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The predictive value of relative fat density for metabolic risk in obese individuals

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Abstract

Background:

Obesity is metabolically heterogeneous, and conventional adiposity measures mainly quantify fat amount rather than adipose tissue quality. This study evaluated computed tomography (CT)-derived relative fat density (RFD), an individualized ratio of visceral to subcutaneous fat attenuation, for metabolic risk stratification in adults with obesity.

Methods:

This retrospective cross-sectional study included adults who underwent routine health examinations between June 2024 and July 2025. Visceral fat area (VFA), subcutaneous fat area (SAT), visceral fat attenuation density (FAD), and subcutaneous adipose density (SAD) were measured on non-contrast abdominal CT images at the L3 level. Sex-specific VFA cutoffs for defining obesity and sex-specific RFD cutoffs were determined using receiver operating characteristic (ROC) curve analysis with the maximum Youden index. Restricted cubic spline (RCS), DeLong tests, and multivariable logistic regression were used to evaluate the association between RFD and metabolic abnormality (MA).

Results:

Among 1,426 participants, 698 (48.9%) were classified as having obesity based on sex-specific VFA cutoffs (123.173 cm^2 for men and 64.87 cm^2 for women). In adults with obesity, the optimal RFD cutoffs were 99.599 in men and 95.356 in women. RFD showed better discriminative performance for MA than FAD in the overall obese population (AUC 0.657 vs. 0.574; DeLong $P < 0.001$) and in obese men (AUC 0.609 vs. 0.509; $P = 0.034$). High RFD was independently associated with MA after adjustment for age, VFA, and BMI (OR = 2.153, 95% CI: 1.565–2.963; $P < 0.001$). MA was more frequent in the high-RFD group than in the low-RFD group (64.53% vs. 37.57%), with a stronger stratification effect in women.

Conclusions:

RFD is independently associated with metabolic abnormality in adults with obesity and may provide individualized, sex-specific risk stratification beyond conventional fat attenuation measures.

1. Background

Obesity has become a major public health challenge of the 21st century. According to the Global Burden of Disease study published in The Lancet in 2025, approximately 2.11 billion adults aged 25 years or older were overweight or obese in 2021 (1). Obesity increases the risk of metabolic diseases, functional impairment, and malignancies such as colorectal and liver cancer (2, 3). It has been projected that by

2030, obesity-related healthcare expenditures in China will exceed 418 billion RMB, accounting for approximately 22% of total national healthcare costs (4).

Obesity is increasingly recognized as a heterogeneous condition (5). Traditional indices, including body mass index (BMI), waist circumference, and waist-to-hip ratio, cannot adequately capture differences in visceral and subcutaneous fat distribution (6, 7). Visceral fat area (VFA) is a more direct marker of central adiposity and has been associated with metabolic disorders, cardiovascular disease, malignancy, and chronic low-grade inflammation (8, 9). However, VFA mainly reflects fat quantity and has limited ability to describe adipose tissue composition and function (10). Although a VFA cutoff of 100 cm^2 has been widely used (11), a single threshold may not adequately reflect sex-specific metabolic risk. Previous studies have also used data-driven approaches to determine sex-specific VFA cutoffs for different outcomes, including type 2 diabetes, metabolic syndrome, and metabolic dysfunction-associated fatty liver disease (12–14).

Fat attenuation density (FAD), derived from CT attenuation values, has attracted increasing attention because it reflects structural characteristics of adipose tissue, including adipocyte size, lipid content, vascularity, fibrosis, and inflammation (15). Nevertheless, the relationship between visceral fat density and adverse outcomes remains inconsistent. Lower visceral fat density has been associated with a higher prevalence of metabolic syndrome and increased cardiometabolic risk (16), whereas higher adipose tissue density has been linked to increased mortality in older adults and patients with advanced cancer (17).

FAD may be influenced by overall adiposity, metabolic status, and individual differences in fat distribution, which limits direct comparability across individuals. To address this limitation, we proposed relative fat density (RFD), defined as the ratio of visceral to subcutaneous fat attenuation within the same individual. Because adipose tissue attenuation is recorded as negative HU values, absolute attenuation values were used for ratio calculation. We hypothesized that RFD may provide a more individualized assessment of visceral adipose tissue quality and improve metabolic risk stratification in adults with obesity.

2. Methods

2.1 Study design and population

This retrospective cross-sectional study consecutively enrolled adults undergoing routine health examinations at the Health Management Center of our hospital between June 2024 and July 2025. This design was consistent with previous health-screening studies using CT-derived visceral fat measurements to evaluate metabolic risk (18). Inclusion criteria were: (1) age ≥ 18 years; (2) availability of non-contrast abdominal CT; and (3) complete anthropometric and metabolic laboratory data. Exclusion criteria were: (1) a history of heart failure, chronic kidney disease, or chronic pulmonary disease requiring ongoing treatment; (2) prior major abdominal surgery or previous cardiovascular or

cerebrovascular events; and (3) a history of malignancy or current antitumor therapy. The study protocol was approved by the Ethics Committee of the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University. The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

2.2 Clinical and laboratory data

Demographic characteristics, anthropometric measurements, blood pressure levels, and medical history were extracted from the electronic medical record system. Laboratory measurements included fasting plasma glucose, glycated hemoglobin, lipid profile, high-sensitivity C-reactive protein, liver function parameters, serum creatinine, uric acid, serum albumin, hemoglobin, and neutrophil percentage.

