</sup>Analysis of variance (ANOVA) for continuous variables and chi-square test for categorical variables.

<sup>d</sup>Monthly household income/number of household members according to sex and 5-year age group.

<sup>e</sup>≥ 150 min/wk moderate-intensity and/or ≥ 75 min/wk vigorous-intensity aerobic physical activity.

<sup>f</sup>ALT, alanine aminotransferase; AST, aspartate aminotransferase; DBP, diastolic blood pressure; FBS, fasting blood sugar; HDL-C, high density lipoprotein cholesterol; HOMA-IR, insulin resistance assessed by homeostasis model assessment; PTH, parathyroid hormone; SBP, systolic blood pressure.

**Table 3** Relationship between the number of adverse body composition<sup>a</sup> and subject characteristics in women<sup>b</sup>

	Women (n = 3423)				P <sup>c</sup>
	0	1	2	3	
<b>General characteristics</b>					
Age (y)	54.2 ± 4.2	62.3 ± 9.0	61.0 ± 8.4	64.2 ± 8.8	<0.001
Education level (>elementary school)	66.2	38.0	41.0	32.4	<0.001
Quartiles of equivalent income <sup>d</sup> (highest)	29.9	24.2	25.5	28.9	0.08
Current smoker	1.4	6.1	3.1	3.9	<0.001
Alcohol consumption (>1 drinks/d)	7.2	3.7	3.1	3.0	0.05
Recommended level of exercise <sup>e</sup> (yes)	50.7	39.2	33.8	31.6	<0.001
Sunlight exposure (≥5 h/d)	18.0	27.1	18.4	14.9	<0.001
Dietary supplement use (yes)	57.9	47.7	46.1	47.0	0.03
Menopause (yes)	71.8	94.2	90.0	96.3	<0.001
<b>Laboratory data<sup>f</sup></b>					
SBP (mmHg)	120.9 ± 18.5	124.3 ± 18.0	125.1 ± 17.7	128.4 ± 18.0	<0.001
DBP (mmHg)	77.0 ± 11.5	75.6 ± 10.0	77.2 ± 9.9	77.5 ± 9.6	0.001
FBS (mg/dL)	98.3 ± 22.3	100.5 ± 24.9	101.3 ± 22.0	104.2 ± 25.4	0.02
HOMA-IR	2.4 ± 1.3	2.4 ± 1.6	2.8 ± 2.0	3.1 ± 3.3	<0.001
Total cholesterol (mg/dL)	196.5 ± 37.0	199.0 ± 35.3	200.9 ± 36.5	207.8 ± 36.6	<0.001
HDL-C (mg/dL)	51.1 ± 10.9	48.4 ± 11.2	48.1 ± 10.9	47.4 ± 10.3	<0.001
Triglyceride (mg/dL)	124.8 ± 88.3	134.6 ± 87.5	139.9 ± 84.6	149.2 ± 84.8	0.002
AST (IU/L)	21.8 ± 6.9	22.8 ± 8.6	23.4 ± 11.1	23.3 ± 9.3	0.06
ALT (IU/L)	19.9 ± 10.2	19.5 ± 11.6	20.8 ± 13.4	21.2 ± 11.6	0.02
Creatinine (mg/dL)	0.7 ± 0.1	0.7 ± 0.2	0.7 ± 0.2	0.7 ± 0.1	0.21
PTH (pg/mL)	61.4 ± 24.3	66.6 ± 32.3	67.2 ± 26.4	73.4 ± 31.6	<0.001
<b>Frequency of food group consumption</b>					
Meats (times/wk)	1.4 ± 1.7	1.1 ± 1.4	1.2 ± 1.3	1.2 ± 1.6	0.13
Egg (times/wk)	2.0 ± 1.8	1.7 ± 1.9	1.8 ± 1.8	1.6 ± 2.0	0.14
Fish (times/wk)	5.1 ± 4.1	4.5 ± 4.2	4.5 ± 4.0	4.1 ± 3.8	0.02
Mushrooms (times/wk)	1.5 ± 2.0	1.1 ± 1.5	1.1 ± 1.3	1.1 ± 1.3	0.002
Milk (times/wk)	2.8 ± 3.3	2.2 ± 3.0	2.1 ± 2.9	1.8 ± 2.7	0.001
<b>Nutrient intake</b>					
Energy (kcal/d)	1620.3 ± 566.4	1591.1 ± 531.6	1587.1 ± 535.9	1499.2 ± 528.6	0.01
Protein (g/d)	57.1 ± 27.8	52.2 ± 23.8	55.2 ± 25.1	51.2 ± 25.0	0.006
Calcium (mg/d)	477.8 ± 321.3	427.8 ± 297.6	440.8 ± 315.5	427.5 ± 598.3	0.17

<sup>a</sup>Multiple adverse body composition: number of osteopenia/osteoporosis, muscle mass loss, or obesity.

