Association Between Relative Fat Mass and Risk of Cardiometabolic Comorbidity: Postprint

Authors: Gu Handong, Lu Hongrun, Gu Keyi, Han Zheng, Yang Fei, FU Xiaoya, Weiqiang Wang, Wang Weiqiang

Date: 2025-11-10T16:56:18+00:00

Abstract

Background Cardiometabolic multimorbidity (CMM) is currently one of the most common and stable multimorbidity patterns. Relative fat mass (RFM), as a novel body fat assessment tool, has demonstrated potential for predicting risk in single cardiometabolic diseases; however, research on the relationship between RFM and CMM risk remains limited. Objective To investigate the relationship between RFM and CMM risk in different gender populations and to evaluate the role of RFM in CMM prevention and treatment. Methods A total of 116,321 permanent residents living in 12 urban communities including Suzhou from March 2017 to July 2021 were selected as study subjects. Based on gender and CMM status, male and female participants were divided into CMM and non-CMM groups, and baseline characteristics were compared between CMM and non-CMM groups by gender. RFM was grouped by gender-specific interquartile range, and multivariate Logistic regression analysis was used to explore the relationship between RFM and CMM risk in different gender populations. Restricted cubic spline (RCS) curves were used to investigate the non-linear relationship between RFM and CMM across genders. Subgroup analysis and interaction tests were performed to explore differences in the association between RFM and CMM across different subpopulations. Results This study included a total of 116,321 participants, including 46,637 males (40.1%), among whom 11,969 (25.7%) were in the CMM group and 34,668 (74.3%) in the non-CMM group; and 69,684 females (59.9%), among whom 16,668 (23.9%) had CMM and 53,016 (76.1%) were in the non-CMM group. RFM levels were higher in the CMM group than in the non-CMM group for both males and females ($P<0.001$). Multivariate Logistic regression analysis showed that after adjusting for confounding factors including age, education level, smoking, alcohol consumption, BMI, low-density lipoprotein cholesterol, remnant cholesterol, blood glucose, systolic pressure, and diastolic pressure, the risk of CMM in males in groups T2–T4 was 1.530, 2.086, and 2.945 times that

of group T1, respectively (P<0.001); for females in groups F2-F4, the risk was 1.205, 1.532, and 1.760 times that of group F1, respectively (P<0.001). Furthermore, for each unit increase in RFM, the risk of CMM increased by a factor of 1.109 in males (OR=1.109, 95%CI=1.101-1.116, P<0.001) and by a factor of 1.054 in females (OR=1.054, 95%CI=1.049-1.060, P<0.001). RCS curve analysis revealed a non-linear relationship between RFM and CMM risk in both males and females (males: inflection point for OR=1 was 25.26, P for non-linearity<0.001; females: inflection point for OR=1 was 38.41, P for non-linearity=0.001). Subgroup analysis indicated that the association between RFM and CMM risk was stronger in males (OR=1.108, 95%CI=1.101-1.115), individuals aged $ $45 years (OR=1.011, 95%CI=1.008-1.013), those with education below high school (OR=1.013, 95%CI=1.011-1.015), current smokers (OR=1.062, 95%CI=1.054-1.069), current drinkers (OR=1.021, 95%CI=1.015-1.028), and those with BMI<24 kg/m2 (OR=1.010, 95%CI=1.007-1.014). Interaction analysis showed that the association between RFM and CMM risk was influenced by interactions between gender, age, education level, smoking, alcohol consumption, and BMI (P for interaction<0.05). Conclusion Higher RFM may be closely associated with increased CMM risk, and this association is more pronounced in males, individuals aged $ $45 years, those with education below high school, smokers, drinkers, and those with BMI<24 kg/m2.

Full Text

Association Between Relative Fat Mass and the Risk of Cardiometabolic Multimorbidity

GU Handong[1,2], **LU Hongrun**[1,2], **GU Keyi**[1,2], **HAN Zheng**[1,2], **YANG Fei**[1,2], **FU Xiaoya**[1,2], **WANG Weiqiang**[1*]

[1]Department of General Medicine, Suzhou Hospital Affiliated to Anhui Medical University/Suzhou Municipal Hospital of Anhui Province, Suzhou 234000, China
[2]Anhui Medical University, Hefei 230000, China

Corresponding author: WANG Weiqiang, Chief physician; E-mail: wwq007@126.com

Abstract

Background: Cardiometabolic multimorbidity (CMM) represents one of the most prevalent and stable multimorbidity patterns. Relative fat mass (RFM), as a novel anthropometric indicator for assessing adiposity, has shown promise as a predictor of individual cardiometabolic diseases. However, evidence regarding its association with the risk of CMM remains limited.

