

Relationships Between Serum Lipoprotein (a) And Sarcopenia In Elderly

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Abstract

Background: Examine the association of serum Lp(a) with sarcopenia in Chinese elderly.

Methods: We conducted this study using 2015–2020 data from hospitalized Chinese people 60 years old and older. Total body fat percentage and appendicular skeletal muscle mass were assessed with a dual-energy X-ray absorptiometry scan. We classified the participants into four sarcopenia/obesity groups based on both total body fat percentage and appendicular skeletal muscle mass.

Results: The analysis included data of 528 participants. the LP(a) level of sarcopenia was significantly higher than no sarcopenia, compared with obese or no obese groups. Furthermore, In the sarcopenic obesity group, the LP(a) level was highest. Correlation analysis showed that ASM/height² was negatively correlated with LP(a). Logistic regression analysis showed that sarcopenia was positively associated with LP(a).

Conclusions: Our study shows that sarcopenia appeared to be significantly associated with Lp(a) no matter the subjects had obesity or not.

Background

Sarcopenia first suggested by Rosenberg in 1989, has been defined as an age-related decline in muscle function (muscle strength or physical performance) as well as skeletal muscle mass[1]. The aging process is associated with progressive loss of lean body mass and the increase of fat mass[2]. Lean body mass makes up 50% of total body weight in adults but declines 25% over about 80 years old[3]. It has been suggested that this loss of muscle mass was strongly connected with increase in fat mass[4], which lead to the concomitant presence of sarcopenia and obesity. And they may potentiate each other and have a synergistic impact on metabolic disorders, reduced physical capability, poorer quality of life and increased mortality[5].

Lp(a) is a plasma lipoprotein synthesized by the liver, consisting of apolipoprotein(a) covalently linked to apolipoprotein B-100[6]. Plasma Lp(a) has been widely identified as independent cardiovascular risk factor[7]. The pathophysiological mechanism of Lp(a) still remains elusive. Aging may be an inflammatory condition such as obesity, cardiovascular disease, insulin resistance, and arthritis[8]. Researches suggested that loss of lean body mass, as well as obesity, was a smoldering inflammatory state driven by cytokines and oxidative stress[9]. And it has been demonstrated that disorder of lipid metabolism affected the atherosclerotic process through the modulation of inflammation[10]. Studies, observed in patients with rheumatoid arthritis, found that elevated levels of Lp(a) was related to low-grade inflammation[11].

Several biomarkers including Lp(a) were associated with sarcopenia in men and women using the new EWGSOP2 statement[12]. However, the relationship between sarcopenia/obesity and Lp(a) in Asian population remain unclear. The aim of this study was to investigate the relationship of LP(a) and sarcopenia and sarcopenic obesity.

Methods

1. Study Subjects

The data were consecutively collected from hospitalized people of Chinese Han population 60 years old and older, who were examined using DXA (Hologic Discovery A; Hologic, Bedford, MA, USA) and measured both muscle strength (grip strength) or/and physical performance (6-m usual gait speed) between 2015 and 2020. All of the information was collected from a large general hospital in Chongqing, a city with a population of 5.4 million in the southwest of China. And most of them were hospitalized because of either acute medical problems or elective admission.

Exclusion criteria for all participants were as follows: 1) acute changes of body composition such as severe edema and dehydration; 2) having a fever or an acute infection; 3) having an end-stage heart failure, renal disease; 4) missing data for clinical laboratory measures, including LP(a) and any body composition measure. All the exclusion criteria were based on medical history, physical examinations, and the laboratory data of participants. Ultimately, 528 subjects were involved in the study and all entered in the final result analysis.

2. Laboratory measurements

All blood samples were obtained in the morning between 7–9 o'clock, after a 12–14h overnight fast. Specimens were collected about 5ml in tubes without anticoagulant. After 30 minutes' standing, samples were centrifuged at 3000 rpm for 15 minutes. Serum samples were divided into aliquots and immediately stored at -80°C for subsequent assays. Serum Lp(a) levels were determined enzymatically using a chemistry analyzer (Hitachi 7020; Tokyo, Japan).

3. Body-composition, grip strength, 6-m usual gait speed measurements

Body compositional analysis was performed using dual energy X-ray absorptiometry (DXA). A whole-body DXA scan was performed for each patient to measure total and regional lean mass (g), total body fat (g), visceral adipose tissue (VAT) (g) and total body fat percentage (%). Appendicular skeletal muscle mass (kg) was defined as the sum of the lean soft tissue masses of the arms and legs [13]. ASM (kg) and ASM/height² (Kg/m²) were obtained [13]. We assessed hand grip strength using a hydraulic jamar dynamometer (Sammons Preston Rplyan, 4 Sammons Court Bolingbrook, IL, 60440). We measured walking speed by having the participant walk at his usual pace over a 6-m course.

