ORIGINAL ARTICLE

High skeletal muscle mass is associated with increased serum 25(OH)D levels in elderly

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ABSTRACT

BACKGROUND

Low vitamin D has been associated with various health problems. Aging influences body composition, especially body fat and fat-free mass. Anthropometric measurements, such as body weight (BW), body mass index (BMI), body fat (BF), skeletal muscle mass (SMM), waist circumference (WC) and the waist-height ratio (WHtR) represent body composition which many studies proposed will influence serum vitamin D [25(OH)D]. The objective of the present study was to determine which anthropometric measurements were determinants of 25(OH)D levels in elderly.

METHODS

A cross-sectional study was conducted involving 126 elderly (>60 years old) men and women at *Pusat Santunan Dalam Keluarga* (PUSAKA) Central Jakarta centers. Anthropometric measurements [body mass index (BMI), skeletal muscle mass (SMM), body fat (BF), and waist circumference (WC)] were determined by bioelectrical impedance analysis using the Omron body composition monitor with scales (HBF-375, Omron, Japan). Fasting blood samples were taken to measure 25(OH)D level by electrochemiluminescence immunoassay. Multivariate linear regression was used to analyze the data.

RESULTS

The data showed that BMI, BF, and WC were higher than recommended, while SMM and serum 25(OH)D were lower. When the analysis was done based on sex, there were significant differences in BF, SMM, WHtR, and serum 25(OH)D. In the linear regression multivariate analysis of log 25(OH)D with age and body anthropometric measurements, only SMM reached significance level (β=0.019; p=0.025).

CONCLUSIONS

This study demonstrated a positive association between skeletal muscle mass and serum levels of vitamin D in elderly.

Keywords : 25(OH)D, elderly, sex, anthropometric measurements

INTRODUCTION

Vitamin D attracted much attention during the last years. The ideas about the importance of vitamin D and its connection with both communicable and non- communicable diseases have made many researchers interested to do various studies. Some of the diseases that have been linked to low vitamin D status are osteoporosis, cancer, the metabolic syndrome, and cardiovascular disease.[1] Vitamin D deficiency is a highly prevalent condition, even in Indonesia, a tropical country with abundant sun exposure.

Vitamin D is a fat-soluble vitamin. There are two major forms of vitamin D, i.e. vitamin D_2 and vitamin D_3. Vitamin D_2 (ergocalciferol) is found in plants and can be consumed as a supplement or in fortified foods.[1] Vitamin D_3 (cholecalciferol) is synthesized in the human epidermis or consumed in the form of natural or fortified food sources or as a supplement.[1] Vitamin D in the form of $1,25(OH)_2D$ is a hormone and the active form of vitamin D. Directly or indirectly $1,25(OH)_2D$ regulates over 200 genes, including those involved in renin production in the kidney, insulin production in the pancreas, release of cytokines from lymphocytes, production of cathelicidin in macrophages, induction of terminal differentiation, and growth and proliferation of both vascular smooth muscle cells and cardiomyocytes.[1,2]

Individual vitamin D status can be estimated by measuring plasma 25-hydroxy vitamin D levels [abbreviated to 25(OH)D]. Most experts define vitamin D deficiency as a 25(OH)D level of <20 ng/mL (50 nmol/l), vitamin D insufficiency as 21-29 ng/mL (525-725 nmol/l) and optimal concentration of vitamin D as at least 30 ng/mL).[2] Vitamin D deficiency may be due to inadequate dietary intake, inadequate exposure to sunlight, or malabsorption.

