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Non-linear relationship between relative fat mass and diabetes risk in Japanese adults: a retrospective cohort study

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Background: Relative fat mass (RFM) represents a newly developed sex-specific anthropometric formula to estimate total body fat percentage. Nonetheless, research examining the correlation between RFM and the risk of diabetes remains scarce. This research assessed the link between RFM and DM risk within the Japanese demographic. Methods: From 2004 to 2015, 15,462 Japanese individuals without diabetes underwent physical evaluations at Murakami Memorial Hospital. The relationship between RFM and the onset of diabetes was analyzed separately using Cox proportional-hazards regression models. This study employed Cox proportional hazards regression incorporating cubic spline functions and smooth curve fitting to detect non-linear associations between RFM and new cases of diabetes, categorized by sex. Sensitivity analyses were performed to confirm the robustness of the link between RFM and incident diabetes. Results: After controlling for confounding factors, a significant positive correlation between RFM and diabetes risk was found in women (HR: 1.13, 95%CI: 1.04–1.24, $P = 0.0061$), while the association in men was not statistically significant (HR: 1.05, 95%CI: 0.98–1.13, $P = 0.1511$). Additionally, a non-linear relationship between RFM and the incidence of diabetes was detected in both genders. The RFM threshold was identified at 39.23 for women and 23.08 for men. For women, HR was 1.11 (95%CI: 1.01–1.21) below the threshold and 1.39 (95%CI: 1.17–1.65) above it. In men, an RFM above 23.08 was positively related to diabetes risk (HR: 1.16, 95%CI: 1.06–1.28, $P = 0.0012$), whereas an RFM below this point did not show a significant association (HR: 0.98, 95%CI: 0.91–1.06, $P = 0.5899$). Conclusion: Our findings suggest a non-linear relationship and threshold effect between RFM and the risk of diabetes. These findings imply that maintaining RFM at lower levels may be beneficial in mitigating the onset of DM.

Keywords Relative fat mass, Adiposity, Waist circumference, Diabetes mellitus, Non-linear

Abbreviations

RFM	Relative fat mass
DM	Diabetes mellitus
BMI	Body mass index
WC	Waist circumference
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
GGT	Gamma-glutamyl transferase

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HDL-C	High-density lipoprotein cholesterol
TC	Total cholesterol
TG	Triglycerides
HbA1c	Glycosylated hemoglobin
FPG	Fasting plasma glucose
HR	Hazard ratio
SD	Standard deviation
CI	Confidence interval

Diabetes mellitus (DM) poses a significant global public health challenge, with its prevalence reaching epidemic proportions. The International Diabetes Federation reports that approximately 463 million adults currently have DM, a number projected to rise to 700 million by 2045[1]. The increasing burden of diabetes underscores the need to identify and understand modifiable risk factors to inform effective prevention and management strategies.

Obesity is a well-established risk factor for DM, accounting for roughly 90% of all cases[2]. Traditional obesity metrics, such as body mass index (BMI), are widely used in epidemiological studies but have notable limitations. BMI does not distinguish between fat and lean mass and overlooks fat distribution, which is crucial for assessing metabolic risk. Relative Fat Mass (RFM) is a novel anthropometric index developed by Woolcott and Bergman in 2018 as a response to the limitations of BMI[3]. RFM considers both height and waist circumference, offering a more nuanced assessment of body composition. It is calculated using a straightforward equation: RFM = 64 - [20 × (height/waist circumference)] for males, and RFM = 76 - [20 × (height/waist circumference)] for females[3]. This formula was derived from a large, diverse sample using dual-energy X-ray absorptiometry (DXA) as the reference standard. RFM provides a more accurate estimation of an individual's body fat percentage compared to traditional metrics like BMI[3]. Recent studies using RFM as an adiposity measure have demonstrated its predictive ability for dyslipidemia, severe liver disease, all-cause mortality, metabolic syndrome, hypertension, and cardiovascular disease[4–8]. However, except for one small sample study from the Netherlands, research on the relationship between RFM and diabetes is minimal[9]. No associations have been reported in the Japanese population, and the potential non-linear relationship between RFM and diabetes remains unexplored. To address this research gap, we conducted a large-sample retrospective cohort study to elucidate the relationship between RFM and diabetes mellitus among the Japanese.

Methods

Data source

This research utilized open-source data from the NAGALA (NAFLD in Gifu Area, Longitudinal Analysis) database, serving as a secondary analysis within a medical examination program. The center responsible for these programs, established in 1994, conducted over 8,000 medical examinations annually, with approximately 60% of participants undergoing one to two examinations per year. Owing to the high frequency of repeated examinations, the original study cohort included all individuals who participated in repeated examinations between 2004 and 2015. Researchers can freely obtain and access the original study data from the Dryad Digital Repository (https://datadryad.org/). This dataset (DOI: https://doi.org/10.5061/dryad.8q0p192) includes data from 15,464 participants who were free of diabetes at baseline[10]. Complying with Dryad's terms of service, we utilized this dataset for secondary analysis. Our research entailed a secondary examination of publicly accessible medical examination program data.

Study participants

Informed written consent was obtained from all participants during the primary study, which received approval from the Clinical Research Ethics Committee at Murakami Memorial Hospital[10]. Additionally, ethical approval for this study was granted by the Shenzhen Dapeng New District Nan'ao People's Hospital Ethics Committee. The research protocol adhered to the Helsinki Declaration's principles and was conducted in strict accordance with applicable regulations and guidelines.

We acquired data from a database made available by the Murakami Memorial Hospital in Japan, encompassing 20,944 participants who underwent medical examinations between 2004 and 2015. The exclusion criteria established in the initial research were as follows: (1) alcohol consumption over 60 g/day for men and 40 g/day for women, (2) presence of viral hepatitis, indicated by the detection of hepatitis B antigen or hepatitis C antibody at baseline, (3) usage of any medication at baseline, (4) diagnosed diabetes at baseline, (5) missing covariate data, (6) fasting plasma glucose levels of $\geq$6.1 mmol/L, and (7) unexplained withdrawal from the survey. Consequently, the original study included 15,464 participants. In our secondary analysis, we excluded an additional 2 subjects whose RFM was $\leq$0. Ultimately, our study's data analysis comprised 15,462 individuals, consisting of 8,428 males and 7,034 females (Fig. 1).

