

Sex-specific associations between total and regional Fat-to-muscle Mass ratio and cardiometabolic risk: findings from the China National Health Survey

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Abstract

Background The fat-to-muscle mass ratio (FMR), integrating the antagonistic effects of fat and muscle mass, has been suggested as a valuable indicator to assess cardiometabolic health independent of overall adiposity. However, the specific associations of total and regional FMR with cardiometabolic risk are poorly understood. We aimed to examine sex-specific associations of total and regional FMR with single and clustered cardiometabolic risk factors (CRFs).

Methods 13,505 participants aged 20 years and above were included in the cross-sectional study. Fat mass and muscle mass were assessed using a bioelectrical impedance analysis device. FMR was estimated as fat mass divided by muscle mass in corresponding body parts (whole body, arm, leg, and trunk). Clustered CRFs was defined as the presence of two or more risk factors, including hypertension, elevated blood glucose, dyslipidemia, insulin resistance (IR), and hyperuricemia. IR was assessed by the triglyceride glucose (TyG) index. Multivariable logistic regression models were applied to explore the associations of FMR in the whole body and body parts with single and clustered CRFs.

Results The odds ratios (ORs) increased significantly for all single and clustered CRFs with the per quartile increase of total and regional FMR in both sexes (*P* for trend<0.001), following adjustment for confounders. Among the regional parts, FMRs of the legs presented the strongest associations for clustered CRFs in both men and women, with adjusted OR of 8.54 (95% confidence interval (CI): 7.12–10.24) and 4.92 (95% CI: 4.24–5.71), respectively. Significant interactions (*P* for interaction < 0.05) were identified between age and FMRs across different body parts, as well as between BMI status and FMRs in different regions for clustered CRFs. Restricted cubic splines revealed significant nonlinear relationships between FMRs of different body parts and clustered CRFs in both sexes (*P* for nonlinear < 0.05).

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Conclusions FMRs in the whole body and different regions were significantly associated with single and clustered CRFs in the general Chinese population. The association between FMR and clustered CRFs was more pronounced in youngers than in the elderly.

Keywords Fat-to-muscle mass ratio, Obesity, Cardiometabolic risk, Muscle mass, Fat mass

Introduction

Cardiovascular diseases (CVDs) are the leading cause of mortality globally [\[1](#page-11-0)]. Cardiometabolic disorders, as main modifiable risk factors for CVD, have posed serious burden on individuals, families and society [\[1\]](#page-11-0). Therefore, it is urgent and crucial to prevent cardiometabolic disorder. Obesity, a well-established risk factor for CVDs and other chronic diseases, is also associated with clustering of other CRFs such as hypertension, elevated glucose and dyslipidemia [[2\]](#page-11-1). Body mass index (BMI) is commonly used to assess overall adiposity in population studies. However, BMI has a major limitation in determining obesity since it cannot discriminate between fat and muscle content [[3](#page-11-2)]. Body composition varies greatly among individuals with the same BMI. In addition, individuals with similar BMI levels can exhibit diverse metabolic characteristics, including differences in lipid profiles, glucose intolerance, and blood pressure (BP) [[4,](#page-11-3) [5\]](#page-11-4).

Several studies have revealed that body composition could play important roles in quantifying CRFs [\[6](#page-11-5)[–8](#page-11-6)]. For example, muscle mass is considered a protective factor and had a negative relationship with cardiometabolic parameters [[9\]](#page-11-7). By contrast, elevated fat mass is strongly related with adverse CRFs, including hypertension, dyslipidemia, and impaired glucose regulation [[6](#page-11-5)]. Furthermore, a significant decrease in muscle mass and an increase in fat mass may lead to sarcopenia or sarcopenia obesity, both of which are proposed to have detrimental effects on cardiometabolic profiles and mortality [\[10](#page-11-8), [11\]](#page-11-9). The components of body composition are intricately interrelated. Fat mass stands for the metabolic load, while muscle mass signifies metabolic capacity; determining CRFs within the context of their interrelationship but rather focusing on their absolute amounts, presents an intriguing avenue for research $[12]$ $[12]$. Hence, the FMR, a novel marker that integrates the effects of muscle and fat mass, has been considered a promising body composition indicator for CRFs, CVDs, and mortality $[13 - 15]$ $[13 - 15]$ $[13 - 15]$ $[13 - 15]$.