Objective: To investigate the association between RFM and the risk of CMM across different genders, and to evaluate the potential role of RFM in the prevention and management of CMM.

Methods: A total of 116,321 permanent residents from 12 urban communities (including Suzhou) were selected as study participants from March 2017 to July 2021. Based on gender and CMM status, participants were stratified into CMM and non-CMM groups. Baseline characteristics were compared between these groups separately for each gender. Multivariable logistic regression analysis was employed to examine the association between RFM and the risk of CMM stratified by sex. Restricted cubic spline (RCS) curves were applied to explore potential non-linear relationships. Subgroup analyses and interaction tests were conducted to investigate variations in the association across different populations.

Results: Among the 116,321 participants, 46,637 (40.1%) were male, with 11,969 cases (25.7%) in the CMM group and 34,668 cases (74.3%) in the non-CMM group; 69,684 (59.9%) were female, with 16,668 cases (23.9%) in the CMM group and 53,016 cases (76.1%) in the non-CMM group. RFM levels were significantly higher in the CMM group than in the non-CMM group for both sexes (P<0.001). After adjusting for confounders including age, education level, smoking, alcohol consumption, body mass index (BMI), low-density lipoprotein cholesterol (LDL-C), remnant cholesterol, blood glucose, systolic blood pressure, and diastolic blood pressure, multivariable logistic regression analysis revealed that among males, the risks of CMM in the T2 to T4 groups were 1.530, 2.086, and 2.945 times that of the T1 group, respectively (P<0.001). Among females, the risks of CMM in the F2 to F4 groups were 1.205, 1.532, and 1.760 times that of the F1 group, respectively (P<0.001). Furthermore, for each unit increase in RFM, the risk of CMM increased by 1.109 times in males (OR=1.109, 95%CI=1.101-1.116, P<0.001) and by 1.054 times in females (OR=1.054, 95%CI=1.049-1.060, P<0.001). Restricted cubic spline (RCS) analysis demonstrated a nonlinear relationship between RFM and CMM risk in both sexes. For males, the inflection point where OR=1 was 25.26 (Pnonlinearity<0.001). For females, the inflection point where OR=1 was 38.41 (Pnonlinearity=0.001). Subgroup analysis showed that the association between RFM and CMM risk was stronger in males (OR=1.108, 95%CI=1.101-1.115), individuals aged $ 45*years*(*OR* = 1.011, 95^{2}$ (OR=1.010, 95%CI=1.007-1.014). Interaction analysis revealed that the association between RFM and CMM risk was significantly influenced by interactions between gender, age, education level, smoking, alcohol consumption, and BMI (Pinteraction<0.05).

Conclusion: Higher RFM is significantly associated with an increased risk of CMM, and this association is more pronounced in males, individuals aged $ 45*years*, *thosewithahighschooleducationorbelow*, *smokers*, *drinkers*, *andindividualswithBMI* < 24*kg*/*m*^{2}$.

Keywords: Relative fat mass; Cardiometabolic multimorbidity; Obesity; Disease risk; Cross-sectional study

1. Introduction

Cardiometabolic multimorbidity (CMM) refers to the coexistence of two or more cardiometabolic diseases in an individual, including stroke, heart disease, diabetes, hypertension, and dyslipidemia [1-2]. Previous studies have demonstrated that the prevalence of CMM is increasing globally, accompanied by reduced life expectancy [3]. CMM has gradually evolved into a global public health challenge that threatens population health and exacerbates the burden on healthcare systems.

Obesity, as a major public health concern, has seen its global prevalence rise annually, intensifying the worldwide disease burden [4]. Obesity is also a key risk factor for CMM with good predictive value [5]. However, traditional obesity assessment indicators such as body mass index (BMI) and waist circumference (WC) cannot accurately quantify fat tissue distribution information. In this context, relative fat mass (RFM) has emerged as a novel, gender-specific obesity assessment indicator [6-7]. RFM is calculated based on the ratio of height to waist circumference, can more accurately reflect body fat content, and is more sensitive to visceral fat accumulation [8]. Due to its simple measurement, ease of calculation, and cost-effectiveness, it has been widely applied in clinical practice. Furthermore, multiple prospective cohort studies and large-sample cross-sectional analyses have shown that RFM is closely associated with obesity-related diseases such as hypertension, cardiovascular disease (CVD), and type 2 diabetes mellitus (T2DM) [9-11].

