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THE CORRELATION BETWEEN SARCOPENIA AND TRANSTHYRETIN LEVELS AMONG COMMUNITY-DWELLING OLDER ADULTS IN PADANG, WEST SUMATRA

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ABSTRACT

The objective of this study was to evaluate the correlation between sarcopenia and transthyretin levels among community-dwelling older adults in Padang. This study employed a cross-sectional design and included 45 community-dwelling individuals aged 60 years and above who visited Andalas Primary Health Care in Padang, West Sumatra, Indonesia. Characteristics of sociodemographic and lifestyle habits were collected using a general questionnaire. Sarcopenia was defined in accordance with the criteria set forth by the Asian Working Group for Sarcopenia (AWGS) criteria encompass three components: low muscle mass, as determined by an index of appendicular skeletal mass/height^2 less than 7,0 kg/m^2 for males and less than 5,7 kg/m^2 for females; low physical performance, as indicated by a gait speed less than 1,0 m/s; low muscle strength, defined as handgrip strength less than 26 kg for males and less than 18 kg for females. Accordingly, sarcopenia was defined as the presence of low muscle mass in conjunction with low physical performance and/or low muscle strength. Transthyretin levels were considered as independent variables in order to evaluate the potential correlation between transthyretin and sarcopenia status using bivariate analysis. The overall prevalence of sarcopenia was 51.1%, with four cases (40%) observed in males and 19 cases (54.3%) in females classified as having sarcopenia. The prevalence of sarcopenia was significantly lower among participants with normal nutritional status. A comparison of the participants with and without sarcopenia revealed that the former exhibited higher levels of transthyretin (p = 0,000). A statistically significant correlation was observed between transthyretin levels and sarcopenia (p = 0,000). The prevalence of sarcopenia among community-dwelling older adults in Padang was notably high. A significant correlation was observed between sarcopenia and transthyretin levels. Further research is required to assess the potential efficacy of maintaining optimal nutritional status in increasing transthyretin levels and reducing the risk of sarcopenia.

KEYWORDS *Sarcopenia, transthyretin, malnutrition*

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INTRODUCTION

As people age, organ function naturally declines, leading to various disorders, including impaired mobility. A key predictor of mobility is muscle strength, which is necessary for performing physical activitie (Amarya et al., 2018). In the elderly, skeletal muscle loss occurs as a result of an imbalance between anabolic and catabolic pathways of muscle protein. This process commences with muscle atrophy and may subsequently progress to sarcopenia (Larsson et al., 2019). Sarcopenia is defined as a progressive and generalized age-related decline in muscle mass, accompanied by a reduction in muscle strength and/or physical performance (Cruz-Jentoft et al., 2019; Sayer & Cruz-Jentoft, 2022).

Sarcopenia is associated with an increased risk of falls, fractures, functional decline, loss of independence, prolonged institutionalization, frailty, and death (Beaudart et al., 2014; Mellen et al., 2023). These factors not only reduce the quality of life for individuals with sarcopenia but also increase healthcare costs and contribute to higher mortality rates. The economic burden of sarcopenia extends to families, communities, and countries (Bruyère et al., 2019). Goates et al. estimated that hospitalization costs for elderly individuals with sarcopenia reached $40.4 billion USD, underscoring the significant strain sarcopenia places on the healthcare system in the U.S (Goates et al., 2019).

Sarcopenia is a complex geriatric syndrome with multifactorial causes. Neuromuscular degeneration, altered muscle protein turnover, hormonal changes, chronic inflammation, oxidative stress, and lifestyle factors all play a role in its pathogenesis (Aryana, 2021; Mellen et al., 2023). The balance between protein synthesis and breakdown is crucial in determining muscle mass. Protein malnutrition further exacerbates sarcopenia, as muscle atrophy occurs when protein degradation outpaces synthesis (Jang et al., 2023; Njoto & Suka Aryana, 2023). Inadequate protein intake accelerates this process, making nutrition a critical factor in the prevention and progression of sarcopenia (Rogeri et al., 2021).

