Association Between Relative Fat Mass and Cardiovascular Disease in Middle-aged and Elderly Populations: A Cross-sectional and Longitudinal Study Based on CHARLS (Postprint)

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Abstract

Background In recent years, medical research has found an association between relative fat mass (RFM) and cardiovascular disease (CVD). However, nationwide cohort studies on the association between RFM and CVD incidence risk in the Chinese population remain limited. Objective Using data from the China Health and Retirement Longitudinal Study (CHARLS), to analyze the relationship between RFM and CVD incidence risk in Chinese middle-aged and elderly population ($ $45 years). Methods This study used CHARLS data from 2011 –2018 for cross-sectional and longitudinal studies. The cross-sectional study included 12,867 middle-aged and elderly individuals aged $ $45 years. The longitudinal study included 11,171 middle-aged and elderly individuals from the 2011 cross-sectional study who were not diagnosed with CVD, with follow-up until 2018. Multivariable logistic regression and restricted cubic spline (RCS) were used to analyze the cross-sectional association between RFM and CVD. Kaplan-Meier curves, multivariable Cox proportional hazards regression model, and RCS were used to analyze the longitudinal association between different baseline RFM levels in 2011 and risk of new-onset CVD. Subgroup analysis was employed to explore consistency of the association across different subgroups, and sensitivity analysis was used to verify model stability. Results Multivariable logistic regression analysis showed that elevated RFM was a risk factor for CVD incidence (OR=1.03, 95%CI=1.02~1.04, P<0.05). Compared with the Q1 group, the Q2 group (OR=1.26, 95%CI=1.07~1.49), Q3 group (OR=1.78, 95%CI=1.47~2.16), and Q4 group (OR=1.81, 95%CI=1.49~2.19) had higher CVD risk (P<0.05). During the follow-up period, a total of 1,655 individuals (14.9%) were newly diagnosed with CVD. Multivariable Cox regression analysis showed that elevated RFM was a risk factor for CVD incidence (HR=1.03,

95%CI=1.02~1.04, P<0.05). Compared with Q1, the Q2 group (HR=1.31, 95%CI=1.12~1.52), Q3 group (HR=1.34, 95%CI=1.12~1.61), and Q4 group (HR=1.79, 95%CI=1.49~2.14) had higher risk of new-onset CVD. Subgroup analysis showed an interaction between RFM and marital status (P=0.022). Sensitivity analysis results were consistent with the trends of the main findings. Conclusion Higher levels of RFM were associated with increased risk of CVD incidence, suggesting that RFM may have potential value in CVD prevention and treatment.

Full Text

Association between Relative Fat Mass and Cardiovascular Disease in Middle-aged and Older Adults: A Cross-sectional and Longitudinal Study Based on CHARLS

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Abstract

Background
In recent years, medical research has identified an association between relative fat mass (RFM) and cardiovascular disease (CVD). However, nationwide cohort studies examining the relationship between RFM and CVD risk in Chinese populations remain limited.

Objective
Using data from the China Health and Retirement Longitudinal Study (CHARLS), this study analyzes the relationship between RFM and CVD incidence risk among middle-aged and elderly Chinese individuals ($ $45 years).

Methods
This study utilized CHARLS data from 2011-2018 for both cross-sectional and longitudinal analyses. The cross-sectional study included 12,867 middle-aged and elderly adults aged $ $45 years. For the longitudinal study, 11,171 individuals without a CVD diagnosis at baseline in 2011 were followed up until 2018. Multivariate logistic regression and restricted cubic splines (RCS) were used to analyze the cross-sectional association between RFM and CVD. Kaplan-Meier curves, multivariate Cox proportional hazards regression models, and RCS were

employed to analyze the longitudinal association between baseline RFM levels in 2011 and new-onset CVD risk. Subgroup analyses were conducted to assess consistency across different subgroups, and sensitivity analyses were performed to verify model stability.

Results
Multivariate logistic regression analysis revealed that elevated RFM was a risk factor for CVD (OR=1.03, 95%CI=1.02-1.04, P<0.05). Compared with the Q1 group, the Q2 group (OR=1.26, 95%CI=1.07-1.49), Q3 group (OR=1.78, 95%CI=1.47-2.16), and Q4 group (OR=1.81, 95%CI=1.49-2.19) showed significantly higher CVD risk (P<0.05). During follow-up, 1,655 individuals (14.9%) were newly diagnosed with CVD. Multivariate Cox regression analysis showed that elevated RFM was a risk factor for CVD (HR=1.03, 95%CI=1.02-1.04, P<0.05). Compared with Q1, the Q2 group (HR=1.31, 95%CI=1.12-1.52), Q3 group (HR=1.34, 95%CI=1.12-1.61), and Q4 group (HR=1.79, 95%CI=1.49-2.14) had significantly higher risk of new-onset CVD. Subgroup analysis indicated an interaction between RFM and marital status (P=0.022). Sensitivity analysis results were consistent with the main findings.