Covariates

Clinical expertise and previous research findings informed the selection of Covariates for this investigation[5,6,9,11–15]. The considered factors included: (1) continuous variables: triglycerides (TG), glycosylated hemoglobin (HbA1c), alanine aminotransferase (ALT), total cholesterol (TC), gamma-glutamyl transferase (GGT), FPG, systolic blood pressure (SBP), aspartate aminotransferase (AST), age, BMI, high-density lipoprotein cholesterol (HDL-C) diastolic blood pressure (DBP) and alcohol consumption; (2) categorical variables: smoking status, exercise habits, and gender. Participants' lifestyle and medical history details were collected using a standardized questionnaire from the initial study. Trained professionals accurately measured waist circumference (WC), weight, height, and blood pressure. The original research team gathered laboratory test results using a consistent protocol under controlled conditions.

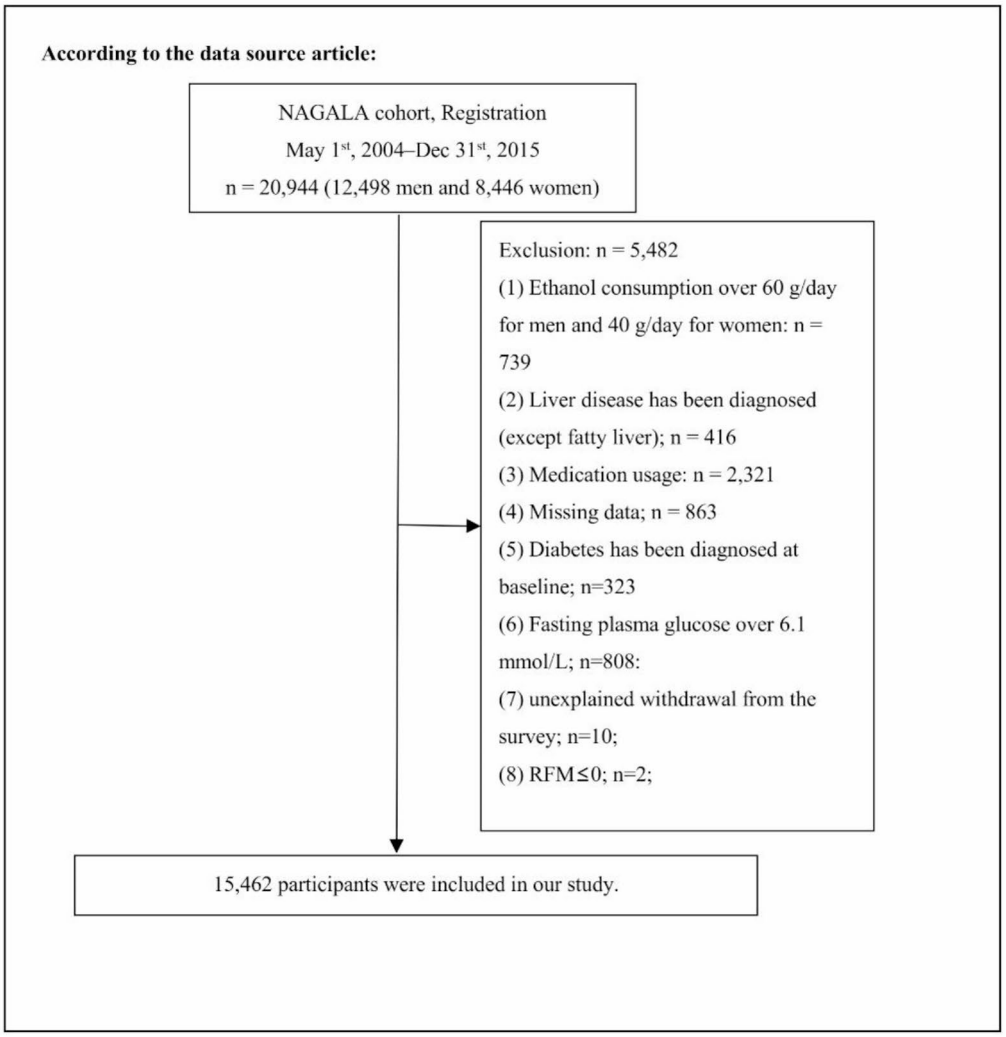

Fig. 1. Study population.

Relative fat mass

RFM is a recently developed anthropometric index designed to estimate an individual's body fat percentage based on their height and waist circumference. The RFM formula addresses several limitations associated with traditional BMI by emphasizing waist measurement, which is a more accurate indicator of adiposity and associated health risks. The formulas used to calculate RFM are gender-specific, reflecting physiological differences in fat distribution. For males, RFM is calculated as: RFM = 64-[20×height/waist circumference] for males, and RFM = 76-[20×height/waist circumference] for females[3,4,16,17].

Diagnosis of incident diabetes

Diabetes was diagnosed through one of the following criteria: fasting plasma glucose levels of 7 mmol/L or above, glycosylated hemoglobin levels of 6.5% or higher[18], or a self-reported diagnosis during the follow-up period.

Statistical analysis

We performed statistical analysis using Empower-Stats. Participants' characteristics were categorized by diabetes status. Continuous variables with skewed and normal distributions were presented as median (quartile) and mean ± standard deviation, respectively. Group differences were analyzed using the Wilcoxon rank-sum test (for skewed distributions), two-sample t-tests (for normal distributions), and the χ^2 test (for categorical variables).

Univariate Cox regression analysis evaluated the impact of individual variables on diabetes risk. Multivariate Cox regression analysis explored the specific association between RFM and DM risk. Model 1 was unadjusted. Model 2 adjusted for gender, age, BMI, alcohol intake, smoking status, exercise habits, SBP, and DBP. Model 3 included all adjustments from Model 2 plus TG, ALT, HbA1c, HDL-C, AST, FPG, GGT, and TC. Hazard ratios (HR) and 95% confidence intervals (CI) were meticulously documented.