Transthyretin (TTR) is an extracellular protein produced by the liver and choroid plexus (Liz et al., 2020). With aging, lean body mass (LBM)—a key component of skeletal muscle—declines, leading to reduced nitrogen levels, which in turn affect TTR production (Ingenbleek, 2019). Studies have shown that TTR levels decline gradually after age 60, paralleling the loss of LBM. TTR is a reliable marker of LBM and is often used to assess nutritional status in older adults (Ingenbleek, 2019; Ribeiro & Kehayias, 2014). The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends using TTR and other biochemical markers to assess malnutrition, as declining TTR levels indicate worsening protein malnutrition (Cederholm et al., 2015).

Several studies have established the link between TTR levels and sarcopenia. Research shows that low TTR levels are associated with an increased risk of sarcopenia (Ingenbleek, 2019). Observed that elderly individuals with sarcopenia

exhibited significantly lower TTR levels than those without the condition (Xiu et al., 2021). Confirmed similar findings, with lower TTR levels correlating with an increased incidence of sarcopenia (B. Xu et al., 2022). However, most studies on this subject have been conducted in European and Chinese populations. Studies using the Asian Working Group for Sarcopenia (AWGS) criteria and its correlation with TTR levels in Indonesia are scarce. Given the unique genetic background and living conditions of the Indonesian population, defining the precise correlation between sarcopenia and TTR levels is essential. This study aims to explore the relationship between sarcopenia and TTR levels in community-dwelling elderly population aged 60 and above in Padang.

RESEARCH METHOD

Study Population and design

A cross-sectional study was conducted at Andalas Primary Health Care in Padang, West Sumatra. From July to Agustus 2024, adults aged 60 years and older who visited healthcare facility were enrolled in the study on a consecutive basis. In order to be eligible for inclusion in this study, participants were required to meet the following criteria: age 60 years or above; able to perform a walking test and handgrip strength test; and able to give written informed consent. Individuals were excluded if they met any of the following criteria: (i) presence of comorbidities, including acute infection, liver disease, renal failure, thyroid dysfunction or malignancy; (ii) steroid use; (iii) severe cognitive impairment (Mini Mental Status Examination (MMSE) score < 10); (iv) use of any implanted electronic device. The data were collected from the recruited patients by trained staff within 24 hours of their visit to healthcare facility, through interviews and medical records. The general characteristics collected for each participant included age, gender, height, weight, body mass index (BMI), smoking status, alcohol consumption status, and the following comorbidities: diabetes, hypertension, dyslipidemia, hyperuricemia, COPD, coronary disease, stroke, liver disease, renal failure, thyroid disease and tumors of any type. Lifestyle data encompassed information regarding smoking and drinking habits. Participants were classified according to their smoking status as current smokers, quitters, and non-smokers. Those who had smoked on a daily basis over the past year were classified as current smokers, those who had smoked daily for a period exceeding two years and ceased smoking a year prior to the study were classified quitters and all others were considered non-smokers. Additionally, participants were classified according to their alcohol consumption habits, with the categories no drinking and drinking being used. Drinking was defined as consumption of alcohol on two occasions per week. Physical activity was evaluated using a form of International Physical Activity Questionnaire (IPAQ). Body mass index (BMI) was defined as weight (kg) divided by height squared in meters (kg/m^2). Blood samples were collected from all participants after overnight fasting for at least eight hours. Transthyretin levels in the blood were quantified using standard laboratory techniques, conducted by a technician in the laboratory of Prodia Indonesia.

