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THE ASSOCIATION BETWEEN SARCOPENIA AND PREALBUMIN LEVELS AMONG ELDERLY CHINESE INPATIENTS

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Abstract: *Objectives:* The goal of the present study was to assess the relationship between sarcopenia and prealbumin levels among hospitalized patients ages 60 and older. *Design:* Cross-sectional study. *Setting:* The geriatric wards in Guizhou Provincial People's Hospital, Guiyang. Guizhou, China. *Measurements:* Sarcopenia was defined according to the Asian Working Group for Sarcopenia (AWGS) criteria, which consist of three components: low muscle mass, assessed based on an index of appendicular skeletal mass/height^2 <7.0kg/m^2 for men and <5.4kg/m^2 for women; low muscle strength, defined as handgrip strength <26kg for men and <18kg for women; and low physical performance, defined as gait speed <0.8m/s. Using these criteria, sarcopenia was defined as presence of low muscle mass in addition to low muscle strength and/or low physical performance. Prealbumin levels and other variables were considered as being independent variables in an effort to evaluate any potential associations between these factors and sarcopenia status using non-adjusted and multivariate-adjusted regression models. *Results:* The overall prevalence of sarcopenia was 60.17%, affecting 65 (70.65%) men and 6 (23.08%) women in the present study. Age, body mass index (BMI), and prealbumin levels were each independently associated with sarcopenia ($p<0.05$). In a multivariate model, after adjusting for all potential covariates, prealbumin levels remained significantly associated with sarcopenia incidence, with an inflection point of 265.9mg/L. The effect sizes and the confidence intervals on the left and right sides of this inflection point were 0.94 (0.90 to 0.99) and 1.07 (0.93 to 1.23), respectively. *Conclusion:* Among older Chinese inpatients in the present study, prealbumin levels were negatively correlated with sarcopenia incidence, when prealbumin levels were below 265.9mg/L.

Key words: Hospitalized patients, sarcopenia, prealbumin, association.

Introduction

Sarcopenia is a geriatric syndrome characterized by the age-related loss of muscle mass and muscle strength (1). Sarcopenia is associated with many adverse outcomes, such as falls, disability, poor quality of life, high health care expenditures, and increased risk of mortality (2-4). According to a recent systematic review of 45 separate studies, the overall prevalence of sarcopenia is 10% in both men and women, but these estimates vary widely across studies (5). Lau and colleagues (6), for example, established a sarcopenia prevalence of 12.3% in men and 7.6% in women, while other studies have found a prevalence as high as 46.9% in males and 46.3% in females (7).

Many factors are associated with the onset and progression of sarcopenia. For example, loss of motor neuron units, decreased anabolic hormone status, and increased insulin sensitivity are all known to be associated with sarcopenia (8). Lifestyle or environmental factors such as cigarette smoking, low BMI, and physical inactivity, as well as disease states such as chronic obstructive pulmonary disease (COPD), stroke, and diabetes mellitus are all further associated with sarcopenia (9-11). Although the risk factors of sarcopenia in community-dwelling elderly persons have been relatively well studied, relatively little research has been done on this among hospitalized patients. In older people, hospitalization itself may represent a risk for functional decline and sarcopenia because of associated prolonged bed-rest, reduced caloric intake, and depressed mood.

Prealbumin is a protein produced by the liver. Serum prealbumin has historically been used as a biomarker of malnutrition and as an important indicator of overall nutrition status among older adults not suffering from acute illness (12). Malnutrition is closely related to sarcopenia in older persons (13, 14). Indeed, our research group has previously found that sarcopenia is associated with lower levels of serum prealbumin in community-dwelling older adults (15). Whether there is any change in this association among older inpatients, however, remains to be assessed. To that end, we studied a cohort of older Chinese inpatients to assess the relationship between prealbumin levels and sarcopenia in this population, using the Asian Working Group for Sarcopenia (AWGS) diagnostic criteria (16).