Previous studies have reported that the FMR was associated with diabetes, hypertension, and metabolic syndrome (MetS) in both men and women $[16–18]$ $[16–18]$ $[16–18]$. However, there is a lack of research exploring the associations between total and regional FMR and insulin resistance, as well as clustered CRFs (two or more factors). Additionally, existing studies have been hampered by small sample sizes, a focus on Western populations, and a failure to consider FMR in different body parts, resulting in limited evidence in large-scale general populations, particularly in China [[17,](#page-11-15) [18](#page-11-14)]. Considering that muscle gain and exercise may have site-specific effects, determining FMR associations at different anatomical sites (including arms, legs, and trunk) could provide segmental body information and enhance comprehension of potential clinical and public health implications, which still requires further research. Given the remarkable sex difference in body composition distribution, such as muscle mass and fat mass, sex-stratified analyses were performed in the current study.

Using data from the China National Health Survey (CNHS), we aimed to comprehensively assess the sexspecific relationship between FMR in various body regions (including the whole body, arm, leg, and trunk) and CRFs, both individually and clustering multiple risk factors.

Materials and methods

Study design and participants

A cross-sectional study was conducted in Guangdong (South China), Jilin (Northeastern China), and Jiangsu (East China) provinces from April to November 2023. The present study originated from the CNHS, an ongoing nationally representative cross-sectional study initiated in 2012. Additional details about the study design have been provided elsewhere [\[19\]](#page-11-16). In short, a multistage stratified cluster sampling method was used to recruit permanent residents aged 20 years and above in both urban and rural areas. In this study, the respondents completed a standardized questionnaire and underwent physical measurements to collect health-related information, including demographic characteristics, lifestyle factors, and personal disease history. Moreover, venous blood samples were collected after an 8-hour fasting period for the measurement of glucose and serum lipid levels.

A total of 13,904 Chinese Han adults completed the survey. We excluded participants under the age of 20, with missing information on the measurement of CRFs, or those with missing data on body composition parameters (muscle mass and fat mass in the trunk, arm, and leg), the remaining 13,505 subjects in the final analysis consisting of 5,208 men and 8,297 women (Supplemental Fig. 1). The study has been carried out in accordance with the Declaration of Helsinki. The Ethical Review Committee of the Institute of Basic Medical Sciences Chinese Academy of Medical Sciences, Beijing, China, has approved this study under the protocol (No. 2022177 and

No. 2022134). Written informed consent was obtained from all participants.

Exposure assessment

Data on height, weight, and body composition were collected by trained program staff using well-calibrated instruments according to a standard protocol. Height was measured in centimeter (to the nearest 0.1 cm) without shoes using a stadiometer (SECA, Germany). After the height measurement, weight (in kilograms to the nearest 0.1 kg) and body composition were measured in light clothes and bare feet using a standard multi-frequency segmental Tanita MC780MA analyzer (Tanita Inc, Japan) by the method of bioelectrical impedance analysis (BIA). To ensure accurate measurements, participants were instructed to place their bare feet on the designated markings on the analyzer platform and to keep their feet still and in full contact with the platform. Simultaneously, participants were asked to grip the two metal handles firmly using their hands, allowing their arms to hang loosely by their sides. The BIA method, validated for accuracy and precision $[20, 21]$ $[20, 21]$ $[20, 21]$ $[20, 21]$, was used to estimate muscle mass and fat mass in the whole body, trunk, left arm, right arm, left leg, and right leg. The right and left arms/legs and trunk were integrated into a whole body. FMR was defined as fat mass divided by estimated muscle mass in the corresponding body parts. Therefore, the total and regional (arm, leg, and trunk) FMRs were the exposures to be examined. In the analysis, FMR values were classified into quartiles (Q1-Q4) from the lowest (Q1) to the highest (Q4).

Outcome assessment

Clustered CRFs was defined as the presence of two or more risk factors, including hypertension, elevated blood glucose, dyslipidemia, IR, and hyperuricemia.

BP was measured three times on the upper right arm using an electronic BP device (Omron HEM-907, Japan) with the participant in a sitting posture. There was one minute between each measurement and the average of three readings was recorded. Hypertension was defined as the participant who had a mean systolic BP≥140 mmHg and/or a mean diastolic BP≥90 mmHg and/ or self-reported diagnosed hypertension by a physician and/or receiving antihypertensive medication [\[22](#page-11-19)]. Elevated blood glucose was defined as a fasting plasma glucose (FPG) level≥6.1 mmol/L, or a self-reported diagnosis of diabetes [\[23](#page-11-20)]. Dyslipidemia was defined as high total cholesterol (high TC, a TC level≥6.2 mmol/L), or high triglyceride (high TG, a TG level≥2.3 mmol/L), or high low-density lipoprotein cholesterol (high LDL-C, a LDL-C level≥4.1 mmol/L), or low high-density lipoprotein cholesterol (low HDL-C, a HDL-C level ≤ 1.0 mmol/L), or a self-reported diagnosed dyslipidemia [\[24](#page-11-21)]. IR was assessed by the TyG index, which is a simple and reliable clinical marker of IR [\[25,](#page-11-22) [26\]](#page-11-23). The TyG index was calculated as Ln [TG (mg/dl)×FPG (mg/dl)/2] [\[27](#page-11-24)]. IR was defined as a TyG index above the 75th percentile for each sex in the study population [[28](#page-11-25)]. Hyperuricemia was defined as a serum uric acid (SUA) level>420 µmol/L in men and SUA>360 µmol/L in women, or current use of SUA-lowering drugs [[29](#page-11-26), [30\]](#page-11-27).