Although previous studies have demonstrated correlations between RFM and various individual diseases, research on its relationship with CMM remains scarce. Moreover, current studies have focused primarily on high-risk populations, with relatively insufficient research on screening for related risk factors in general community residents. Therefore, this study investigates the relationship between RFM and CMM risk in different gender populations, aiming to provide evidence-based support for early intervention in CMM.

2. Methods

2.1 Study Population

A total of 116,321 permanent residents from 12 urban communities in Suzhou, Anqing, Bengbu, Chizhou, Fuyang, Hefei, Lu'an, Ma'anshan, Wuhu, Xuancheng, Bozhou, and Tongling were selected as study participants from March 2017 to July 2021. Inclusion criteria were: (1) age >18 years; (2) residence in the area for $ $6 months before the project; and (3) voluntary signed informed consent. Exclusion criteria were: (1) missing important baseline data such as blood glucose, blood lipids, blood pressure, or medical history; and (2) pregnant women or individuals with malignant tumors. This study was approved by the Ethics Committee of Suzhou Hospital Affiliated to Anhui Medical University (approval number: A2022033), and all participants provided informed consent.

2.2 Data Collection and Definitions

2.2.1 General Data Collection Standardized trained investigators collected demographic data, physical measurements, and relevant laboratory biochemical indicators. Demographic information included gender, age, smoking and drinking status, and disease history. Physical measurements included blood pressure, height, weight, and waist circumference. Laboratory biochemical indicators included fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). All participants were required to fast overnight before examination, and venous blood samples (6 mL) were collected the following morning for these biochemical tests.

2.2.2 Calculation Methods RFM was calculated as: RFM = 64 - (20 × height/WC) + (12 × sex) [6-7], where sex was coded as 1 for female and 0 for male. Participants were grouped by RFM quartiles separately for each gender:

Males:
- T1 group: RFM = 7.33~22.43, n=11,678
- T2 group: RFM = 22.44~25.26, n=11,642
- T3 group: RFM = 25.27~27.78, n=11,702
- T4 group: RFM = 27.79~40.50, n=11,615

Females:
- F1 group: RFM = 19.21~35.36, n=17,436
- F2 group: RFM = 35.37~38.34, n=17,603
- F3 group: RFM = 38.35~41.11, n=17,249
- F4 group: RFM = 41.12~53.32, n=17,396

Remnant cholesterol (RC) was calculated as: RC = TC (mmol/L) - LDL-C (mmol/L) - HDL-C (mmol/L) [12].

2.2.3 Definitions Cardiometabolic multimorbidity (CMM) was defined as an individual having two or more cardiometabolic diseases (CMD), including hypertension, dyslipidemia, diabetes, heart disease, and stroke [1-2]. Specifically: - **Hypertension** was defined as systolic blood pressure $ $140 mmHg and/or diastolic blood pressure $ $90 mmHg measured on different days by medical personnel, or meeting clinical diagnostic criteria, or currently receiving antihypertensive medication [13]. - **Diabetes** was defined as meeting clinical diagnostic criteria or currently using hypoglycemic agents (oral/insulin) [14]. - **Dyslipidemia** was defined as meeting any of the following: total cholesterol $ $240 mg/dL or >6.2 mmol/L, triglycerides $ $200 mg/dL or >2.3 mmol/L, self-reported hyperlipidemia, medical history, and/or any lipid-lowering therapy [2]. - **Stroke** was defined as a history of cerebral infarction/cerebral hemorrhage confirmed by CT/MRI or a history of transient ischemic attack (TIA). - **Heart disease** was categorized as having any of the following conditions: angina, arrhythmia, atrial fibrillation, heart failure, myocardial infarction, or related treat-

ments [2]. - **Smoking** was defined as current smoking behavior reported by the participant at the time of the survey. - **Alcohol consumption** was defined as current drinking behavior reported by the participant at the time of the survey.

2.3 Statistical Analysis

Statistical analysis was performed using SPSS 27.0 and R 4.4.3. Normally distributed continuous variables were expressed as mean ± standard deviation ($\bar{x}\pm s$) and compared among groups using one-way ANOVA. Non-normally distributed continuous variables were expressed as median (interquartile range) [M(P25, P75)] and compared using the Kruskal-Wallis H test. Categorical variables were expressed as relative frequencies (%) and compared using the ^{2} test.

Multivariate logistic stepwise regression analysis was used to explore the effect of RFM quartiles on CMM. Restricted cubic spline (RCS) curves were plotted to calculate the inflection point where OR=1. Additionally, interaction analysis and subgroup analysis were performed to explore differences in the association between RFM and CMM across different populations. $P<0.05$ was considered statistically significant.