2.3 CT image analysis and adipose tissue measurement

Non-contrast abdominal CT images at the third lumbar vertebra (L3) level were analyzed using the INFINITT PACS system (INFINITT Healthcare, Seoul, Korea). Adipose tissue was identified using a predefined attenuation threshold from − 150 to − 50 Hounsfield units (HU). Visceral and subcutaneous adipose tissue regions were manually delineated, and the corresponding VFA, SAT, FAD, and SAD were automatically calculated. FAD and SAD were originally recorded as negative HU values and were converted to absolute values for RFD calculation. RFD was calculated as |FAD|/|SAD| × 100%. All measurements were independently performed by two trained investigators, and discrepancies were resolved by consensus.

2.4 Definition of study variables

Optimal VFA cutoff values for MA were determined by ROC curve analysis using the maximum Youden index, and obesity was defined accordingly. MA was defined as the presence of at least two of the following criteria: (1) hyperglycemia, defined as fasting plasma glucose ≥ 5.6 mmol/L and/or 2-hour postprandial glucose ≥ 7.8 mmol/L, or previously diagnosed diabetes under treatment; (2) hypertension, defined as blood pressure ≥ 140/90 mmHg or previously diagnosed hypertension under treatment; (3) hypertriglyceridemia, defined as TG ≥ 1.7 mmol/L; and (4) reduced high-density lipoprotein cholesterol (HDL-C), defined as HDL-C < 0.9 mmol/L in men and < 1.0 mmol/L in women (19).

2.5 Statistical analysis

Statistical analyses were performed using Decision Chain software (version 1.0). Continuous variables are presented as mean ± standard deviation or median (interquartile range), as appropriate. Between-group differences were analyzed using Student's t-test, the Mann–Whitney U test, Pearson's chi-square test, or Fisher's exact test, as appropriate. RCS models were used to examine potential nonlinear associations between RFD and MA. ROC curve analysis was performed to evaluate discriminative performance and determine optimal cutoff values. AUCs were compared using the DeLong test. Variables with a trend toward significance in univariate analysis ($P < 0.10$) were entered into a forward stepwise multivariable logistic regression model. All tests were two-sided, and $P < 0.05$ was considered statistically significant.

3. Results

3.1 Sex-specific VFA cutoffs for defining obesity

RCS analysis showed significant overall associations between VFA and MA in both men and women (both $P < 0.001$), while tests for nonlinearity were not statistically significant (both $P > 0.05$). These findings suggested a monotonic association between VFA and MA and supported subsequent ROC analysis. Based on the maximum Youden index, the optimal VFA cutoff for defining obesity was 123.173 cm^2 in men (AUC = 0.772) and 64.87 cm^2 in women (AUC = 0.853).

Figure 1. RCS and ROC curves of VFA for metabolic risk stratification. (a,b) Men; (c,d) women.

3.2 Baseline characteristics of the study population

A total of 1,426 participants were enrolled, including 728 non-obese and 698 obese individuals (Table 1). Compared with the non-obese group, the obese group was older, had a higher proportion of men, and showed significantly higher BMI, VFA, SAT, and RFD (all $P < 0.001$). Obese individuals also had higher rates of hyperglycemia and hypertension, accompanied by higher TG, fasting blood glucose, ALT, BUN, SCr, UA, WBC, and NLR levels, as well as lower HDL-C, lymphocyte percentage, and PLR (all $P < 0.05$). In the carotid ultrasonography subcohort, carotid plaque was more frequently detected in the obese group than in the non-obese group (29.28% vs. 15.04%). Overall, MA was significantly more prevalent in the obese group than in the non-obese group (50.86% vs. 9.34%, $P < 0.001$).