Assessment of sarcopenia

Muscle mass was quantified through the utilization of bioelectrical impedance analysis Omron Karada Scan model HBF-362 (Omron Corporation, Kyoto, Japan). Appendicular skeletal mass (ASM) was calculated as the sum of the muscle mass in the arms and legs. The ratio of ASM to height in meters squared (ASM/height^2) was employed as a measure of sarcopenia. A cutoff point for sarcopenia was established at ASM/height^2 < 7.0 kg/m^2 for males and <5.7 kg/m^2 for females. Muscle strength was evaluated through the measurement of grip strength using Lafayette Dynamometers model J00105 (Lafayette Instrument Company, Lafayette, United States). The participants were instructed to exert their maximum effort on two occasions with their dominant hand, and the highest reading was recorded. Low handgrip strength was defined in accordance with Asian Working Group for Sarcopenia (AWGS) consensus criteria as < 28 kg for males and < 18 kg for females. Gait speed was calculated using the gait speed test, whereby each subject was instructed to walk in a straight line for a distance of six meters, and the time was recorded using a stopwatch. Low physical performance was defined as a gait speed of less than 1.0 m/s. In accordance with the AWGS criteria, sarcopenia was defined as the presence of low muscle mass concomitant with low physical performance and/or low muscle strength.

Assessment of nutritional status

The Mini Nutritional Assessment (MNA) form, which is specific for older people was utilized. Participants were classified according to their MNA scores as follows: normal (score 24 – 30), at risk of malnutrition (score 17 – 23,5), and malnourished (score < 17).

Assessment of physical activity

The level of physical activity was evaluated using the International Physical Activity Questionnaire (IPAQ) form. The intensity of physical activity was expressed in metabolic equivalents (MET). In accordance with IPAQ guidelines, MET-min per week for a given activity were calculated by multiplying the MET level by the minutes of activity per day by the number of days per week and the total physical activity MET-min/week were summed within each item. The participants were classified according to the intensity of their physical activity, which was divided into three levels: high, moderate and low. Participants were classified as high if they met either of the following two criteria: (i) engagement in vigorous-intensity activity on at least three days, with a minimum accumulation of 1500 MET-min/week; (ii) completion of seven or more days of any combination of walking, moderate or vigorous-intensity activities, with a minimum accumulation of 3000 MET-min/week. Participants were classified as moderate if they met any one of the following three criteria: (i) Three or more days of vigorous-intensity activity of at least 20 minute per day; (ii) Five or more days of moderate-intensity activity and/or walking of at least 30 minutes per day; (iii) Five or more days of any combination of walking, moderate-intensity or vigorous-intensity activities achieving a minimum of at least 600 MET-min/week. Those participants who had no activity reported or who had some activity reported, but whose activity did not meet the criteria for either the moderate or high categories, were classified as having low-level activity.

Ethical issues

The study protocol was approved by the Padang City Investment and One Stop Integrated Service. Written informed consent was obtained from all participants or their legal proxies.

Statistical analyses

The statistical analyses were conducted using SPSS 25.0 (IBM, New York, USA). Continuous variables are presented as the mean ± standard deviation. The significance of the mean difference in transthyretin levels between the sarcopenic and non-sarcopenic group was evaluated using an independent samples t-test. The correlation between transthyretin levels and either sarcopenia prevalence or sarcopenia parameter was investigated using the Pearson bivariate correlation test for parametric tests and the Spearman bivariate correlation test for non-parametric tests. A two-sided p-value of less than 0.05 was considered to indicate a statistically significant result.

RESULT AND DISCUSSION

Baseline characteristic of participants

Table 1 Estimated prevalence of low appendicular skeletal muscle index, low grip strength, low physical performance and sarcopenia

	n	Low ASMI, n (%)	Low grip strength, n (%)	Low physical performance, n (%)	Sarcopenia, n (%)
Male	10	4 (40)	2 (20)	4 (40)	4 (40)
Female	35	19 (54.3)	9 (25.7)	24 (68.5)	19 (54.3)
Total	45	23 (51.1)	11 (24.4)	28 (62.2)	23 (51.1)

The analysis was based on data from 45 participants. The mean age of the participants was 67.91 ± 5.79 years (ranging from 60 to 78 years), and 35 (77.8%) were female. Of the 45 community-dwelling older individuals, 23 (51.1%) were identified as having sarcopenia. Among these, 4 (40%) were male and 19 (54.3%) were female. In data of male, 40% of the participants exhibited low ASMI, 20% demonstrated low grip strength and 40% displayed low physical performance. In female, the corresponding rates were 54.3%, 25.7% and 68.5%, respectively (Table 1).