Given that RFM is a continuous variable, we examined potential nonlinear relationships between RFM and DM using Cox proportional hazards regression with cubic spline functions and smooth curve fitting. If a nonlinear connection was identified, a two-piecewise Cox proportional hazards regression model was applied to determine the inflection point. Log-likelihood ratio analysis selected the most appropriate model for RFM and DM connection.

The validity of our findings was confirmed through sensitivity analyses. RFM was categorized by quartile, and a P-value for trend was calculated to validate the results from RFM as a continuous variable. Additional sensitivity analyses excluded individuals with hypertensive (SBP ≥ 140 mmHg and DBP ≥ 90 mmHg) or aged ≥ 65 years to evaluate RFM's association with diabetes risk. The study adhered to the STROBE statement for all outcomes[19]. Statistical significance was determined using two-tailed tests with a threshold of $P < 0.05$.

Results

Characteristics of participants

This study analyzed data from 15,089 participants without DM and 373 with DM. The average age of the cohort was 43.71 ± 8.90 years, with males comprising 54.51% of the sample. Table 1 presents the results, highlighting significant differences between non-DM and DM groups across various metrics. The DM group had notably higher levels of blood pressure, BMI, RFM, WC, alcoholic intake, age, AST, ALT, GGT, TC, TG, FPG, and HbA1c. Additionally, the DM cohort had a higher proportion of males, smokers, and drinkers. Conversely, the DM group showed reduced levels of HDL-C and a lower prevalence of regular exercise compared to the non-DM group.

Univariate analysis

The univariate analysis results are displayed in Table 2. The findings indicated that higher levels of DBP, SBP, age, WC, BMI, RFM, TG, HbA1c, TC, FPG, ALT, GGT, and AST, along with increased alcohol consumption and smoking, were associated with an elevated risk of diabetes. Conversely, HDL-C was inversely related to diabetes risk. Additionally, males exhibited a greater propensity for diabetes compared to females.

Figures 2 and 3 display Kaplan-Meier curves of diabetes likelihood, stratified by RFM quartiles according to sex. The probability of diabetes varied significantly among RFM groups in both genders (log-rank test, $P < 0.001$), with the risk progressively increasing with higher RFM levels. This trend suggests that individuals in the highest RFM quartile had the highest diabetes risk.

The incidence rate of DM

As illustrated in Table 1S, over a median follow-up period of 6.04 years, 373 participants developed DM. The cumulative incidence rates of DM were 3.99 per 1,000 person-years for the entire cohort, 2.10 for females, and 5.48 for males. The incidence rates were 2.41% for the overall study population, 1.24% for women, and 3.39% for men. Within the female subgroup, the cumulative incidence rates of DM for the four quartiles of RFM (Q1, Q2, Q3, Q4) were 0.52, 0.95, 1.52, and 5.91 per 1,000 person-years, respectively. Correspondingly, the incidence rates were 0.34%, 0.57%, 0.85%, and 3.18%. A significant positive correlation was observed between higher RFM values and increased incidence rates of DM in females. This pattern was similarly observed among male participants.

The connection between RFM and DM risk

Table 3 illustrates the Cox proportional hazards regression analysis, detailing the HR and 95%CI to elucidate the relationship between RFM and diabetes risk. The analysis includes three models: unadjusted (Model 1) and two adjusted (Models 2 and 3). A significant positive association was found between RFM and diabetes incidence in the unadjusted Model 1 (HR: 1.28, 95%CI: 1.22–1.33, $P < 0.0001$ for females; HR: 1.22, 95%CI: 1.18–1.26, $P < 0.0001$ for males). This association remained in Model 2, which adjusted for age, smoking status, BMI, alcohol intake, exercise habits, SBP, and DBP, with similar results (HR: 1.19, 95%CI: 1.09–1.30, $P < 0.0001$ for females; HR: 1.11, 95%CI: 1.04–1.18, $P = 0.0023$ for males). In Model 3, following adjustments for covariates from Model 2 along with TG, ALT, HbA1c, HDL-C, AST, FPG, GGT, and TC, the HR for the relationship between RFM levels and diabetes risk was 1.13 for females and 1.05 for males (HR: 1.13, 95%CI: 1.04–1.24, $P = 0.0061$ for females; HR: 1.05, 95%CI: 0.98–1.13, $P = 0.1511$ for males).

We also transformed RFM from continuous data to a definite format and incorporated it into Model 3. Compared to the Q1 reference group of RFM, the HR (95% CI) for the Q2, Q3, and Q4 groups were 0.72 (0.51–

Baseline characteristic	Non-DM	DM	*P*-value
Participants	15,089	373	
Gender			< 0.001
Female	6947 (46.04%)	87 (23.32%)	
Male	8142 (53.96%)	286 (76.68%)	
Age(years)	43.62 ± 8.89	47.14 ± 8.52	< 0.001
Alcoholic intake (g/wk)	1 (0–60)	4.20 (0–90)	0.006
Smoking status			< 0.001
Never-smoker	8886 (58.89%)	145 (38.87%)	
Ex-smoker	2874 (19.05%)	77 (20.64%)	
Current-smoker	3329 (22.06%)	151 (40.48%)	
Exercise habits			0.048
No	12,432 (82.39%)	322 (86.33%)	
Yes	2657 (17.61%)	51 (13.67%)	
SBP (mmHg)	114.31 ± 14.91	122.03 ± 15.59	< 0.001
DBP (mmHg)	71.44 ± 10.47	77.18 ± 10.23	< 0.001
BMI (kg/m^2)	22.05 ± 3.07	25.03 ± 3.82	< 0.001
WC (cm)	76.26 ± 8.97	85.08 ± 10.20	< 0.001
RFM	25.75 ± 6.75	27.14 ± 6.82	< 0.001
ALT (IU/L)	17 (13–23)	24 (18–39)	< 0.001
AST (IU/L)	17 (14–21)	20 (16–26)	< 0.001
GGT (IU/L)	15 (11–22)	24 (17–36)	< 0.001
HDL-C (mmol/L)	1.47 ± 0.40	1.19 ± 0.33	< 0.001
TG (mmol/L)	0.72 (0.49–1.11)	1.21 (0.86–1.93)	< 0.001
TC (mmol/L)	5.12 ± 0.86	5.43 ± 0.90	< 0.001
HbA1c (%)	5.16 ± 0.32	5.53 ± 0.37	< 0.001
FPG (mmol/L)	5.15 ± 0.41	5.61 ± 0.36	< 0.001

Table 1. The baseline characteristics of participants. Values are n (%) or mean ± SD or median (quartile) RFM: relative fat mass; BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyl transferase; HDL-C: high-density lipoprotein cholesterol; TC: total cholesterol; TG: triglycerides; HbA1c: hemoglobin A1c; FPG: fasting plasma glucose

1.03), 0.96 (0.63–1.47), and 1.18 (0.58–2.39), respectively, indicating no statistically significant relationship between categorically transformed RFM and diabetes.