Table 1
Baseline characteristics of the study population

Factors	All (N = 1426)	Non-obesity (N = 728)	Obesity (N = 698)	P value
Age, mean (SD), years	44.78 ± 12.88	40.75 ± 11.64	48.99 ± 12.77	< 0.001
BMI, mean (SD), kg/m²	23.72 ± 3.30	21.89 ± 2.44	25.63 ± 2.98	< 0.001
VFA, median (IQR), cm²	95.99 (107.10)	48.26 (47.66)	156.69 (68.26)	< 0.001
SAT, median (IQR), cm²	114.60 (57.52)	97.06 (51.52)	132.60 (54.22)	< 0.001
FAD, median (IQR), |HU|	97.70 (10.60)	91.95 (9.55)	102.00 (5.20)	< 0.001
SAD, median (IQR), |HU|	103.60 (5.70)	103.15 (6.55)	103.90 (5.00)	< 0.001
RFD, median (IQR), %	94.24 (9.79)	89.83 (7.59)	98.31 (6.38)	< 0.001
TC, median (IQR), mmol/L	4.91 (1.23)	4.84 (1.12)	4.99 (1.34)	0.002
TG, median (IQR), mmol/L	1.24 (1.02)	0.95 (0.57)	1.66 (1.17)	< 0.001
HDL-C, median (IQR), mmol/L	1.32 (0.40)	1.44 (0.40)	1.22 (0.33)	< 0.001
LDL-C, median (IQR), mmol/L	3.19 (0.96)	3.07 (0.85)	3.32 (1.05)	< 0.001
FBG, median (IQR), mmol/L	4.75 (0.67)	4.60 (0.58)	4.94 (0.80)	< 0.001
ALB, median (IQR), g/L	44.25 (3.10)	44.20 (3.20)	44.30 (3.20)	0.935
ALT, median (IQR), U/L	21.00 (18.00)	17.00 (11.00)	27.00 (21.00)	< 0.001
BUN, median (IQR), mmol/L	5.10 (1.50)	5.00 (1.60)	5.20 (1.50)	< 0.001
SCr, median (IQR), μmol/L	72.00 (22.00)	70.00 (23.00)	74.00 (21.00)	< 0.001
UA, median (IQR), μmol/L	361.00 (128.00)	334.50 (115.00)	389.00 (135.00)	< 0.001
WBC, median (IQR), ×10⁹/L	5.77 (1.86)	5.43 (1.61)	6.20 (1.93)	< 0.001
PLT, median (IQR), ×10⁹/L	229.00 (68.00)	225.00 (62.00)	234.00 (72.00)	0.005

Note: Data are presented as mean ± standard deviation, median (interquartile range), or n (%). FAD and SAD are presented as absolute HU values. Carotid ultrasonography was evaluated in a nested subcohort of 986 participants (non-obesity: n = 419; obesity: n = 567). Percentages for carotid status were calculated using the corresponding subcohort as the denominator. Abbreviations: BMI, body mass index; VFA, visceral fat area; SAT, subcutaneous fat area; FAD, fat attenuation density; SAD, subcutaneous adipose density; RFD, relative fat density; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FBG, fasting blood glucose; ALB, albumin; ALT, alanine aminotransferase; BUN, blood urea nitrogen; SCr, serum creatinine; UA, uric acid; WBC, white blood cell count; PLT, platelet count; Hb, hemoglobin; NEU, neutrophil percentage; LYM, lymphocyte percentage; PLR, platelet-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; IMT, intima-media thickness; MN, metabolically normal; MA, metabolically abnormal.

Factors	All (N = 1426)	Non-obesity (N = 728)	Obesity (N = 698)	P value
Hb, median (IQR), g/L	142.00 (22.00)	137.50 (23.00)	146.00 (20.00)	< 0.001
NEU, median (IQR), %	55.80 (10.20)	55.15 (10.10)	56.55 (10.20)	0.006
LYM, median (IQR), %	34.60 (9.70)	35.15 (9.70)	33.65 (10.00)	0.004
PLR, median (IQR)	116.05 (50.31)	118.59 (49.71)	112.24 (47.59)	< 0.001
NLR, median (IQR)	1.61 (0.75)	1.57 (0.72)	1.66 (0.77)	0.004
Gender, n (%)				**< 0.001**
Male	817 (57.29%)	361 (49.59%)	456 (65.33%)	
Female	609 (42.71%)	367 (50.41%)	242 (34.67%)	
Hyperglycemia, n (%)				**< 0.001**
No	1249 (87.59%)	702 (96.43%)	547 (78.37%)	
Yes	177 (12.41%)	26 (3.57%)	151 (21.63%)	
Hypertension, n (%)				**< 0.001**
No	909 (63.74%)	573 (78.71%)	336 (48.14%)	
Yes	517 (36.26%)	155 (21.29%)	362 (51.86%)	
Carotid atherosclerosis subcohort, n (%) ‡				**< 0.001**
Normal	479 (48.58%)	235 (56.09%)	244 (43.03%)	
IMT thickening	278 (28.19%)	121 (28.88%)	157 (27.69%)	
Carotid plaque	229 (23.23%)	63 (15.04%)	166 (29.28%)	
Metabolic status, n (%)				**< 0.001**
MN	1003 (70.34%)	660 (90.66%)	343 (49.14%)	
MA	423 (29.66%)	68 (9.34%)	355 (50.86%)	

Note: Data are presented as mean ± standard deviation, median (interquartile range), or n (%). FAD and SAD are presented as absolute HU values. Carotid ultrasonography was evaluated in a nested subcohort of 986 participants (non-obesity: n = 419; obesity: n = 567). Percentages for carotid status were calculated using the corresponding subcohort as the denominator. Abbreviations: BMI, body mass index; VFA, visceral fat area; SAT, subcutaneous fat area; FAD, fat attenuation density; SAD, subcutaneous adipose density; RFD, relative fat density; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FBG, fasting blood glucose; ALB, albumin; ALT, alanine aminotransferase; BUN, blood urea nitrogen; SCr, serum creatinine; UA, uric acid; WBC, white blood cell count; PLT, platelet count; Hb, hemoglobin; NEU, neutrophil percentage; LYM, lymphocyte percentage; PLR, platelet-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; IMT, intima-media thickness; MN, metabolically normal; MA, metabolically abnormal.

