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Association between stroke and relative fat mass: a cross-sectional study based on NHANES

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Abstract

Background This study was aimed at investigating the correlation between the occurrence of stroke and relative fat mass (RFM), a novel metric for determining total body fat.

Methods This cross-sectional study employed the National Health and Nutrition Examination Survey (NHANES) dataset, which encompassed the years 2005 to 2018 to assess the independent relationship between RFM and stroke. Moreover, multinomial logistic regression, subgroup analysis, smooth curve fitting, and interaction testing were also used.

Results This study included 35,842 participants and 1,267 (3.53%) of them were diagnosed with stroke. Fully adjusted Models showed that RFM was positively associated with stroke (odds ratio [OR] = 1.02; 95% confidence interval [CI] = 1.01–1.03). The odds of having a stroke in quartile 4 were significantly elevated by 44%, compared to quartile 1 (OR = 1.44,95%CI:1.09–1.90). In addition, a subgroup analysis also demonstrated that age and BMI significantly impacted the association between RFM and stroke (*P* for interaction<0.01).

Conclusions Elevated RFM is associated with increased odds of stroke, suggesting that RFM may have potential value in the prevention and management of stroke.

Keywords Relative fat mass, Stroke, Cardiovascular disease, NHANES, Obesity

Introduction

Stroke refers to a common neurological disorder arising from either diminished blood supply to the brain due to occlusion or stenosis, or from anatomical impairments in vascular tissues, which causes parenchymal bleeding and resultant neuronal damage [1]. Stroke is also the second most common reason for death worldwide and ranks third among factors that significantly impact mortality and disability. The frequency of strokes and stroke-related fatalities increased from 1990 to 2019; enhanced body mass index (BMI) was established as the stroke risk indicator with a fast rate of growth [2]. Stroke is a serious public health concern owing to its high morbidity, death, and disability rates, respectively [3].

Obesity is a major global health issue that is steadily increasing in frequency every year [4, 5]. Numerous conditions, like diabetes, cardiovascular disease (CVD), stroke, and non-alcoholic fatty liver disease, are linked to obesity [6]. Traditional obesity assessment indicators like BMI and waist circumference (WC) cannot effectively differentiate between body weight components like fat and muscle [7, 8]. Therefore, additional research is needed to explore novel scientific indicators of obesity

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like visceral adiposity index (VAI), waist-to-hip ratio (WHR), weight-adjusted waist index (WWI), etc [9–11]. Orison et al. proposed relative fat mass (RFM), a novel obesity index. Validated by dual-energy X-ray absorptiometry (DXA), it is a more accurate predictor of total body fat percentage for both sexes than the BMI. This is based on a waist-to-height ratio algorithm, which is simple and cross-racially validated [12]. Moreover, RFM is closely associated with several diseases, like hypertension, coronary artery disease (CAD), as well as type 2 diabetes mellitus (T2DM) [13–15].

Although previous studies have established a correlation between RFM and several diseases, its association with stroke is unclear. Thus, this cross-sectional study utilizes NHANES data to investigate the correlation between RFM and stroke.

Materials and methods

Study population

Conducted by the National Center for Health Statistics (NCHS), the Nutrition and Health Examination Survey (NHANES) is a continuous research project that collects health and nutrition data across the American population. NHANES implemented a complex, two-year cycle multi-stage stratified probability sampling procedure to ensure broadly representative sample data. All participants offered informed consent and the NCHS Ethics Committee officially authorized all research protocols. Access to all pertinent data is available at: https://www.cdc.gov/nchs/nhanes/.

This study investigated a dataset derived from the 2005–2018 NHANES survey, with an initial sample size of 70,190 participants. It excluded 30,442 participants with incomplete stroke data, 2,060 participants without height data, and 1,846 participants with missing WC data; all remaining participants were adults. Finally, 35,842 participants were involved in the analysis (Fig. 1).

Variables

Stroke

The Medical Condition Questionnaire (MCQ) self-report interview data provided information on stroke. The following question was asked: "Has a doctor or relevant health care professional ever told you directly that you have suffered from a stroke?" People who said "yes" were considered to have experienced a stroke, but those who said "no" were not.

Relative fat mass

The formula for calculating RFM is as follows: RFM = 64 - (20 × Height/WC) + (12 × Gender), where Genders 1 and 0 denoted females and males, respectively [12]. Height and WC were measured by the Mobile Examination Center (MEC) professionals. The iliac crests' superior border was the location for the measuring WC [16], while height was measured with a specialized height-measuring MEC device [17]. Both were measured in centimeters (cm).