Conclusion
Higher levels of RFM are associated with increased CVD risk, suggesting that RFM may have potential value in CVD prevention and treatment.

Keywords: cardiovascular disease; relative fat mass; middle-aged and elderly people; China Health and Retirement Longitudinal Study; cohort study

Introduction

According to the *China Cardiovascular Health and Disease Report 2023* [1], approximately 330 million people in China currently suffer from cardiovascular disease (CVD), with prevalence continuing to rise. CVD has become the leading cause of death among urban and rural residents. Obesity, a global public health concern, represents one of the key risk factors for CVD [2]. By 2022, the global number of adults with obesity had reached nearly 880 million, with obesity rates among Chinese women increasing from 2.0% in 1990 to 7.8% in 2022, and among men from 0.8% to 8.9% [3].

Although traditional obesity assessment indices such as BMI are widely used, they have limitations in distinguishing between fat and muscle mass components [4] and cannot accurately reflect individual fat distribution patterns. Furthermore, the correlation between BMI and various diseases remains controversial [5]. Consequently, identifying more precise obesity assessment indicators to better measure CVD risk has become a research priority [6-8].

Visceral and ectopic fat distributions exert significantly more negative cardiovascular effects than subcutaneous fat [9-10]. While clinical techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) can assess

visceral fat accumulation, their high cost and radiation risks limit widespread application. In recent years, researchers have proposed a new obesity assessment index—relative fat mass (RFM)—based on sex, height, and waist circumference [11]. Compared with BMI, RFM more effectively reflects visceral fat accumulation by incorporating waist circumference and accounts for sex differences in body structure and fat distribution, thereby providing more accurate estimates of whole-body fat percentage. This index has been widely applied in clinical and public health settings for metabolic diseases and cerebrovascular conditions [12].

However, nationwide studies on the association between RFM and CVD in Chinese populations remain limited [13]. Therefore, this study utilizes the China Health and Retirement Longitudinal Study (CHARLS) database to explore the relationship between RFM and CVD among middle-aged and elderly Chinese individuals, aiming to provide new perspectives and evidence for health management in this population.

Methods

Study Population

This study was based on the CHARLS database, a national population cohort study that includes basic demographic information and health status data [14]. The national baseline survey (Wave 1) was conducted from June 2011 to March 2012, enrolling 17,705 participants using multistage probability sampling from 150 counties/districts and 450 villages/communities across China. Follow-up surveys have been conducted every two years (Wave 2 in 2013, Wave 3 in 2015, Wave 4 in 2018, and Wave 5 in 2020). The CHARLS study was approved by the Peking University Ethics Committee (approval number: IRB00001052-11015), and all participants provided informed consent.

Using CHARLS data from 2011–2018, this study conducted both cross-sectional and longitudinal analyses. The cross-sectional study included 12,867 middle-aged and elderly adults based on the following criteria: (1) age $ $45 years; (2) participation in physical examinations with complete data for RFM calculation; and (3) reported CVD diagnosis status in 2011. For the longitudinal study, 11,171 individuals without a CVD diagnosis at baseline in 2011 were followed until 2018.

Assessment of CVD

Heart disease diagnosis was determined based on participants' responses to the question: "Have you been diagnosed with a heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems by a doctor?" Stroke diagnosis was based on responses to: "Have you been diagnosed with stroke

by a doctor?" CVD was defined as self-reported heart disease or stroke. Participants who reported heart disease or stroke in previous waves were required to reaffirm in subsequent waves, and inconsistencies were corrected when participants denied previous self-reported diagnoses. Prior research has demonstrated high consistency between self-reported disease diagnoses and medical records in CHARLS [15].

