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Association between serum insulin level and low muscle mass in older individuals: evidence from the China Health and Nutrition Survey

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Abstract

Background The link between serum insulin level and low muscle mass among older adults is not yet fully understood. This study seeks to investigate this association using data from a nationally representative large-scale survey.

Methods The study utilized data from two waves of the China Health and Nutrition Survey (CHNS) conducted in 2009 and 2015. Subjects meeting the inclusion criteria were classified according to the Asia Working Group for Sarcopenia 2019 criteria. The study employed ordinary least squares (OLS) regression models to analyze the cross-sectional association between appendicular skeletal muscle mass (ASM) and serum insulin level. Additionally, based on the median insulin level in the population without low muscle mass in 2009, these individuals were divided into high insulin and low insulin groups. Logistic regression models were utilized to examine the longitudinal association between low muscle mass and serum insulin level.

Results In 2009, a cross-sectional association study enrolled a total of 2329 participants aged over 60 years, with 53.1% women and a median age of 68.00 years. The prevalence of low muscle mass in the study population was 30.83%, with females accounting for 60.03%. In the adjusted OLS regression model based on blood biomarker, serum insulin level was positively associated with ASM (β = 0.075, 95% confidence interval (95% CI): 0.034–0.117, $P < 0.01$). A total of 944 individuals from the 2009 population without low muscle mass were divided into high insulin and low insulin groups based on the median insulin level, and were followed up until 2015. It was found that there was a significant difference in the incidence of low muscle mass between the two groups. (12.44% vs. 7.45%, $P = 0.01$). The adjusted logistic regression models indicated that higher serum insulin levels were associated with a reduced incidence of low muscle mass (Hazard ratio = 0.958, 95% CI: 0.925–0.989, $P = 0.01$).

Conclusions Adequate serum insulin level could potentially serve as a protective factor in preserving healthy muscle mass among Chinese adults aged 60 and above.

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Clinical trial number Not applicable.

Keywords CHNS, Sarcopenia, Muscle mass, Serum insulin level

Introduction

As aging process accelerates worldwide as well as in China, the proportion of older population is steadily rising, leading to a significant increase in societal burdens [1]. With the growing older population, the demand for social pension security, healthcare services, and other related resources will also see a substantial surge. This will impose heavy pressure on the country's social security system, healthcare system, and family economies [2, 3]. Therefore, addressing the challenges brought about by aging to society, such as sarcopenia, requires concerted efforts from the government, various sectors of society, and families.

Sarcopenia, characterized by progressive loss of skeletal muscle mass, strength, and function, represents a prevalent geriatric syndrome associated with adverse outcomes [4]. Its epidemiology demonstrates a rising prevalence worldwide, particularly in aging populations. The multifactorial etiology involves age-related hormonal changes, chronic inflammation, sedentary lifestyle, and inadequate nutrition. Clinically, sarcopenia manifests as decreased muscle mass and strength, impaired physical performance, and increased risk of falls and fractures [5]. Prevention and management strategies encompass a multidisciplinary approach, including nutritional optimization with adequate protein intake and vitamin D supplementation, resistance exercise training, and addressing underlying comorbidities [6, 7]. Pharmacological interventions such as anabolic agents and myostatin inhibitors are emerging as potential therapeutic options [8].

Insulin, primarily secreted by pancreatic beta cells, plays a pivotal role in glucose homeostasis by facilitating glucose uptake into muscle and adipose tissue. Impaired insulin signaling pathways contribute to insulin resistance, leading to decreased glucose uptake and utilization in skeletal muscle [9]. Therefore, insulin resistance has been unequivocally established as a pivotal contributor to the pathogenesis of sarcopenia, eliciting muscle wasting primarily through the subsequent mechanisms: (1) heightened protein catabolism coupled with diminished protein synthesis within the skeletal musculature; (2) upregulated expression of the FoxO family, orchestrating skeletal muscle attenuation either through direct means or by fostering protein degradation; and (3) induction of autophagy within skeletal muscle cells [10].

