09. Comparison of the 25 D Levels Between Sarcopenia and Frailty in Elder Women

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Comparison of the 25(OH)D Levels Between Sarcopenia and Frailty in Elder Women: A Cross-Sectional Observation Analytic Study in Elderly Community in Surabaya

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ABSTRACT
The prevalence of vitamin D deficiency in the elderly, specifically in post-menopausal women, are very high. Deficiency of 25(OH)D has a direct impact on decreasing muscle strength and mass that can lead into sarcopenia and frailty. This study aimed to compare the difference levels of 25(OH)D between sarcopenia and frailty in elderly community.
Methods: This was a cross-sectional design study. The blood sample were collected to evaluate the levels of 25(OH)D using The Chemiluminescent Immune Assay (CLIA) method.
Results: Most of the subjects were at deficiency of 25(OH)D with mean of 16.1 (range level of 6.2-32.7). Subjects with deficiency level of 25(OH)D were 20 (71.4%) with sarcopenia and 23 (85.1%) with frailty. Subjects with an insufficiency level of 25(OH)D were 6 (21.4%) with sarcopenia and 23 (85.1%) with frailty. Subjects with sufficiency level of 25(OH)D were 2 (7.1%) with sarcopenia and 1 (3.7%) with frailty. The median 25(OH)D levels were 17.1 and 13.2 for sarcopenia and frailty, respectively. There was significant differences in levels of 25(OH)D in both groups (p = 0.014).
Conclusions: The levels of 25(OH)D of subjects with sarcopenia was significantly higher than those with frailty.
Keywords: 25(OH)D, vitamin D, sarcopenia, frailty, elder women
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INTRODUCTION

Health problems in the elderly come from declining body cells, so the function and body endurance decreases along with increased risk factors for diseases and infections.[1,2] One of health problems is vitamin D deficiency. The prevalence of vitamin D deficiency in the elderly, specifically in post-menopausal women, is very high. The incidence rate reaches 90% in Asia and 41.1% in Europe.[3] Vitamin D deficiency in the elder women in Jakarta reaches 35%.[4] The elderly with obesity are at risk for suffering vitamin D deficiency.[5] Vitamin D deficiency can lead to sarcopenia and frailty. Sarcopenia and frailty can influence the quality of life of the elderly, resulting in an adverse outcome, such as falls, fractures, hospitalization, and high comorbidity, disability, and mortality rates.

Technically, vitamin D is a prohormone that is produced by the photochemical process on the skin with the initial form of 7-dehydrocholesterol. The synthesis of vitamin D is mainly in the skin, and less than 10% is earned from the food source. Vitamin D deficiency can lean into the decrease in muscle mass and muscle strength. Besides, vitamin D deficiency affects to tooth loss that may be considered an early marker of decline and weakness in the elderly.[6] It mainly occurs in the elderly because there is a low intake of food that contains vitamin D, lowest of sun exposure, intestinal malabsorption, and decreased vitamin D hydroxylase activity in the kidneys. The main synthesis of vitamin D is on the skin. Less than 10% comes from the diet. 7-dehydrocholesterol converts to pre-vitamin D3 on the skin with the aid of ultraviolet-B exposure from sunlight. Pre-vitamin D3 undergoes an isomerase, which depends on the temperature to form vitamin D3. Enzymatically, vitamin D3 will be converted to 25-hydroxyvitamin D3 (25(OH)D) by the enzyme 25-hydroxylase in the liver and converted to 1.25-dihydroxy vitamin D3 (biologically active form) in the kidney by the enzyme 1-alpha-hydroxylase. The 25(OH)D is in the form of an inactive version of vitamin D and has a longer half time compare with another form of vitamin D.[7–9]

The person in advanced age is likely to experience a decrease in physical quality, such as a weakness in his legs.[10] The aging process in bones and muscles is characterized by the decrease of muscle mass and strength, and if both of that process occurs in a person, it is called sarcopenia. If sarcopenia develops continuously, it will lead to frailty. Deficiency of 25(OH)D has a direct impact on decreasing muscle strength and mass. The muscle strength is correlated with physical performance.[11] Decreased strength and muscle mass can lead to the lowering of mechanical myokines, which can also lead to the lowering of mineral bone density.[12]