3.3 Discriminative performance of RFD for metabolic abnormality

RCS analysis suggested approximately linear associations between both FAD and RFD and MA in the overall, male, and female obese populations, supporting further ROC analysis. ROC analysis showed that RFD had better discriminative performance than FAD for identifying MA in obese participants. In the overall obese population, the AUC of RFD was higher than that of FAD (0.657 vs. 0.574), and the difference was significant by the DeLong test (ΔAUC = 0.083, P < 0.001). The full DeLong test results comparing the AUCs of RFD and FAD are summarized in Table 2. FAD showed poor discriminative ability in obese men (AUC = 0.509), whereas RFD showed relatively better performance in both obese men (AUC 0.609 vs. 0.509, ΔAUC = 0.100, P = 0.034) and obese women (AUC 0.712 vs. 0.676, ΔAUC = 0.036, P = 0.167). Although the improvement in women did not reach statistical significance, RFD had the highest AUC in the obese female subgroup.

Based on sex-stratified ROC curves, the optimal RFD cutoffs were 99.599 in obese men and 95.356 in obese women. Obese participants were therefore classified into low- and high-RFD groups using these sex-specific thresholds.

Figure 2. RCS and ROC analyses of FAD and RFD in obese participants. (a,d) FAD in all obese participants; (b,e) FAD in obese men; (c,f) FAD in obese women; (g,j) RFD in all obese participants; (h,k) RFD in obese men; (i,l) RFD in obese women.

Table 2
DeLong test comparing AUCs between RFD and FAD

Population	RFD AUC	FAD AUC	AUC difference	DeLong P value
Obese individuals	0.657	0.574	0.083	P < 0.001
Obese males	0.609	0.509	0.100	P = 0.034
Obese females	0.712	0.676	0.036	P = 0.167

3.4 Baseline characteristics and metabolic status according to RFD group

Among obese participants, the high-RFD group showed a more unfavorable metabolic risk profile than the low-RFD group (Table 3). Compared with the low-RFD group, the high-RFD group had higher age, BMI, VFA, FAD, and RFD, but lower SAT and SAD. Biochemical analyses showed higher TG, GLU, ALT, SCr, and UA levels and lower HDL-C levels in the high-RFD group, suggesting that high RFD was associated with dyslipidemia, higher glucose levels, and abnormal liver and renal metabolic markers. ALB and Hb were also slightly higher in the high-RFD group. However, WBC, PLT, LYM%, NEU%, PLR, and NLR did not differ significantly between the two groups. The proportions of glucose abnormality and hypertension were significantly higher in the high-RFD group. Accordingly, MA was markedly more prevalent in the high-RFD

group than in the low-RFD group (64.53% vs. 37.57%, P < 0.001). In the carotid ultrasonography subgroup, plaque formation was numerically more frequent in the high-RFD group than in the low-RFD group (31.83% vs. 26.62%), although the overall distribution of carotid plaque status was not significantly different (P = 0.366).

Table 3
Baseline characteristics according to RFD group in obese participants

Variable	Overall (n = 698)	Low RFD (n = 354)	High RFD (n = 344)	P value
Age, mean ± SD, years	48.99 ± 12.77	48.07 ± 12.95	49.94 ± 12.53	0.025
BMI, mean ± SD, kg/m²	25.63 ± 2.98	25.14 ± 3.01	26.14 ± 2.86	< 0.001
VFA, median (IQR), cm²	156.69 (68.26)	139.83 (74.62)	178.70 (76.05)	< 0.001
FAD, median (IQR), |HU|	102.00 (5.20)	99.90 (4.60)	104.10 (3.90)	< 0.001
RFD, median (IQR), %	98.31 (6.38)	95.31 (4.65)	101.70 (3.76)	< 0.001
SAT, median (IQR), cm²	132.60 (54.23)	136.79 (50.81)	127.28 (58.65)	< 0.001
SAD, median (IQR), |HU|	103.90 (5.00)	104.95 (4.00)	102.50 (5.40)	< 0.001
ALB, median (IQR)	44.30 (3.20)	44.05 (3.10)	44.50 (3.30)	0.016
WBC, median (IQR)	6.20 (1.93)	6.08 (1.90)	6.27 (1.91)	0.176
PLT, median (IQR)	234.00 (72.00)	234.00 (70.00)	234.00 (72.00)	0.619
LYM%, median (IQR)	33.65 (10.00)	33.60 (10.60)	33.75 (9.65)	0.782
Hb, median (IQR)	146.00 (20.00)	145.00 (23.00)	147.50 (20.50)	0.023
NEU%, median (IQR)	56.55 (10.20)	56.50 (11.70)	56.55 (9.25)	0.903
TC, median (IQR)	4.99 (1.34)	5.08 (1.24)	4.90 (1.36)	0.128
TG, median (IQR)	1.66 (1.17)	1.50 (1.10)	1.81 (1.16)	< 0.001
HDL-C, median (IQR)	1.22 (0.33)	1.25 (0.32)	1.19 (0.34)	< 0.001
LDL-C, median (IQR)	3.32 (1.05)	3.36 (1.01)	3.27 (1.07)	0.226
GLU, median (IQR)	4.94 (0.80)	4.88 (0.67)	5.01 (0.94)	< 0.001
ALT, median (IQR)	27.00 (21.00)	24.00 (20.00)	28.50 (21.00)	< 0.001
SCr, median (IQR)	74.00 (21.00)	73.00 (23.00)	75.50 (20.50)	0.031
UA, median (IQR)	389.00 (135.00)	370.00 (124.00)	408.50 (141.50)	< 0.001
PLR, median (IQR)	112.24 (47.59)	116.57 (50.86)	109.88 (45.95)	0.098
NLR, median (IQR)	1.66 (0.77)	1.66 (0.81)	1.66 (0.72)	0.915
Gender, n (%)				**0.189**