Covariates

This study included the following covariates: age, gender, race, education level, marital status, Family Poverty Income Ratio (Family PIR), smoking and drinking status, diabetes, hypertension, CAD, total cholesterol (mg/dL), and BMI (kg/m^2). Specifically, a person's smoking status was characterized as either a nonsmoker (having smoked < 100 tobacco products in their lifespan) or a smoker (having smoked > 100 tobacco products in their lifetime) [18, 19].

Statistical analysis

The R (version 3.4.3) and EmpowerStats (version 2.0) were used to perform statistical analysis. A threshold of $P < 0.05$ denoted statistical significance. For continuous and categoric variables, mean ± standard deviation (SD) and percentages were used, respectively. To investigate disparities comparing the stroke and the non-stroke cohorts, t-tests and chi-square analysis were used for continuous and categorical variables, respectively. Using multivariate logistic regression analysis, the odds ratio (OR) and 95% confidence interval (CI) between stroke and RFM were calculated. Three distinct Models were formulated for multivariate analysis: Model 1 exhibited no variable adjustment; Model 2 included gender, age, and race adjustments while Model 3 was based on Model 2 and included education, marital status, Family PIR, total cholesterol, alcohol consumption, smoking, T2DM, and CAD adjustments. Additionally, a generalized additive model helped to create smooth curves and investigate the nonlinear connection between stroke and RFM. Furthermore, subgroup and interaction analyses were conducted with stratification factors like age, gender, and race. For missing values, imputation was performed using the mode or the median for categorical and continuous variables, respectively.

Results

Baseline characteristics

Totally 35,842 participants were included in the present study, and the mean age of participants was 49.15 ± 17.69 years, among which 48.62% were male and 51.38% were female. Among them, 1267 had stroke (3.53%). The mean RFM value of the patients was 35.67 ± 8.70, which was notably higher in stroke patients than in non-stroke patients, 37.63 ± 8.16 versus 35.60 ± 8.71, respectively. Participants who suffered a stroke were often older, non-Hispanic White, had less education, lived alone, smoked, had T2DM, hypertension, CAD, lower total cholesterol levels, consumed less alcohol, and had a lower Family