Methods

Study population and design

A cross-sectional study was conducted in geriatric wards in Guizhou, China. Between July 2017 and October 2017, consecutively admitted patients were prospectively recruited for this study. The inclusion criteria were as follows: age ≥60 years; able to perform a handgrip strength test or a walking test and to give informed written consent. The exclusion criteria

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were: (i) Severe cognitive impairment (Mini-Mental Status Examination (MMSE) score ≤10) (17); (ii) Presentation with any of the following comorbidities: acute infection, liver disease, renal failure, thyroid dysfunction, or iron-deficiency anemia (18); (iii) Steroid use; (iv) The presence of any tumor; (v) The presence of any implanted electronic device. Trained staff collected pertinent data from recruited patients within 48 hours of admission through face-to-face interviews and electronic medical records. The general characteristics collected for each patient included age, sex, height, weight, education level, alcohol consumption status, smoking status, marriage status, polypharmacy (defined as the concomitant use of ≥5 medications at time of admission) (19), and the following comorbidities: hypertension, coronary disease, stroke, COPD, liver disease, diabetes, renal failure, tumors of any type, dyslipidemia, and thyroid dysfunction. 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 8h from 6AM to 7AM. Blood levels of hemoglobin, plasma glucose, total protein, serum albumin, prealbumin, total cholesterol, triglycerides, creatinine, and estimated glomerular filtration rate were measured using standard laboratory techniques, which were carried out by a technician in the biochemistry laboratory of Guizhou Provincial People's Hospital.

Assessment of sarcopenia

Muscle mass was measured using dual-energy X-ray absorptiometry (DEXA) (LUNAR Prodigy, GE, USA). Appendicular skeletal mass (ASM) was calculated as the sum of muscle mass in the arms and legs. ASM divided by height in meters squared ($ASM/height^2$) was measured to gauge sarcopenia. A sarcopenia cutoff point of $ASM/height^2$ <7.0 kg/m^2 (men) and <5.4kg/m^2 (women) was used. (16) Fat mass was estimated for the whole body.

Muscle strength was assessed by measuring grip strength using a dynamometer (CAMRY EH 101; Zhongshan, Guangdong, China). Participants were asked to exert maximum effort three times with their dominant hand and the highest reading was recorded. Low grip strength was defined as <26 kg for men and <18 kg for women in accordance with the AWGS consensus criteria (16).

According to these same AWGS criteria, typical gait speed (m/s) on a 6-m course can also be used as a measure of physical performance, with low physical performance being defined as a usual walking speed slower than 0.8 m/s (16). Patients were asked to walk a 6-m course at their usual speed, using canes or walkers if necessary. The best time from two separate attempts was recorded.

Based on the AWGS criteria, we defined sarcopenia as the presence of low muscle mass co-presenting with low muscle strength or/and low physical performance (16).

Assessment of covariates

Functional ability, nutritional status, cognitive function, and the presence of depression were assessed in all participants. Functional ability was assessed using the Barthel Index, with scores ranging from 0 to 100 and low scores indicating less activity, with 0 points indicating complete care dependency (20). Nutritional status was assessed using the revised Mini-Nutritional Assessment short-form (MNA-SF). MNA-SF scores were rated as follows: malnutrition (score of ≤7), risk of malnutrition (score of 8-11) and normal nutritional state (score of 12-14) (21). Cognitive impairment was judged based on an MMSE score of ≤17 for persons who had not attended school, ≤20 for those with primary school education, and ≤24 for those with high school or higher level of education (22). Depression status was assessesed using the 15-item Geriatric Depression Scale (GDS-15), and depression was defined as a score more than 5/15 (23).