During aging, body composition changes, leading to increased adiposity and decreased skeletal muscle mass (SMM).[3] Obesity, defined as excessive fat accumulation, is associated with low 25(OH)D. Low levels of vitamin D in obesity has been suggested as due to sequestration in fat, increased clearance by a larger body-fat pool, and decreased sun exposure.[4]

Several cross-sectional studies have investigated the relation between vitamin D to body mass index (BMI) dan body fat (BF), and those findings were inconsistent. Han et al.[5] showed that there was a significant negative association between BF in adult men and women, but BMI and waist circumference (WC) were not significant in men. A meta-analysis showed a significant inverse weak correlation between serum vitamin D and BMI in the adult population, except for women living in developing countries.[6] A recent meta-analysis concluded that vitamin D deficiency is associated with obesity irrespective of age, latitude, cut-offs to define vitamin D deficiency and the Human Development Index of the study location.[7] Regarding the muscle mass, a study on subjects younger than 65 years showed that there was a statistically significant association between low $1,25(OH)D_2$ levels and low muscle mass both in men and women.[8] A study on elderly concluded that lower 25(OH)D increased the risk of sarcopenia in older men and women.[9]

The elderly have a strong need to maintain normal vitamin D status. It has been estimated that 20-100% of elderly men and women are vitamin D deficient.[2] Considering the importance of vitamin D and obesity in general health and the tendency to vitamin D deficiency in the elderly, this study's objective was to determine the relationship between vitamin D and anthropometric measurements in the elderly population.

METHODS

Research design

This cross-sectional study was conducted in the *Pusat Santunan Dalam Keluarga* (PUSAKA) non-institutional elderly care centers II, V and X in Central Jakarta between January-March 2016.

Research subjects

Subjects were men or women >60 years old and willing to participate in the study. Exclusion criteria were: being bedridden, on dialysis and having consumed vitamin D supplements for the last 3 months. The number of subjects needed in the current study was 126, on the basis of r=0.455, with μ=0.05 and power = 90%.[10] The study subjects were selected by simple random sampling from a total of 245 elderly. Written informed consent was obtained from each subject.

Anthropometric measurements

The collected data included subject characteristics, such as age, sex, and history of family illness. Height was measured using a stadiometer or as sitting knee height. Body weight (BW), BF, and SMM percentage was assessed by means of bioelectrical impedance analysis (BIA) using the body composition monitor with scales (HBF-375, Omron, Japan). Body mass index was calculated as weight (kg) divided by height (m) squared. Waist circumference was measured with a non-stretch tape with a precision of one millimeter. The measurement was made at the level of the umbilicus, with the subject in the erect position, breathing silently. Waist-to-height ratio (WHtR) was calculated by dividing waist circumference by height in centimeters.

Serum 25(OH)D measurement

The serum level of 25(OH)D is a good indicator of vitamin D, because it has a slower clearance than 1,25 $(OH)_2$ D.[11,12] Venous blood samples of 5 mL were obtained in the morning after an overnight fast. Blood was collected in evacuated tubes and stored at 2-8°C and transported to the designated laboratory. Serum 25(OH)D levels were determined using direct competitive chemoluminescent immunoassay (CLIA) (DiaSorin, Stillwater, MN). This assay can detect levels ranging from 4.0 to 150 ng/mL, based on 3.90% CV inter-assay precision.[13] The examination for serum 25(OH)D was done simultaneously at one point in time.

Statistical analysis

We performed a sex-stratified analysis. The Kolmogorov-Smirnov normality test was used to assess the normality of distribution of all data. The differences between mean values for each tested variable between man and women were tested by independent Student t test or Mann-Whitney test.

Multivariate linear regression analysis was used to evaluate associations between anthropometric measurements and serum 25(OH)D. A p-value of <0.05 was considered statistically significant.

Ethical clearance

Ethical clearance No. 77/KER/FK/V/2015 was obtained from the Ethics Committee for Medical Research, Faculty of Medicine, Trisakti University, prior to the study.

RESULTS

Most of the subjects were women (86.5% vs. 13.5%). Mean BMI was categorized as obese. Mean WC was high for women but within a normal range for men. Mean WHtR was still in the normal category for people older than 60 years. The median of BF was high for men but in the normal range for women. Median 25(OH)D concentration of all subjects indicated vitamin D deficiency (Table 1). Based on serum 25(OH)D, there were 80.2% subjects who had vitamin D

Table 1. Characteristics distribution of all subjects (n=126)

Variable	
Sex	
Men	17 (13.5%)
Women	109 (86.5%)
Age (years)	70.07 ± 6.39
Body Mass Index (kg/m^2)	23.41 ± 5.10
Body fat (%)	33.83 ± 7.54
Skeletal muscle mass (%)	21.72 ± 3.48
Waist circumference (cm)	81.22 ± 1.75
Waist-to-height ratio (WHtR)	0.55 ± 0.08
25(OH)D (ng/dL)	13.9 (4.0 - 59.3)

*Data presented as mean ± SD, except for 25(OH)D level as median (min.-max.)