The analyses of the non-linear relationship

Figure 4 illustrates the nonlinear connection between RFM and DM risk. Table 4 further highlights this nonlinear association in both male and female cohorts after adjusting for confounders. This research applied a segmented Cox proportional hazards regression model to determine the inflection points for RFM, which were 39.23 in females and 23.08 in males (P for log-likelihood ratio test = 0.009 for females, 0.002 for males). For females, the HR was 1.11 (95% CI: 1.01–1.21) to the left of the inflection point, increasing to 1.39 (95% CI: 1.17–1.65) to the right. In males, the RFM exceeding 23.08 demonstrated a positive association with diabetes risk (HR: 1.16, 95% CI: 1.06–1.28), whereas an RFM below 23.08 did not show a statistically significant correlation (HR: 0.98, 95% CI: 0.91–1.06).

Sensitive analysis

We conducted sensitivity analyses on participants under 65 to validate our findings, carefully adjusting for multiple potential confounders. The results confirmed a nonlinear relationship between RFM and diabetes risk in both sexes (Table 5, Model 4). We refined our analysis by excluding individuals with hypertension (SBP ≥ 140 mmHg or DBP ≥ 90 mmHg). After applying similar adjustments for confounding variables, we observed similar results in both females and males (Table 5, Model 5).

Discussion

In this retrospective cohort study, we identified a correlation between elevated RFM and incident diabetes in females after adjusting for confounding factors. The analysis revealed a nonlinear relationship between RFM levels and diabetes onset, differentiated by gender, with inflection points at 39.23 for females and 23.08 for males. Sensitivity analyses further validated the robustness of these findings.

The prevalence of diabetes has been rising globally in recent decades, placing significant economic strain on national healthcare systems[20,21]. Obesity is a major risk factor for diabetes development[22]. Although BMI

	Statistics	HR (95% CI)	*P* value
Gender			
Female	7034 (45.492%)	ref	
Male	8428 (54.508%)	2.522 (1.984, 3.207)	< 0.0001
Age(years)	43.709 ± 8.898	1.056 (1.044, 1.069)	< 0.0001
Alcoholic intake (g/wk)	47.741 ± 82.321	1.002 (1.001, 1.003)	0.0012
Smoking status			
Never-smoker	9031 (58.408%)	ref	
Ex-smoker	2951 (19.085%)	1.655 (1.255, 2.182)	0.0004
Current-smoker	3480 (22.507%)	2.583 (2.056, 3.244)	< 0.0001
Exercise habits			0.0641
No	12,754 (82.486%)	ref	
Yes	2708 (17.514%)	0.756 (0.563, 1.016)	
SBP (mmHg)	114.497 ± 14.974	1.032 (1.026, 1.037)	< 0.0001
DBP (mmHg)	71.581 ± 10.506	1.049 (1.040, 1.058)	< 0.0001
BMI (kg/m^2)	22.117 ± 3.127	1.242 (1.216, 1.268)	< 0.0001
WC (cm)	76.475 ± 9.098	1.093 (1.083, 1.103)	< 0.0001
RFM	25.788 ± 6.758	1.044 (1.028, 1.060)	< 0.0001
ALT (IU/L)	19.989 ± 14.344	1.006 (1.005, 1.007)	< 0.0001
AST (IU/L)	18.401 ± 8.642	1.008 (1.006, 1.010)	< 0.0001
GGT (IU/L)	20.309 ± 18.136	1.011 (1.009, 1.013)	< 0.0001
HDL-C (mmol/L)	1.461 ± 0.404	0.148 (0.109, 0.202)	< 0.0001
TG (mmol/L)	0.912 ± 0.655	1.798 (1.681, 1.923)	< 0.0001
TC (mmol/L)	5.126 ± 0.864	1.493 (1.342, 1.661)	< 0.0001
HbA1c (%)	5.172 ± 0.322	54.273 (39.491, 74.588)	< 0.0001
FPG (mmol/L)	5.161 ± 0.413	25.377 (18.710, 34.421)	< 0.0001

Table 2. The results of the univariate analysis.

is commonly used to diagnose obesity, it has limitations as it cannot differentiate between weight gain due to muscle and that due to fat[23]. Recently, RFM has been a novel metric for estimating body fat percentage based on sex, WC, and height. RFM emerged as the most accurate and user-friendly measure in a comprehensive analysis of 365 anthropometric metrics[3]. In recent years, RFM has garnered increasing attention, with numerous studies demonstrating its close association with diabetes mellitus, dyslipidemia, metabolic syndrome, severe liver disease, hypertension, and cardiovascular disease[4–9]. In a cross-sectional study including 20,167 patients, RFM was more predictive of various dyslipidemias and metabolic syndrome than BMI[6]. In a cross-sectional study including 3,406 individuals from China, RFM was strongly associated with hypertension risk after adjusting for confounders (HR:2.032, 95%CI: 1.567–2.634)[4]. Furthermore, a prospective longitudinal study from the Netherlands involving 7,961 participants found that a one-unit increment in RFM corresponded to a 119% higher risk of DM (HR:2.19, 95%CI: 1.96–2.44) after adjusting for prevalent hypertension, smoking, age, sex, and family history of diabetes[9]. This retrospective analysis demonstrated a gender-specific correlation between RFM and diabetes incidence. A significant positive association was observed in females, whereas male subjects exhibited no statistically meaningful relationship. After adjusting for confounding factors, each unit increase in RFM raised the diabetes risk by 13% in females. Sensitivity analyses confirmed the robustness of these findings, demonstrating a consistent link between RFM and diabetes risk. These results provide clinical guidelines for RFM-level interventions to reduce diabetes risk.