Table 2 Characteristics profile of participants

	Male (n = 10)		Female (n = 35)	
	Sarcopenia n = 4	Non-sarcopenia n = 6	Sarcopenia n = 19	Non-sarcopenia n = 16
Mean age (years)	69.25 ± 2.63	69.67 ± 8.11	68.16 ± 5.91	66.63 ± 5.46
Mean weight (kg)	58.0 ± 4.54	62.0 ± 5.89	55.32 ± 9.58	58.38 ± 5.62

Mean height (cm)	161.0 ± 8.24	157.6 ± 2.58	154.26 ± 4.12	153.88 ± 3.12
Mean BMI (kg/m^2)	22.4 ± 2.11	24.7 ± 1.61	23.34 ± 3.41	24.60 ± 2.13
Mean appendicular muscle mass (kg)	16.19 ± 3.29	17.74 ± 0.81	12.09 ± 1.69	14.08 ± 0.68
Mean ASMI (kg/m^2)	6.20 ± 0.77	7.13 ± 0.14	5.06 ± 0.56	5.95 ± 0.18
Mean grip strength (kg)	32.25 ± 13.96	45.83 ± 12.01	21.58 ± 7.02	29.75 ± 6.86
Mean gait speed (m/s)	0.76 ± 0.27	1.00 ± 0.18	0.64 ± 0.14	0.94 ± 0.27
Smoking, n (%)				
Non-smokers	0 (0)	0 (0)	19 (100)	16 (100)
Quitters	4 (100)	5 (83.3)	0 (0)	0 (0)
Current Smokers	0 (0)	1 (16.7)	0 (0)	0 (0)
Drinking, n (%)				
No drinking	4 (100)	6 (100)	19 (100)	16 (100)
Drinking	0 (0)	0 (0)	0 (0)	0 (0)
Diseases, n (%)				
Hypertension	2 (50)	5 (83.3)	5 (26.4)	6 (37.5)
Diabetes	2 (50)	1 (16.7)	3 (15.7)	1 (6.25)
Dyslipidemia	0 (0)	0 (0)	3 (15.7)	5 (31.25)
Hyperuricemia	0 (0)	0 (0)	8 (42.2)	4 (25)
Nutrition status, n (%)				
Normal	0 (0)	6 (100)	7 (36.8)	16 (100)
Risk of malnutrition	3 (75)	0 (0)	10 (52.6)	0 (0)
Malnutrition	1 (25)	0 (0)	2 (10.6)	0 (0)
Physical activity, n (%)				
Low	4 (100)	2 (33.3)	15 (78.9)	4 (25)
Moderate	0 (0)	4 (66.7)	4 (21.1)	10 (62.5)
High	0 (0)	0 (0)	0 (0)	2 (12.5)
Mean transthyretin (mg/dL)	9.975 ± 5.41	21.117 ± 2.54	11.053 ± 2.81	20.175 ± 2.49

The clinical characteristics of the participants are presented in table 2, stratified by sex and sarcopenia status. Individuals with sarcopenia exhibited diminished appendicular muscle mass, ASMI, handgrip strength, physical performance, and lower transthyretin levels compared to those without sarcopenia. Among the female participants, those with sarcopenia were more likely to be older and have a lower body mass index. The prevalence of hyperuricemia was higher among sarcopenic female participants, whereas hypertension and diabetes were more prevalent among sarcopenic male than among non-sarcopenic participants.

Among the participants with sarcopenia, 13 (56.5%) were identified as being at risk of malnutrition, while three (13.1%) were confirmed to be malnourished. In both sexes, all of the participants with malnutrition were diagnosed with sarcopenia. In males, 75% of those at risk of malnutrition were diagnosed with sarcopenia,

compared to 52.6% in females. The prevalence of sarcopenia was found to be lower among those with a normal nutritional status, irrespective of gender.