Note: Data are presented as mean ± standard deviation, median (interquartile range), or n (%). FAD and SAD are presented as absolute HU values. Carotid plaque status was available in 573 participants. Percentages were calculated using the corresponding subgroup as the denominator. Abbreviations are as defined in Table 1.

Variable	Overall (n = 698)	Low RFD (n = 354)	High RFD (n = 344)	P value
Male	456 (65.33%)	223 (62.99%)	233 (67.73%)	
Female	242 (34.67%)	131 (37.01%)	111 (32.27%)	
Glucose abnormality, n (%)				**0.002**
No	547 (78.37%)	294 (83.05%)	253 (73.55%)	
Yes	151 (21.63%)	60 (16.95%)	91 (26.45%)	
Hypertension, n (%)				**< 0.001**
No	336 (48.14%)	194 (54.80%)	142 (41.28%)	
Yes	362 (51.86%)	160 (45.20%)	202 (58.72%)	
Carotid plaque status, n (%)†				**0.366**
Normal	244 (43.03%)	126 (45.32%)	118 (40.83%)	
IMT thickening	157 (27.69%)	78 (28.06%)	79 (27.34%)	
Plaque formation	166 (29.28%)	74 (26.62%)	92 (31.83%)	
Metabolic abnormality, n (%)				**< 0.001**
No	343 (49.14%)	221 (62.43%)	122 (35.47%)	
Yes	355 (50.86%)	133 (37.57%)	222 (64.53%)	

Note: Data are presented as mean ± standard deviation, median (interquartile range), or n (%). FAD and SAD are presented as absolute HU values. Carotid plaque status was available in 573 participants. Percentages were calculated using the corresponding subgroup as the denominator. Abbreviations are as defined in Table 1.

Sex-stratified analysis further showed that the increase in MA associated with high RFD was present in both men and women, with a more pronounced stratification effect in women (Table 4). In men, MA prevalence increased from 44.84% in the low-RFD group to 65.67% in the high-RFD group. In women, MA prevalence increased from 25.19% to 62.16% (both P < 0.001).

Table 4
Sex-stratified MA prevalence by RFD group

Sex	Low RFD	High RFD	Absolute difference	P value
Male	44.84%	65.67%	+ 20.85%	< 0.001
Female	25.19%	62.16%	+ 36.97%	< 0.001

3.5 Independent association between RFD and metabolic abnormality

Logistic regression analysis showed that RFD was closely associated with MA in obese participants (Table 5). In univariate analysis, high RFD was significantly associated with an increased risk of MA. After further multivariable adjustment for age, VFA, and BMI, high RFD remained independently associated with MA (OR = 2.153, 95% CI: 1.565–2.963, P < 0.001).

Table 5
Logistic regression analyses for metabolic abnormality in obese participants

Factors	Univariate analysis OR (95% CI)	P	Multivariate analysis OR (95% CI)	P
GENDER	0.403 (0.315–0.516)	< 0.001*		
AGE	1.056 (1.046–1.066)	< 0.001*	1.044 (1.032–1.056)	< 0.001*
RFD_group	6.680 (5.156–8.656)	< 0.001*	2.153 (1.565–2.963)	< 0.001*
VFA	1.018 (1.016–1.020)	< 0.001*	1.012 (1.008–1.015)	< 0.001*
SAT	1.007 (1.004–1.009)	< 0.001*		
BMI	1.314 (1.260–1.372)	< 0.001*	1.076 (1.012–1.144)	0.019*

Note: OR, odds ratio; CI, confidence interval; RFD, relative fat density; VFA, visceral fat area; SAT, subcutaneous adipose tissue area; BMI, body mass index. *P < 0.05.

4. Discussion

To our knowledge, this is the first study to introduce RFD by normalizing visceral fat density to subcutaneous fat density within the same individual and to evaluate its value for metabolic risk stratification in adults with obesity. High RFD was independently associated with MA after adjustment for age, VFA, and BMI (OR = 2.153, 95% CI: 1.565–2.963). MA prevalence was 64.53% in the high-RFD group, compared with 37.57% in the low-RFD group. RFD also showed stronger discriminative performance in women, suggesting that sex-related differences may influence its ability to identify metabolic risk.

