

Lean Mass Index, Not Body Mass Index, is Essentially Associated with Arterial Stiffness in Chinese Adults: A Cross-Sectional Study

Xinyi Wang^{1,*}, Ming Yi^{1,*}, Yinghua Zhang², Keling Xiao¹, Jin Si¹, Lijie Sun¹, Haoyu Zhang¹, Jinghao Sun¹, Zhaoli Liu¹, Jiaying Lin¹, Yuxin Xie¹, Bingyan Zhang¹, Jing Zhao³, Xi Chu³, Jing Li¹

¹Department of Geriatrics, Xuanwu Hospital, Capital Medical University, National Clinical Research Center for Geriatric Diseases, Beijing, 100053, People's Republic of China; ²Department of Cardiology, Chui Yang Liu Hospital Affiliated to Tsinghua University, Beijing, 100021, People's Republic of China; ³Health Management Center, Xuanwu Hospital, Capital Medical University, Beijing, 100053, People's Republic of China

*These authors contributed equally to this work

Correspondence: Jing Li, Department of Geriatrics, Xuanwu Hospital, Capital Medical University, National Clinical Research Center for Geriatric Diseases, Beijing, 100053, People's Republic of China, Tel +86-13611092728, Email shpxbb@sina.com; Xi Chu, Health Management Center, Xuanwu Hospital, Capital Medical University, Beijing, 100053, People's Republic of China, Tel +86-15699959668, Email cissy9007@163.com

Purpose: Although body mass index (BMI) is an established risk factor for cardiovascular diseases (CVD), many studies found that obese patients with established CVD had better prognosis than their lean counterparts. The study aimed to investigate whether this inverse association between BMI and arterial stiffness can be explained by body composition analysis.

Patients and Methods: Participants, aged from 26 to 86 years, were included in the cross-sectional study from October 2016 to January 2020. The brachial-ankle PWV (baPWV) was measured to assess arterial stiffness. Body composition was measured using bioelectrical impedance analysis (BIA). Lean Mass Index (LMI) and Fat Mass Index (FMI), calculated as lean mass and fat mass divided by squared height (kg/m²) respectively, are complementary indices that quantitatively assess individual's non-fat and fat compartments. Multiple linear regression analysis was conducted to investigate the associations between BMI, LMI and arterial stiffness. Mediation analysis was performed to examine the effect of bone mineral density (BMD) on the association between LMI and baPWV.

Results: A total of 744 participants were included. The median age was 61.00 (55.00, 67.00) years, and 502 (67.47%) of them were men. The median BMI, FMI and LMI were 25.56 (23.35, 28.01) kg/m², 7.18 (5.81, 8.68) kg/m² and 18.45 (17.10, 19.73) kg/m² respectively. The median baPWV was 1514.50 (1358.00, 1689.00) cm/s. Among all the anthropometric parameters, only BMI ($r=-0.150$, $p<0.001$) and LMI ($r=-0.206$, $p<0.001$) were significantly correlated with baPWV. Although BMI was inversely associated with baPWV [$\beta=-5.99$, 95% CI (-11.10, -0.89), $p=0.022$], the association became insignificant after LMI [$\beta=-25.85$, 95% CI (-44.73, -6.96), $p=0.007$] was included in the model. Furthermore, 19.68% of the association between LMI and baPWV was mediated by BMD.

Conclusion: Lean mass is the essential body component that determines the inverse association between BMI and arterial stiffness. Body composition analysis may provide important information for subclinical atherosclerosis beyond BMI.