Among the participants with sarcopenia, four (17.4%) were engaged in moderate physical activity, while 19 (82.6%) were engaged in low physical activity. In both sexes, all participants with low physical activity were diagnosed with sarcopenia. In males, 100% of those with low-activity were diagnosed with sarcopenia, while in females, this rate was 78.9% and 21.1%, respectively, among those with low and moderate physical activity.

Comparison of transthyretin levels between sarcopenia and non-sarcopenia

The mean transthyretin levels for participants with sarcopenia was 10.86 ± 3.26 mg/dL which had a lower transthyretin level than participants without sarcopenia (20.43 ± 2.48 mg/dL). Mean difference between two group was statistically significant ($p = 0.000$).

Correlations between transthyretin levels and sarcopenia

Overall, sarcopenia was positively correlated with transthyretin ($r = 0.86$, $p = 0.000$). Sarcopenia parameter (ASMI, grip strength, and physical performance) were all positively correlated with transthyretin ($r = 0.68$, $p = 0.000$; $r = 0.51$, $p = 0.000$; $r = 0.63$, $p = 0.000$, respectively).

DISCUSSION

The objective of this study was to evaluate the prevalence of sarcopenia among community-dwelling older adults using the AWGS definition. The prevalence of sarcopenia was found to be 51.1%, which is higher than previously reported rates in Asia. There is considerable variation in the reported prevalence of sarcopenia across Asia, with studies showing rates ranging from 9.1% to 91.3%.19–21 The high and rising prevalence of sarcopenia in Indonesia is likely due to the widespread decrease in muscle mass, strength, and physical performance among the elderly population (Budiartha et al., 2019; Harimurti et al., 2023; Wardhana et al., 2019; Widajanti et al., 2020). Moreover, differences in sarcopenia definitions, as well as factors such as country-specific conditions, age, gender, population charac-teristics, and measurement methods, contribute to this inconsistency (Boshnjaku & Krasniqi, 2024; Yuan & Larsson, 2023).

The prevalence of sarcopenia in men was found to be 40%, which is lower than in women, where it was 54.3%. This discrepancy may be attributed to the fact that the majority of health center users were women. In accordance with the findings of a preceding study, the majority of respondents were elderly women, comprising 58% to 63.6% of study populations (Boshnjaku & Krasniqi, 2024) (Sumandar et al., 2023). Another study demonstrated that females have a threefold increased risk of sarcopenia compared to males (OR 3.01, 95% CI 1.34–6.73; OR 1.52, 0.88–2.63, respectively) (Boshnjaku & Krasniqi, 2024). Older women tend to have reduced muscle mass and strength compared to men, likely due to the sig-nificantly higher prevalence of physical inactivity among women (Yang et al., 2022; Yerrakalva et al., 2024). Furthermore, the decline in estrogen levels during menopause may result in alterations to body composition, leading to a reduction in lean body mass and an increase in body weight, fat mass, and deposition, which contributes to sarcopenia in older wom-en (Black & Matkin-Hussey, 2024). However, a recent systematic review and

meta-analysis of randomized con-trolled trials suggested that estrogen supplementation may not increase muscle mass (Y. Xu et al., 2020). Furthermore, it is noteworthy that muscle mass and strength decline more rapidly in older men than in older women (Mitchell et al., 2012).

The etiology of sarcopenia is multifactorial. While some contributing factors are fixed, many are modifiable, leading to growing interest in lifestyle factors, particularly the influence of modifiable elements such as nutritional status on muscle mass and function in older adults (Eglseer et al., 2016; Shokri-Mashhadi, 2023). The relationship between nutritional status and sarcopenia is clinically significant, with both factors being interrelated in their underlying pathophysiology. Increasing evidence suggests that nutritional defi-ciencies, including inadequate intake of protein, energy, specific micronutrients, and malabsorption, are associated with the development of sarcopenia. Malnour-ished individuals are at a higher risk of developing sarcopenia due to decreased muscle protein synthesis (Beaudart et al., 2019; Sieber, 2019).