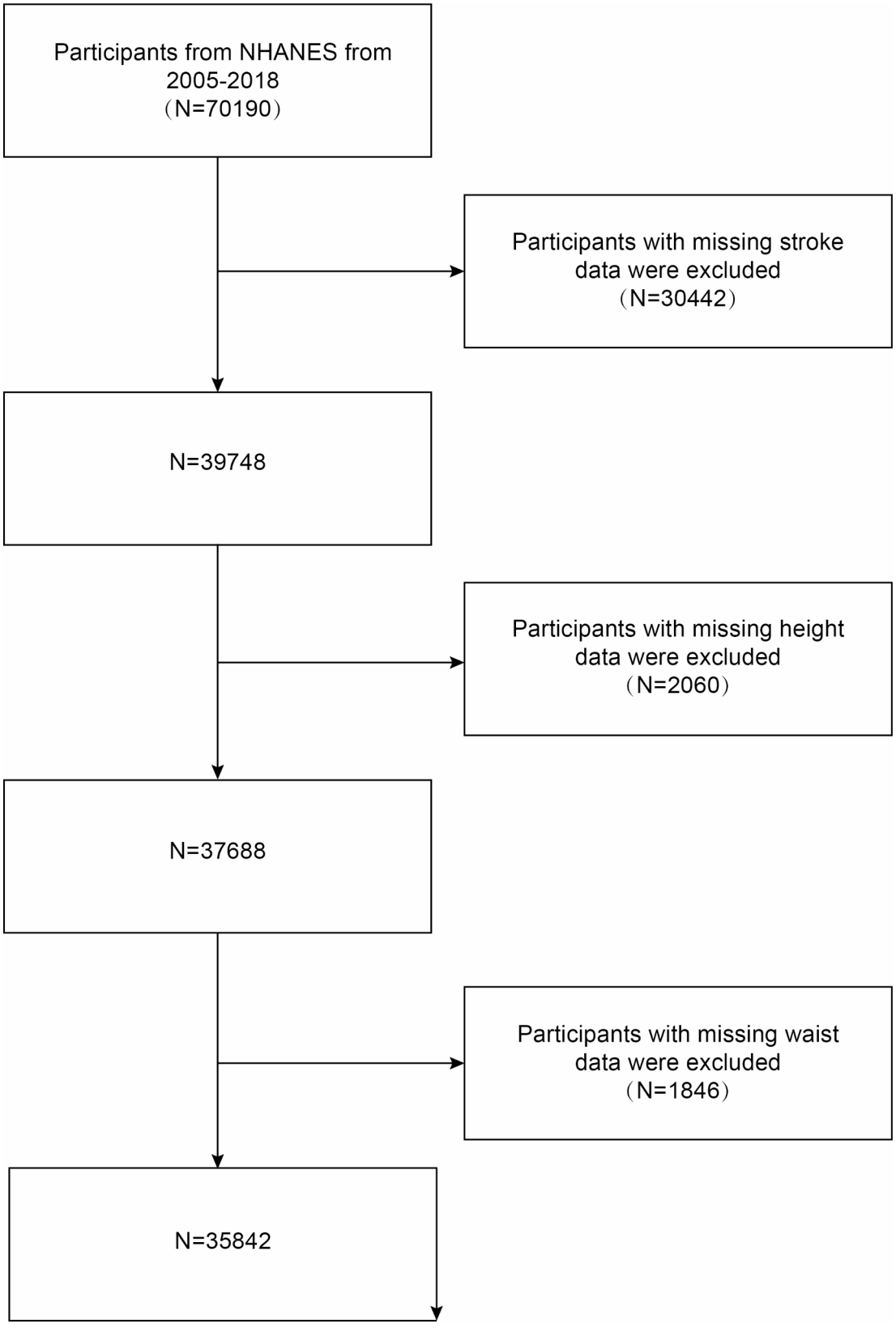

Fig. 1 Flow chart of participants selection

PIR, and a higher BMI, compared to those who did not experience a stroke (all $P<0.001$, Table 1).

Association of RFM with Stroke

A positive correlation between stroke and RFM scores in the crude (Model 1) and partially adjusted (Model 2) Models, respectively. This positive correlation was stable in the comprehensively refined Model 3 (OR = 1.02, 95% CI: 1.01–1.03). This indicated a 2% increase in the odds of stroke for each increment in the RFM score. The RFM was further converted from a continuous variable to a categorical variable (quartiles) for sensitivity analysis. The probabilities of suffering a stroke in quartile 4 of Model 3 were significantly greater than in quartile 1 by 44% (OR = 1.44,95%CI:1.09–1.90, Table 2). Furthermore, the P for trend = 0.0104 showed that elevated RFM leads to an increase in the odds of stroke. Additionally, smooth curve modeling demonstrated a positive relationship between RFM and stroke (Fig. 2).

Subgroup analyses

Using subgroup analysis and interaction testing, the correlation's robustness was evaluated. The outcomes demonstrated inconsistent relationships between the different subgroups. The correlation between RFM and stroke was significantly impacted by age and BMI (all P for interaction < 0.05). RFM values were significantly and positively correlated with stroke among participants who were male, aged 20–59, Non-Hispanic white, had a BMI of 25–29 kg/m², smoking (yes/no), non-diabetic, and non-coronary heart disease ($P<0.05$, Fig. 3).