Given the shared underlying determinants between muscle mass and insulin resistance, recent investigations have posited a potential nexus between low muscle mass and serum insulin level. Therefore, the present study utilized data sourced from the China Health and Nutrition Survey (CHNS), a nationally representative dataset. By conducting a cross-sectional analysis in 2009, we scrutinized the relationship between low muscle mass and serum insulin level in Chinese older individuals aged 60 years and above. Furthermore, we undertook longitudinal analyses based on data from 2015 to explore the enduring association of serum insulin level with low muscle mass. This endeavor aimed to furnish robust scientific evidence pertaining to the etiology, early intervention, and preventive measures against low muscle mass.

Methods

Data source

The study cohort was drawn from the CHNS, a nationwide longitudinal study administered by the Chinese Center for Disease Control and Prevention in collaboration with the University of North Carolina. Employing a multi-stage, random cluster sampling methodology, the CHNS sought representation across socioeconomic strata, encompassing low, middle, and high-income brackets. Within each province, a weighted sampling framework guided the selection of four counties and two cities. Subsequently, villages within counties and urban as well as suburban neighborhoods within cities were chosen through random sampling procedures. Within these locales, households were randomly identified, and all household members were included in the survey. Comprehensive descriptions of the cohort and sampling methodology have been previously published [11]. Blood biomarker assessments were conducted in 2009, and the last round of follow-up data collection occurred in 2015. Accordingly, data from the 2009 survey wave were used for cross-sectional analysis, while the 2015 data were used for longitudinal cohort analysis. Based on the median serum insulin level in the 2009 population without low muscle mass, individuals with insulin levels greater than or equal to this value were classified into the high insulin group, while those with levels below this value were classified into the low insulin group. Figure 1 presents the schematic diagram of research process.

Assessment of low muscle mass

Low muscle mass evaluation followed the Asia Working Group for Sarcopenia (AWGS) 2019 guidelines, incorporating assessments of muscle strength, appendicular skeletal muscle mass (ASM), and physical performance [12]. Among these, ASM plays a pivotal role in fundamental functions such as mobility. The calculation formula is as follows: $ASM = 0.193 \times \text{weight (kg)} + 0.107 \times \text{height}$