This study was the first to examine the nonlinear connection between RFM and diabetes across genders. After controlling for confounding covariates, the smooth curve analysis revealed a nonlinear relationship in both sexes. Using a two-piecewise Cox proportional hazards regression model, we identified RFM inflection points: 39.23 for females and 23.08 for males. In females, a one-unit increment in RFM below 39.23 was associated with an 11% increase in diabetes risk (HR: 1.11, 95% CI: 1.01–1.21), while above 39.23, the risk increased by 39% (HR: 1.39, 95% CI: 1.17–1.65). In males, RFM above 23.08 correlated with a 16% increase in diabetes risk (HR: 1.16, 95% CI: 1.06–1.28), whereas RFM below 23.08 showed no significant correlation (HR: 0.98, 95% CI: 0.91–1.06). Therefore, our findings suggest that maintaining lower RFM levels can reduce the risk of diabetes.

The relationship between RFM, a metric that accounts for body fat percentage, and the development of diabetes is not well understood. This association may be linked to excess fatty tissue's metabolic and inflammatory effects. Adipose tissue, particularly visceral fat, secretes a variety of bioactive molecules known as adipokines and inflammatory cytokines, which can induce insulin resistance and impair glucose metabolism[24]. Adipose tissue contributes to chronic low-grade inflammation, affecting the signal transduction pathways of neighboring cells, including eosinophils, macrophages, B-regulatory cells, and T cells (including invariant natural killer cells)[25]. These interactions further exacerbate metabolic disturbances, leading to pancreatic β-cell dysfunction, reduced insulin sensitivity, and ultimately contribute to the development of diabetes[26].

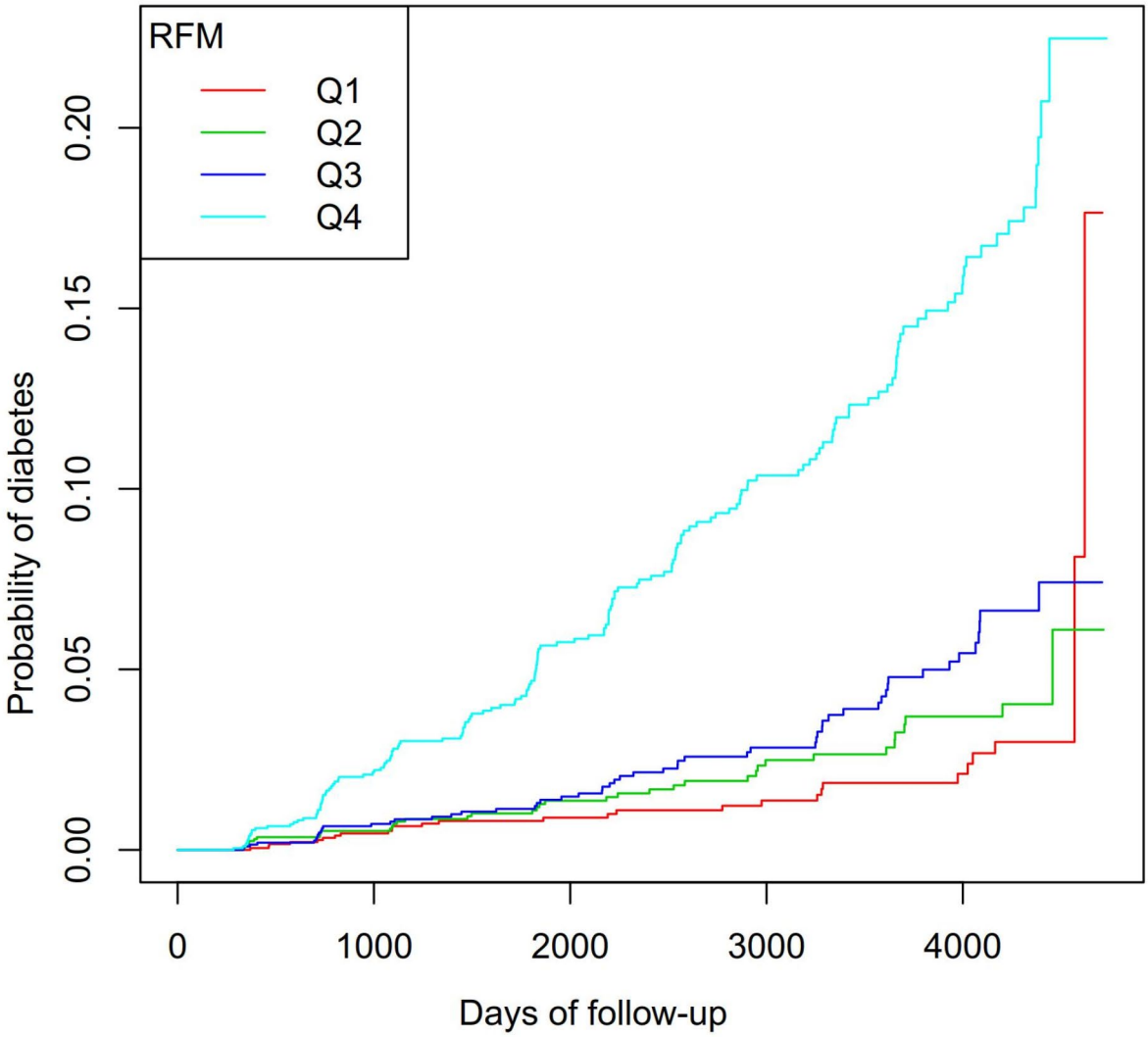

Fig. 2. Kaplan–Meier event-free survival curve. Kaplan–Meier analysis of incident diabetes based on RFM quartiles in males (log-rank, $P < 0.0001$).