Keywords: arterial stiffness, bioelectrical impedance analysis, body composition, body mass index

Introduction

The global obesity epidemic is well-established,¹ as the prevalence of obesity has tripled over the past four decades.² Body mass index (BMI) is widely accepted as a measurement of general adiposity for its convenience and feasibility.³ Well-documented epidemiologic studies have established BMI as an independent risk factor for diabetes mellitus (DM), cardiovascular diseases (CVD), cancer and mortality.⁴⁻⁷ Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of global morbidity and mortality. Atherosclerosis may initiate during early life and progress silently for many

years, culminating in severe complications such as myocardial infarction or ischemic stroke.⁸ Arterial stiffness is an early stage of atherosclerosis that can be detected before clinical symptoms, served as important surrogate for cardiovascular risk.^{9,10} Brachial–ankle pulse wave velocity (baPWV) is widely used as a non-invasive measurement to assess arterial stiffness for its simplicity and repeatability.¹¹ A previous meta-analysis based on data from 14 cohort studies including 14,673 participants showed that one standard deviation unit elevation in baPWV was related to 1.2 times increased cardiovascular risk.¹²

Although BMI is a well-known risk factor for CVD, many studies have reported its paradoxical association with better prognosis in patients with CVD, which has been termed “obesity paradox”.¹³ Accumulating studies have also reported the “obesity paradox” in the inverse association between BMI and arterial stiffness.^{14–20} For example, a cross-sectional study including 578 healthy participants found reduced arterial stiffness with increasing BMI.¹⁹ Hu et al found BMI was inversely correlated with baPWV in 4322 Chinese adults with hypertension. The underlying mechanism for the inverse association remains to be elucidated.²⁰

A potential explanation is that BMI cannot distinguish between lean mass and fat mass, which may have disparate effects on the development of arterial stiffness.^{21,22} In particular, higher lean mass is generally associated with improved metabolic health and enhanced insulin sensitivity, which may attenuate arterial stiffening.^{23,24} In contrast, excess fat mass, especially visceral fat, promotes inflammation, insulin resistance, and endothelial dysfunction, thereby accelerating arterial stiffness.^{25–27} However, limited data are available on the correlation between body composition and arterial stiffness. Bioelectrical impedance analysis (BIA) is a non-invasive, low-cost, quick, and simple method to estimate body composition.²⁸ Lean Mass Index (LMI) and Fat Mass Index (FMI) are complementary indices defined as lean mass and fat mass (kg) divided by height squared. Therefore, the current study used BIA to measure participants’ body composition and hypothesized that the inverse correlation between BMI and PWV could be explained by body composition analysis.

Materials and Methods

Study Population

Participants in the present study include: 1) participants who had regular physical examinations at the Health Management Department of Xuanwu Hospital, Capital Medical University; 2) patients who had a history of CVD and took regular visits at the Cardiology Outpatient Department of Xuanwu Hospital. A total of 744 participants who have examined baPWV and body composition from October 2016 to January 2020 were included. Participants with incomplete primary data, end-stage liver or renal disease, acute infection, malignancy, hematologic disease, autoimmune diseases were excluded.

Data Collection

Demographic characteristics, lifestyle factors, and medical history were extracted from electronic medical records of participants at Xuanwu Hospital, Capital Medical University. Hypertension and diabetes mellitus (DM) cases were defined based on either self-reported medical history or current use of disease-specific medications. Hypercholesterolemia was defined as either low density lipoprotein-cholesterol (LDL-C) ≥ 3.4 mmol/l, self-reported physician diagnosis, or use of lipid-lowering medication.

Anthropometric Measurements

The standing height was measured using a fixed stadiometer, and weight was measured using a calibrated digital scale. BMI was calculated as body weight (kg) divided by square of body height (m²). Anthropometric indices (waist, abdominal and hip circumferences) were measured with a soft non-stretchable tape while participants were barefoot and wearing light indoor clothing. Waist circumference (WC) was measured at the midpoint between the lowest costal margin and the iliac crest. Abdominal circumference (AC) was measured at the level of the umbilicus in the standing position at the end of expiration while breathing normally. Hip circumference (HC) was measured at the level of the maximal protrusion of the gluteal muscles, with the tape parallel to the floor. Each circumference was measured twice

non-consecutively, and the mean of both measurements was used for the analysis. The waist–hip ratio (WHR) was calculated as waist circumference (cm) divided by hip circumference (cm).