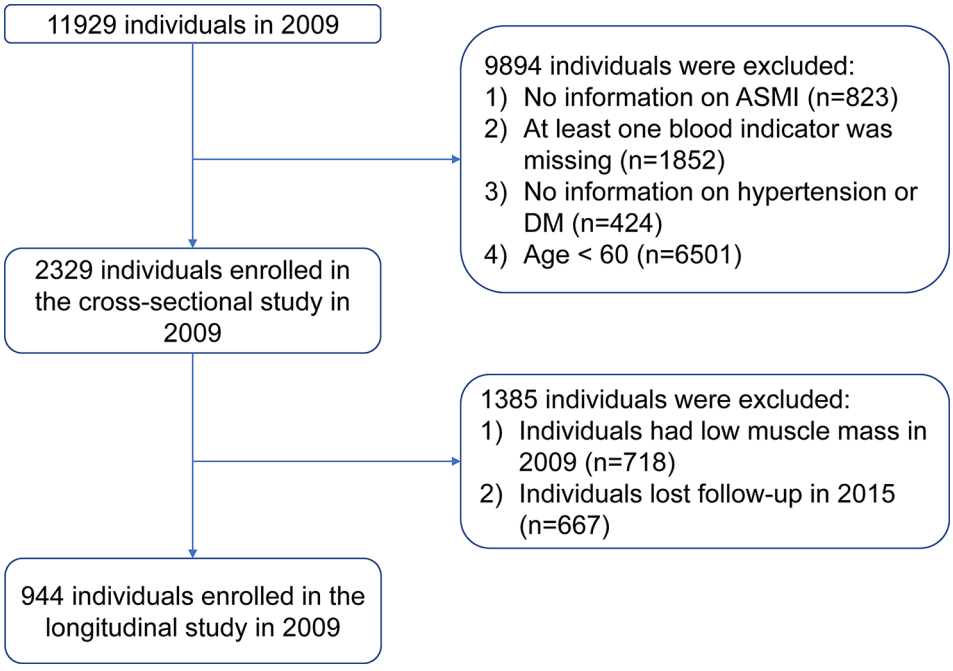

Fig. 1 Diagram illustrating the process of sample selection

(cm) – 4.157×gender – 0.037×age (years) – 2.631. In this formula, gender is coded as 1 for males and 2 for females [13]. His equation has a high R^2 value of 0.90, which indicates strong predictive accuracy for ASM in Chinese adults. Cross-validation further demonstrated a strong correlation coefficient of 0.941 with dual X-ray absorptiometry (DXA), underscoring its reliability. Moreover, this equation has been widely used in studies involving similar Chinese populations [14, 15]. The ASM index (ASMI), calculated by dividing ASM by the square of height in meters, serves as a key metric for categorizing low muscle mass. In accordance with the 2021 Chinese consensus on sarcopenia, low muscle mass was delineated by ASMI values below 7.0 kg/m^2 for males and 5.4 kg/m^2 for females [16].

Covariates

This study employed adjustments for demographic factors, medical history, and blood biomarkers. Covariates were carefully chosen in alignment with existing research and clinical directives [17, 18]. Demographic variables encompassed age, sex, and ASM. Medical history, including a record of diabetes mellitus (DM) [19] and hypertension [20], was included because these conditions may affect dietary habits due to treatment regimens.

In the 2009 survey, blood samples were critical specimens. All individuals aged seven years and older were asked to provide a 12 ml fasting blood sample, divided into three 4 ml tubes. Detailed procedures for blood sample collection and analysis can be found in the CHNS operational manual. The blood sample indicators included in this study encompassed the following items: serum insulin level, glucose, triglyceride (TG), total cholesterol (TC), apolipoprotein a1 (ApoA1), apolipoprotein b (Apo-B), lipoprotein a (LPA), C-reactive protein (CRP), creatinine (CR), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). To minimize the influence of outliers that may be erroneous or skew the analysis, values below the 5th percentile were adjusted to the 5th percentile, while values above the 95th percentile were set to the 95th percentile [21].

Statistical analysis

Descriptive statistics were utilized to compare patients from different groups. Continuous variables were summarized using mean and standard deviation or medians and interquartile ranges, while categorical variables were presented as frequencies. Normality of continuous variables were assessed using the Shapiro-Wilk test. Parametric data were analyzed using the two-tailed T-test, while nonparametric data were compared using the Wilcoxon rank-sum test. Categorical data were analyzed using the $\chi 2$ test.

In 2009, we utilized an Ordinary Least Squares (OLS) regression model to explore the cross-sectional relationship between ASMI and serum insulin level. The results were reported as regression coefficients (β) with corresponding 95% confidence intervals (95% CI). Additionally, longitudinal data from 2009 to 2015 were used to investigate the association between serum insulin levels and the development of low muscle mass through logistic

regression, with results expressed as Hazard ratio (HR) and 95% CI. Based on the overall average serum insulin level of the population included in 2009, those with levels below the average were categorized as the low insulin group, while those with levels above the average were categorized as the high insulin group. We developed three models to account for various covariates. Initially, Model 1 included only serum insulin level as the sole continuous independent variable. Subsequently, Model 2 expanded to include additional blood sample indicators, such as glucose, TG, TC, Apo-A1, Apo-B, LPA, CRP, and CR. The factors ultimately included in the Model 2 were determined by the backward method. Model 3 further adjusted for demographic and clinical factors, including age, gender, hypertension, and DM. A significance level of $P<0.05$ was used. All statistical analyses were performed using R version 4.4.0 (The R Foundation, Vienna, Austria).

Results

Table 1 provides the characteristics of the study population in 2009. The median age of the 2329 participants was 68.00 years (63.00–73.00 years), with females comprising 53.07% of the cohort. According to AWGS criteria, 718 participants (30.83%) were diagnosed with low muscle mass. The low muscle mass group was more likely to comprise females and older individuals ($P<0.01$). Regarding blood test indicators, the low muscle mass group exhibited lower levels of glucose, insulin, TC, TG, LDL-C, ApoB, and CRP ($P<0.01$). On the other hand, the low muscle mass group had higher levels of HDL-C, ApoA1, and LPA ($P<0.01$). There was no significant difference in CR levels between the two groups ($P=0.11$).