Statistical analyses

Continuous variables were expressed as median (quartile) or mean ± standard deviation, depending on the data distribution. Categorical variables were provided as percentages (%). One-Way ANOVAs, Kruscal Whallis H tests, and chi-squared tests were used to determine whether any statistical differences existed between groups, with distribution and data type being used to select appropriate statistical tests. A univariate linear regression model was used to evaluate the associations between factors of interest and sarcopenia status. Both non-adjusted and multivariate-adjusted models were used. According to the recommendations of the STROBE statement, we examined the results from unadjusted or minimally adjusted analyses and those from fully adjusted analyses in parallel. Whether the covariance was adjusted was determined based on the following principle: if, when added to this model, this changed the matched odds ratio by at least 10 percent the an adjustment was made (24). We also used a generalized additive model (GAM) to identify non-linear relationships. If a non-linear relationship was observed, a two-piecewise linear regression model was constructed to calculate the threshold effect of prealbumin levels on sarcopenia status according to the resultant smoothing plot. When the relationship between sarcopenia status and prealbumin levels appears obvious in this smoothed curve, a recursive method was used to automatically the inflection point, which was then used in subsequent analyses (25). All of these analyses were performed using the statistical software packages R (http://www.R-project.org, The R Foundation) and EmpowerStates (http://www.empowerstates.com, X & Y Solutions, Inc., Boston, MA). P values less than 0.05 (two-sided) were considered statistically significant.

Table 1
The baseline characteristics of participants according to the levels of Prealbumin

Prealbumin	Low (T1) (N=39)	Middle (T2) (N=39)	High (T3) (N=40)	P-value
Mean age (years)	86.46(5.12)	85.69(4.64)	80.75(8.27)	<0.001
Mean BMI(kg/m^2)	23.03 (4.48)	23.79(2.67)	25.30(3.35)	0.018
Mean hemoglobin(g/l)	129.10(17.79)	130.62(18.52)	139.30(14.43)	0.019
Mean length of stay(days)	25.10(5.18)	25.28(6.14)	21.75(7.11)	0.042
Mean fat mass (kg)	16.80(8.08)	16.80(8.08)	21.60(6.64)	0.007
Number of Drugs, mean (SD)	6.31(3.40)	6.46(3.02)	6.22(3.33)	0.948
Education level				0.961
illiterate	1(2.56%)	1(2.56%)	0(0.00%)	
elementary school	5(12.82%)	5(12.82%)	6(15%)	
middle school	16(41.03%)	15(38.46%)	14(35%)	
≥high school	17(43.59%)	18(46.15%)	20(50%)	
SEX				0.471
female	10(25.64%)	6(15.38%)	10(25.00%)	
male	29(74.36%)	33(84.62%)	30(75%)	
Smoking status				0.503
never smokers	20(51.28%)	24(61.54%)	23(57.50%)	
former smokers	14(35.90%)	12(30.77%)	12(30.00%)	
current smokers	5(12.82%)	3(7.69%)	5(12.50%)	
Marital status				0.386
married	26(66.67%)	32(82.05%)	31(77.50%)	
widowed /divorced	13(33.33%)	7(17.95%)	9(22.50%)	
ALCOHOL				0.238
never	31(79.49%)	26(66.67%)	27(67.50%)	
former drinkers	2(5.13%)	8(20.51%)	5(12.50%)	
occasional drinkers	6(15.38%)	4(10.26%)	5(12.50%)	
everyday drinkers	0(0.00%)	1(2.56%)	3(7.50%)	
ADL	93.92±8.59	95.69±6.67	97.84±5.84	0.065
Diabetes				0.414
yes	13(33.33%)	8(20.51%)	14(35.00%)	
no	26(66.67%)	31((79.49%)	26(65%)	
COPD				0.001
yes	26(66.67%)	15(38.46%)	11(27.5%)	
no	13(33.33%)	24(61.54%)	29(72.50%)	
Sarcopenia				<0.001
yes	32(82.05%)	24(61.54%)	15(37.50%)	
no	7(17.95%)	15(38.46%)	25(62.50%)	

Results

Description of the study population

Of the 138 enrolled participants, 20 participants were excluded from the study. Among these 20 patients , 4 exhibited acute infections, 4 had thyroid dysfunction, 7 had severe cognitive impairment, 2 had tumors, 2 had liver disease, and 1 was suffering from renal failure. Four patients did not agree to join the study. As a result, a total of 118 patients were included in the final study.