Covariates

The following potential confounding factors were considered in the present study: age, residential area (rural/ urban), region, educational level (elementary school or below, or secondary school, or college or higher), smoking status (never, ever, or current), drink status (never, ever, or current), physical activities [light level of both occupational and leisure-time physical activity (low); moderate or high level of either occupational or leisuretime physical activity (moderate); moderate or high level of both occupational and leisure-time physical activity (high)]. The information on menopausal status was obtained through self-reported in the face-to-face questionnaire, where they were asked whether they had experienced menstrual bleeding within the past 12 months. BMI was calculated as weight in kilograms divided by the square of the height in meters $(kg/m²)$. BMI categories were defined as underweight $\left($ < 18.5 kg/m²), normal $(18.5-23.9 \text{ kg/m}^2)$, overweight, or obesity (224 kg/m^2) [[31\]](#page-11-28).

Statistical analysis

Continuous variables were expressed as mean±standard deviation (SD) or median (interquartile range, IQR), and categorical variables were reported as frequency (percentage, %). Comparisons of baseline characteristics between men and women were conducted using a *t*-test or Mann-Whitney U-test for continuous variables and a Chi-square-test for categorical variables.

Multivariable logistic regression models were applied to estimate ORs and 95% CIs for the associations between quartiles of total and regional FMR and CRFs in men and women. Models were adjusted for age (continuous variable), residential area, region, educational level, smoking status, drinking status, physical activities, and menopausal status in women. The associations of FMR in total and body parts with the specific dyslipidemia components, including high TC, high TG, high LDL-C, and low HDL-C, were also examined. The linear trend test was performed using the median value of sex-specific FMR for each quartile estimated as a continuous variable in the models. We further performed restricted cubic splines (RCS) with four knots at the 5th, 35th, 65th, and 95th percentiles to explore the potential nonlinear association between FMR and clustered CRFs. RCS analysis was

conducted using R software (version 4.2.2). The interaction analyses were performed to investigate the relationship between FMR and clustered CRFs stratified by age (20–39 years, 40–59 years, or ≥ 60 years), BMI categories $(BMI < 24 \text{ kg/m}^2 \text{ and } BMI \geq 24 \text{ kg/m}^2)$, and menopausal status in women (yes/no). The potential interactions were measured by using the likelihood ratio test to compare models with and without a cross-product term. We further conducted a sensitivity analysis to assess the robustness of our results. Participants with a previous diagnosis of hypertension, diabetes, dyslipidemia, and hyperuricemia were excluded to minimize the potential impact of reverse causality. Data analyses were performed using

SAS, version 9.4 (SAS Institute Inc, Cary, NC, USA). A two-sided *P* value<0.05 was considered to be statistically significant.

Results

General characteristics of participants

Table [1](#page-3-0) summarizes the general characteristics of the study population by sex. A total of 13,505 participants were included in the present study, which comprised 5,208 men (mean age, 53.27±12.93 years) and 8,297 women (mean age, 51.82±12.31 years). Among the women, 58.48% (4,852 out of 8,297) had experienced menopause. Overall, the total and regional