Body Composition and BMD Measurement

Body Composition Analyzer (ACCUNIQ, SELVAS Healthcare Co, Korea) was used to estimate participants' body composition. Participants were fully informed of the purpose, procedure, and precautions of the test, rested for more than 30 minutes in a comfortable position, removed any metal accessories, and put on light clothing before measurement. The participants were required to step on the plate electrodes barefoot, grip the handle electrodes and stretch both arms. Participants were not allowed to talk or move during the measurement if not necessary. Lean mass, fat mass, visceral fat area (VFA), and body fat percent (BFP) were collected for analysis. Lean mass index (LMI) and fat mass index (FMI) were calculated as dividing the subjects' lean mass or fat mass in kg by the square of the subject's height in meters. Dual-energy X-ray absorptiometry (DEXA) scan (EXA3000, OsteoSys Co, Korea) was used to determine the BMD (g/cm²) at the non-dominant arm, following the standard protocol. All subjects were required to remove from the participants before measurement. Participants' forearm was positioned laterally between the X-ray source and detector of the DEXA machine.

BaPWV Measurement

The present study measured baPWV using an automatic waveform analyzer with appropriate-sized cuffs (BP-203RPE III, Omron-Colin Co, Japan). After maintaining a supine position for at least 10 minutes, occlusion cuffs were applied to both upper arms and ankles for baPWV measurement. BaPWV was determined as the distance between brachial and posterior tibial arterial recording sites divided by pulse wave transmission time.²⁵ The mean value of the left and right baPWV value was used in the statistical analyses.

Statistical Analysis

Baseline characteristics of participants were reported as means \pm standard deviations (SD) for normally distributed data or medians (inter-quartile ranges) for skewed data. Categorical variables were described as number (percentage). Correlations between BMI and body components as well as the correlations between baPWV and anthropometric parameters were assessed using Spearman correlation analyses. Multiple linear regression analysis was conducted to explore the relationship between BMI and baPWV. Model 1 was adjusted for age, sex, smoking history, low-density lipoprotein-cholesterol (LDL-C) level, and history of coronary heart disease (CHD), hypertension and DM. Model 2 was further adjusted for LMI based on Model 1. Mediation analysis was conducted to investigate the role of BMD in the association between LMI and baPWV. Variance inflation factors (VIF) were calculated to diagnose collinearity among multiple variables. P-value < 0.05 was considered as statistically significant. Statistical analyses were performed using SPSS version 26.0 and PROCESS 4.2.

Results

Seven hundred and forty-four participants were included in the cross-sectional study from October 2016 to January 2020. The demographic and clinical characteristics of participants are shown in [Table 1](#). The median age of the study participants was 61.00 (55.00, 67.00) years, and 502 (67.74%) of them were male. About 50.81% of participants had a history of smoking. The proportions of participants with CHD, hypertension, DM and hypercholesterolemia was 60.22%, 61.89%, 28.09%, and 55.24%, respectively. The median value of BMI, FMI and LMI were 25.56 (23.35, 28.01) kg/m², 7.18 (5.81, 8.68) kg/m² and 18.45 (17.10, 19.73) kg/m². The median baPWV was 1514.50 (1358.00, 1689.00) cm/s.

As shown in [Figure 1](#), BMI was both positively correlated with FMI ($r=0.782$, $p<0.001$) and LMI ($r=0.744$, $p<0.001$). [Table 2](#) showed the results of Spearman correlation analyses between baPWV and multiple anthropometric parameters. Only BMI ($r=-0.150$, $p<0.001$) and LMI ($r=-0.206$, $p<0.001$) were significantly correlated with baPWV among all the parameters. As shown in [Table 3](#), the univariate analysis showed BMI [$\beta=-9.76$, 95% CI (-15.47, -4.04), $p<0.001$] and LMI [$\beta=-25.98$, 95% CI (-35.15, -16.81), $p<0.001$] were negatively associated with baPWV. Model 1 showed that the