4. The definition of sarcopenia and obesity

In the study, sarcopenia was defined by using height-adjusted skeletal muscle mass (the ASM/height² index) and gait speed or handgrip strength based on the definition of sarcopenia for Asian population in 2019 [14]. For the ASM/height² index, the cut-off values are 7.0 kg/m² for men and 5.4 kg/m² for women. The cut-off values of handgrip strength are 26 kg for men and 18 kg for women, while gait speed are 0.8 m/s. The ASM/height² index is correlated with body mass index (BMI) [15]. BMI is used as a current criterion for obesity, which could have limited applications for underestimating obese subjects with sarcopenia [16]. In our study, obesity was defined as values greater than 27% for men and 38% for women, based on the New Mexico Aging Process Study (NMAPS) and the New Mexico Elder Health Survey (NMEHS) [17]. We classified the subjects as the following: sarcopenia without obesity, without sarcopenia obesity, obesity without sarcopenia, and sarcopenic obesity, according to the definitions above.

5. Statistical Analysis

The numerical data were expressed as mean and standard deviation (SD). The normally distributed of examined variables were verified by Kolmogorov-Smirnov test. If the variables were normally distributed, we performed statistical comparisons applying student's t-test. If not, we applied nonparametric test. The correlation coefficient test was applied in order to assess the existence of significant interdependence between ASM/height² and Lp(a), as well as total body fat percentage and Lp(a). In addition, we used multiple binary logistic regression models to evaluate the relationship between sarcopenia, as well as obesity, as the dependent variable, and Lp(a). The regression models were adjusted for age, sex, and diseases. P <0.05 was considered to be statistically significant. Statistical analysis was performed using the SPSS program, version 19.0.

Results

The analysis included data of 528 participants (184 males and 344 females). The mean age of the participants was 71.77 years. As shown in Table 1, the subjects were classified as the following: sarcopenia without obesity (n=70, M/F=23/47), without sarcopenia and obesity (n=248, M/F=81/167), obesity without sarcopenia (n=154, M/F=62/92), sarcopenic obesity (n=56, M/F=18/38). In both the obese and non-obese groups, subjects with sarcopenia were older. And the sarcopenic obesity were oldest among all groups. The incidence of the muscle wasting appeared to be higher in female than in male. In the obese or no obese group, the Lp(a) level of subjects with sarcopenia was significantly higher. Furthermore, In the sarcopenia obesity group, the Lp(a) level was highest.

Table 1
Clinical characteristic of study population

	Non-obesity			Obesity		
	Sarcopenia (+)	Sarcopenia (-)	P	Sarcopenia (+)	Sarcopenia (-)	P
N	70	248		56	154	
Male/Female	23/47	81/167		18/38	62/92	
Age (yrs)	73.93±8.19	70.18±7.41		77.95±9.28	71.12±7.87	
Smoking (%)	36.20%	17.14%		57.18%	20.13%	
Drinking (%)	12.86%	17.74%		37.50%	17.53%	
CHD (%)	15.71%	25.81%		32.14%	28.57%	
Hypertension (%)	62.86%	70.97%		73.21%	78.57%	
PA (%)	54.29%	52.02%		60.71%	44.81%	
DM (%)	37.14%	66.94%		44.64%	69.48%	
Lp(a) (g/L)	311.93±369.21	240.86±231.20	0.048	319.80±407.87	197.29±224.97	0.006

Data are presented as mean± standard deviation; N: number; LP(a): Lipoprotein (a) ;CHD: coronary heart disease; PA: peripheral atherosclerosis; DM: diabetes mellitus;

Correlation analysis showed that ASM/height² was negatively correlated with Lp(a) (R=-0.121, P=0.005) (Table 2). However, there was no significant correlation between total body fat percentage and Lp(a).

Table 2. Correlation coefficients between ASM/height², total body fat percentage and Lp(a)

	LP(a)	
	R	P
ASM/height ²	-0.121	0.005
total body fat percentage	0.003	0.944

R: correlation coefficients; LP(a): Lipoprotein (a)

Multiple binary logistic regression analysis was performed using sarcopenia and obesity as dependent variables and Lp(a) levels as independent variables (Table 3). In the unadjusted model, sarcopenia was positively associated with Lp(a) (OR=1.541, P= 0.008). There was no significant correlation between obesity and Lp(a). After adjusting for age, sex, hypertension, coronary heart disease, diabetes mellitus and peripheral atherosclerosis, the relationship between sarcopenia and Lp(a) was not significantly changed (OR=1.587, P= 0.009).