Sarcopenia is described as the loss of muscle mass and strength inherent to the aging process.[13] Frailty is a condition that is prone to the exposure of a stressor related to an aging process with the disorder of neuromuscular, metabolic, and immune systems that are at risk of comorbidities, disability, and mortality.[14] Previous study in America showed that in the elder women (age >65 y.o), the deficiency of 25(OH)D can be used as a predictor of the risk of sarcopenia and frailty.[15] Other studies in South Korea showed that levels of 25(OH)D less than 10 ng/dL are associated with the incidence of sarcopenia.[16] Sarcopenia is a condition of pre-frailty and also the precursor of frailty.[17] The elderly people with sarcopenia are three times as likely to develop frailty.[18]

Generally, the pathogenesis of sarcopenia and frailty are broadly the same. It begins with the changes in size and length of muscle fibers, loss of type-2 muscle fibers, the resistance of anabolic signal, and low physical performance which lead to the decrease of ATP production by muscle, denervation of type-2 muscle fiber, and decrease of the neuromuscular junction. All the processes mentioned above can cause a decrease in muscle mass, muscle strength, and physical performance.

The involvement of vitamin D in physical performance is at the cellular level and the structure of muscle. Deficiency of 25(OH)D can cause a decrease/atrophy of type II muscle fibers and increase infiltration adipocyte between muscle fibers. Another study stated that in post-menopausal women who consumed an additional intake of vitamin D and calcium had better physical performance than if they only consumed calcium.[19,20] This study aimed to compare the different levels of 25(OH)D between sarcopenia and frailty in the elderly community in Surabaya.

MATERIALS AND METHODS

This study used a cross-sectional design to compare the levels of 25(OH)D between the subjects with sarcopenia and frailty by using a ratio scale data. The subjects of this study were the elder women from five regions of public health center (Puskesmas) in Surabaya, Indonesia, they were: Puskesmas Menur from East region of Surabaya, Puskesmas Perak Timur from North Region of Surabaya, Puskesmas Tambak Rejo from Central Region of Surabaya, Puskesmas Sememi from West Region of Surabaya, and Puskesmas Putat Jaya from South Region of Surabaya. The subjects must undergo the interview, physical examinations, and undersign the inform consent and informed to consent.

The subjects were categorized into two groups; sarcopenia and frailty based on the examination before. The diagnose of sarcopenia was based on physical examination that found a decrease in muscle mass, muscle strength, and physical performance. The diagnose of frailty was based on the criteria of the Cardiovascular Health Study (CHS). Afterward, the subject must be screened and divided into inclusion and exclusion criteria. The inclusion criteria in this study were elder women >60 years old, able to do active communication, met the criteria of sarcopenia, met the criteria of frailty, and willing to be involved in this study by undersigning the inform consent an informed to consent. The exclusion criteria in this study were obesity (BMI >25kg/m^2), history of kidney disease, history of liver disease, and subjects with supplementation of vitamin D. Subjects that were qualified into inclusion criteria must be examined the level of 25(OH)D serum by using The Chemiluminescent Immune Assay (CLIA) method. The levels of 25(OH)D were classified into three groups, they were; sufficient (levels of 25(OH)D>30ng/dL), insufficient (levels of 25(OH)D29-20ng/dL), and the deficiency (levels of 25(OH)D<20ng/dL).

Statistical Analysis

Baseline characteristics were presented descriptively, in frequency, and in percentage for all categorical data. All data of normality distribution were tested using the Kolmogorov Smirnov test because the subjects of this study were more than 50 subjects. To compare the different levels of 25(OH)D between sarcopenia and frailty, we used the Mann-Whitney test. The Mann-Whitney test was utilized because the data did not have normal distribution. The statistical significance was achieved if p-value was <0.05. All statistical analyses were undertaken using the SPSS program version 25.0.

RESULTS

The general characteristics of subjects are shown in Table 1. The total subjects of this study were 55 samples; they were 28 subjects with sarcopenia and 27 subjects with frailty. The ranged age of the total subjects were 60-100 years with the median age of 66 years. Most of the subjects in this study were in sarcopenia (88%) and frailty (89%) and living at their own house (not joining their relatives). The marital status of the subjects was mostly marriage and widow, most of them were unemployed, some of them were retirement, and some of them were still working as an enterpriser. The financial support of the subjects was varying, most of them got their financial support from their child, some of them were from retirement fund, and some others got from their own. Physical activity in the daily exercise of the subjects found that subjects with sarcopenia were more active than those with frailty. Most of the subjects had sarcopenia of 85.7% and frailty of 92.6% and did not use walking aid. Mostly, from both groups, subjects did not have a history of falls for the last one year.

For the comorbid factor, this study found that subjects mostly got a musculoskeletal disorder, diabetes, and hypertension. Based on Table 2, comprehensive geriatric assessment for Barthel Activity Daily Living (ADL) showed that subjects with sarcopenia (71.4%) were more independent than those with frailty (66.7%). For Mini Nutritional Assessment (MNA), both groups of sarcopenia (50%) and frailty (51.8%) were at risk of malnutrition.