The median level of ASMI of the two groups were 7.11 and 5.27, respectively. These scores demonstrated a significant decline from the control group to the low muscle mass group ($P<0.01$). Figure 2 illustrates the cross-sectional relationship between serum insulin level and ASMI in the 2009 wave. In the crude model, serum insulin levels were positively correlated with ASMI ($P<0.01$; Fig. 2A). In the adjusted model by glucose, HDL-C, LPA, CR, and insulin, similar patterns were also observed with statistical significance ($P<0.01$, Fig. 2B).

Among the 944 longitudinal analytic samples, 92 participants (9.75%) developed new-onset low muscle mass in 2015. The incidence rate of low muscle mass was 7.45% in the high insulin group, whereas it was 12.44% in the low insulin group, indicating a significant difference ($P=0.01$) (Table 2). Figure 3 presents the longitudinal association between low muscle mass and serum insulin level using logistic regression models. In the unadjusted model, compared to the high insulin group, individuals with low insulin level had a higher risk of developing low muscle mass (HR = 0.955, 95% CI: 0.923–0.985, $P<0.01$).

Table 1 Characteristics of study population in 2009

	Total ($N=2329$)	Control group ($N=1611$)	Low muscle mass group($N=718$)	*P* value
Age (year)	68.00 (63.00,73.00)	66.00 (63.00,72.00)	71.00 (65.00,77.00)	< 0.01
Gender				< 0.01
Female	1236 (53.07%)	805 (49.97%)	431 (60.03%)	
Male	1093 (46.93%)	806 (50.03%)	287 (39.97%)	
Hypertension				< 0.01
No	1681 (72.18%)	1090 (67.66%)	591 (82.31%)	
Yes	648 (27.82%)	521 (32.34%)	127 (17.69%)	
DM				< 0.01
No	2183 (93.73%)	1472 (91.37%)	711 (99.03%)	
Yes	146 (6.27%)	139 (8.63%)	7 (0.97%)	
ASMI (Kg/m^2)	6.61 (5.66,7.44)	7.11 (6.12,7.72)	5.27 (4.90,6.62)	< 0.01
Glucose (mmol/L)	5.29 (4.84,5.93)	5.39 (4.92,6.11)	5.13 (4.70,5.61)	< 0.01
Insulin (uIU/mL)	10.49 (7.19,15.90)	11.90 (8.16,17.51)	8.36 (6.05,12.18)	< 0.01
TG (mg/dL)	116.03 (79.72,173.60)	131.09 (89.46,195.31)	91.23 (67.32,130.20)	< 0.01
TC (mg/dL)	192.96 (169.76,219.64)	196.06 (171.69,222.35)	187.16 (165.89,212.68)	< 0.01
HDL-C (mg/dL)	54.52 (45.63,64.58)	51.82 (44.08,61.87)	59.94 (51.04,70.38)	< 0.01
LDL-C (mg/dL)	120.26 (98.61,145.01)	122.97 (100.93,148.30)	114.66 (93.58,138.44)	< 0.01
Apo-A1 (mg/dL)	112.00 (97.00,131.00)	110.00 (95.00,128.00)	116.00 (102.00,138.00)	< 0.01
Apo-B (mg/dL)	95.00 (78.00,113.00)	98.00 (81.00,116.00)	87.00 (73.00,103.00)	< 0.01
LPA (mg/L)	0.92 (0.50,2.00)	0.87 (0.50,1.79)	1.06 (0.53,2.48)	< 0.01
CRP (mg/L)	2.00 (1.00,4.00)	2.00 (1.00,4.00)	1.00 (1.00,3.00)	< 0.01
CR (mg/dL)	1.01 (0.89,1.15)	1.01 (0.89,1.15)	1.00 (0.88,1.14)	0.11

ApoA1: apolipoprotein a1; Apo-B: apolipoprotein b; ASMI: appendicular skeletal muscle mass index; CR: creatinine; CRP: C-reactive protein; DM: diabetes mellitus; HDL-C: high-density lipoprotein cholestero; LDL-C: low-density lipoprotein cholesterol; LPA: lipoprotein a; TC: total cholesterol; TG: triglyceride. The values are presented as median (quartiles)