3. Results

3.1 Baseline Characteristics by Gender and CMM Status

This study included 116,321 participants, of whom 46,637 (40.1%) were male. Among males, 11,969 (25.7%) were in the CMM group and 34,668 (74.3%) in the non-CMM group. Among the 69,684 (59.9%) female participants, 16,668 (23.9%) were in the CMM group and 53,016 (76.1%) in the non-CMM group. RFM levels were significantly higher in the CMM group than in the non-CMM group for both sexes ($P<0.001$).

Among male participants, the CMM group had significantly higher age, TC, TG, LDL-C, RC, FPG, BMI, proportion with high school education or above, and higher prevalence of hypertension, diabetes, heart disease, and stroke compared to the non-CMM group, while the proportion of smokers and HDL-C levels were lower ($P<0.05$). There was no significant difference in alcohol consumption between the two groups ($P>0.05$).

Among female participants, the CMM group had significantly higher age, BMI, TC, TG, LDL-C, RC, FPG, and higher prevalence of diabetes, heart disease, stroke, hypertension, and smoking compared to the non-CMM group, while the proportion with high school education or above, alcohol consumption, and HDL-C levels were lower ($P<0.05$). These results are presented in Table 1 .

3.2 Multivariate Logistic Regression Analysis of RFM and CMM Risk by Gender

Using CMM status as the dependent variable (no=0, yes=1) and gender-specific RFM quartile groups as the independent variable [T1(F1)=1, T2(F2)=2, T3(F3)=3, T4(F4)=4], multivariate logistic stepwise regression analysis showed:

- **Model 1** (unadjusted): Male T2-T4 groups had 1.980, 3.145, and 5.327 times higher CMM risk than T1 (P<0.001). Female F2-F4 groups had 1.756, 2.735, and 4.154 times higher risk than F1 (P<0.001).
- **Model 2** (adjusted for age): Male T2-T4 groups had 1.996, 3.180, and 5.337 times higher risk than T1 (P<0.001). Female F2-F4 groups had 1.605, 2.326, and 3.245 times higher risk than F1 (P<0.001).
- **Model 3** (further adjusted for education, smoking, alcohol consumption, BMI, LDL-C, RC, blood glucose, systolic and diastolic blood pressure): Male T2-T4 groups had 1.530, 2.086, and 2.945 times higher risk than T1 (P<0.001). Female F2-F4 groups had 1.205, 1.532, and 1.760 times higher risk than F1 (P<0.001). These results are shown in Table 2 .

When RFM was analyzed as a continuous variable, Model 3 showed that each unit increase in RFM increased CMM risk by 1.109 times in males (OR=1.109, 95%CI=1.101-1.116, P<0.001) and by 1.054 times in females (OR=1.054, 95%CI=1.049-1.060, P<0.001), as presented in Table 3 .

3.3 Non-linear Relationship Between RFM and CMM Risk

RCS curve analysis, after adjusting for age, smoking, alcohol consumption, education, BMI, LDL-C, RC, blood glucose, systolic and diastolic blood pressure, revealed non-linear relationships between RFM and CMM risk in both sexes (males: inflection point at OR=1 was 25.26, Pnonlinearity<0.001; females: inflection point at OR=1 was 38.41, Pnonlinearity=0.001). These findings are illustrated in Figure 1 [Figure 1: see original paper].

3.4 Subgroup Analysis

Subgroup analysis showed that the association between RFM and CMM risk was stronger in males (OR=1.108, 95%CI=1.101-1.115), individuals aged \$ $45 years (OR = 1.011, 95\hat{}\{2\}\$$ (OR=1.010, 95%CI=1.007-1.014). Interaction tests showed that the association between RFM and CMM risk was significantly influenced by interactions between gender, age, education level, smoking, alcohol consumption, and BMI (Pinteraction<0.05), as shown in Table 4 .

4. Discussion

This study systematically investigated the association between RFM and CMM in 116,321 permanent residents. The results showed an overall CMM prevalence of 24.6%, with a higher prevalence in males (25.7%) than in females (23.9%),

consistent with previous research. A cohort study of Chinese adults aged 45 and above reported a cardiometabolic multimorbidity prevalence of 24.5% [1]. Another longitudinal cohort study in China showed that the prevalence of cardiometabolic multimorbidity more than doubled among Chinese adults during a 5-year follow-up period [15]. Additionally, a meta-analysis of 67 studies indicated that approximately 25% of Chinese adults had multiple diseases, with prevalence increasing rapidly with age and showing significant regional variation [16]. These findings highlight the rapid progression of CMM in China and the potential public health management challenges it poses.