Table 2. Characteristics of subjects based on sex

Variable	Men (n=17)	Women (n=109)	p
Age (years)	69.71 ± 7.50	70.15 ± 6.29	0.612
Body Mass Index (kg/m^2)	22.29 ± 4.88	23.57 ± 5.17	0.333
Body fat (%)	24.17 ± 6.28	35.30 ± 6.60	0.0001*
Skeletal muscle mass (%)	27.39 ± 2.82	20.84 ± 2.66	0.0001*
Waist circumference (cm)	81.52 ± 13.48	81.18 ± 11.63	0.911
Waist-to-height ratio (WHtR)	0.51 ± 0.08	0.55 ± 0.07	0.043*
25(OH)D (ng/dL)	16.9 (12.4-59.3)	13.4 (4.7-30.1)	0.004**

*p<0.05 t-test; ** p<0.05 Mann-Whitney; Data presented as mean ± SD, except for 25(OH)D level as median (min.-max.)

deficiency, 15.9% vitamin D insufficiency and only 4% reached a sufficient level of vitamin D.

When an analysis was done by sex, there were significant differences in body fat, skeletal muscle mass, WHtR, and serum 25(OH)D, while the other variables were not significantly different (Table 2).

In the multivariate linear regression analysis between log 25(OH)D and all variables, only SMM correlated significantly with serum level of log 25(OH)D. (Table 3). High skeletal muscle mass was associated with increased serum level of log 25(OH)D (β=0.019; p=0.025).

DISCUSSION

Our study showed that there was a significant difference in BF percentage between men and women. This result agrees with one other study which showed that women have a higher fat tissue percentage (73.6%) compared to men (16.5%).[14] Mean BMI in our study was categorized as obese grade 1 according to the classification for obesity in the Asia-Pacific population.[15]

A study in Mexico on 1,968 subjects older than 60 years showed that 62.3% of the subjects were obese.[14] In Indonesia, the prevalence of overweight is higher in women (22.9%) compared with men (16.0%).[16] Aging is related to changes in body composition, usually marked by a decrease in fat-free mass (FFM) and an increase in body fat mass (BFM).

The WC in our study was 81.22 ± 11.75 cm. The simplest method to examine excess abdominal fat (central body fat) is WC, because it correlates with abdominal fat mass (subcutaneous and intra-abdominal). The WHtR is a very simple, low-cost anthropometric measurement as an indicator of early health risk if the WHtR is >0.5 for the age group between 40-50 years, while the critical value for people over 50 years is >0.6.[17-19] The WHtR in our study was borderline, between 0.5 and 0.6, so that we can conclude that there is an increased health risk. The SMM was significantly different between men and women. This was in line with the theory that there is sexual dimorphism of SMM, with higher SMM in men. The recommended level of serum 25(OH)D is higher

Table 3. Multivariate linear regression analysis between
the log-transformed 25(OH)D and other parameters

Variable	log 25(OH)D		p
	β	Beta	
Age (years)	0.001	0.048	0.619
Body Mass Index (kg/m^2)	0.005	0.146	0.541
Body fat (%)	- 0.001	- 0.047	0.745
Skeletal muscle mass (%)	0.019	0.344	0.025*
Waist circumference (cm)	- 0.001	- 0.087	0.801
Waist-to-height ratio (WHtR)	- 0.232	- 0.099	0.785

*p<0.05; β: regression coefficient; Beta: standardized regression coefficient

for people living in tropical countries. Unfortunately, a high prevalence of vitamin D deficiency is also reported in tropical countries, including Indonesia.[20] Our study showed very low serum vitamin D levels in the elderly. A previous study in Indonesia showed the same result, i.e. that there is a high prevalence of vitamin D deficiency in the elderly.[21] An increase in 24(OH)ase gene expression and in $1,25\,(OH)_2D_3$ clearance with age has been reported. The study of Angel et al.[22] showed an increase in the proportion of vitamin D deficiency in older age, especially in women.