Our study has several notable strengths. Firstly, we identified the nonlinear relationship between RFM and diabetes, accurately pinpointing the optimal inflection point for RFM's impact on diabetes by gender. Secondly, our results underwent rigorous statistical adjustments to minimize confounding effects, enhancing their credibility. Thirdly, the robustness of our conclusions was confirmed through sensitivity analyses, which included transforming RFM and reevaluating the RFM-diabetes relationship after excluding participants with a BMI ≥ 24 kg/m^2 or hypertension.

However, this investigation has some limitations. Firstly, the investigation was limited to the Japanese population, restricting the generalizability of our findings to other ethnic and geographical groups. Secondly, the original research excluded individuals with ≥ 6.1 mmol/L those with viral hepatitis, those exhibiting excessive alcohol consumption, those using any medications at baseline, and those with missing covariate data. Such exclusion criteria may have influenced the representativeness of the sample. In future research, we aim to design a study that includes a more diverse population with a larger sample size to validate our findings and enhance their generalizability. Thirdly, as with all retrospective studies, unmeasured or uncontrolled confounding variables, such as dietary patterns or family history of diabetes, could influence our results despite efforts to account for known covariates. Fourthly, In the original study upon which our secondary analysis is based, participants with impaired fasting glucose (IFG) were excluded, and data on glucose tolerance tests or glycated hemoglobin levels were not available. Consequently, we were unable to identify or include individuals with impaired glucose tolerance (IGT) or IFG in our current analysis. In the future, we will undertake future research that will include

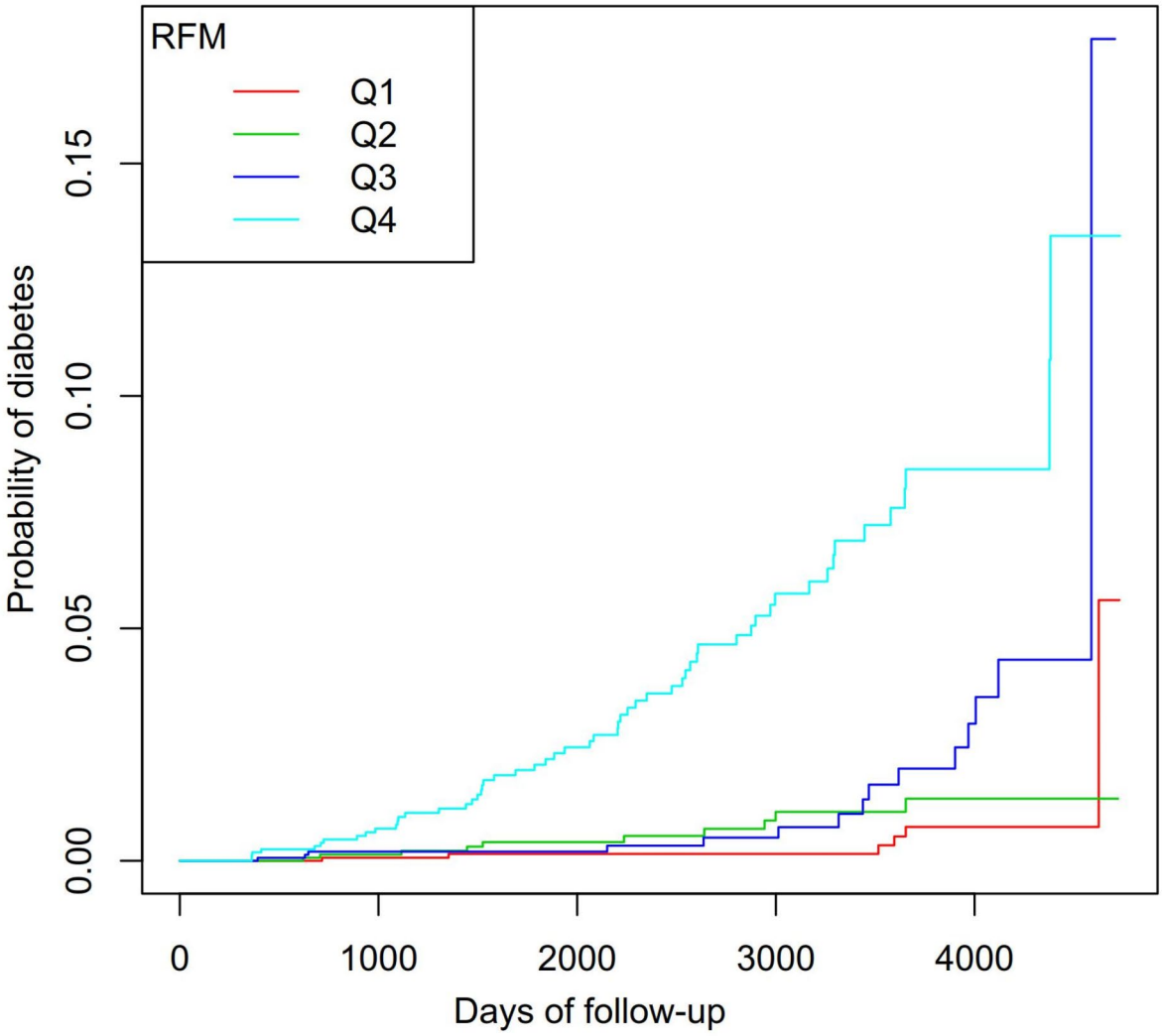

Fig. 3. Kaplan–Meier event-free survival curve. Kaplan–Meier analysis of incident diabetes based on RFM quartiles in females (log-rank, $P < 0.0001$).

participants with both IFG and IGT. This will enable a more comprehensive evaluation of the risk associated with RFM during these intermediary stages. Lastly, our study measured baseline WC and height without considering changes over time. Future research should include more comprehensive monitoring of confounding factors, including fluctuations in WC and height during follow-up, to explore the impact of changes in RFM on future diabetes risk.

Conclusion

Our study elucidated a nonlinear relationship and threshold effect between RFM and diabetes risk, stratified by gender. Specifically, we observed that RFM levels exceeding 39.23 were strongly associated with an increased risk of diabetes in females. In contrast, in males, only RFM levels above 23.08 were linked to an elevated risk of diabetes. These findings underscore the critical importance of maintaining lower RFM levels as a strategy to mitigate diabetes risk, thereby providing a theoretical foundation for targeted intervention measures.