In this study, when RFM was grouped by quartiles and confounders were adjusted, a positive correlation was observed between RFM and CMM risk in both sexes. Notably, after adjusting only for age, the increased risk of CMM in female groups F2-F4 compared to F1 was significantly lower than in the unadjusted model, suggesting that age may have a stronger influence on the relationship between RFM and CMM risk in women. TANG et al. [17] reported that the proportion of obesity and abdominal obesity in women gradually increases after menopause, with abdominal obesity increasing faster than general obesity. Another cohort study of menopausal transition women in the United States indicated that declining estrogen levels during menopause are associated with harmful changes in inflammatory markers and adipokines, significantly promoting abdominal obesity [18].

When RFM was analyzed as a continuous variable, each unit increase was associated with a 1.1-fold increase in CMM risk in males and a 1.05-fold increase in females after controlling for confounders. This finding aligns with previous research. CAO et al. [8] found that RFM levels were positively associated with non-alcoholic fatty liver disease (NAFLD) in both sexes, with a 1.15-fold increase in NAFLD risk after adjusting for confounders.

Using RCS models adjusted for multiple confounders, this study found nonlinear associations between RFM and CMM risk in both sexes (Pnonlinearity<0.05), with gender differences in inflection points (25.26 for males, 38.41 for females). Below these inflection points, CMM risk increased significantly, after which the risk rose more slowly. The lower inflection point in males may be related to their physiological predisposition to accumulate visceral fat [19]. Compared to subcutaneous fat, visceral fat has stronger secretory capacity for pro-inflammatory cytokines and lipolytic activity [20]. On one hand, it induces insulin resistance (IR) through secretion of pro-inflammatory cytokines [21]; on the other hand, high lipolysis rates in visceral fat produce large amounts of free fatty acids, leading to vascular endothelial dysfunction and atherosclerosis progression [22]. Additionally, the progressive decline in testosterone levels with age in males [23] reduces its protective effects on fat distribution and insulin sensitivity [24], resulting in earlier and more severe IR and central obesity. Consequently, males enter an accelerated CMM risk phase at lower RFM levels. In contrast, premenopausal women have protective factors such as estrogen that promote subcutaneous fat distribution [19], and estrogen can enhance lipolysis

and energy metabolism efficiency through activation of the AMPK pathway [26], requiring higher RFM levels before CMM risk increases. This is consistent with findings from WANG et al. [27], who reported that the RFM values corresponding to significant increases in all-cause and cardiovascular mortality were lower in males than in females.

Furthermore, when populations (especially middle-aged and elderly individuals) have multimorbidity and polypharmacy [28], this may partially mask underlying non-linear relationships, as some medications can indirectly affect the relationship between RFM and CMM risk through various pathways such as improving insulin sensitivity (e.g., metformin [29]) or vascular endothelial function (e.g., sacubitril/valsartan [30]). Therefore, while CMM risk increases rapidly with RFM at lower levels, risk growth tends to plateau at higher RFM levels due to factors such as polypharmacy. A cross-sectional study based on NHANES 2017-2020 data also indicated that maintaining lower RFM levels may help reduce the risk of metabolic dysfunction-associated steatotic liver disease and severe hepatic steatosis [31], highlighting the importance of early-life intervention to control RFM.

Subgroup analysis revealed that the association between RFM and CMM risk was stronger in males, individuals aged $ 45*years*, *thosewithhighschooleducationorbelow*, *smokers*, *drinkers*, *a*
24*kg*/*m*^{2}).*Aprospectivecohortstudyshowedthathigher**RFM**levelswere**more**strongly**associated**withimpai*
*sectionalstudyindicatedthatalthoughwomengenerallyhavehigherbody**fat**percentagesthanmen*, *theprevalence*
agedandolderadults($45 years) is consistent with existing research. A prospective study of 500,000 Chinese adults found that multimorbidity prevalence increased with age, with cardiometabolic comorbidity being the main pattern and associated with the highest mortality risk [33]. This may be because metabolic rates decline in this population, making them more susceptible to IR, hypertension, and lipid metabolism disorders as RFM increases.

A longitudinal cohort study from the UK showed that several health-related behaviors, including smoking, alcohol consumption, physical activity, and nutrition, were associated with multiple chronic diseases and life expectancy, with non-smoking having the greatest impact on life expectancy in both multimorbid and non-multimorbid patients [34], emphasizing the importance of smoking cessation. DI CHIARA et al. [35] confirmed that low education level was associated with significantly higher global cardiovascular risk, which was strongly correlated with cardiometabolic comorbidities. This may stem from health literacy deficits associated with low education, manifested as decreased awareness of cardiovascular risk factors, reduced communication effectiveness due to information asymmetry between doctors and patients, and inadequate access to primary healthcare and prevention compliance.