Table 1 Demographic and Clinical Characteristics of Participants

Variables	Total (n=744)
Age (years)	61.00 (55.00, 67.00)
Males, n (%)	502 (67.47)
Smoking history, n (%)	378 (50.81)
History of CHD, n (%)	448 (60.22)
Hypertension, n (%)	453 (61.89)
Diabetes mellitus, n (%)	209 (28.09)
Hypercholesterolemia, n (%)	411 (55.24)
SBP (mmHg)	133.00 (120.00, 147.00)
DBP (mmHg)	77.00 (69.00, 86.00)
Serum uric acid (umol/l)	344.00 (287.00, 400.00)
Serum creatinine (umol/l)	67.00 (57.00, 77.00)
Glycosylated hemoglobin (%)	5.80 (5.50, 6.60)
TC (mmol/l)	4.06 (3.45, 4.81)
TG (mmol/L)	1.47 (1.08, 2.15)
LDL-C (mmol/l)	1.91 (2.41, 3.00)
Waist circumference (cm)	93.00 (86.00, 98.00)
Abdominal circumference (cm)	95.00 (88.00, 101.00)
Hip circumference (cm)	98.75 (94.00, 104.00)
Waist-to-hip ratio	0.94 (0.88, 0.98)
Visceral fat area (cm ²)	123.00 (97.00, 150.00)
Body fat percent (%)	27.70 (24.43, 31.80)
BMI (kg/m ²)	25.56 (23.35, 28.01)
FMI (kg/m ²)	7.18 (5.81, 8.68)
LMI (kg/m ²)	18.45 (17.10, 19.73)
BaPWV (cm/s)	1514.50 (1358.00, 1689.00)

Abbreviations: CHD, coronary heart disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; LDL-C, low density lipoprotein cholesterol; BMI, body mass index; FMI, fat mass index; LMI, lean mass index; BaPWV, brachial-ankle pulse wave velocity.

association between BMI [$\beta=-5.99$, 95% CI (-11.10, -0.89), $p=0.022$] and baPWV remained significant after adjustment of age, sex, smoking history, LDL-C, history of CHD, hypertension, and DM. However, BMI [$\beta=5.61$, 95% CI (-4.28, 15.49), $p=0.266$] became insignificant after LMI [$\beta=-25.85$, 95% CI (-44.73, -6.96), $p=0.007$] was included in the model 2. The variance inflation factors for all variables were less than 10.

Table 4 shows the results of mediation analysis performed to identify the mediating effect of BMD on the association between LMI and baPWV. LMI had a significant direct effect on baPWV [direct effect=-24.53, 95% CI (-35.95, -13.11), $p<0.001$], whereas BMD partially mediated the effect of LMI on baPWV [indirect effect=-6.01, 95% CI (-11.61, -0.96), $p<0.001$]. BMD elucidates 19.68% of the association between connecting LMI and baPWV, visually depicted in Figure 2.

Discussion

This cross-sectional study included 744 participants from October 2016 to January 2020. BIA was further performed to examine lean mass and fat mass, which were expressed as LMI and FMI by dividing the squared height. LMI and BMI were significantly correlated with baPWV among all the anthropometric parameters. Although BMI was inversely associated with baPWV, the association became insignificant when LMI was included in the model. To the best of our knowledge, this study was the first to identify lean mass as the predominant body component that determines the relationship between BMI and arterial stiffness.