<sup>b</sup>Values are mean ± SD, or percentage.

<sup>c</sup>Analysis of variance (ANOVA) for continuous variables and chi-square test for categorical variables.

<sup>d</sup>Monthly household income/number of household members according to sex and 5-year age group.

<sup>e</sup>≥150 min/wk moderate-intensity and/or ≥75 min/wk vigorous-intensity aerobic physical activity.

<sup>f</sup>ALT, alanine aminotransferase; AST, aspartate aminotransferase; DBP, diastolic blood pressure; FBS, fasting blood sugar; HDL-C, high density lipoprotein cholesterol; HOMA-IR, insulin resistance assessed by homeostasis model assessment; PTH, parathyroid hormone; SBP, systolic blood pressure.

compared with those in the lowest tertile, were significantly less likely to have osteosarcopenic obesity (OR = 0.55, 95% CI: 0.33, 0.93).

The association between vitamin D deficiency and the number of adverse body composition is shown in *Table 5*. In men, vitamin D deficiency was significantly associated with an increased likelihood of multiple adverse body composition, adjusting for covariates, especially for osteosarcopenic obesity (OR = 2.08, 95% CI: 1.42, 3.03). In women, vitamin D deficiency was significantly associated with osteosarcopenic obesity (OR = 1.99, 95% CI: 1.30, 3.05).

## Discussion

Serum vitamin D levels were significantly associated with multiple adverse body composition in middle-aged and older Korean adults. After adjusting for covariates, in men, higher

serum vitamin D levels were negatively associated, while deficiency of serum vitamin D was positively associated, with the number of abnormal body composition. In women, higher serum vitamin D levels were negatively associated with osteosarcopenic obesity and deficiency of serum vitamin D was positively associated with osteosarcopenic obesity. To our knowledge, this is the first study to demonstrate the significant association between serum vitamin D levels and multiple adverse body composition in community-dwelling people in their mid- and late-life.

Numerous studies have investigated the relationship between serum 25(OH)D levels and individual body composition. Calcium and vitamin D were positively associated with bone health in several studies.<sup>10–14</sup> A study involving a nationwide sample of Koreans aged 40 years and older showed a lower mean value of appendicular skeletal muscle mass index (ASSMI) in men, but not in women, with hypovitaminosis, defined as serum 25(OH)D < 20 ng/mL.<sup>15</sup>

**Table 4** Likelihood of multiple adverse body composition according to serum vitamin D levels: multinomial logistic regression analysis

Adverse body composition <sup>a</sup>	Men (n = 2485)				
	Tertiles (T) of serum vitamin D	Crude OR (95% CI)	P for trend	Adjusted OR <sup>b</sup> (95% CI)	P for trend
1 vs. 0	T1 (median, 14.6)	1.00	0.08	1.00	0.02
	T2 (median, 21.1)	0.65 (0.48, 0.89)		0.62 (0.45, 0.87)	
	T3 (median, 29.0)	0.75 (0.56, 1.01)		0.67 (0.49, 0.92)	
2 vs. 0	T1	1.00	<0.001	1.00	<0.001
	T2	0.60 (0.42, 0.87)		0.65 (0.44, 0.96)	
	T3	0.45 (0.31, 0.65)		0.49 (0.33, 0.73)	
3 vs. 0	T1	1.00	<0.001	1.00	<0.001
	T2	0.40 (0.27, 0.59)		0.46 (0.30, 0.70)	
	T3	0.35 (0.23, 0.54)		0.42 (0.26, 0.67)	

  