Table 2
The results of the univariate analysis for factors related to sarcopenia

	Statistics	YY
Prealbumin	206.75±4.4	1.0 (1.0, 1.0) <0.001
AGE	84.2±6.7	1.1 (1.0, 1.2) 0.002
BMI	24.0±3.6	0.7 (0.6, 0.8) <0.001
Education level		
illiterate	2 (1.6%)	1.0
elementary school	16 (13.1%)	0.0 (0.0, 1.0) 0.989
middle school	47 (38.5%)	0.0 (0.0, 1.0) 0.988
≥high school	57 (46.7%)	0.0 (0.0, 1.0) 0.988
Length of stay	23.96±6.4	1.0 (1.0, 1.1) 0.188
Sex		
female	26 (21.3%)	1.0
male	96 (78.7%)	6.3 (2.4, 16.5) <0.001
Number of drug	6.3+3.2	1.1 (0.9, 1.2) 0.311
Hemoglobin	133.6+17.7	1.0 (1.0, 1.0) 0.828
Fat mass	19.0+7.0	0.9 (0.8, 0.9) <0.001
COPD		
yes	54 (44.3%)	1.0
no	68 (55.7%)	0.5 (0.2, 1.0) 0.052
Marital status		
married	91 (74.6%)	1.0
widowed /divorced	31 (25.4%)	1.2 (0.5, 2.9) 0.611
Alcohol		
never	86 (70.5%)	1.0
former drinkers	15 (12.3%)	1.1 (0.4, 3.3) 0.893
occasional drinkers	17 (13.9%)	1.7 (0.6, 5.3) 0.342
everyday drinkers	4 (3.3%)	2.2 (0.2, 21.6) 0.512
Diabetes		
yes	36 (29.5%)	1.0
no	86 (70.5%)	1.1 (0.5, 2.5) 0.734
Smoking		
never smokers	69 (56.6%)	1.0
former smokers	40 (32.8%)	1.4 (0.6, 3.0) 0.450
current smokers	13 (10.7%)	4.5 (0.9, 28.1) 0.063
ADL	95.96±7.16	0.97(0.91,1.04) 0.419

Baseline characteristics of participants

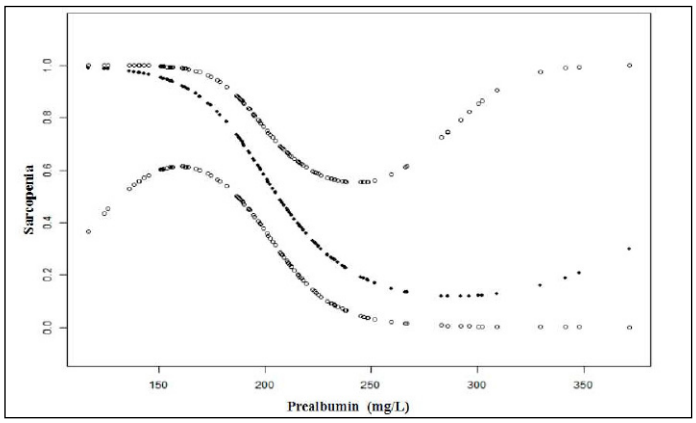
The mean participant age was 84.2±6.7 years, and 77.97% of the participants were male. The overall prevalence of sarcopenia was 60.17% in the overall study population. Male patients were more likely to be sarcopenic than female patients (70.65% vs 23.08%). Baseline patient characteristics are summarized in Table 1. Among groups of patients with different prealbumin levels, there were no statistically significant differences in sex, number of drugs taken, education level, ADL, smoking, alcohol consumption, marital status, or diabetes. Patients with low levels of prealbumin (group T1) were significantly older, and had significantly lower BMI, lower hemoglobin, lower fat mass, and longer length of days than those patients in the other two groups (T2-T3). The proportion of participants with COPD in group T3 was significantly lower than in the other two groups (T1-T2). The proportion of participants with sarcopenia in group T3 was significantly lower than in the other two groups (T1-T2).