In this study, Table 3 shows most of the total subjects, as many as 43 (78.2%), were at deficiency 25(OH)D with range level of 6.2-32.7 and mean of 16.1. Subjects with deficiency level of 25(OH)D were 20 (71.4%) with sarcopenia and 23 (85.1%) with frailty. Subjects with an insufficiency level of 25(OH)D were 6 (21.4%) with sarcopenia and 23 (85.1%) with frailty. Subjects with sufficiency level of 25(OH)D were 2 (7.1%) with sarcopenia and 1 (3.7%) with frailty.

Physical examination of the subjects are shown in Table 4. The sarcopenia's subjects had a better physical condition than frailty in each component of the physical examination. While Table 5 shows the mean and median differences between two groups. The mean 25(OH)D levels of sarcopenia was 18.05 and frailty was 14.1, the median value was 17.1 for sarcopenia and 13.2 for frailty. Analysis for normality of distribution data concluded that this study data was not normal, and the analysis of the Mann-Whitney test showed that p-value = 0.014 so that sarcopenia subjects had higher levels of 25(OH)D compared to frailty subjects.

DISCUSSION

Most of the subjects in this study were at the deficiency of 25(OH)D. The comparison between two groups revealed there was a higher level of 25(OH)D in subjects with sarcopenia than those with frailty. The subjects with

sarcopenia will third times be at risk to fall into frailty, so it was concluded that sarcopenia could be an indicator of frailty.[18,21]

This study only used woman subjects. The study in Malaysia showed that the prevalence of 25(OH)D deficiency was greater in elder women than men.[22] Decreased growth hormone (GH) and Insulin-Like Growth Factor (IGF-1) in post-menopausal women causes a decrease in muscle protein synthesis. Levels of IGF and estrogen decrease in post-menopausal women.[23] On the contrary, an increase in proinflammatory cytokines such as IL-6 and TNF-α can increase the risk of sarcopenia and frailty by reducing muscle protein synthesis. Estrogen has an anabolic mechanism in the muscles; the actions of estrogen in the muscle are by stimulating the IGF-1 receptor. Estrogen receptors in post menopause are lower than at perimenopause, so it is prone to get sarcopenia and frailty.[24]

Most of the subjects in this study were retirement and unemployment and got financial support from their child or retirement fund. It is similar to another study revealed that most of the subjects were widows with financial support from the retirement fund.[21] Most of the subjects were at risk of malnutrition based on the MNA scoring system. It is related to the circumstances of socio-economics of the subjects with their nutritional status. It was shown that the elderly are really close to the malnutrition.

In this study, socio-economic data had a strong relation to employment status. It had a statistically significant value. Subjects who were unemployed were more frequent in frailty than sarcopenia. The impact of socio-economic factors on low levels of 25(OH)D in the elderly had an adverse nutritional status.[25] Relationship between subject's income with low levels of 25(OH)D was the subjects with low income were unable to buy nutritious food sources containing vitamin D. it was in line with study in Poland that suggested that low-income subjects rarely consumed food sources of vitamin D.[26] As many as 90.4% in female subjects had levels of 25(OH)D <30 ng/dL. The main source of vitamin D in the body is through exposure to UV-B rays and vitamin D-rich food ingredients.[26]

Based on US Endocrine society, the levels of 25(OH)D were classified into three classifications: sufficiency when the levels of 25(OH)D serum >30ng/mL; insufficiency when the levels of 25(OH)D serum 21-29 ng/mL; deficiency when the levels of 25(OH)D serum <20ng/mL. It is suitable according to the theory that explained the involvement of 25(OH)D levels with physical performance and muscle structure. This study found that at each component of the physical examination, the sarcopenia's subjects had a better physical condition than frailty. Vitamin D deficiency can lead to a decrease/atrophy of type II muscle fibers and increase fat cell infiltration between muscle fibers so that it can cause sarcopenia and frailty.[7–9]

This study has a several limitations. It is only a cross sectional research in a several times, so it cannot describe the process of the occurrence of deficiency 25(OH)D. The exclusion criteria of this study were only based on interviews and physical examinations of the subjects so that exclusion criteria were difficult to objectively assess. This study has several confounding factors that cannot be excluded, such as a history of nutrient content of daily food, a history of sun exposure, and the magnitude/level of spectrum of UV-B ray exposure.