This study found a significantly lower prevalence of sarcopenia in individuals with normal nutritional status in both sexes. Consistent with findings from a previous systematic review and meta-analysis of observational studies, poor macronutrient and micronutrient intake is common among community-dwelling older adults in Indonesia (Dewiasty et al., 2022). Other studies have shown that older adults who are mal-nourished or at risk of malnutrition have a higher likelihood of developing sarco-penia compared to those with normal nutritional status, with odds ratios ranging from 9.9 to 13.6 in at-risk groups (Lu et al., 2020; Sato et al., 2020). A meta-analysis further demonstrated that malnutrition or malnutrition risk was associated with an increased risk of sarcope-nia (OR 2.99, 95% CI 2.40–3.72) among community-dwelling older adults (Gao et al., 2021).

Malnourished individuals are often deficient in essential dietary nutrients such as protein, vitamin D, calcium, and those involved in maintaining acid-base balance. These deficiencies contribute to the loss of muscle mass, strength, and physical performance (Norman et al., 2021). Additionally, diminished muscle protein synthesis in mal-nourished individuals may further explain the development of sarcopenia (Beaudart et al., 2019). Re-duced nutrient intake, impaired protein synthesis, acute injury, and periods of im-mobilization can all contribute to sarcopenia, characterized by a decline in the body's protein reserves.

Albumin and transthyretin have long been used as markers for the diagnosis of malnutrition (Keller, 2019). Several studies suggest that low transthyretin levels are associat-ed with sarcopenia, but these findings are inconsistent. To our knowledge, studies specifically investigating the relationship between transthyretin and sarcopenia remain scarce. Chen et al. found that transthyretin levels were negatively associat-ed with sarcopenia when transthyretin levels were below 266 mg/L in elderly Chi-nese inpatients (Chen et al., 2019). Similarly, in our study we found that low transthyretin levels were significantly associated with sarcopenia. Transthyretin, a thyroid hormone transport protein, is produced by the liver and partially metabolized by the kid-neys (Ingenbleek, 2023). Serum transthyretin levels below 10 mg/dL are typically associated with malnutrition. Lower levels are linked to reduced muscle mass and lean body mass (LBM). The liver produces less

transthyretin in both protein-deficient states and during cytokine-induced inflammatory disorders. Therefore, reduced transthyretin values can serve as indicators of the severity of involutional LBM loss. In a clinical investigation of elderly individuals with sarcopenia, transthyretin (TTR) exhibited the highest positive correlation with LBM (r = 0.64), compared to reti-nol-binding protein (r = 0.57) and albumin (r = 0.52).43 Transthyretin appears to be superior to other hepatic biomarkers, reflecting the same evolutionary patterns in both healthy and disease states for visceral and structural LBM compartments. Consequently, TTR maintains positive correlations with muscle mass decline in elderly individuals.

Our study had several limitations. Firstly, the study was a single-center observational study with a relatively small sample size, and confounding factors were present. A multi-center study with a larger number of subjects is planned in order to address this issue. Secondly, the assessment of physical activity and nutri-tional status was based on cross-sectional data, which precludes the possibility of establishing causal relationships. Thirdly, the results of the serological tests may have been influenced by environmental and personal factors. Therefore, caution is required when interpreting the findings of this study. Larger, prospective studies are required to validate our results. Furthermore, it is important to note that this sample was selected on the basis of convenience and therefore it cannot be as-sumed to be fully representative of the larger population of Padang, the province, or the country. These characteristics highlight the necessity for the early identifica-tion, screening, and evaluation of sarcopenia in older patients. We hope our work will contribute to further research on the factors influencing sarcopenia, as well as strategies for prevention and targeted treatment.

CONCLUSION

The present study suggested that low levels of transthyretin were related to an increased risk for sarcopenia in adults aged 60 years and older. Thus, comprehensive clinical evaluation of transthyretin levels in older patients might be helpful for early identification of those at high risk for sarcopenia. Further studies should evaluate the potential efficacy of maintaining optimal nutritional status in increasing transthyretin levels and reducing the risk of sarcopenia.

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