The association between RFM and CMM was less pronounced in the overweight/obese group (BMI$ 24*kg*/*m*^{2})*comparedtothenormalweightgroup*(*BMI* < 24*kg*/*m*^{2}$).
This may be because in individuals with normal BMI, elevated RFM often indicates abnormal fat distribution (especially visceral fat accumulation) [36], which is typically associated with metabolic diseases and adverse cardiovascular

outcomes. Additionally, overweight/obese individuals are more likely to have long-term unhealthy lifestyle habits (e.g., high-sugar/high-fat diet, sedentary behavior), gut microbiota dysbiosis, or chronic inflammatory states, which can directly promote CMM while also increasing RFM, thereby diluting the relationship between RFM and CMM in this population. Therefore, RFM may serve as a potential indicator for preventing or managing CMM in males, individuals aged $ 45 *years*, *thosewithhighschooleducationorbelow*, *smokers*, *drinkers*, *andparticularlyinindividualswithnorm* $ 24 *kg*/*m*^{2}$).

The strengths of this study include its systematic investigation of the association between RFM and CMM, subgroup analyses to enhance understanding of disease association patterns, and adjustment for multiple potential confounders including gender, age, and BMI to more accurately assess the relationship between RFM and CMM. However, several limitations should be acknowledged. First, limited by database information, the study could not collect detailed data on participants' dietary habits, precise physical activity levels, or medical insurance status. The absence of these important confounders may lead to residual confounding bias. Second, as a cross-sectional study, it cannot infer causality between RFM and CMM, only revealing their association. Future studies with longer follow-up periods or prospective designs are needed to clarify potential causal relationships. Finally, the study population was drawn from a single region, limiting the generalizability of the findings. Multi-center studies covering different regions across the country are warranted to validate the general applicability of these results.

In summary, this study demonstrates that higher RFM is significantly associated with CMM risk across genders. Based on these findings, we recommend that clinical practice should include early identification of individuals with elevated RFM levels as a high-risk group for CMM. For these individuals, comprehensive prevention and intervention measures (such as lifestyle management and metabolic risk factor control) should be actively implemented to effectively reduce their future risk of developing CMM.

References

[1] HUANG Z T, LUO Y, HAN L, et al. Patterns of cardiometabolic multimorbidity and the risk of depressive symptoms in a longitudinal cohort of middle-aged and older Chinese[J]. J Affect Disord, 2022,301:1-7. DOI:10.1016/j.jad.2022.01.030.

[2] ZHAO X H, XU X L, YAN Y F, et al. Independent and joint associations of cardiometabolic multimorbidity and depression on cognitive function: findings from multi-regional cohorts and generalisation from community to clinic[J]. Lancet Reg Health West Pac, 2024,51:101198. DOI:10.1016/j.lanwpc.2024.101198.

[3] Emerging Risk Factors Collaboration, DI ANGELANTONIO E, KAPTOGE S, et al. Association of cardiometabolic multimorbidity with mortality[J]. JAMA,

2015,314(1):52-60. DOI:10.1001/jama.2015.7008.

[4] KIVIMÄKI M, STRANDBERG T, PENTTI J, et al. Body-mass index and risk of obesity-related complex multimorbidity: an observational multicohort study[J]. Lancet Diabetes Endocrinol, 2022,10(4):253-263. DOI:10.1016/S2213-8587(22)00033-X.

[5] KIVIMÄKI M, KUOSMA E, FERRIE J E, et al. Overweight, obesity, and risk of cardiometabolic multimorbidity: pooled analysis of individual-level data for 120,813 adults from 16 cohort studies from the USA and Europe[J]. Lancet Public Health, 2017,2(6):e277-e285. DOI:10.1016/S2468-2667(17)30074-9.

[6] WOOLCOTT O O, BERGMAN R N. Relative fat mass (RFM) as a new estimator of whole-body fat percentage—a cross-sectional study in American adult individuals[J]. Sci Rep, 2018,8(1):10980. DOI:10.1038/s41598-018-29362-1.

[7] FAN Y J, FENG Y J, MENG Y, et al. The relationship between anthropometric indicators and health-related quality of life in a community-based adult population: a cross-sectional study in Southern China[J]. Front Public Health, 2022,10:955615. DOI:10.3389/fpubh.2022.955615.