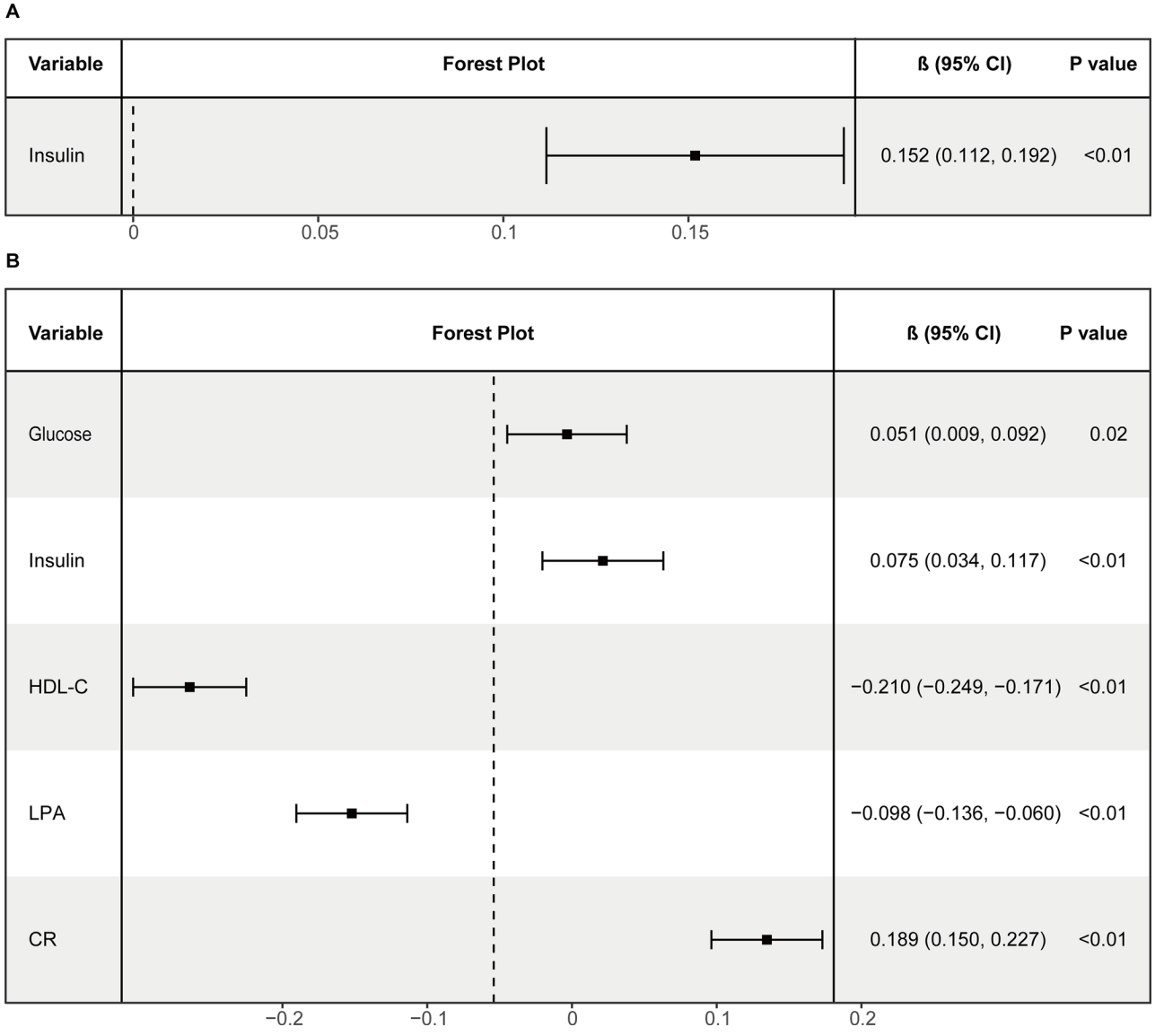

Fig. 2 OLS regression model on ASMI and insulin. **A**: The crude model based on insulin only. **B**: The adjusted model using backward method included glucose, HDL-C, LPA, CR, and insulin

This pattern persisted in the fully adjusted model, accounting for age, gender, hypertension, DM, HDL-C, and insulin, with the result remaining statistically significant (HR = 0.958, 95% CI: 0.925–0.989, $P = 0.01$).