Table 1 Characteristics of participants according to sex

IC I Characteristics of participarits according to sext Characteristics	Total($n = 13505$)	$Men(n=5208)$	Women($n = 8297$)	P value
Age, years	52.38 ± 12.57	53.27 ± 12.93	51.82 ± 12.31	< 0.001
Residential area				< 0.001
Urban	8418 (62.33)	3116 (59.83)	5302 (63.90)	
Rural	5087 (37.67)	2092 (40.17)	2995 (36.10)	
Educational level				< 0.001
Elementary school or below	2856 (21.19)	771 (14.83)	2085 (25.18)	
Secondary school	7192 (53.35)	3035 (58.39)	4157 (50.19)	
College or higher	3432 (25.46)	1392 (26.78)	2040 (24.63)	
Smoking				< 0.001
Never	10261 (75.98)	2154 (41.36)	8107 (97.72)	
Ever	940 (6.96)	895 (17.18)	45 (0.54)	
Current	2303 (17.06)	2159 (41.46)	144 (1.74)	
Drinking				< 0.001
Never	9658 (71.52)	2039 (39.16)	7619 (91.83)	
Ever	572 (4.24)	486 (9.33)	86 (1.04)	
Current	3274 (24.24)	2682 (51.51)	592 (7.14)	
BMI, $kg/m2$	24.41 ± 3.45	24.94 ± 3.44	24.08 ± 3.42	< 0.001
BMI categories				< 0.001
Underweight	395 (2.92)	117 (2.25)	278 (3.35)	
Normal weight	6050 (44.80)	1966 (37.75)	4084 (49.22)	
Overweight or obesity	7060 (52.28)	3125 (60.00)	3935 (47.43)	
Physical activity				< 0.001
Low	10394 (77.02)	3483 (66.93)	6911 (83.36)	
Moderate	1454 (10.77)	857 (16.47)	597 (7.20)	
High	1647 (12.20)	864 (16.60)	783 (9.44)	
Menopause			4852 (58.48)	
Fat-to-muscle mass ratio				
Whole body	0.42(0.31, 0.55)	0.30(0.23, 0.36)	0.51(0.42, 0.62)	< 0.001
Arm	0.33(0.22, 0.48)	0.21(0.17, 0.26)	0.44(0.34, 0.55)	< 0.001
Leg	0.47 (0.32, 0.58)	0.30(0.25, 0.34)	0.56(0.49, 0.63)	< 0.001
Trunk	0.42(0.31, 0.55)	0.32(0.24, 0.40)	0.50(0.39, 0.62)	< 0.001
Cardiometabolic risk factors				
Hypertension	5011 (37.10)	2361 (45.33)	2650 (31.94)	< 0.001
Elevated blood glucose	2691 (19.93)	1298 (24.92)	1393 (16.79)	< 0.001
Dyslipidemia	6172 (45.70)	2652 (50.92)	3520 (42.42)	< 0.001
Insulin resistance	3388 (25.09)	1310 (25.15)	2078 (25.05)	0.888
Hyperuricemia	3502 (25.93)	1867 (35.85)	1635 (19.71)	< 0.001
\geq 2 risk factors	6088 (45.08)	2824 (54.22)	3264 (39.34)	< 0.001

Mean±SD or median (IQR) for continuous variables and number (percentage) for categorical variables. BMI, body mass index

FMR significantly differed between men and women (*P*<0.001). It was observed that there were notable sex differences in single CRFs, with men presenting higher prevalence in various aspects, excluding IR. Additionally, the prevalence of clustered CRFs was higher in men compared to women and increased with age (Supplemental Table 1). The demographic characteristics of the participants according to the quartiles FMR of the whole body in men and women are shown in Supplemental Table 2. Participants in Q4 of whole FMR had the highest prevalence of hypertension, elevated blood glucose, dyslipidemia, hyperuricemia, and clustered CRFs compared to participants in the other three FMR quartiles in both sexes (all *P*<0.001).

Total and regional fat-to-muscle mass ratio and cardiometabolic risk

The associations of total and regional FMR with CRFs were examined using multivariable logistic regression models by sex as shown in Table [2](#page-5-0). After adjusting for confounding factors, the FMR in whole body and body parts exhibited significant associations with all examined risk factors (all *P*<0.05) in men and women. Compared with the Q1, the multivariable-adjusted ORs of the Q4 of total FMR for hypertension, elevated blood glucose, dyslipidemia, insulin resistance, and hyperuricemia were 5.28 (95% CI: 4.39–6.34), 2.33 (95% CI: 1.92–2.83), 4.15 (95% CI: 3.50–4.91), 5.47 (95% CI: 4.39–6.82), and 4.11 (95%CI: 3.42–4.93), respectively, for men and 3.29 (95% CI: 2.82–3.85), 2.47 (95% CI: 2.06–2.96), 2.42 (95% CI: 2.11–2.78), 5.10 (95% CI: 4.28–6.07), and 3.92 (95%CI: 3.29–4.67), respectively, for women. The associations of the total and regional FMR with the risk of dyslipidemia components are shown in Supplemental Table 3. Compared with the Q1, the effect of the FMR Q4 was significant for high TC, high TG, high LDL-C, and low HDL-C in women, whereas the association of FMR in the arms for high TC and high LDL-C was not statistically significant in men.