Adverse body composition <sup>a</sup>	Women (n = 3423)				
	Tertiles (T) of serum vitamin D	Crude OR (95% CI)	P for trend	Adjusted OR <sup>c</sup> (95% CI)	P for trend
1 vs. 0	T1 (median, 12.2)	1.00	0.63	1.00	0.47
	T2 (median, 18.0)	1.08 (0.75, 1.56)		1.18 (0.79, 1.77)	
	T3 (median, 26.1)	1.10 (0.75, 1.62)		0.86 (0.55, 1.35)	
2 vs. 0	T1	1.00	0.6	1.00	0.39
	T2	0.91 (0.60, 1.38)		1.02 (0.65, 1.59)	
	T3	0.89 (0.58, 1.37)		0.81 (0.50, 1.32)	
3 vs. 0	T1	1.00	0.02	1.00	0.03
	T2	0.85 (0.57, 1.27)		1.03 (0.66, 1.60)	
	T3	0.58 (0.37, 0.91)		0.55 (0.33, 0.93)	

<sup>a</sup>Number of osteopenia/osteoporosis, muscle mass loss, and obesity.

<sup>b</sup>Adjusted for age, education level, quartiles of equivalent income, smoking, alcohol consumption, recommended level of exercise, sun-light exposure, dietary supplement use, fasting blood sugar, insulin resistance assessed by homeostasis model assessment, high density lipoprotein cholesterol, triglyceride, alanine aminotransferase, creatinine, parathyroid hormone, frequency of food group consumption (meats, egg, fish, mushrooms, milk), and nutrient intake (energy, protein, calcium).

<sup>c</sup>Adjusted for age, education level, quartiles of equivalent income, smoking, alcohol consumption, recommended level of exercise, sun-light exposure, dietary supplement use, menopausal status, systolic blood pressure, diastolic blood pressure, triglyceride, parathyroid hormone, frequency of food group consumption (meats, egg, fish, mushrooms, milk), and nutrient intake (energy, protein, calcium).

**Table 5** Likelihood of multiple adverse body composition by the presence of vitamin D deficiency: multinomial logistic regression analysis

Adverse body composition <sup>a</sup>	Men (n = 2485)		
	Deficiency of serum vitamin D (<20 ng/mL)	Crude OR (95% CI)	Adjusted OR <sup>b</sup> (95% CI)
1 vs. 0	No	1.00	1.00
	Yes	1.29 (1.00, 1.67)	1.35 (1.03, 1.77)
2 vs. 0	No	1.00	1.00
	Yes	1.91 (1.40, 2.61)	1.71 (1.21, 2.41)
3 vs. 0	No	1.00	1.00
	Yes	2.52 (1.78, 3.57)	2.08 (1.42, 3.03)

  

Adverse body composition <sup>a</sup>	Women (n = 3423)		
	Deficiency of serum vitamin D (<20 ng/mL)	Crude OR (95% CI)	Adjusted OR <sup>c</sup> (95% CI)
1 vs. 0	No	1.00	1.00
	Yes	0.99 (0.71, 1.37)	1.31 (0.90, 1.90)
2 vs. 0	No	1.00	1.00
	Yes	1.05 (0.73, 1.52)	1.22 (0.82, 1.82)
3 vs. 0	No	1.00	1.00
	Yes	1.71 (1.17, 2.51)	1.99 (1.30, 3.05)

<sup>a</sup>Number of osteopenia/osteoporosis, muscle mass loss, and obesity.

<sup>b</sup>Adjusted for age, education level, quartiles of equivalent income, smoking, alcohol consumption, recommended level of exercise, sun-light exposure, dietary supplement use, fasting blood sugar, insulin resistance assessed by homeostasis model assessment, high density lipoprotein cholesterol, triglyceride, alanine aminotransferase, creatinine, parathyroid hormone, frequency of food group consumption (meats, egg, fish, mushrooms, milk), and nutrient intake (energy, protein, calcium).

<sup>c</sup>Adjusted for age, education level, quartiles of equivalent income, smoking, alcohol consumption, recommended level of exercise, sun-light exposure, dietary supplement use, menopausal status, systolic blood pressure, diastolic blood pressure, triglyceride, parathyroid hormone, frequency of food group consumption (meats, egg, fish, mushrooms, milk), and nutrient intake (energy, protein, calcium).