Discussion

This study investigated the relationship between low muscle mass and serum insulin level among individuals aged over 60 within Chinese communities, utilizing nationally representative data. Our cross-sectional analysis revealed a positive correlation between ASMI and serum insulin level. Moreover, our longitudinal analysis demonstrated that older adults with lower insulin level were at an elevated risk of developing new-onset low muscle mass.

In this study, the prevalence of low muscle mass falls within the intermediate range compared to previous research [22, 23]. There are several reasons that could explain this discrepancy [24]. First, estimates of low muscle mass prevalence are influenced by the diagnostic criteria employed. Second, prevalence estimates may differ based on the assessment techniques utilized. Third, prevalence estimates can vary across different populations and regions. On the other hand, the incidence of new-onset low muscle mass observed in this study is similar to that reported in a previous study [25].

As an anabolic hormone, insulin promotes protein synthesis by facilitating the uptake of amino acids into muscle tissues [26]. Our study results indicate that serum insulin levels are positively correlated with ASMI and

Table 2 Characteristics of the follow-up cohort from 2015

	Total (*N* = 944)	High insulin level group (*N* = 510)	Low insulin level group (*N* = 434)	*P* value
Age (year)	71.00 (68.00,75.00)	71.00 (68.00,76.00)	71.00 (68.00,75.00)	0.73
Gender				< 0.01
Female	485 (51.38%)	288 (56.47%)	197 (45.39%)	
Male	459 (48.62%)	222 (43.53%)	237 (54.61%)	
Hypertension				0.29
No	593 (62.82%)	312 (61.18%)	281 (64.75%)	
Yes	351 (37.18%)	198 (38.82%)	153 (35.25%)	
DM				< 0.01
No	853 (90.36%)	443 (86.86%)	410 (94.47%)	
Yes	91 (9.64%)	67 (13.14%)	24 (5.53%)	
Low muscle mass:				0.01
No	852 (90.25%)	472 (92.55%)	380 (87.56%)	
Yes	92 (9.75%)	38 (7.45%)	54 (12.44%)	
Glucose (mmol/L)	5.35 (4.88,5.98)	5.59 (5.07,6.53)	5.15 (4.71,5.54)	< 0.01
Insulin (uIU/mL)	11.37 (7.71,17.15)	16.58 (13.35,23.04)	7.34 (5.51,9.01)	< 0.01
HDL-C (mg/dL)	52.20 (44.76,61.87)	49.11 (42.92,59.16)	55.10 (46.79,63.81)	< 0.01
LPA (mg/L)	0.85 (0.50,1.76)	0.76 (0.50,1.55)	0.94 (0.55,1.92)	0.01
CR (mg/dL)	1.00 (0.88,1.13)	1.00 (0.90,1.12)	0.98 (0.87,1.13)	0.37

CR: creatinine; DM: diabetes mellitus; HDL-C: high-density lipoprotein cholestero; LPA: lipoprotein a. The values are presented as median (quartiles)

serve as a protective factor against low muscle mass. A previous study has reached similar conclusions, but our larger sample size strengthens the evidence in this area [27]. The relationship between serum insulin levels and the decline in muscle mass and function in older adults, particularly those with DM, is complex. Traditionally, insulin resistance has been considered central to the onset of DM, leading to opposing hypotheses [28]: one suggests that insulin resistance contributes to the development of sarcopenia, while the other posits that sarcopenia is a risk factor for insulin resistance and DM. However, mounting evidence indicates that disordered insulin secretion, rather than insulin resistance, plays a crucial role in the progression of DM [29, 30]. In aging and diabetes, diminished insulin signaling impairs muscle protein synthesis and enhances muscle protein degradation, resulting in muscle mass loss and eventual sarcopenia. Therefore, insulin therapy slows the progression of sarcopenia in individuals with DM [31]. However, in a cohort study from Mexico involving community-dwelling older adults without other chronic health conditions, hyperinsulinemia, an early indicator of insulin resistance, was linked to a reduction in ASM [32]. Given the considerable heterogeneity of sarcopenia across diverse populations, further investigation is warranted to determine whether this could elucidate the conflicting results observed in different population.