Figure [1](#page-6-0) illustrates the effect [OR (95% CI)] of FMR quartiles on clustered CRFs by sex. Following adjustment for confounding factors, the FMR in whole body and body parts were significantly associated with clustered CRFs (all *P*<0.05) in men and women. FMRs were more strongly associated with clustered CRFs in men compared to women. Among the regional body parts, FMR of the legs presented the strongest associations in both men and women, with adjusted OR of 8.54 (95% CI: 7.12–10.24) and 4.92 (95% CI: 4.24–5.71), respectively. Notably, the adjusted ORs displayed a significant increase with ascending FMR quartiles from Q1 to Q4 (all *P* for trend<0.001), for both the whole body and regional body parts. Figure [2](#page-7-0) visualized the nonlinear associations between FMRs and clustered CRFs using RCS analysis. A J-shaped association were observed between total and regional FMR and clustered CRFs in both men and women (all *P* for non-linear < 0.05).

Age-stratified, BMI-stratified analyses and sensitivity analyses

Stratified analysis by age group was conducted to identify whether age modified the relationship between FMR and clustered CRFs (Table [3\)](#page-8-0). Interestingly, the association between FMR and clustered CRFs was more pronounced in youngers (adults aged 20–39 years) than in the elderly (adults aged 60 years or above) in both sexes. The significant modifying effect was observed in women (all *P* for interaction<0.001); while the effect was only observed in the arms and legs of men. We also observed a significant interaction between FMR in the whole body and specific body parts and BMI category on clustered CRFs in both sexes, excepting FMR of the whole body and legs in men (all *P* for interaction<0.05; Table [4](#page-9-0)). Similarly, significant interaction effects were observed for menopausal status in women (all *P* for interaction<0.05; Supplemental Table 4). In sensitivity analysis, similar findings were found when excluding the participants with a previous diagnosis of hypertension, diabetes, dyslipidemia, and hyperuricemia (Supplemental Table 5).

Discussion

In the large-scale cross-sectional study that covered northeast, north, and south China, we found a promising and easy-to-use body composition indicator—FMR and explored its association with cardiometabolic health. The findings demonstrated a significant association between FMRs in various body regions and single as well as clustered CRFs in both sexes. In addition, these associations were strongly modified by age group and BMI category for both sexes. Among the regional body parts, FMRs of the legs presented the strongest associations in men and women. To our knowledge, the present study is the first to identify the sex-specific associations of FMRs in different body regions with single and clustered CRFs among the general Chinese population.

Several studies have identified the relationships of fat mass and muscle mass separately with CRFs in diverse populations. However, these findings have exhibited inconsistent conclusions. A perspective cohort study of 132,324 participants (mean age, 37.1 years) with a 4-year follow-up, revealed a significant association between low relative skeletal muscle mass and the incidence of hypertension in men after adjustment for confounding factors, whereas, no statistically significant association was observed in women $[32]$ $[32]$. A cross-sectional study included 1,413 community-dwelling older adults found that muscle mass was negatively associated with MetS in both sexes [\[33](#page-11-30)]. Another study involving older people

Table 2 The effect [OR (95% CI)] of quartiles of FMR on cardiometabolic risk factors by sex

Table 2 (continued)

Data are presented as OR (95% CI). Adjusted models were adjusted for age, physical activity, education level, smoking status, residential area, drinking, region, and menopausal status in women

FMR: Fat-to-muscle mass ratio; OR: odds ratio; CI: confidence interval; Ref: reference

Fig. 1 The effect [OR (95% CI)] of quartile of FMR on clustered cardiometabolic risk factors by sex. All models were adjusted for age, physical activity, education level, smoking status, residential area, drinking, region, and menopausal status in women. Clustered cardiometabolic risk was defined as the presence of 2 or more risk factors, including hypertension, elevated blood glucose, dyslipidemia, insulin resistance, and hyperuricemia. (**a**) FMR of the whole body, trunk, arm and leg in men; (**b**) FMR of the whole body, trunk, arm and leg in women. FMR: Fat-to-muscle mass ratio; OR: odds ratio; CI: confidence interval

Fig. 2 Association of fat-to-muscle mass ratio (FMR) with clustered cardiometabolic risk by sex. All models were adjusted for age, physical activity, education level, smoking status, residential area, drinking, region, and menopausal status in women. Clustered cardiometabolic risk was defined as the presence of 2 or more risk factors, including hypertension, elevated blood glucose, dyslipidemia, insulin resistance, and hyperuricemia. (**a**-**d**) FMR of the whole body, trunk, arm and leg in men; (**e**-**h**) FMR of the whole body, trunk, arm and leg in women. Odds ratios are reported by solid lines and 95% CIs by shaded areas. The reference point is the 50th percentile for each FMR, using four knots at the 5th, 35th, 65th, and 95th percentiles. FMR: Fat-to-muscle mass ratio; OR: odds ratio; CI: confidence interval