An inverse relationship between body fat percentage (BF) and serum 25(OH)D or vitamin D deficiency, irrespective of the fat location, has also been reported.<sup>16</sup>

However, relatively few studies have examined the relationship between serum vitamin D levels and combined indices of body composition. Favourable effects of vitamin D on the interaction between bone and muscle have been suggested.<sup>20,21</sup> In Korean men, those in the combined group with the highest third of total fat percentage (TFP) and the lowest third of total lean mass (TLM), compared with those in the lowest tertile of TFP and highest tertile of total TLM, were 2.2 times more likely to exhibit vitamin D deficiency.<sup>22</sup> In a study of Thai populations without diabetes, vitamin D status and male sex were identified as significant positive predictors of percent skeletal muscle mass.<sup>23</sup> In lifestyle intervention therapies for obese older adults, vitamin D supplementation is recommended when inducing weight loss, for minimizing bone and muscle mass loss.<sup>34</sup>

The potential roles of vitamin D in bone, muscle, and body fat have been suggested. Vitamin D is known to have beneficial effects on the bone by suppressing PTH levels and promoting calcium absorption, and further lowering the risk of falls and fracture.<sup>7,17</sup> Vitamin D, in its active form, can stimulate muscle cell proliferation and growth by activating vitamin D receptors (VDR) that mediates both gene transcription and rapid non-transcriptional signal transduction, regulating protein synthesis and calcium handling involved in muscle cell development.<sup>35</sup> In body fat, vitamin D may modulate VDR that can affect energy metabolism<sup>19</sup> and also potentially modulate adipogenesis and preadipocyte differentiation.<sup>8</sup> Vitamin D deficiency might induce adipogenesis, whereas higher vitamin D concentration attenuates the effect.<sup>36</sup> Alternatively, obesity may be a risk factor for vitamin D deficiency.<sup>37</sup> Anti-inflammatory effects of vitamin D have been suggested as well.<sup>38</sup> Vitamin D may mediate bone-muscle cross-talk. It inhibits myostatin production, while stimulating vascular endothelial growth factor, insulin-like growth factor-1, and osteoglycin production in muscle that have beneficial effects on bone.<sup>5</sup> Alternatively, vitamin D may increase the production of sclerostin, osteocalcin, and fibroblast growth factor-23 in bone that can potentially stimulate myogenic activity.

In this study, the magnitude of the association between serum 25(OH)D levels and multiple adverse body composition was stronger in men than women. This gender difference could be because of in part the effect of the genotype of VDR (FokI) polymorphism, the risk allele (F allele), found in older men that increases the risk of sarcopenia.<sup>39</sup> More men than women may have the risk allele, leading to a more rapid decline in skeletal muscle mass. Also, vitamin D co-regulates the synthesis of sex hormones,<sup>40</sup> with adverse skeletal effects of low sex steroid levels being pronounced among men with low

25(OH)D levels.<sup>41</sup> Further study is needed to confirm the gender difference.

The strength of this study lies in the representativeness of the study sample, giving credence to the external validity of the results. Moreover, numerous potential confounders were adjusted in the analysis, demonstrating the robustness of the findings.

In interpreting the results of this study, however, several limitations need to be considered. First, data on the seasonal variation of exposure to solar ultraviolet-B radiation and diets enriched with vitamin D, including supplements, that could modify 25(OH)D blood levels were not available for analysis. Second, sarcopenia was defined by muscle mass loss only, because muscle performance was not assessed in the survey. Third, the association of vitamin D with mutually exclusive combinations of abnormal body composition could not be analysed because of insufficient sample size. Finally, the cross-sectional design of the survey prevents us from making any causal inferences of vitamin D's possible effect on multiple adverse body composition. A reverse causality cannot be ruled out, as vitamin D may be sequestered in adipose tissues of obese individuals.<sup>37</sup>

In conclusion, we found that higher serum vitamin D levels were associated with a reduced likelihood of concurrent adverse body composition in middle-aged and older adults, with a deficiency of serum vitamin D being associated with an elevated risk. Our findings suggest that maintaining serum vitamin D levels may potentially protect against combined abnormalities in body composition, especially osteosarcopenic obesity, in midlife and late life. Longitudinal studies are warranted to better understand whether differences in serum vitamin D levels affect multiple components of body composition.

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## Conflict of interests

Jinhee Kim, Yunhwan Lee, Seunghee Kye, Yoon-Sok Chung, and Okhee Lee declare that they have no conflict of interest.

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