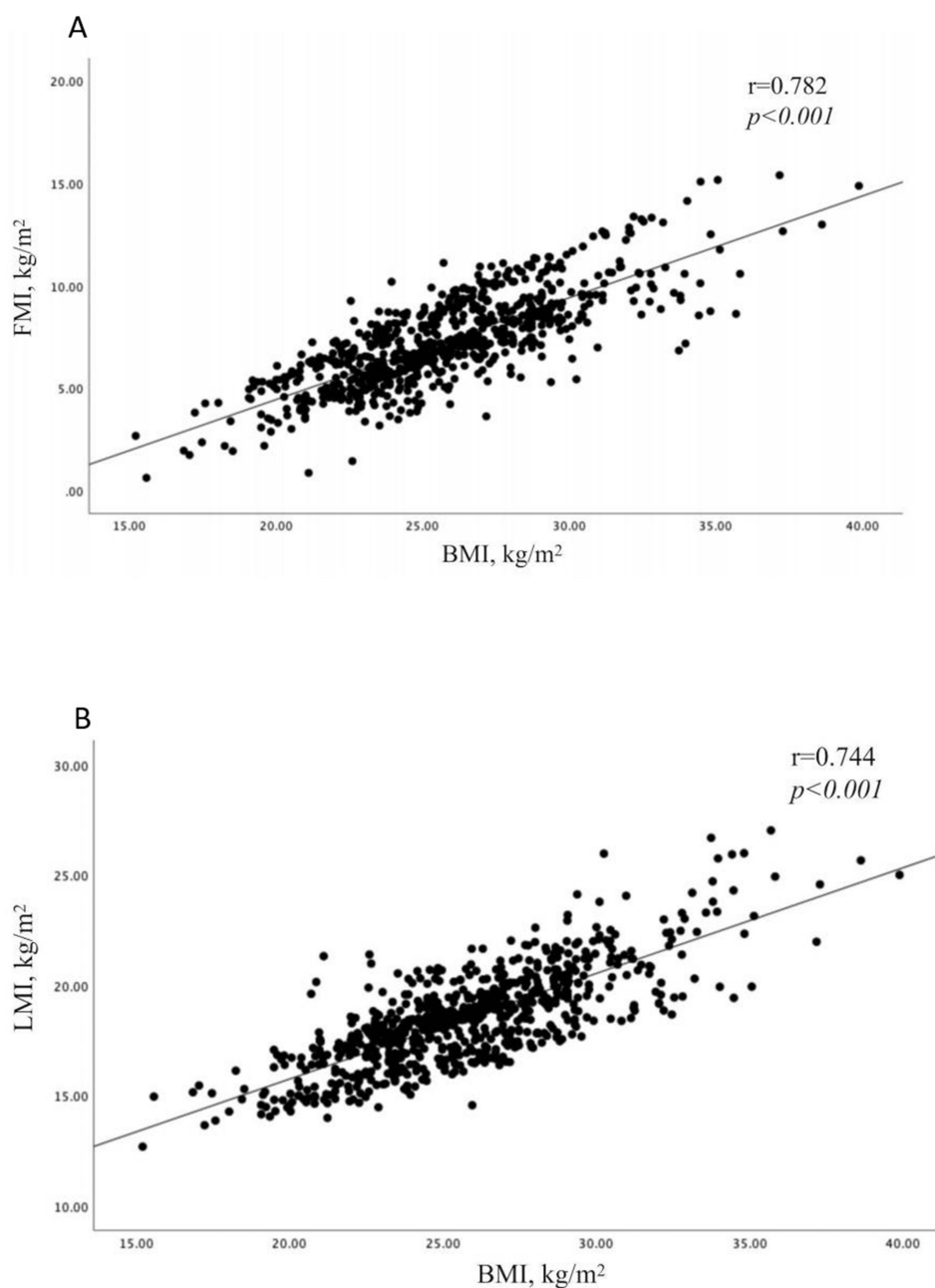


Figure 1 Correlations between BMI and FMI, LMI. **(A)** Correlation between BMI and FMI. **(B)** Correlation between BMI and LMI. **Abbreviations:** BMI, body mass index; FMI, fat mass index; LMI, lean mass index.