Table 3. Multiple binary logistic regression analysis of the association between LP(a) and muscle wasting and obesity

	Sarcopenia				Obesity			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	OR (95%CI)	P						
Lp(α)	1.613 (1.130-2.263)	0.008	1.594 (1.125-2.213)	0.009	0.779 (0.591-1.041)	0.087	0.794 (0.579-1.051)	0.102

OR: odds ratio; CI: confidence interval; LP(a): Lipoprotein (a);

Adjusted for age, sex, hypertension, coronary heart disease, diabetes mellitus, peripheral atherosclerosis

Discussion

Sarcopenia has been reported to affect more than approximately 600 million elderly in 2000 worldwide[18] .It will become a common and important public health challenge as the proportion of aged population rapid increase in worldwide. But the mechanism of sarcopenia has still not been completely uncovered. There are several identified risk factors that may be involved in the onset and progression of sarcopenia: inadequate nutrition, hormonal factors, chronic state of inflammation, oxidative stress, declines in neural function, apoptosis, reduced protein synthesis, loss of mitochondrial function, reduced satellite cell function and telomere length[19] .In the study, we observed that subjects with sarcopenia had higher Lp(a) level in obese or no obese groups. At the same time, sarcopenia was positively associated with LP(a) no matter adjusted or unadjusted for additional potential confounders.

The level of serum lipids and lipoproteins have been risk predictors for cardiovascular disease. Lp(a) is one of plasma lipoproteins. In our study, we found that sarcopenia was associated with the Lp (a) level. Lp(a) associated independently with coronary heart disease (CHD) and cardiovascular mortality, which is not affected by age, gender, weight and exercise.[20] And Lp(a) are predominantly determined by the size of the apolipoprotein-a isoforms which are encoded by the LPA-gene.[21] Subjects rolled into the study were hospitalized elderly patients, who had wide difference in diet and exercise. The characteristics of Lp(a) can avoid possible possible confounding factors, improving the accuracy and reliability of the research. Many researches have shown that the level of Lp(a) is associated with CHD,diabetes mellitus[22],peripheral atherosclerosis[23] .after adjusted for these confounders, we found sarcopenia was still associated with the Lp(a), which indicated the Lp(a) may be an independent risk factor for sarcopenia.

The mechanism of the relationship between serum Lp(a) and sarcopenia is not well elucidated. Research has indicated that Lp(a) was involved in the development of arteriosclerosis, which may contribute to sarcopenia because of reducing blood supply to skeletal muscle[24] .Second, it has been proposed that Lp(a) are associated with proinflammatory oxidized phospholipids, which may explain some of the potential effect of Lp(a) on sarcopenia[25] .Dursunoglu D and Wang J s have shown that elevated levels of lipoprotein(a) were associated with increased low grade inflammation as measured through CRP[26]. And there are several indirect mechanisms, through which inflammation affect body composition: enhancing catabolic effects,

anorexia[8], promoting insulin resistance, reducing growth hormone and insulin-like growth factor-1 levels[27]. Furthermore, the available evidence at present suggests that hormones have effects on serum Lp(a). Ane study showed suppression of endogenous testosterone increased serum levels of Lp(a)[28]. As we all known, normal testosterone levels are necessary for maintenance of muscle mass. Low plasma testosterone levels can cause or accelerate sarcopenia.

Total body mass contains adipose tissue and lean mass. There is a progressive decrease of muscle mass and a rise in fat mass between the age of 20 and 70 years. Muscle mass is twice as much as fat mass in young men, but this ratio is almost reversed in elderly[29]. sarcopenia and obesity might act synergistically on metabolic and functional impairments in the elderly[30]. In our study, we also found that the subjects with sarcopenia and obesity have the highest level of Lp(a). Obesity have a greater burden of chronic disease, which contributed to sarcopenia. At the same time, sarcopenia also was one major contributor to fat gain.

There were several limitations in our study. First, it was performed using baseline data from a cross-sectional design of the study, which did not allow us to investigate the cause-effect relation. Second, the subjects in the study had cardiovascular disease, diabetes mellitus and other disease, which may influence the outcome. Third, we used height measured by people to calculate BMI and weight-adjusted appendicular lean mass, which may have a potential bias in our findings.

Conclusion

We found that sarcopenia appeared to be significantly associated with Lp(a) no matter the subjects had obesity or not.

Abbreviations

Lp(a):Lipoprotein (a);ASM: appendicular skeletal muscle mass;DXA:dual energy X-ray absorptiometry;BMI:body mass index ;NMAPS:New Mexico Aging Process Study;NMEHS:New Mexico Elder Health Survey;SD:standard deviation;PA:peripheral atherosclerosis;OR:odds ratio;DM:diabetes mellitus;CHD:coronary heart disease ;

Declarations

Ethics approval and consent to participate

Research involving human data was performed in accordance with the Declaration of Helsinki and informed consent was waived approved by the Ethics Committee of The First Affiliated Hospital of Chongqing Medical University(2021-506).

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due individual privacy but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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No funding was received for the study.

Authors' contributions

LJX,LSZ and QX designed the study. LJX, TZ, KXZ, JLC and CL performed the data collection. LSZ, YXZ, QL and YS processed the data collected and performed the statistical analyses. LJX and LSZ wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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