[8] CAO C C, HUANG M L, HAN Y, et al. The nonlinear connection between relative fat mass and non-alcoholic fatty liver disease in the Japanese population: an analysis based on data from a cross-sectional study[J]. Diabetol Metab Syndr, 2024,16(1):236. DOI:10.1186/s13098-024-01472-z.

[9] YU P, HUANG T, HU S L, et al. Predictive value of relative fat mass algorithm for incident hypertension: a 6-year prospective study in Chinese population[J]. BMJ Open, 2020,10(10):e038420. DOI:10.1136/bmjopen-2020-038420.

[10] ZWARTKRUIS V W, SUTHAHAR N, IDEMA D L, et al. Relative fat mass and prediction of incident atrial fibrillation, heart failure and coronary artery disease in the general population[J]. Int J Obes (Lond), 2023,47(12):1256-1262. DOI:10.1038/s41366-023-01380-8.

[11] WANG D, CHEN Z T, WU Y R, et al. Association between two novel anthropometric measures and type 2 diabetes in a Chinese population[J]. Diabetes Obes Metab, 2024,26(8):3238-3247. DOI:10.1111/dom.15651.

[12] HU X M, LIU Q Z, GUO X Y, et al. The role of remnant cholesterol beyond low-density lipoprotein cholesterol in diabetes mellitus[J]. Cardiovasc Diabetol, 2022,21(1):117. DOI:10.1186/s12933-022-01554-0.

[13] Chinese Hypertension Prevention and Treatment Guidelines Revision Committee, Hypertension Alliance (China), Chinese Healthcare International Exchange Promotion Association Hypertension Branch, et al. Chinese guidelines for the prevention and treatment of hypertension (2024 revision)[J]. Chinese Journal of Hypertension, 2024,32(07):603-700. DOI:10.16439/j.issn.1673-7245.2024.07.002.

[14] YIN J X, YU L, PU D L, et al. Interpretation of the "Chinese Guidelines for the Prevention and Treatment of Diabetes (2024 Edition)" [J]. Journal of Chongqing Medical University, 2025,50(05):557-564. DOI:10.13406/j.cnki.cyxb.003749.

[15] ZHANG D D, TANG X, SHEN P, et al. Multimorbidity of cardiometabolic diseases: prevalence and risk for mortality from one million Chinese adults in a longitudinal cohort study[J]. bmjopen-2018-024476.

[16] HU Y D, WANG Z X, HE H J, et al. Prevalence and patterns of multimorbidity in China during 2002-2022: a systematic review and meta-analysis[J]. Ageing Res Rev, 2024,93:102165. DOI:10.1016/j.arr.2023.102165.

[17] TANG R Y, FAN Y B, LUO M, et al. General and central obesity are associated with increased severity of the VMS and sexual symptoms of menopause among Chinese women: a longitudinal study[J]. Front Endocrinol (Lausanne), 2022,13:814872. DOI:10.3389/fendo.2022.814872.

[18] JUPPI H K, SIPILÄ S, FACHADA V, et al. Total and regional body adiposity increases during menopause-evidence from a follow-up study[J]. Aging Cell, 2022,21(6):e13621. DOI:10.1111/acel.13621.

[19] PALMER B F, CLEGG D J. The sexual dimorphism of obesity[J]. Mol Cell Endocrinol, 2015,402:113-119. DOI:10.1016/j.mce.2014.11.029.

[20] KAHN D, MACIAS E, ZARINI S, et al. Exploring visceral and subcutaneous adipose tissue secretomes in human obesity: implications for metabolic disease[J]. Endocrinology, 2022,163(11):bqac140. DOI:10.1210/endocr/bqac140.

[21] AHMED B, SULTANA R, GREENE M W. Adipose tissue and insulin resistance in obese[J]. Biomed Pharmacother, 2021,137:111315. DOI:10.1016/j.biopha.2021.111315.

[22] YU F Z, ZONG B Y, JI L L, et al. Free fatty acids and free fatty acid receptors: role in regulating arterial function[J]. Int J Mol Sci, 2024,25(14):7853. DOI:10.3390/ijms25147853.

[23] FAULKNER J L, BELIN DE CHANTEMÈLE E J. Sex hormones, aging and cardiometabolic syndrome[J]. Biol Sex Differ, 2019,10(1):30. DOI:10.1186/s13293-019-0246-6.

[24] SCHIFFER L, KEMPEGOWDA P, ARLT W, et al. MECHANISMS IN ENDOCRINOLOGY: The sexually dimorphic role of androgens in human metabolic disease[J]. Eur J Endocrinol, 2017,177(3):R125-R143. DOI:10.1530/EJE-17-0124.