Table 1 Baseline characteristics of patients with or without stroke

Characteristics	Total	Without stroke	With stroke	*P*-value
	N = 35,842	*N* = 34,575	*N* = 1267	
Age(years)	49.15 ± 17.69	48.56 ± 17.55	65.27 ± 13.21	< 0.001
Gender, n(%)				0.821
Male	17,427 (48.62%)	16,807 (48.61%)	620 (48.93%)	
Female	18,415 (51.38%)	17,768 (51.39%)	647 (51.07%)	
Race, n(%)				< 0.001
Non-Hispanic White	14,961 (41.74%)	14,344 (41.49%)	617 (48.70%)	
Non-Hispanic Black	7712 (21.52%)	7346 (21.25%)	366 (28.89%)	
Mexican American	5654 (15.77%)	5538 (16.02%)	116 (9.16%)	
Other Race	7515 (20.97%)	7347 (21.25%)	168 (13.26%)	
Education level, n(%)				< 0.001
< High school	8884 (24.79%)	8459 (24.47%)	425 (33.54%)	
High school	8212 (22.91%)	7865 (22.75%)	347 (27.39%)	
> high school	18,746 (52.30%)	18,251 (52.79%)	495 (39.07%)	
Marital status, n(%)				< 0.001
Living alone	14,301 (39.90%)	13,683 (39.57%)	618 (48.78%)	
Married or living with a partner	21,541 (60.10%)	20,892 (60.43%)	649 (51.22%)	
Smoking, n(%)				< 0.001
Never	19,903 (55.53%)	19,417 (56.16%)	486 (38.36%)	
Ever	15,939 (44.47%)	15,158 (43.84%)	781 (61.64%)	
Diabetes, n(%)				< 0.001
Yes	5287 (14.75%)	4815 (13.93%)	472 (37.25%)	
No	30,555 (85.25%)	29,760 (86.07%)	795 (62.75%)	
Hypertension, n(%)				< 0.001
Yes	12,597 (35.15%)	11,645 (33.68%)	952 (75.14%)	
No	23,245 (64.85%)	22,930 (66.32%)	315 (24.86%)	
Coronary heart disease, n(%)				< 0.001
Yes	1400 (3.91%)	1173 (3.39%)	227 (17.92%)	
No	34,442 (96.09%)	33,402 (96.61%)	1040 (82.08%)	
Total Cholesterol (mg/dL, mean ± SD)	193.25 ± 40.95	193.54 ± 40.75	185.46 ± 45.46	< 0.001
Drinking (mean ± SD)	2.94 ± 28.35	2.96 ± 28.36	2.38 ± 28.07	< 0.001
Family PIR (mean ± SD)	2.48 ± 1.56	2.50 ± 1.56	2.04 ± 1.34	< 0.001
BMI (kg/m², mean ± SD)	29.08 ± 6.80	29.06 ± 6.80	29.78 ± 6.68	< 0.001
RFM (mean ± SD)	35.67 ± 8.70	35.60 ± 8.71	37.63 ± 8.16	< 0.001

Abbreviation: BMI: body mass index; PIR: the ratio of income to poverty; RFM: relative fat mass

Table 2 Association between RFM and stroke

Exposure	Model 1 [OR (95%CI)]	Model 2[OR (95%CI)]	Model 3 [OR (95%CI)]
RFM	1.03 (1.02, 1.03) ***	1.04 (1.03, 1.06) ***	1.02 (1.01, 1.03) **
RFM			
Quartile 1	reference	reference	reference
Quartile 2	1.71 (1.43, 2.03) ***	1.35 (1.13, 1.62) ***	1.20 (0.99, 1.44)
Quartile 3	1.40 (1.17, 1.68) ***	1.57 (1.25, 1.98) ***	1.19 (0.94, 1.50)
Quartile 4	2.07 (1.75, 2.46) ***	2.30 (1.76, 3.01) ***	1.44 (1.09, 1.90) *
P for trend	< 0.0001	< 0.0001	0.0104

Abbreviation: RFM: relative fat mass. Model 1: adjusted for no covariates. Model 2: adjusted were race, gender, and age. Model 3: adjusted for age, gender, race, education, marital status, family PIR, total cholesterol, drinking, smoking, diabetes, and coronary heart disease. *$P<0.05$, ** $P<0.01$, *** $P<0.001$; a $P<0.05$ was considered statistically significant