	Variable	Model 1 (HR,95%CI, *P*)	Model 2 (HR,95% CI, *P*)	Model 3 (HR,95% CI, *P*)
All	RFM	1.24 (1.21, 1.27) < 0.0001	1.13 (1.08, 1.19) < 0.0001	1.08 (1.02, 1.14) 0.0055
	RFM (quartile)			
	Q1	ref	ref	ref
	Q2	2.01 (1.46, 2.76) < 0.0001	0.98 (0.69, 1.38) 0.9003	0.72 (0.51, 1.03) 0.0719
	Q3	5.19 (3.79, 7.11) < 0.0001	1.32 (0.87, 2.00) 0.1972	0.96 (0.63, 1.47) 0.8539
	Q4	19.03 (12.27, 29.53) < 0.0001	1.65 (0.84, 3.25) 0.1484	1.18 (0.58, 2.39) 0.6543
	P for trend	< 0.0001	0.1033	0.6038
Female	RFM	1.28 (1.22, 1.33) < 0.0001	1.19 (1.09, 1.30) < 0.0001	1.13 (1.04, 1.24) 0.0061
	RFM (quartile)			
	Q1	ref	ref	ref
	Q2	2.11 (0.76, 5.81) 0.1502	1.40 (0.50, 3.90) 0.5190	1.34 (0.48, 3.75) 0.5814
	Q3	3.59 (1.39, 9.29) 0.0084	1.61 (0.60, 4.29) 0.3442	1.28 (0.47, 3.49) 0.6335
	Q4	14.42 (6.17, 33.68) < 0.0001	2.86 (1.04, 7.88) 0.0419	1.63 (0.56, 4.72) 0.3711
	P for trend	< 0.0001	0.0240	0.3942
Male	RFM	1.22 (1.18, 1.26) < 0.0001	1.11 (1.04, 1.18) 0.0023	1.05 (0.98, 1.13) 0.1511
	RFM (quartile)			
	Q1	ref	ref	ref
	Q2	1.40 (0.86, 2.30) 0.1791	0.96 (0.58, 1.60) 0.8867	0.60 (0.36, 1.01) 0.0547
	Q3	1.99 (1.26, 3.15) 0.0034	0.97 (0.59, 1.59) 0.9002	0.50 (0.30, 0.85) 0.0107
	Q4	6.09 (4.05, 9.15) < 0.0001	1.76 (1.04, 3.00) 0.0367	0.82 (0.47, 1.46) 0.5031
	P for trend	< 0.0001	0.0085	0.7088

Table 3. Relationship between RFM and incident diabetes in different models. Model 1: we did not adjust for any covariants. Model 2: we adjusted for gender, age, BMI, alcoholic intake, smoking status, exercise habits, SBP, and DBP. Model 3: we adjusted for gender, age, BMI, alcoholic intake, smoking status, exercise habits, SBP, DBP, ALT, AST, GGT, HDL-C, TC, TG, HbA1c, and FPG. Note: The models were not adjusted for gender variables in both male and female models. HR: hazard ratio; CI: confidence interval; Ref: Reference; RFM: relative fat mass.