In addition to serum insulin level, ASMI exhibited positive correlations with glucose and CR, while demonstrating negative correlations with HDL-C and LPR among the blood indicators. Similar findings have also been reported in a previous study [33]. Therefore, ASMI is also associated with liver function, and renal function other than β cell function. Sarcopenia correlates with fibrotic burden in individuals diagnosed with chronic hepatitis B. Moreover, ASMI experiences a notable decrease during antiviral therapy for chronic hepatitis B [34]. Progressive renal dysfunction is linked to diminished muscle strength and physical performance. Among older men residing in the community, even mild-to-moderate renal impairment at the outset is correlated with deteriorations in grip strength, gait speed, and overall muscle function over time [35].

Our longitudinal analysis, utilizing nationally representative data, indicated that the protective factors of low muscle mass include hypertension besides serum insulin level, while the risk factors include age and HDL-C. Within this study, hypertension was found to reduce the risk of sarcopenia, a finding consistent with prior research [36]. Generally, nutritional and exercise therapies are advocated for hypertension management [37], both of which have been shown to mitigate sarcopenia [38]. Nevertheless, further investigation is warranted to elucidate the relationship between hypertension and sarcopenia prevention. In middle-aged and older Chinese adults, each incremental unit rise in HDL-C levels corresponds to a 42% increase in the likelihood of developing sarcopenia at 4 years follow up, emphasizing the importance of effectively managing high HDL-C levels in sarcopenia prevention [39]. A study from China indicates that the prevalence of sarcopenia among males aged 60–69 years, 70–79 years, and over 80 years is 1.5%, 9.6%, and 33.1%, respectively. Therefore, prior to reaching 80 years of age, preserving muscle mass warrants primary