RFM Calculation

RFM was calculated using validated formulas that incorporate sex, age, waist circumference, and height to reflect visceral fat distribution [11]. Height and waist circumference were measured in meters. The formulas were:
Males: RFM = 64 - (20 × height / waist circumference)
Females: RFM = 64 - (20 × height / waist circumference) + 12

Covariates

Collinearity analysis was performed with a variance inflation factor threshold of <5 to determine covariates. These included sociodemographic characteristics (age, education level, residence, marital status, smoking and drinking status) and health conditions (diabetes, hypertension, dyslipidemia). Smoking was defined as current or former smoking; drinking as current or former alcohol consumption. Hypertension was defined as systolic blood pressure $ $140 mmHg (1 mmHg=0.133 kPa) or diastolic blood pressure $ $90 mmHg, self-reported hypertension diagnosis, or use of antihypertensive medication. Diabetes was defined as fasting glucose $ $7.0 mmol/L, random glucose $ $11.1 mmol/L, HbA1c $ $6.5%, self-reported diabetes diagnosis, or use of glucose-lowering medication. Dyslipidemia was defined as total cholesterol $ $240 mg/dL, triglycerides $ $150 mg/dL, LDL-C $ $160 mg/dL, HDL-C <40 mg/dL, self-reported dyslipidemia diagnosis, or lipid-lowering therapy.

Results

Baseline Characteristics

A total of 12,867 respondents were included in the cross-sectional study, with a flowchart shown in [Figure 1: see original paper]. The sample comprised 6,117 males (47.54%) and 6,750 females (52.46%), with a mean age of $59.5\$\pm9.6 years; BMI 23.5\pm3.9 kg/m\hat{}\{2\}; body weight 58.8\pm11.7 kg; waist circumference 85.3\pm10.2 cm; and RFM$
When stratified by CVD diagnosis, 1,696 individuals (13.18%) had CVD and 11,171 (86.82%) did not. The CVD and non-CVD groups showed no statistically significant differences in education level or smoking status (P>0.05). However, significant differences were observed between groups in age, RFM, BMI, body weight, waist circumference, sex, marital status, residence, drinking status,

diabetes, hypertension, dyslipidemia, heart disease, and stroke (P<0.05), as detailed in .

Cross-sectional Association between RFM and CVD Risk

Multivariate Logistic Regression Analysis Using CVD occurrence as the dependent variable (yes=1, no=0) and RFM (both continuous and quartiles) as independent variables, multivariate logistic regression was performed. RFM quartiles were: Q1 (RFM 0.76-25.27, n=3,217), Q2 (RFM 25.28-32.83, n=3,217), Q3 (RFM 32.84-40.47, n=3,216), and Q4 (RFM 40.48-53.97, n=3,217). Model 1 was unadjusted; Model 2 adjusted for age (continuous), marital status (married/cohabiting=1, unmarried/separated/widowed=2), education (below primary=1, primary=2, secondary=3, high school and above=4), and residence (rural=1, urban=2); Model 3 additionally adjusted for smoking (never=1, current=2), drinking (never=1, current=2), hypertension (no=1, yes=2), diabetes (no=1, yes=2), and dyslipidemia (no=1, yes=2). All models showed that elevated RFM was a risk factor for CVD, with increasing CVD risk as RFM levels rose (P<0.05), as shown in .

RCS Analysis of RFM and CVD Risk RCS curves were used to explore the dose-response relationship between RFM and CVD risk. The results indicated no non-linear association (P-overall<0.001, P-non-linear=0.655), as illustrated in [Figure 2: see original paper].

Longitudinal Association between RFM and New-onset CVD Risk

Kaplan-Meier Cumulative Incidence Analysis During follow-up, 1,655 individuals (14.9%) were newly diagnosed with CVD. The Q1, Q2, Q3, and Q4 groups had 294, 430, 368, and 563 new cases, respectively. Kaplan-Meier analysis revealed that cumulative incidence of new-onset CVD increased over time across all four groups, with statistically significant differences among groups (^{2}=109.165, P<0.05), as shown in [Figure 3: see original paper].

Multivariate Cox Regression Analysis Using new-onset CVD as the dependent variable and RFM (continuous and quartiles) as independent variables, multivariate Cox regression was performed. Quartiles for this analysis were: Q1 (RFM 0.76-24.98, n=2,793), Q2 (RFM 24.99-32.29, n=2,793), Q3 (RFM 32.30-40.19, n=2,794), and Q4 (RFM 40.20-53.97, n=2,791). Model 1 was unadjusted; Model 2 adjusted for age, residence, marital status, and education; Model 3 additionally adjusted for smoking, drinking, hypertension, diabetes, and dyslipidemia. All models demonstrated that elevated RFM was a risk factor for CVD, with increasing risk as RFM levels rose (P<0.05), as presented in .

RCS Analysis of RFM and New-onset CVD Risk RCS curves examining the dose-response relationship between RFM and new-onset CVD risk showed

no non-linear association (P-overall<0.001, P-non-linear=0.153), as depicted in [Figure 4: see original paper].