The relationship between prealbumin levels and sarcopenia

The results of a univariate analysis are shown in Table 2. These results revealed that age, BMI, prealbumin, and fat mass were all correlated with sarcopenia. We also found that smoking, hemoglobin levels, alcohol consumption, marriage status, number of drugs taken, and education level were not associated with sarcopenia.

We used a univariate linear regression model to evaluate the association between prealbumin levels and sarcopenia status. The non-adjusted and adjusted models are both shown in Table 3. In the non-adjusted model, prealbumin levels were positively correlated with the prevalence of sarcopenia (β=0.98, 95% CI: 0.97 to 0.99, P=0.0002). In adjusted model I (adjusted age, sex, BMI), the result remained significant (β=0.99, 95% CI: 0.97 to 1.00, P=0.0267). However, we did not detect this association in adjusted model II (β=0.97, 95% CI: 0.93 to 1.00, P=0.0693).

Figure 1
The nonlinear relationship between prealbumin and sarcopenia after adjusting for age, BMI, education level, length of stay, sex, number of drugs, marital status, hemoglobin, fat mass, alcohol, diabetes, COPD, smoking, ADL



In this study, we found that the relationship between prealbumin levels and sarcopenia was non-linear (after adjusting for age, sex, BMI, education level, length of stay, number of drugs, marital status, hemoglobin levels, fat mass, alcohol consumption, diabetes, COPD, smoking, and ADL)

Table 3
The association of prealbumin and sarcopenia in different models

Variable	Non-adjusted(β,95%CI,P)	Adjusted I (β,95%CI,P)	AdjustII (β,95%CI,P)
Prealbumin	0.98(0.97,0.99)0.0002	0.99(0.97,1.00)0.0267	0.97(0.93,1.00)0.0693
Prealbumin(quartile)			
T1	1.0	1.0	1.0
T2	0.35(0.12,0.99)0.0482	0.08(0.01,0.49)0.0062	0.01(0.00,0.65)0.0302
T3	0.13(0.05,0.37)0.0001	0.08(0.01,0.47)0.0053	0.01(0.00,0.99)0.0204
P for trend	0.36(0.22,0.61)0.0001	0.35(0.16,0.77)0.0088	0.20(0.04,0.99)0.0582

Non-adjusted model; Adjust model I: adjust for age, sex, BMI; Adjust model adjust II: adjust for age, sex, BMI, education level, length of stay, number of drugs, marital status, hemoglobin, fat mass, alcohol, diabetes, COPD, smoking, ADL

(Figure 1). Based on a two-piecewise linear regression model, we calculated the inflection point was 265.9mg/L. The effect sizes and the confidence intervals on the left side of this model was 0.94 (0.90 to 0.99), P = 0.0225. However, we could not observe any relationship between prealbumin levels and sarcopenia to the right side of this inflection point (1.07,0.93 to 1.23, 0.3306) (Table 4).

Table 4
Piecewise linear regression model was used to detect the association of prealbumin and sarcopenia according to the prealbumin cut points

Cut points	Hazard ratio (HR)	95%CI	P value
≤ 265.9	0.94	0.90 to 0.99	0.022
> 265.9	1.07	0.93 to 1.23	0.330

Adjusted variables: age, BMI, education level, length of stay, sex, number of drugs, marital status, hemoglobin, fat mass, alcohol, diabetes, COPD, smoking, ADL