Arterial stiffness, commonly assessed using baPWV, is a feature of vascular aging and an independent predictor of cardiovascular events beyond conventional risk factors.²⁹ BMI, a simple anthropometric measurement for obesity, was an established risk factor for CVD.^{7,8} However, a great number of studies found an inverse association between BMI and arterial stiffness.^{14–20} For example, a cross-sectional study including 7750 healthy participants found BMI was negatively correlated with arterial stiffness.³⁰ Misako et al found arterial stiffness reduced with elevating BMI in 724 patients with diabetes mellitus.³¹ Huang et al found an inverse relationship between BMI and baPWV in 14866 hypertensive participants.³² The inverse relationship was also observed in several cross-sectional studies based on the general population.^{16,33} Our finding was in line with previous studies, as we consistently observed an inverse association between BMI and baPWV even after adjusting for multiple risk factors. Previous studies have proposed several possible

Table 2 Correlations Between Anthropometric Parameters and baPWV

Variables	r	P Value
WC (cm)	-0.040	0.285
AC (cm)	-0.045	0.272
HC (cm)	-0.052	0.208
WHR	0.005	0.897
VFA (cm ²)	0.001	0.970
BFP (%)	0.051	0.168
BMI (kg/m ²)	-0.150	<0.001
FMI (kg/m ²)	-0.031	0.404
LMI (kg/m ²)	-0.206	<0.001

Note: Spearman correlation analyses were used to analyze the correlations between anthropometric parameters and BaPWV.

Abbreviations: BaPWV, brachial-ankle pulse wave velocity; WC, waist circumference; AC, abdominal circumference; HC, hip circumference; WHR, waist-to-hip ratio; VFA, visceral fat area; BFP, body fat percent; BMI, body mass index; FMI, fat mass index; LMI, lean mass index.

Table 3 Univariate and Multivariate Linear Regression Model for baPWV

Variables	Univariate Analysis			Model 1			Model 2		
	β	95% CI	P value	β	95% CI	P value	β	95% CI	P value
Age (years)	14.79	(13.13, 16.45)	<0.001	13.75	(11.93, 15.57)	<0.001	13.49	(11.67, 15.32)	<0.001
Sex (Female, %)	56.49	(13.42, 99.57)	0.01	9.27	(-37.15, 55.70)	0.695	-39.73	(-98.20, 18.74)	0.183
Smoking history (%)	-38.59	(-79.04, 1.86)	0.061	20.09	(-23.32, 63.50)	0.364	26.30	(-17.16, 69.76)	0.235
CHD (%)	46.06	(4.77, 87.34)	0.029	-17.70	(-55.59, 20.18)	0.359	-16.56	(-54.29, 21.17)	0.389
Hypertension (%)	96.62	(55.67, 137.57)	<0.001	40.57	(3.22, 77.92)	0.033	42.47	(5.25, 79.68)	0.025
DM (%)	144.64	(100.76, 188.52)	<0.001	79.75	(39.55, 119.94)	<0.001	80.38	(40.35, 120.40)	<0.001
LDL-C (mmol/L)	-17.20	(-42.39, 7.99)	0.180	14.68	(-6.93, 36.29)	0.183	13.63	(-7.91, 35.16)	0.215
BMI (kg/m ²)	-9.76	(-15.47, -4.04)	<0.001	-5.99	(-11.10, -0.89)	0.022	5.61	(-4.28, 15.49)	0.266
LMI (kg/m ²)	-25.98	(-35.15, -16.81)	<0.001	NA	NA	NA	-25.85	(-44.73, -6.96)	0.007

Abbreviations: BaPWV, brachial-ankle pulse wave velocity; CI, confidence interval; DM, diabetes mellitus; CHD, coronary heart disease; LDL-C, low density lipoprotein-cholesterol; BMI, body mass index; LMI, lean mass index; NA, not applicable.

Table 4 Mediation Analysis of BMD on LMI and baPWV

	Effect	SE	95% CI	Proportion Mediated
Total effect	-30.54	5.43	(-41.20, -19.87)	
Direct effect	-24.53	5.81	(-35.95, -13.11)	80.32%
Indirect effect	-6.01	2.74	(-11.61, -0.96)	19.68%

Abbreviations: BMD, bone mineral density; LMI, lean mass index; BaPWV, brachial-ankle pulse wave velocity; SE, standard error; CI: confidence interval.

explanations. Some studies hypothesized that residual confounding factors such as hypertension, smoking history and cardiorespiratory fitness were not adjusted in the model.^{16,19} Several studies have applied other anthropometric indices including a body shape index (ABSI), WC, WHR and VFA to assess obesity but have shown inconsistent results.^{15,20,34,35} So far, no study has analyzed participants' body composition to explain the inverse association.