CONCLUSION

In the conclusion of this study, it is obvious that subjects with sarcopenia has better physical condition than frailty, so the results of this research showed that the levels of 25(OH)D of subjects with sarcopenia were significantly higher than those with frailty. Further research with retrospective design could be done, so the relationship between deficiency 25(OH)D with sarcopenia and frailty will be clear, and the research of vitamin D supplementation with a certain dose in some certain periods is needed to be done to find out the optimal dose to reach optimal levels of 25(OH)D.

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CONFLICT OF INTEREST

The authors in this study declared that they do not have any conflict of interest concerning this manuscript.

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Table 1: Baseline characteristics

Characteristics	Sarcopenia (n=28)		Frailty (n=27)		p-value
	n	%	n	%	
Residence					
• Private house	25	89.3	24	88.9	
• Joint house (Family)	2	7.1	1	3.7	0.136
• Rent house	1	3.6	1	3.7	
• etc.	0	0.0	1	3.7	
Status					
• Marriage	13	46.4	15	55.6	0.659
• Widow	13	46.4	11	40.7	
• Unmarried	2	7.1	1	3.7	
Job					
• Unemployment	17	60.7	23	85.2	
• Enterpriser	6	21.4	2	7.4	
• Employee of a private company	1	3.6	1	3.7	0.039
• Retirement	3	10.7	0	0.0	
• Etc.	1	3.6	1	3.7	
Financial Support					
• Independent cost	6	21.4	5	18.5	
• Support from another family member and independent cost	4	14.3	2	7.4	0.325
• Support from another family member	14	50.0	18	66.7	
• Retirement fund	4	14.3	2	7.4	
Gait style					
• No walking aid	24	85.7	25	92.6	0.104
• With walking aid	4	14.3	2	7.4	
Exercise					
• Yes	22	78.6	11	40.7	0.070
• No	6	21.4	16	59.3	
History of fall					
• Yes	2	7.1	4	14.8	0.070
• No	26	92.9	23	85.2	

Table 2: Comprehensive Geriatric Assessment

Comprehensive Geriatric Assessment	Sarcopenia(n=28)		Frailty(n=27)		p-value
	n	%	n	%	
Barthel Activity Daily Living (ADL)					
Independent	20	71.4	18	66.7	0.17
Mild dependency	8	28.6	8	29.6	
Moderate dependency	0	0.0	1	3.7	
MMSE					
Normal	26	92.9	22	81.5	0.095
Mild Cognitive disorder	1	3.6	4	14.8	
Severe Cognitive disorder	1	3.6	1	3.7	
Mini Nutritional Assessment (MNA)					
Malnutrition	6	21.4	7	25.9	0.19
Risk of Malnutrition	14	50.0	14	51.8	
Normal	8	28.5	6	22.2	
GDS					0.95

Comprehensive Geriatric Assessment	Sarcopenia(n=28)		Frailty(n=27)		p-value
	n	%	n	%	
Normal	27	96.4	26	96.3	
Possible Depression	1	3.6	1	3.7	

Table 3: 25(OH)D Levels in sarcopenia and frailty

25(OH)D Levels	Sarcopenia (n=28)		Frailty (n=27)	
	n	%	n	%
Deficiency	20	71.4	23	85.1
Insufficiency	6	21.4	3	11.1
Sufficiency	2	7.1	1	3.7

Table 4: Physical examination of the subjects

Physical examination	Sarcopenia		Frailty		P-value
	Median	Mean±SD	Median	Mean±SD	
Muscle strength					
<18Kg	14.5	14.91±1.5	15	13.72±3.1	0.04
>18Kg	21	21.75±2.3	20	20.77±2.8	
Muscle mass					
<3Kg/m^2	2.54	2.6±0.39	2.63	2.56±0.2	0.037
>3Kg/m^2	-	-	3.36	3.50±0.4	
Gait-speed test					
>0.8m/mnt	0.64	0.60±0.1	0.61	0.58±0.1	0.51
<0.8m/mnt	-	-	-	-	
PASE score					
≤126.50Kkal/week	58.09	64.27±29.1	55.25	54.19±32.2	0.001
>126.51Kkal/week	180.39	187.46±42.2	-	-	

Table 5: Physical examination components

Variable	Groups	Median	Mean	p-value	Conclusion
25(OH)D	Sarcopenia	17.1ng/dL	18.05 ng/dL	0.014	Significantly different
	Frailty	13.2ng/dL	14.1 ng/dL		

09. Comparison of the 25 D Levels Between Sarcopenia and Frailty in Elder Women

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PAGE 1

PAGE 2

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PAGE 4

PAGE 5

PAGE 6