	Men [OR (95% CI)]			Women [OR (95% CI)]				
	$20-39$ years	40-59 years	≥ 60 years	P for interaction	$20-39$ years	40-59 years	≥ 60 years	P for in- teraction
Whole body				0.215				< 0.001
Q1(lowest)	1 (Ref)	1 (Ref)	1 (Ref)		1 (Ref)	1 (Ref)	1 (Ref)	
Q2	3.53(2.22, 5.59)	2.30 (1.81, 2.92)	2.61 (1.98, 3.44)		2.53 (1.25, 5.15)	1.99 (1.63, 2.42)	2.10 (1.65, 2.67)	
Q3		5.36 (3.36, 8.56) 4.50 (3.52, 5.75)	3.63 (2.72, 4.84)		4.80 (2.48, 9.30)	3.08 (2.54, 3.75)	2.62(2.04, 3.35)	
Q4(highest)	14.47 (8.93, 24.10	7.12 (5.49, 9.23)	6.41 (4.70, 8.73)		13.02 (6.87, 24.66)	5.03 (4.14, 6.12)	3.51 (2.72, 4.53)	
Arm				0.032				< 0.001
Q1(lowest)	1 (Ref)	1 (Ref)	1 (Ref)		1 (Ref)	1 (Ref)	1 (Ref)	
Q2	4.28 (2.68, 6.83)	2.21 (1.74, 2.79)	2.04 (1.55, 2.69)		2.82 (1.36, 5.83)	1.87 (1.54, 2.28)	1.75 (1.38, 2.22)	
Q ₃	5.12 (3.18, 8.22)	3.77 (2.96, 4.80)	3.11 (2.34, 4.14)		4.74 (2.39, 9.40)	2.74 (2.25, 3.32)	2.20 (1.72, 2.82)	
Q4(highest)	14.49 (8.81, 23.84)	7.05 (5.45, 9.13)	5.33 (3.93, 7.22)		13.31 (6.89, 25.73)	4.63 (3.82, 5.62)	3.13(2.43, 4.03)	
Leg				0.005				< 0.001
Q1(lowest)	1 (Ref)	1 (Ref)	1 (Ref)		1 (Ref)	1 (Ref)	1 (Ref)	
Q2	2.88(1.81, 4.61)	2.85 (2.24, 3.63)	2.30 (1.74, 3.03)		3.03 (1.47, 6.26)	1.97 (1.62, 2.40)	1.87(1.47, 2.38)	
Q ₃		5.90 (3.68, 9.44) 4.63 (3.62, 5.93)	3.82 (2.86, 5.10)		5.71 (2.89, 11.30)	3.18 (2.61, 3.86)	2.49 (1.95, 3.19)	
Q4(highest)	18.02 (10.78, 30.12)	9.09 (6.96, 11.86)	5.57 (4.11, 7.56)		13.72 (7.04, 26.74)	5.16 (4.23, 6.28)	3.30 (2.56, 4.26	
Trunk				0.372				< 0.001
Q1(lowest)	1 (Ref)	1 (Ref)	1 (Ref)		1 (Ref)	1 (Ref)	1 (Ref)	
Q2	3.01 (1.92, 4.74)	2.13 (1.68, 2.71)	2.62 (1.99, 3.47)		2.31 (1.16, 4.62)	1.95 (1.60, 2.37)	2.07 (1.62, 2.63)	
Q3		4.76 (3.01, 7.51) 4.07 (3.19, 5.20)	3.53 (2.65, 4.71)		4.03 (2.11, 7.70)	2.98 (2.45, 3.62)	2.63 (2.06, 3.37)	
Q4(highest)	11.66 (7.18, 18.93)	6.87 (5.30, 8.90)	6.27(4.59, 8.55)		11.86 (6.40, 21.96)	4.92 (4.05, 5.98)	3.43 (2.66, 4.42)	

Table 3 Association of FMRs with clustered cardiometabolic risk by age group

Data are presented as OR (95% CI). All models were adjusted for physical activity, education level, smoking status, residential area, drinking, region, and menopausal status in women. Clustered cardiometabolic risk was defined as the presence of 2 or more risk factors, including hypertension, elevated blood glucose, dyslipidemia, insulin resistance, and hyperuricemia

FMR: Fat-to-muscle mass ratio; OR: odds ratio; CI: confidence interval; Ref: reference

aged 75 years and above, indicated that muscle mass was associated with Mets in women, while no significant association was evidenced in men after adjusting for fat mass [\[34](#page-11-31)]. Likewise, the evidence regarding the association between fat mass and CRFs is not always consistent, with some studies reporting a positive association between arm fat mass and CRFs [\[35\]](#page-11-32) and others finding no such association [\[36](#page-11-33)]. The reasons for the apparent discrepancies in these associations remain unclear, but the metabolic load-capacity model provides a plausible explanation. Thus, it is important to consider fat mass and muscle mass together to mitigate such inconsistencies. FMR may be a potential index reflecting the combined effects of fat mass and skeletal muscle mass [[37\]](#page-11-34).