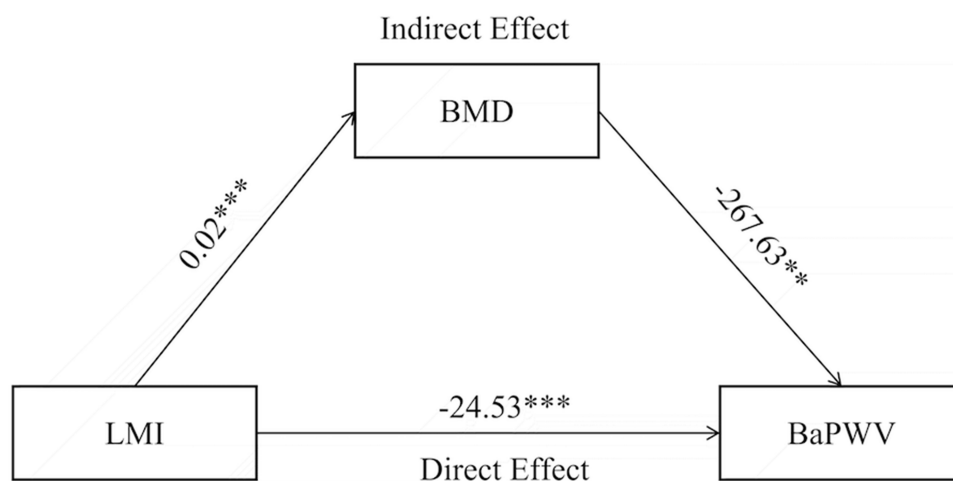


Figure 2 The mediating effect model of BMD on LMI and baPWV. *** $p < 0.001$, ** $p < 0.01$.

Abbreviations: BMD, bone mineral density; LMI, lean mass index; BaPWV, brachial-ankle pulse wave velocity.

BMI is a crude measurement of general adiposity that cannot discriminate between lean mass and fat mass, which have distinct associations with arterial stiffness. Bioelectrical impedance analysis (BIA) is a non-invasive and simple method that estimates body composition by measuring the resistance to a low-intensity electrical current, providing valuable data on fat mass and lean mass.³⁶ Previous studies showed that lean mass was negatively correlated with baPWV. A cross-sectional study including 186 middle-aged participants showed that arterial stiffness increased with decreasing lean mass.³⁷ Another study showed that reduced lean mass was an independent predictor for arterial stiffness in the elderly.³⁸ The inverse association remained significant in healthy participants as well as in patients with chronic kidney disease and peripheral artery disease.^{39–41} In contrast, the correlation between fat mass and arterial stiffness was inconsistent in previous studies. Several studies showed that fat mass was not significantly associated with baPWV.^{37,42,43} The observed inconsistencies may be attributed to the limited capacity of fat mass to reflect fat distribution.³⁴ Consistent with previous studies, we found that lean mass instead of fat mass was significantly correlated with baPWV. Furthermore, the association between BMI and baPWV became insignificant when LMI was included in the model. BMI represents a composite measure of both lean and fat mass, whereas our findings identify lean mass as the component strongly associated with arterial stiffness, indicating the superior predictive value of the LMI over BMI.