Subgroup Analysis Subgroup analyses revealed that elevated RFM remained a risk factor for new-onset CVD across most subgroups, including age >60 years, age 45–60 years, males, females, married individuals, various education levels, urban residents, normal weight, overweight, smokers, non-smokers, drinkers, non-drinkers, and those with or without diabetes, hypertension, or dyslipidemia (P<0.05). However, no significant association was found among unmarried individuals, rural residents, or underweight participants (P>0.05). Interaction analysis showed no significant interactions for age, sex, education, residence, BMI, smoking, drinking, diabetes, hypertension, or dyslipidemia (P>0.05), but a significant interaction was observed for marital status (P<0.05), as shown in [Figure 5: see original paper].

Sensitivity Analysis Three sensitivity analyses were conducted: (1) examining RFM in relation to CVD subtypes (heart disease and stroke); (2) winsorizing RFM at the 0.5th and 99.5th percentiles to reduce extreme value effects; and (3) excluding participants with new-onset CVD within the first two years of follow-up to eliminate potential bias from early incidence. All sensitivity analyses yielded results consistent with the main findings, as detailed in .

Discussion

This large-scale cross-sectional and longitudinal study of Chinese middle-aged and older adults found a positive association between RFM and CVD risk, with consistent trends across most subgroups. These findings suggest that RFM may serve as an effective biomarker for CVD risk stratification, and that close monitoring and maintenance of lower RFM levels may be important for primary prevention of CVD.

RFM is an obesity index calculated based on sex, height, and waist circumference, offering convenience, simplicity, and high accuracy. Compared with BMI, it more accurately reflects whole-body fat percentage. WANG et al. [16] found in a U.S. prospective cohort study of 26,754 participants that elevated RFM increased metabolic abnormalities, cardiovascular risk factors, and CVD incidence. Additionally, a U.S. cross-sectional study demonstrated a significant positive association between RFM and stroke [12]. A survey in East China (SPECT-China) also showed significant associations between RFM and CVD prevalence [13], consistent with our findings.

Several potential mechanisms may explain the relationship between RFM and CVD. First, individuals with elevated RFM often have dyslipidemia [17], particularly increased LDL-C levels, which oxidizes and deposits in arterial walls, triggering inflammatory responses and plaque formation that lead to atherosclerosis.

Second, in obesity, adipose tissue (especially visceral fat) releases excessive free fatty acids and induces chronic low-grade inflammation [18], causing metabolic dysfunctions including insulin resistance [19]. Inflammatory mediators and reactive oxygen species from epicardial adipose tissue can promote atherosclerosis progression [20]. Additionally, obesity contributes to microvascular complications through multiple pathways [21].

Subgroup and interaction analyses revealed an interaction between marital status and RFM. The positive association between RFM and CVD was particularly pronounced among married individuals, possibly because middle-aged married people often bear dual family and social responsibilities—including career development, child-rearing, and elder care—that create high psychosocial stress [22], while also facing unhealthy lifestyle factors such as unbalanced diets and physical inactivity.

This study has several strengths. First, it utilized the large, nationally representative CHARLS cohort with multistage stratified probability sampling, ensuring data representativeness and reliability. Second, the study focused on the relationship between RFM and CVD, with RFM calculated from sex, age, waist circumference, and height, and CVD diagnosis based on reliable participant questionnaire data. To enhance generalizability, we conducted stratified analyses across several subgroups and adjusted for exposure- and outcome-related variables to obtain more precise estimates of the RFM-CVD association.

Several limitations should be noted. First, CVD diagnosis was based solely on self-reported medical history rather than clinical diagnosis, which may involve recall bias. Second, the study lacked detailed information on specific CVD subtypes. Additionally, due to the long follow-up period, RFM may have changed over time, and baseline measurements may not fully reflect participants' true long-term exposure.

In conclusion, higher levels of RFM show a linear positive association with CVD risk among Chinese middle-aged and older adults. RFM may serve as an effective biomarker for CVD risk stratification, and close monitoring and maintenance of lower RFM levels may be important for primary prevention of CVD. These findings provide a theoretical basis for developing risk stratification and intervention strategies for CVD in this population.

Author Contributions

LIANG Wenjian proposed the main research objectives, designed the study, and revised the manuscript. CHEN Huilong performed statistical analysis, drafted the manuscript, and contributed to methodological design. LIAO Yunchu and LIU Yuwei assisted with data analysis and manuscript writing. KONG Zhenghui, HUANG Xinghui, and XU Jiahui conducted data application and preprocessing. QI Na and WANG Yuanping designed and prepared the

figures and tables. All authors reviewed and approved the final manuscript.

Conflict of Interest: The authors declare no conflict of interest.

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