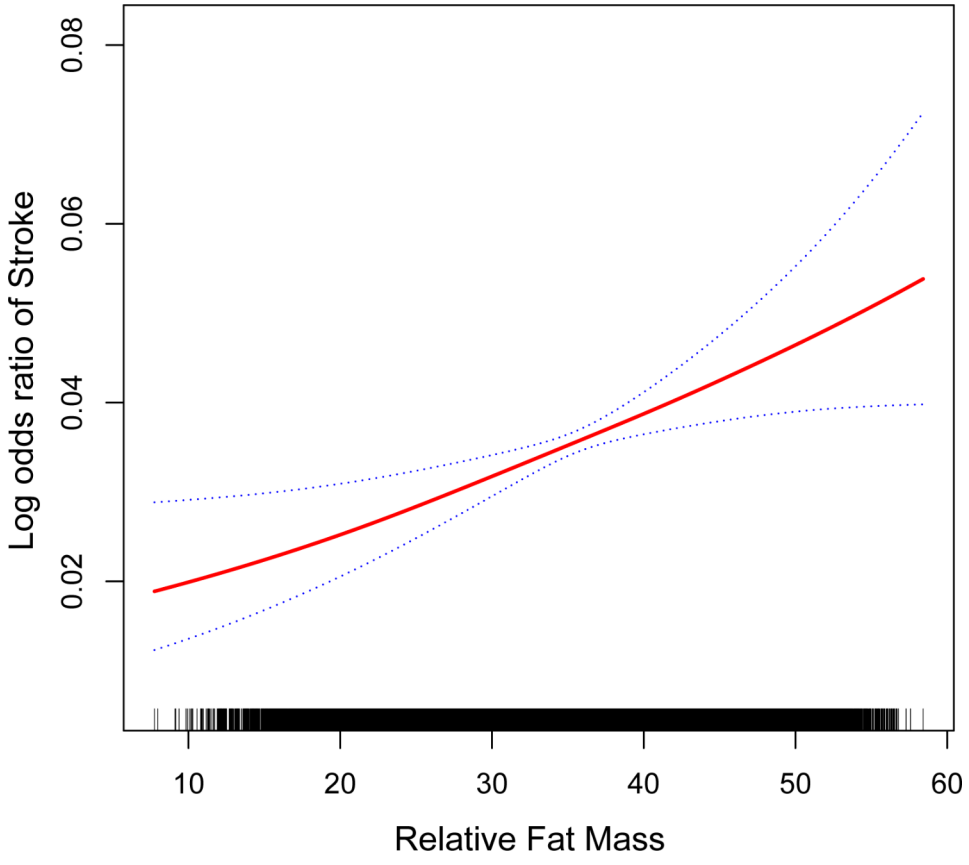

Fig. 2 Nonlinear association between RFM and stroke. The solid red line represents a smooth curve fit between the variables. Blue bars represent 95% confidence intervals for the fit results

Discussion

In this cross-sectional study involving 35,842 adults, individuals who experienced a stroke had significantly higher RFM scores than those who did not. Even after considering several confounding factors, a substantial positive correlation between RFM and the likelihood of stroke was noticed. Additionally, the association of RFM with stroke was impacted by age and BMI, thereby maintaining a positive relationship in individuals aged 20–59 or those with a BMI between 25 and 29 kg/m².

This study is the first to assess the association between RFM and stroke. Previous studies have investigated the association between RFM and CVD to emphasize the significance of RFM for cardiovascular health. Wang et al. found that an elevated RFM leads to abnormal metabolic markers, cardiovascular risk factors and increased CVD a prospective trial involving 26,754 participants. Additionally, a nonlinear correlation was observed between RFM and cardiovascular mortality. This indicated that when RFM levels exceeded the 30 and 45 threshold values for males and females, the cardiovascular death risk increased significantly [20]. In a longitudinal Chinese study, Peng et al. discovered that RFM can accurately predict hypertension occurrence among the Chinese