Multiple epidemiologic studies have confirmed the association of FMR with CRFs. A nationally

representative study including Korean adults reported a positive relationship between FMR and the prevalence of MetS and insulin resistance [[38\]](#page-11-35). Chen et al. performed a population-based observational study of 66,829 adults and found a strong association of FMR with hypertension, prediabetes, and diabetes mellitus [[16\]](#page-11-13). Another cross-sectional study involving 875 participants yielded similar results, demonstrating that a higher FMR was significantly linked with impaired fasting glucose metabolic risk [\[39](#page-11-36)]. These findings support our hypothesis that FMR is a valuable indicator for screening CRFs, suggesting the significance of considering the balance of fat mass and muscle mass when exploring CRFs in the general population.

Our study demonstrated that FMRs were more strongly associated with clustered CRFs in men compared to

	Men [OR (95% CI)]			Women [OR (95% CI)]		
	BMI < 24 kg/m ²	BMI \geq 24 kg/m ²	P for interaction	BMI < 24 kg/m ²	BMI \geq 24 kg/m ²	P for interaction
Whole body			0.060			< 0.001
Q1(lowest)	1 (Ref)	1 (Ref)		1 (Ref)	1 (Ref)	
Q ₂	2.17 (1.61, 2.92)	1.48 (1.20, 1.82)		2.28 (1.81, 2.88)	1.01(0.84, 1.22)	
Q3	3.13 (2.32, 4.22)	1.84 (1.49, 2.28)		2.83(2.25, 3.56)	1.18(0.98, 1.43)	
Q4(highest)	4.98 (3.67, 6.77)	3.14 (2.50, 3.94)		3.25 (2.58, 4.09)	1.76(1.45, 2.14)	
Arm			0.010			< 0.001
Q1(lowest)	1 (Ref)	1 (Ref)		1 (Ref)	1 (Ref)	
Q2	2.06 (1.52, 2.79)	1.53 (1.24, 1.88)		2.42 (1.92, 3.05)	0.98(0.81, 1.18)	
Q3	3.40 (2.51, 4.59)	1.69 (1.37, 2.09)		2.67(2.12, 3.36)	1.09 (0.90, 1.32)	
Q4(highest)	4.17 (3.05, 5.68)	3.03 (2.41, 3.80)		2.84 (2.26, 3.56)	1.65(1.36, 2.00)	
Leg			0.209			< 0.001
Q1(lowest)	1 (Ref)	1 (Ref)		1 (Ref)	1 (Ref)	
Q2	1.79 (1.33, 2.40)	1.36(1.10, 1.67)		2.68(2.11, 3.40)	1.15(0.95, 1.39)	
Q3	2.85(2.13, 3.82)	1.94 (1.57, 2.40)		3.14 (2.48, 3.98)	1.25(1.03, 1.51)	
Q4(highest)	4.91 (3.64, 6.62)	3.40 (2.70, 4.28)		3.62 (2.85, 4.59)	1.81(1.49, 2.19)	
Trunk			0.048			0.001
Q1(lowest)	1 (Ref)	1 (Ref)		1 (Ref)	1 (Ref)	
Q2	2.27(1.68, 3.05)	1.46(1.19, 1.79)		2.18(1.73, 2.76)	1.08(0.90, 1.31)	
Q ₃	2.96 (2.19, 3.99)	1.70(1.38, 2.10)		2.71(2.15, 3.41)	1.21(1.00, 1.46)	
Q4(highest)	4.86 (3.58, 6.61)	2.95 (2.35, 3.70)		3.12 (2.48, 3.93)	1.83 (1.51, 2.22)	

Table 4 Association of FMRs with clustered cardiometabolic risk by BMI group

Data are presented as OR (95% CI). All models were adjusted for age, physical activity, education level, smoking status, residential area, drinking, region, and menopausal status in women. Clustered cardiometabolic risk was defined as the presence of 2 or more risk factors, including hypertension, elevated blood glucose, dyslipidemia, insulin resistance, and hyperuricemia

BMI: body mass index; FMR: Fat-to-muscle mass ratio; OR: odds ratio; CI: confidence interval; Ref: reference

women. This may be caused by differences in fat distribution, estrogen, and androgen levels, and sex-specific genetics $[40, 41]$ $[40, 41]$ $[40, 41]$ $[40, 41]$. However, few of these studies have explored the associations between FMR and CRFs in different body regions. In the present study, we found that FMR of the legs presented the strongest associations for clustered CRFs in men and women. This result is similar to a study of a British population that revealed a stronger association between FMR in legs and diabetes than FMR in the arms and trunk [[17](#page-11-15)]. The findings suggest that the balance of muscle and fat in the legs is more important for cardiometabolic health. They also emphasize the importance of targeted interventions to improve muscle and fat mass in specific body regions as a preventative measure for CRFs in clinical and public health settings.