In recent years, fat density has gained attention as an imaging-derived marker of adipose tissue quality. However, FAD alone is susceptible to individual differences. Previous studies have shown that lower visceral fat density is associated with an increased risk of metabolic syndrome (20), whereas higher adipose tissue radiodensity may reflect lipid depletion, fibrosis, or inflammatory remodeling and has been associated with adverse prognosis or aggressive tumor features in several cancer settings (21–23). These findings indicate a complex relationship between fat density and adverse outcomes. In obesity, visceral adipocytes often undergo pathological hypertrophy, lipid accumulation, impaired angiogenesis, and chronic low-grade inflammation, all of which may reduce CT attenuation values (24).

In the present study, RFD showed better discriminative performance for MA than FAD in obese individuals (AUC 0.657 vs. 0.574, DeLong P < 0.001). Individuals with similar FAD levels may therefore have different metabolic profiles. Subcutaneous fat has relatively low metabolic activity and mainly serves as an energy reservoir and metabolic buffer (25). Using SAD as an internal reference may help correct for individual differences in baseline fat distribution and metabolic status. On this basis, RFD may provide additional metabolic risk information by integrating the relative attenuation difference between visceral and subcutaneous fat, rather than acting as a simple numerical transformation of FAD.

Elevated RFD may not only reflect increased visceral fat burden and impaired adipose tissue quality, but also indicate a higher systemic metabolic burden under obese conditions. In obesity, adipose tissue undergoes sustained expansion to store excess energy (26). When visceral adipose tissue becomes dysfunctional, it can release excessive free fatty acids and inflammatory cytokines, which enter the liver directly through the portal circulation and affect hepatic lipid uptake, synthesis, and inflammatory responses (27), thereby promoting insulin resistance, hypertriglyceridemia, reduced HDL-C, and other forms of dyslipidemia (28, 29). In some individuals, these changes may also be accompanied by elevated liver enzyme levels. Meanwhile, obesity-related lipotoxicity may increase renal metabolic stress, and abnormalities in uric acid metabolism may further promote metabolic risk progression through oxidative stress, endothelial dysfunction, and inflammatory responses (30). In addition, RAAS activation may promote sodium and water retention, vasoconstriction, and renal injury, thereby contributing to elevated blood pressure and increased renal metabolic burden (31).

In the present study, the high-RFD group exhibited a broader adverse metabolic phenotype. Compared with the low-RFD group, participants in the high-RFD group had higher VFA [178.70 (76.05) vs. 139.83 (74.62) cm^2], TG [1.81 (1.16) vs. 1.50 (1.10) mmol/L], but lower HDL-C [1.19 (0.34) vs. 1.25 (0.32) mmol/L]. The proportions of glucose abnormality, hypertension, and MA were also higher in the high-RFD group than in the low-RFD group (26.45% vs. 16.95%, 58.72% vs. 45.20%, and 64.53% vs. 37.57%, respectively). These findings suggest that high RFD is not merely an imaging-based change in fat density, but coexists with dysregulation of glucose and lipid metabolism, increased hepatic and renal metabolic burden, and blood pressure abnormalities. RFD may reflect an integrated link between impaired visceral adipose tissue quality and increased systemic metabolic burden in adults with obesity.

Another important finding of this study is that RFD showed stronger risk-stratification value in obese women. The AUC of RFD for identifying MA was higher in women than in men (0.712 vs. 0.609). After RFD stratification, MA prevalence increased from 25.19% to 62.16% in women, with an absolute difference of 36.97%, compared with 20.85% in men. This sex difference may be related to differences in fat distribution and adipose tissue function. Women generally have a higher proportion of subcutaneous fat, which plays an important role in energy storage and metabolic buffering (32). Therefore, abnormal attenuation of visceral fat relative to subcutaneous fat may more sensitively reflect the transition of visceral adipose tissue from compensated storage to functional impairment. In contrast, metabolic risk in men may be more strongly influenced by visceral fat volume, overall adiposity, and other metabolic factors, thereby weakening the advantage of a density-based ratio. These findings suggest that sex

differences should be considered in metabolic risk assessment and that RFD may be particularly useful for identifying high-risk obese women.

This study has several limitations. First, its retrospective cross-sectional design precludes causal inference and limits evaluation of the longitudinal predictive value of RFD. Second, the study population was derived from a single health management center, which may limit generalizability. Third, RFD calculation requires abdominal CT imaging; although the measurements were obtained from routine health examinations in this study, radiation exposure and accessibility may restrict its broad use in general screening. Fourth, medication use, menopausal status, lifestyle factors, and longitudinal changes in adipose tissue density were not fully evaluated. Future multicenter prospective cohort studies are needed to validate RFD, assess its dynamic changes, and determine whether it improves prediction of diabetes, dyslipidemia, cardiovascular events, and other metabolism-related outcomes.

5. Conclusions

This study demonstrated that CT-derived RFD was independently associated with MA in adults with obesity. Compared with conventional FAD, RFD provided more stable risk stratification, particularly in women. High RFD was accompanied by a broader adverse metabolic phenotype involving dyslipidemia, glucose abnormality, hepatic and renal metabolic burden, and hypertension. Overall, RFD may serve as an individualized imaging-derived marker for metabolic risk stratification in adults with obesity and may have value for future dynamic metabolic management.