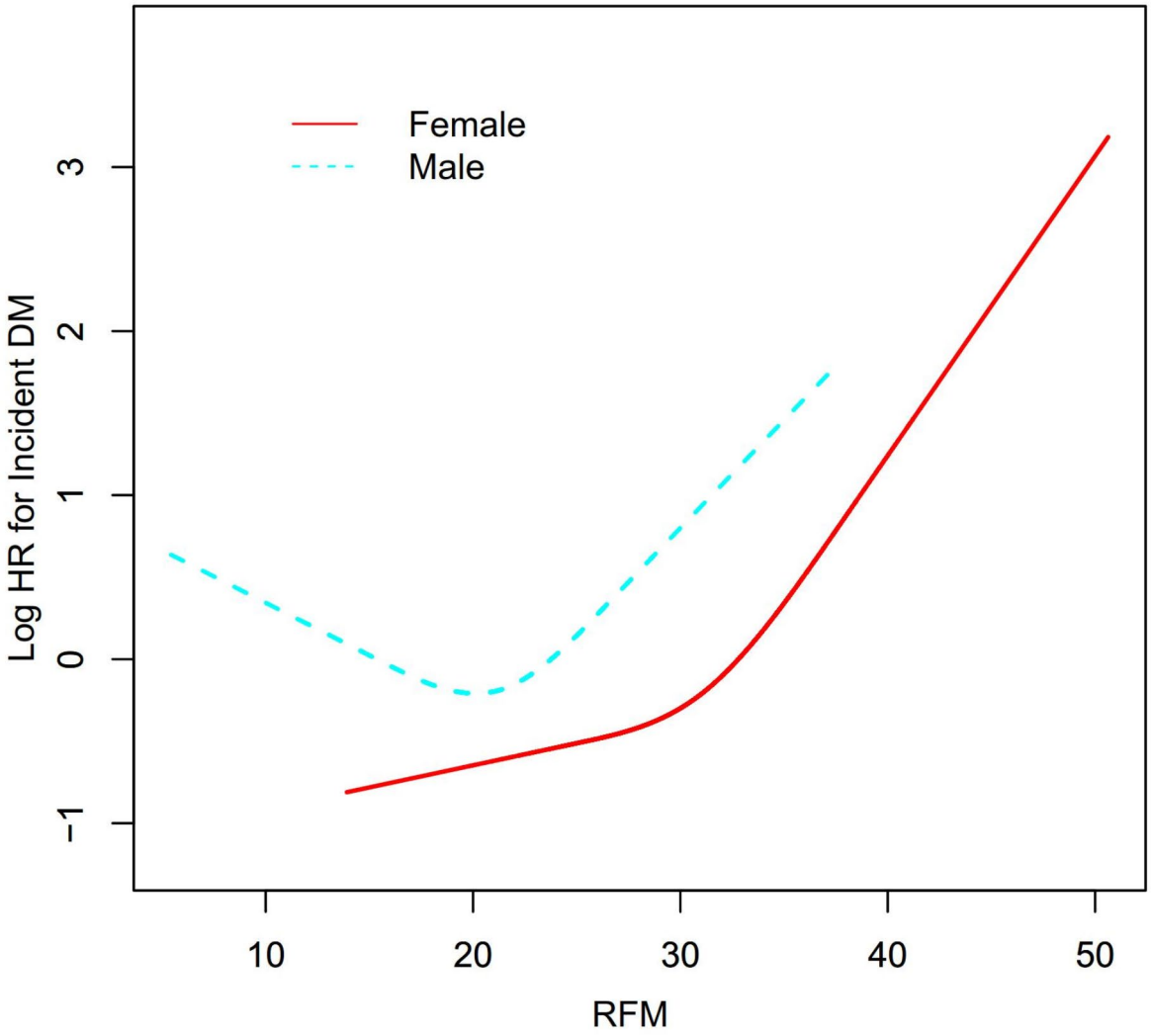

Fig. 4. The nonlinear relationship between RFM and incident diabetes stratified by gender. The nonlinear relationship was detected after adjusting for age, BMI, alcoholic intake, smoking status, exercise habits, SBP, DBP, ALT, AST, GGT, HDL-C, TC, TG, HbA1c, and FPG.

Incident DM	All participants (HR, 95%CI, *P*)	Female (HR, 95%CI, *P*)	Male (HR, 95%CI, *P*)
Fitting model by standard linear regression	1.08 (1.02, 1.14) 0.0055	1.13 (1.04, 1.24) 0.0061	1.05 (0.98, 1.13) 0.1511
Fitting model by two-piecewise Cox proportional hazards regression			
The inflection point of RFM	22.06	39.23	23.08
≤ Inflection point	0.97 (0.90, 1.05) 0.4941	1.11 (1.01, 1.21) 0.0256	0.98 (0.91, 1.06) 0.5899
> Inflection point	1.12 (1.06, 1.19) 0.0002	1.39 (1.17, 1.65) 0.0002	1.16 (1.06, 1.28) 0.0012
P for log-likelihood ratio test	0.002	0.009	0.002

Table 4. The result of the two-piecewise Cox proportional hazards regression model by gender. Note 1: In all participants, we adjusted gender, age, BMI, alcoholic intake, smoking status, exercise habits, SBP, DBP, ALT, AST, GGT, HDL-C, TC, TG, HbA1c, and FPG. Note 2: For female and male subgroups, we adjusted for age, BMI, alcoholic intake, smoking status, exercise habits, SBP, DBP, ALT, AST, GGT, HDL-C, TC, TG, HbA1c, and FPG. HR: hazard ratios; CI: confidence; DM: diabetes mellitus; RFM: relative fat mass

Incident DM	Female (HR, 95%CI, *P*)	Male (HR, 95%CI, *P*)	All participants (HR, 95%CI, *P*)
Model 4			
Fitting model by standard linear regression	1.15 (1.05, 1.27) 0.0026	1.06 (0.99, 1.13) 0.1181	1.08 (1.03, 1.14) 0.0033
Fitting model by two-piecewise Cox proportional hazards regression			
The inflection point of RFM	38.99	21.54	21.08
≤ Inflection point	1.12 (1.02, 1.23) 0.0141	0.95 (0.87, 1.04) 0.2724	0.96 (0.88, 1.05) 0.3448
> Inflection point	1.40 (1.18, 1.67) 0.0002	1.15 (1.05, 1.25) 0.0018	1.12 (1.06, 1.19) 0.0001
P for log-likelihood ratio test	0.011	0.002	0.003
Model 5			
Fitting model by standard linear regression	1.13 (1.03, 1.24) 0.0104	1.04 (0.97, 1.12) 0.2628	1.07 (1.01, 1.14) 0.0143
Fitting model by two-piecewise Cox proportional hazards regression			
The inflection point of RFM	38.66	23.29	22.29
≤ Inflection point	1.10 (1.00, 1.20) 0.0525	0.97 (0.89, 1.05) 0.4154	0.97 (0.89, 1.05) 0.3934
> Inflection point	1.42 (1.19, 1.68) < 0.0001	1.17 (1.06, 1.29) 0.0025	1.12 (1.05, 1.19) 0.0005
P for log-likelihood ratio test	0.003	0.001	0.001

Table 5. The relationship between RFM and incident diabetes is analyzed using a two-piecewise Cox proportional hazards regression model in different sensitivity analyses. Model 4 was a sensitivity analysis in participants with age < 65 years. Model 5 was a sensitivity analysis conducted on participants with SBP < 140mmHg and DBP < 90mmHg. Note 1: In all participants, we adjusted gender, age, BMI, alcoholic intake, smoking status, exercise habits, SBP, DBP, ALT, AST, GGT, HDL-C, TC, TG, HbA1c, and FPG. Note 2: For female and male subgroups, we adjusted for age, BMI, alcoholic intake, smoking status, exercise habits, SBP, DBP, ALT, AST, GGT, HDL-C, TC, TG, HbA1c, and FPG. HR: hazard ratios; CI: confidence; DM: diabetes mellitus; RFM: relative fat mass

Data availability

The raw data can be downloaded from the 'DATADRYAD' database (www.Datadryad.org). Dryad Digital Repository. https://datadryad.org/stash/dataset/doi:10.5061%2Fdryad.8q0p192.

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Author contributions

Binhui Xiao, and Changchun Cao contributed to the study concept and design, researched and interpreted the data, and drafted the manuscript. Yong Han, Haofei Hu, and Yongcheng He analyzed the data and reviewed the manuscript. Binhui Xiao and Changchun Cao oversaw the project's progress, contributed to the discussion and reviewed the manuscript. Yong Han, Yong Han, Haofei Hu, and Yongcheng He are the guarantors of this work and, as such, had full access to all the data in the study and took responsibility for the data's integrity and the data analysis's accuracy. All authors read and approved the final manuscript.

Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

In the initial study, informed written consent was obtained from all participants after receiving approval from the Clinical Research Ethics Committee at Murakami Memorial Hospital. In addition, the study has also been approved by the Ethics Committee of the Shenzhen Dapeng New District Nan'ao People's Hospital (2022082201) and was conducted under the ethical principles of the Declaration of Helsinki.

Additional information

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