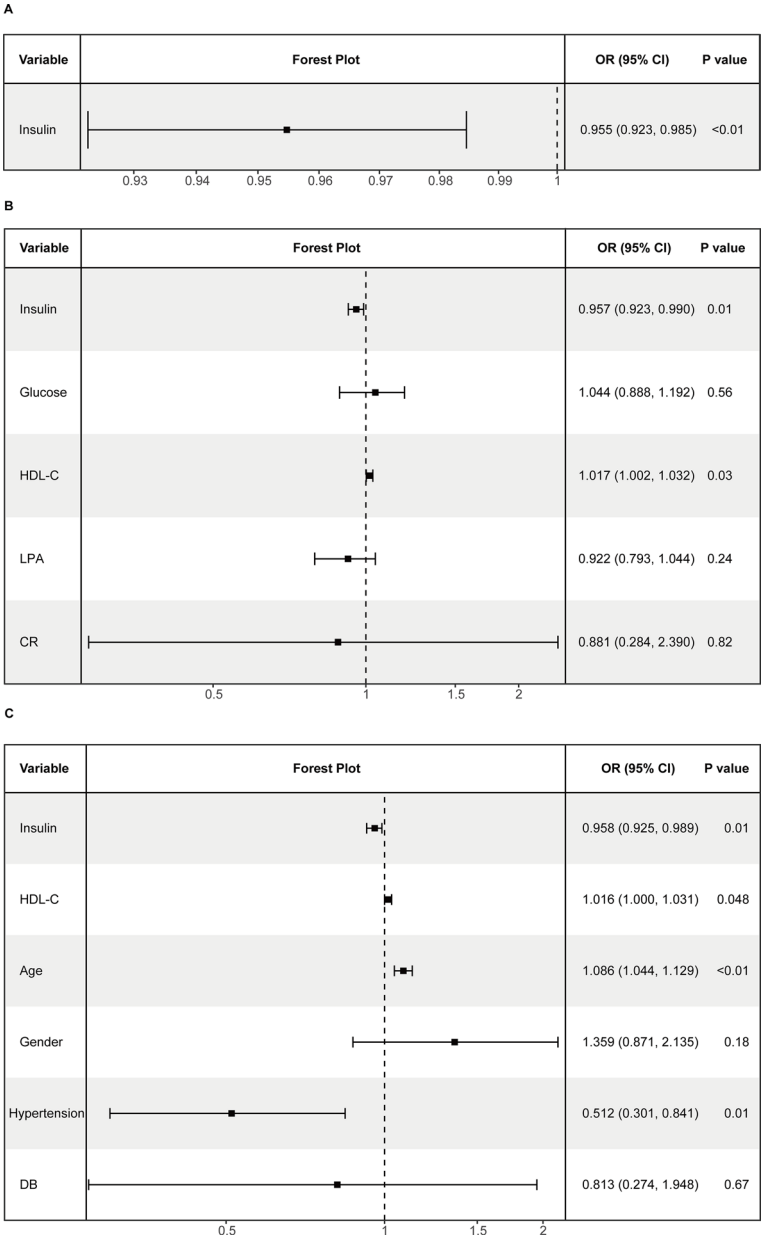

Fig. 3 Forest plot depicting the results of the logistic regression analysis. **A**: The crude model based on insulin only. **B**: The adjusted model based on blood biomarkers included glucose, HDL-C, LPA, CR, and insulin. **C**: The fully adjusted model included age, gender, hypertension, DM, HDL-C, and insulin

consideration, whereas after surpassing this age threshold, emphasis should shift towards enhancing muscle strength and function to mitigate disability risk [40].

It is important to acknowledge the limitations of this study. Firstly, while we adjusted for a comprehensive set of potential confounders based on existing knowledge, certain additional confounding factors, such as physical activity and dietary intake, were not accounted for in our analysis. Secondly, the observational nature of our study made it susceptible to recall bias inherent in questionnaire surveys. Thirdly, the diagnostic criteria for sarcopenia include DXA, the SARC-F questionnaire, grip strength measurement, and other functional tests. Due to limitations in the data recorded in the database, this study only used anthropometric measurements, which may introduce some bias. Last, while our cross-sectional study suggested a potential correlation between low muscle mass and serum insulin level, the underlying biological mechanisms remain unclear. Therefore, further experimental studies are warranted to elucidate and confirm this association.

Conclusions

In summary, this study highlights a potential association between serum insulin level and the onset of low muscle mass in Chinese individuals aged 60 and above, offering novel insights into a potential causal relationship. This endeavor will facilitate the exploration of efficacious approaches for treating low muscle mass using insulin prior to the establishment of evidence-based clinical guidelines.

Abbreviations

ApoA1	Apolipoprotein a1
Apo-B	Apolipoprotein b
ASM	Appendicular skeletal muscle mass
ASMI	Appendicular skeletal muscle mass index
AWGS	Asia Working Group for Sarcopenia
CHNS	China Health and Nutrition Survey
95% CI	95% confidence interval
CR	Creatinine
CRP	C-reactive protein
DM	Diabetes mellitus
DXA	Dual X-ray absorptiometry
HDL-C	High-density lipoprotein cholesterol
HR	Hazard ratio
LDL-C	Low-density lipoprotein cholesterol
LPA	Lipoprotein a
OLS	Ordinary least squares
TC	Total cholesterol
TG	Triglyceride

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Author contributions

Wangmi Liu conceived and designed the experiments. Guofang Sun and Jianjun Liang analyzed the data. Guofang Sun wrote the manuscript. Dechao Chen and Kongjun Zhao collected and visualized data. All authors read and approved the manuscript.

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Data availability

The datasets for this study can be found in the China Health and Nutrition Survey (https://www.cpc.unc.edu/projects/china). Codes are available on request from the authors.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Second Affiliated Hospital of Zhejiang University. Due to the study based on public data, the requirement for written informed consent was waived. The study adhered to the Declaration of Helsinki.

Consent for publication

Not Applicable.

Informed consent

Not applicable.

Competing interests

The authors declare no competing interests.

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