Abbreviations

AUC
area under the curve
BMI
body mass index
CT
computed tomography
FAD
fat attenuation density
FBG
fasting blood glucose
HDL-C
high-density lipoprotein cholesterol
HU
Hounsfield units
LDL-C
low-density lipoprotein cholesterol
MA

metabolic abnormality
MAFLD
metabolic dysfunction-associated fatty liver disease
MN
metabolically normal
RCS
restricted cubic spline
RFD
relative fat density
ROC
receiver operating characteristic
SAD
subcutaneous adipose density
SAT
subcutaneous fat area
SCr
serum creatinine
TG
triglycerides
UA
uric acid
VFA
visceral fat area.

Declarations

Ethics approval and consent to participate

This study involving human participants was approved by the Ethics Committee of the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University. The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

X-YW: Investigation, Formal analysis, Data curation, Writing – original draft. M-FY: Data curation, Investigation, Writing – original draft. Z-QM: Data curation, Investigation, Writing – original draft. Y-LL: Data curation, Investigation, Writing – original draft. H-LW: Data curation, Investigation, Writing – original draft. C-JZ: Formal analysis, Investigation, Writing – original draft. C-GZ: Conceptualization, Project administration, Supervision, Writing – original draft. HW: Conceptualization, Supervision, Writing – review & editing. All authors read and approved the final manuscript.

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Not applicable.

Data Availability

The datasets that support the findings of this study are derived from routine health examination records of the Health Management Center of the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University. Restrictions apply to the availability of these data because they contain potentially sensitive clinical information and were used under the approval of the institutional Ethics Committee for the current study. Therefore, the data are not publicly available. The anonymized data may be available from the corresponding author upon reasonable request and with permission from the Ethics Committee of the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University.