[25] SANTOS-MARCOS J A, MORA-ORTIZ M, TENA-SEMPERE M, et al. Interaction between gut microbiota and sex hormones and their relation to sexual dimorphism in metabolic diseases[J]. Biol Sex Differ, 2023,14(1):4. DOI:10.1186/s13293-023-00490-2.

[26] KVANDOVA M, PUZSEROVA A, BALIS P. Sexual dimorphism in cardiometabolic diseases: the role of AMPK[J]. Int J Mol Sci, 2023,24(15):11986. DOI:10.3390/ijms241511986.

[27] WANG J, GUAN J Y, HUANG L Y, et al. Sex differences in the associations between relative fat mass and all-cause and cardiovascular mortality: a population-based prospective cohort study[J]. Nutr Metab Cardiovasc Dis, 2024,34(3):738-754. DOI:10.1016/j.numecd.2023.10.034.

[28] JUNGO K T, CHEVAL B, SIEBER S, et al. Life-course socioeconomic conditions, multimorbidity and polypharmacy in older adults: a retrospective cohort study[J]. PLoS One, 2022,17(8):e0271298. DOI:10.1371/journal.pone.0271298.

[29] HERMAN R, KRAVOS N A, JENSTERLE M, et al. Metformin and insulin resistance: a review of the underlying mechanisms behind changes in GLUT4-mediated glucose transport[J]. Int J Mol Sci, 2022,23(3):1264. DOI:10.3390/ijms23031264.

[30] SHI Y J, YANG C G, QIAO W B, et al. Sacubitril/valsartan attenuates myocardial inflammation, hypertrophy, and fibrosis in rats with heart failure with preserved ejection fraction[J]. Eur J Pharmacol, 2023,961:176170. DOI:10.1016/j.ejphar.2023.176170.

[31] WANG J J, HE W, CAI X F, et al. Relative fat mass and risk of metabolic dysfunction associated steatotic liver disease and severe hepatic steatosis in U.S. adults: analysis of NHANES 2017-2020 data[J]. BMC Gastroenterol, 2025,25(1):410. DOI:10.1186/s12876-025-04006-7.

[32] STRACK C, BEHRENS G, SAG S, et al. Gender differences in cardiometabolic health and disease in a cross-sectional observational study[J]. Biol Sex Differ, 2022,13(1):8. DOI:10.1186/s13293-022-00416-4.

[33] FAN J N, SUN Z J, YU C Q, et al. Multimorbidity patterns and association with mortality in 0.5 million Chinese adults[J]. Chin Med J (Engl), 2022,135(6):648-657. DOI:10.1097/CM9.0000000000001985.

[34] CHUDASAMA Y V, KHUNTI K, GILLIES C L, et al. Healthy lifestyle and life expectancy in people with multimorbidity in the UK Biobank: a longitudinal cohort study[J]. PLoS Med, 2020,17(9):e1003332. DOI:10.1371/journal.pmed.1003332.

[35] DI CHIARA T, SCAGLIONE A, CORRAO S, et al. Association between low education and higher global cardiovascular risk[J]. J Clin Hypertens (Greenwich), 2015,17(5):332-337. DOI:10.1111/jch.12506.

[36] WOOLCOTT O O, BERGMAN R N. Defining cutoffs to diagnose obesity using the relative fat mass (RFM): Association with mortality in NHANES 1999-2014[J]. Int J Obes (Lond), 2020,44(6):1301-1310. DOI:10.1038/s41366-019-0516-2.

Author Contributions: GU Handong conceptualized the study, designed the research, implemented the investigation, and wrote the manuscript. LU Hongrun and GU Keyi collected and organized data, performed statistical analysis, and prepared figures and tables. HAN Zheng, YANG Fei, and FU Xiaoya revised the manuscript. WANG Weiqiang was responsible for quality control, review, and overall supervision of the manuscript.

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

Funding: Anhui Provincial Science and Technology Innovation Strategy and Soft Science Research Special Project (202106f01050042)

Citation: GU H D, LU H R, GU K Y, et al. Association research between relative fat mass and the incidence risk of cardiometabolic multimorbidity[J]. Chinese General Practice, 2025. DOI:10.12114/j.issn.1007-9572.2025.0266. [Epub ahead of print]

Editor: LI Weixia

Received: 2025-08-04
Revised: 2025-09-05
Accepted: [Not provided]

Note: Figure translations are in progress. See original paper for figures.