We observed that the positive association between FMR and clustered CRFs was remarkably strengthened among younger participants, suggesting that the early improvements in muscle mass and strength have a more pronounced impact on overall health outcomes. This finding is consistent with a prior study utilizing the UK Biobank database, revealing a heightened association between FMRs and diabetes in young adults compared to older adults [\[17](#page-11-15)]. Individuals aged 20–60 typically experience stronger metabolic activity with a relatively faster metabolic rate than older people [\[42](#page-11-39)]. At this stage, the body may exhibit increased sensitivity to fluctuations in

the FMRs, making it more susceptible to such variations. Furthermore, the elderly faced challenges of decline in physical abilities, increased comorbidities, impairment of mental health, and limited life expectancy [\[43](#page-11-40)]. These factors may offset the clinical benefits derived from the improvement of body composition.

The underlying biological mechanisms have been proposed to understand the relationship between FMR and CRFs. Adipose tissue serves not only as an energy reservoir but also as an active endocrine organ, secreting various pro-inflammatory cytokines such as tumor necrosis factor and interleukin 6, thereby leading to chronic inflammation [\[44](#page-11-41)]. The chronic inflammation in adipose tissue may cause IR and metabolic disorders, consequently increasing the risk of high blood glucose, hypertension, and dyslipidemia [\[45\]](#page-11-42). On the other hand, skeletal muscle stands as the principal site for insulinregulated glucose uptake. A decline in muscle mass is significantly correlated with decreased insulin sensitivity [[46\]](#page-11-43). Our study identified a positive association between FMR and IR, providing further support for this correlation. Whole-body IR is the important pathogenic factor of cardiometabolic diseases including dyslipidemia and type 2 diabetes mellitus [\[47\]](#page-11-44). Given the advantageous and adverse attributes of muscle and fat mass, the cumulative effect of the balance between the two body components could potentially impact CRFs.

The strengths of the study include the large sample size of the Chinese general population, which enables sufficient statistical power to examine the associations and interactions. In addition, the data collection process across three provinces adhered to standardized protocols, with subsequent analysis meticulously adjusting for multiple confounders. Notably, the study used a comprehensive index that evaluates both total and body regions, integrating the impacts of muscle and fat mass to evaluate CRFs in the study. Meanwhile, we acknowledge some potential limitations. First, the study is a cross-sectional design, it is limited in interpreting causality between FMR and CRFs. Second, fat mass and muscle mass were not measured by high precision imaging techniques such as magnetic resonance imaging or dual x-ray absorptiometry (DXA). Nevertheless, BIA was a feasible method and an adequate measurement to estimate body composition such as body fat and muscle in large-scale epidemiological studies due to it is convenient, fast, noninvasive, cost-effective and easy to implement [\[48](#page-12-0)]. Last, our study included the general Han population in three provinces in China, which may affect the generalizability of the findings to other regions or countries. Large-scale prospective cohort studies involving multi-ethnic adults are needed in the future to further validate the association between FMR and CRFs and to explore the complex mechanisms.

In conclusion, the findings of this study demonstrated a significant association between FMR and both single and clustered cardiometabolic risk factors in the general Chinese population, regardless of body region. These associations were particularly pronounced among young adults. Our finding highlights the importance of early surveillance of muscle mass, fat mass, and FMR to alleviate the burden of cardiometabolic disease.

Abbreviations

Supplementary Information

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Supplementary Material 1

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Author contributions

Study concept and design: SG, HH, and LZ; Acquisition of data: SG, HH, LZ, HY, CX, OQ, LY, XT, TJ, LA, LB, LQ, XT, WW, HH, XD, CZ, and WZ; Analysis and interpretation of data: LZ; Drafting of the manuscript: LZ; Critical revision of the manuscript for important intellectual content: SG and HH. All authors reviewed the manuscript.

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Data availability

"The datasets analyzed during the present study are available from the corresponding author on reasonable request."

Declarations

Ethics approval and consent to participate

The Ethical Review Committee of the Institute of Basic Medical Sciences Chinese Academy of Medical Sciences, Beijing, China, has approved this study under the protocol (No. 2022177 and No. 2022134). Written informed consent was obtained from all participants.

Competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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