Although the underlying mechanism for the association between LMI and baPWV remains unknown, previous studies have suggested several potential explanations. Skeletal muscle, the primary component of lean mass could secrete myokines including irisin that reduce inflammation and improve insulin sensitivity to protect against arterial stiffness.⁴⁴ Additionally, higher lean mass could enhance glucose metabolism, reducing oxidative stress and endothelial dysfunction.^{44–46} The current study was the first to report that BMD partially mediate this association. Lean mass reflects the non-fat constituents of body weight such as muscles, bones, and blood. A great number of studies showed that lean mass was positively correlated with BMD. A Mendelian randomization study confirmed lean mass as a risk factor for osteoporosis.⁴⁷ Besides, recent studies found that BMD was an independent predictor for arterial stiffness.⁴⁸ We found 19.68% of the association between LMI and baPWV was mediated by BMD. The possible mechanisms include abnormal calcium homeostasis and vitamin D insufficiency, which may induce bone-turnover disturbances and enhance vascular calcification.^{49,50}

Interestingly, a large amount of studies found BMI was inversely associated with mortality in individuals with heart failure (HF), atrial fibrillation and coronary heart disease (CHD) which has been termed as “obesity paradox”.^{51–53} Furthermore, accumulating studies showed lean mass was an independent predictor for CVD prognosis.^{54–56} Our study provided a novel insight into the obesity paradox that the decreased mortality risk at higher BMI range may be attributed to increased lean mass. Compared with body weight management, interventions aimed at preserving or increasing muscle

mass through resistance and aerobic exercise may yield superior prognostic outcomes.^{57,58} Further research is needed to vary our findings.

There are some limitations in the present study. First, due to the cross-sectional design of our study, we could not make inferences about the causality between lean mass and arterial stiffness. Prospective cohort studies are warranted to verify the conclusions. Second, the participants were recruited from a single Chinese ethnic group with established cardiovascular risk factors, which limit the generalizability of our findings to other ethnic populations and healthier population. Third, we used BIA instead of DEXA to measure body composition. However, evidence have shown that body composition measured by BIA was strongly correlated with that measured by DEXA and have been widely used in epidemiological and clinical studies.⁵⁹ Finally, carotid-femoral pulse wave velocity (cfPWV) was accepted as the “gold standard” for arterial stiffness assessment, but the present study used baPWV to evaluate arterial stiffness since it is more simple, acceptable and reproducible.

Conclusions

LMI, rather than BMI, is significantly and inversely associated with arterial stiffness. BMD partially mediate the association between LMI and baPWV. Our findings provide a novel explanation for the widely observed “obesity paradox” by highlighting the protective role of lean mass in vascular health. The results underscore the clinical importance of assessing body composition to better evaluate cardiovascular risk beyond conventional anthropometric measures. Future longitudinal studies are warranted to establish causality and explore underlying mechanisms.

Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Informed Consent

Informed written consent was obtained from all subjects. The study protocol complied with the Declaration of Helsinki and was approved by the Ethics Committee of the Xuanwu Hospital, Capital Medical University (Protocol No [2023] 047). Participants consented to the publishing of all clinical data included in the manuscript.

Author Contributions

Xinyi Wang: Conceptualization, Data curation, Formal analysis, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Ming Yi:** Data curation, Formal analysis, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Yinghua Zhang:** Formal analysis, Software, Writing – original draft, Writing – review & editing. **Keling Xiao:** Formal analysis, Software, Writing – original draft, Writing – review & editing. **Jin Si:** Formal analysis, Software, Writing – original draft, Writing – review & editing. **Lijie Sun:** Formal analysis, Software, Writing – original draft, Writing – review & editing. **Haoyu Zhang:** Software, Writing – review & editing. **Jinghao Sun:** Formal analysis, Visualization, Writing – review & editing. **Zhaoli Liu:** Formal analysis, Visualization, Writing – review & editing. **Jiaying Lin:** Formal analysis, Visualization, Writing – review & editing. **Yuxin Xie:** Formal analysis, Visualization, Writing – review & editing. **Bingyan Zhang:** Formal analysis, Visualization, Writing – review & editing. **Jing Zhao:** Formal analysis, Visualization, Writing – review & editing. **Xi Chu:** Conceptualization, Resources, Supervision; Validation, Writing – original draft; and Writing – review & editing. **Jing Li:** Conceptualization, Formal analysis, Funding acquisition, Methodology, Project administration, Resources, Supervision; Validation, Writing – original draft; and Writing – review & editing. All gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests.

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