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Figures

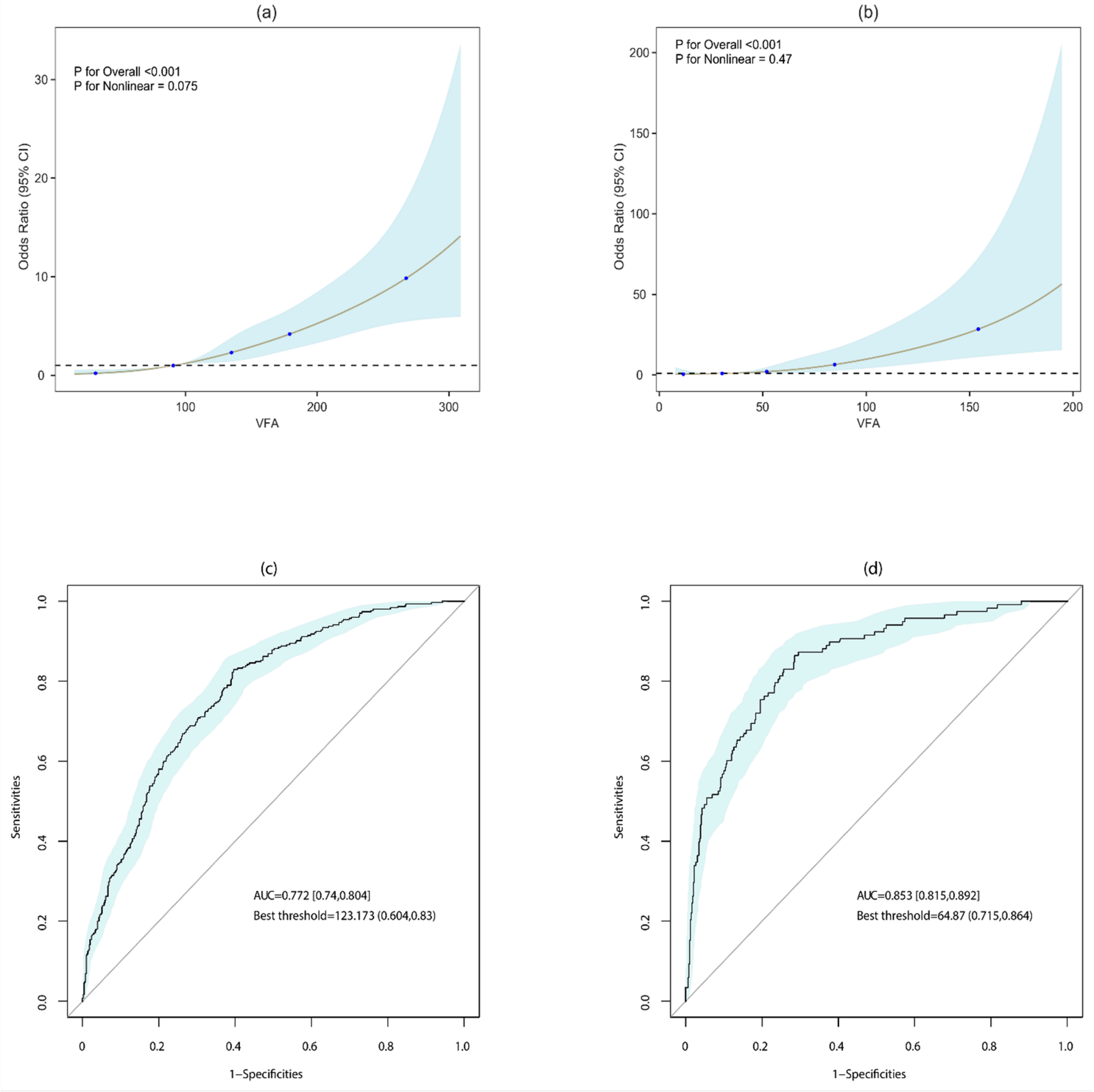


Figure 1

RCS and ROC curves of VFA for metabolic risk stratification. (a,b) Men; (c,d) women.

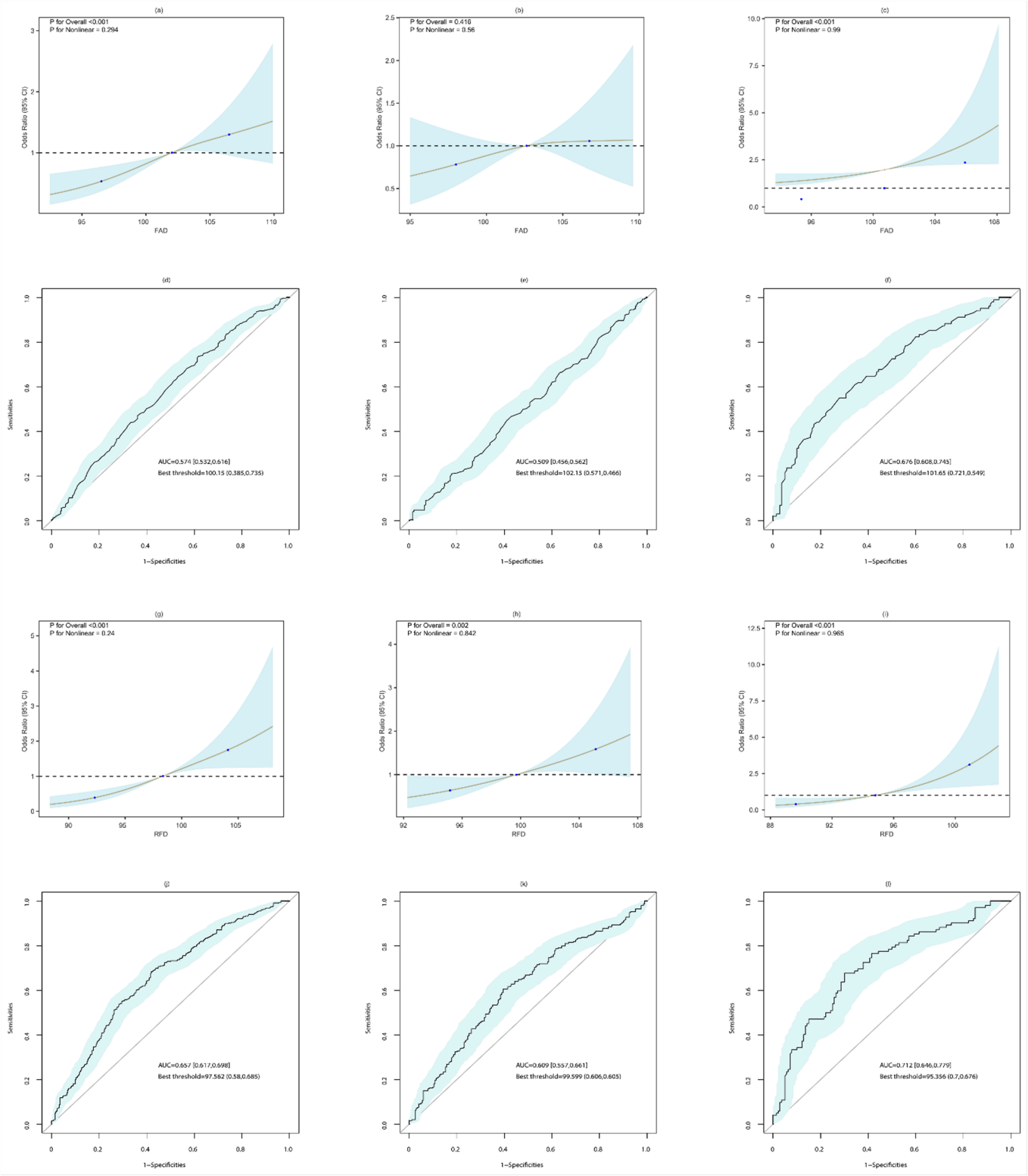


Figure 2

RCS and ROC analyses of FAD and RFD in obese participants. (a,d) FAD in all obese participants; (b,e) FAD in obese men; (c,f) FAD in obese women; (g,j) RFD in all obese participants; (h,k) RFD in obese men; (i,l) RFD in obese women.