Discussion

This study was conducted to evaluate the relationship between sarcopenia and prealbumin levels among elderly Chinese inpatients. The overall prevalence of sarcopenia in our study sample was 60.17%, with 23.08% of women and 70.65% of men affected. The prevalence of sarcopenia varies widely from study to study, owing to different characteristics of study populations, multiple sets of diagnostic criteria, and different methodological approaches to assessing muscle mass and muscle function (26). Christine et al., for example, applied a bio-impedance-based analysis, and they reported a sarcopenia prevalence of 25.3% in 139 hospitalized geriatric subjects on the basis of the EWGSOP (27). Most recently, Simone et al. (28) used dual-energy X-ray absorptiometry (DXA) to estimate muscle mass and handgrip tests to measure muscle strength. They reported that the prevalence of sarcopenia was 12.42% in women and 23.47% in men among 639 hospitalized older patients. A study of community-dwelling older adults in China, meanwhile, has previously found a sarcopenia prevalence of 10.6% based on the AWGS diagnostic criteria – an incidence rate lower than that in our population (29). Moreover, we found that the prevalence of sarcopenia in women (23.08%) was lower than that in men (70.65%). These findings were in agreement with several previous studies (30-32). We also found that increasing age and lower BMI were both associated with sarcopenia, consistent with earlier findings (33-35). As a marker of nutritional status, BMI was inversely associated with the prevalence of sarcopenia. BMI is itself a key risk factor for sarcopenia, with patients with lower BMIs having a significantly higher likelihood of being sarcopenic. Skeletal muscle levels decrease rapidly as age increases, likely explaining the association between age and sarcopenia.

Kim et al. have reported that higher albumin levels are associated with a protective effect against declines in skeletal muscle index (SMI), walking speed, and the development of sarcopenia among old women (35). Prealbumin is an acute phase protein and a blood biomarker reflective of nutrition status (36). Interestingly, we found that prealbumin, rather than albumin, was associated with sarcopenia. However, we also found a non-linear relationship between prealbumin levels and sarcopenia. Distinct correlations between prealbumin levels and sarcopenia were found on the left and right sides of the inflection point (prealbumin = 265.9mg/L) in this model. Prealbumin was negatively associated with the prevalence of sarcopenia on the left side of the inflection point, but there was no significant association on the right side.

The etiology of sarcopenia is complex – the disease is likely to be explained by several associated factors, some factors are not modifiable. Because of reduced muscle protein synthesis with age, malnourished older persons have an inherently increased risk of sarcopenia (37). There is also growing evidence that nutritional supplements, particularly protein, also contribute to the lower incidence of sarcopenia (13). There is likely to be some overlap between the incidence of sarcopenia and malnutrition. In the present study, we found that lower BMI and prealbumin levels were associated with increased sarcopenia prevalence, and therefore higher BMI and prealbumin levels may be protective factors against sarcopenia development among older adults. Muscle strength or mass

might decline due to degradation of protein synthesis associated with low prealbumin, which may lead to an increased risk of sarcopenia(35).

There are several strengths to this study. The GAM to clarify the nonlinear relationship between prealbumin levels and sarcopenia was used in this study, which thereby helping to discover the true relationship between exposure and outcome. We were also able to use more reliable assessments of muscle mass via the DEXA approach.

There are certain limitations to the present study. As this was a cross-sectional study, determining causal relationships was not possible. The sample size was small (n=118), and as such the results regarding prevalence need to be interpreted with caution. There may also have some selection bias, as the populations excluded from these analyses were those individuals with worse health and functional conditions, thus potentially underestimating the prevalence of sarcopenia in the population as a whole.

Conclusion

Sarcopenia is highly prevalent among hospitalized individuals in China. The association between prealbumin levels and sarcopenia is non-linear. Prealbumin is negatively correlated with sarcopenia when prealbumin levels were below 265.9mg/L in this study. Prospective studies with large sample size are needed to confirm this finding.

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Ethical standards: All participants or their legal proxies signed a statement of informed consent and the study protocol received approval from the Ethics Committee of Guizhou Provincial People's Hospital.

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