Serum 25(OH)D was significantly different between men and women in our study, where women were found to be at higher risk of vitamin D deficiency. The study by Huang et al. [23] showed that in the elderly, the female gender is a risk factor for low vitamin D status. The sex difference in correlation with vitamin D was also found in other studies.[24-26] The low serum level of 25(OH)D in our study might have been influenced by the great number of female participants. This may be explained by the observation that women generally prefer indoor activities and take more precautions against sunlight exposure. Avoidance of sunlight exposure was found to be the reason for the low serum 25(OH)D, especially in women. Moreover, most of the women in this study wear the hijab (headscarf) which will reduce sun exposure of the skin. To the best of our knowledge, no studies have examined the correlation between vitamin D level and WHtR. Although in our study the correlation between WHtR was not statistically significant, it could be considered for further exploration.

The multivariate linear analysis in our study showed that high skeletal muscle mass was significantly associated with increased serum 25(OH)D level. The study of Ko et al.[25] showed similar results, in that there might be a positive relationship between 25(OH)D and SMM. On the contrary, Meng at al.[27] found no significant association between 25(OH)D and appendicular SMM in elderly.

Other parameters in our study showed no significant association with log 25(OH)D. A linear regression analysis conducted by Han et al.[5] also showed no association between BMI and WC, although BF was inversely associated with serum 25(OH)D. Aging is related to changes in body composition, usually marked by a decrease in fat-free mass (FFM) and an increase in body fat mass (BFM). BMI may reasonably predict adverse outcomes in global population-based adult studies, but recent studies have demonstrated that BMI cutoffs may misrepresent the degree of adverse outcomes in the older population.[28,29] That is why, in older adults, BMI may be a suboptimal marker for adiposity.

This study used Bioimpedance Analysis (BIA) to assess body fat. BIA is less accurate in older adults and can be influenced by food consumption, exercise, ethnicity, and certain medical conditions. A limitation of the present study is that food intake of the subjects was not assessed because nearly all of the subjects have the same meal pattern as part of PUSAKA policies. The use of WHtR as a tool to assess visceral fat could be considered besides WC and BMI. Most of the studies used BMI or WC to analyze obesity or fat content, a smaller number used BF analysis and only very few of the published studies used WHtR. Another limitation of the present study is the lack of data on physical activity.

In the elderly, the tendency to vitamin D deficiency is relatively high, so that they should be advised to increase serum 25(OH)D by more direct sunlight exposure and higher intake of food sources of vitamin D. It is recommended that Indonesians should have sunlight exposure for 25 minutes at 09.00, or 15 minutes at 09.00-10.00 to have a vitamin D concentration of 2700 IU in the blood for each exposure, and minimally 3x/week to prevent the development of vitamin D deficiency.[26]

The elderly should be advised to maintain their level of SMM by consuming a moderate amount (25-30 g) of high-quality protein and do

resistance exercises. [30] It is suggested that the elderly also maintain a normal body weight so that their BMI, WC, BF, WHtR remain in the normal range. This can be done by showing healthy food models to the elderly and the PUSAKA policymakers. Supplementation of either vitamin D2 or vitamin D3 can be used to treat and prevent vitamin D deficiency.

CONCLUSIONS

Our study demonstrated that high skeletal muscle mass is associated with increased serum levels of vitamin D in the elderly. Further studies of prospective design are needed to examine whether vitamin D supplementation has beneficial effects on muscle mass among the elderly.

CONFLICT OF INTEREST

Competing interests: No relevant disclosures. The authors declare no conflict of interest in relation to this article.

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CONTRIBUTORS

VS originated the idea for this study, did the research proposal, data analysis and prepared the manuscript. LH contributed to the research proposal, reviewed the analysis and participated in the manuscript preparation. VS and LH conducted the data analysis and revised the manuscript. Both authors read and approved the final version.

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