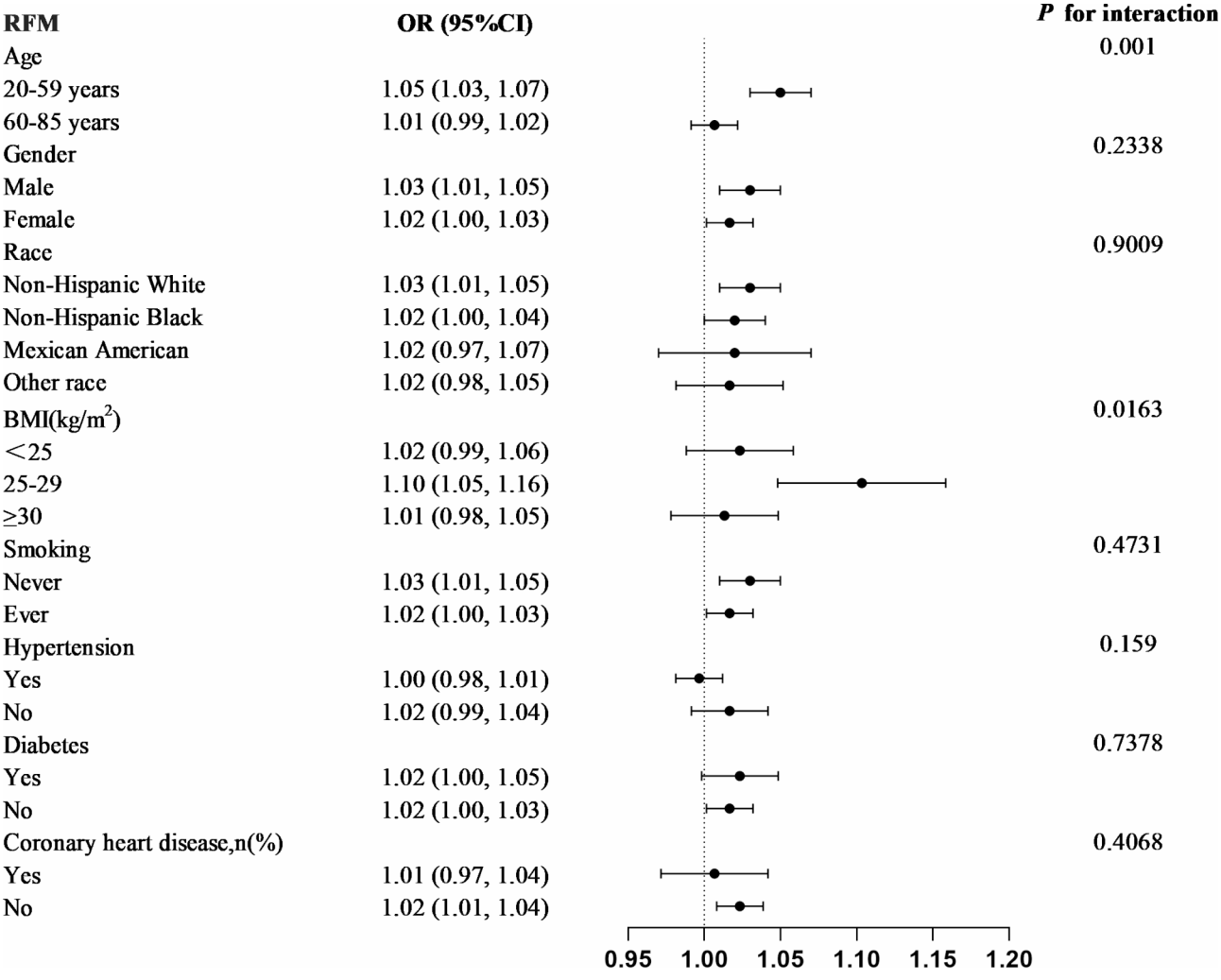

Fig. 3 Subgroup Analyses of Stroke and RFM

population. The optimal cut-off male and female RFM values were 24.67 and 35.73, respectively. Persons exceeding these cut-off values exhibited an increased risk of developing hypertension [13]. By examining 95,003 participants, Zwartkruis et al. discovered a significant correlation between RFM and CAD, heart failure (HF), and atrial fibrillation (AF). They also suggested that RFM can be a simple and intuitive marker for assessing obesity and cardiovascular risk in the general population [21]. Shen et al. suggested that RFM was significantly associated with CVD frequency in the general Chinese population, indicating that it might be used as an initial tool clinically for CVD screening [22]. The present study found that an elevated RFM being associated with increased chances of stroke is consistent with earlier studies describing the adverse consequences of RFM on cardiovascular health. Thus, this finding supports the hypothesis that RFM is an important indicator for assessing the odds of stroke and maintaining cardiovascular health.

Obesity is commonly associated with several risk factors for stroke, like hypertension, dyslipidemia, and T2DM. This makes obesity an important contributor to stroke and CVD [23]. Obesity and overweight individuals displayed an enhanced probability of ischemic stroke [24]. In a follow-up study on 26,815 Chinese adults, Liu et al. discovered that abdominal or generalized obesity degree was positively associated with the risk of stroke [25]. Cong et al. investigated a prospective cohort of 36,632 Chinese individuals to assess the correlation between the combined measurements of BMI and WC and the propensity for stroke occurrence. Their findings demonstrated that the coexistence of overweight status with abdominal obesity as well as the pairing of normal BMI and abdominal obesity was correlated with an enhanced stroke risk in male participants. Notably, excess weight with abdominal adiposity also increased the likelihood of stroke in females [26]. RFM, as a novel obesity indicator, reflects the total body fat percentage precisely, is easy to calculate, cost-effective, and simple to

use [27]. Additionally, RFM might be the strongest predictor of several CVDs. Suthahar et al. analyzed the associations between HF and several obesity indices in cohort research involving 8,295 Dutch participants. When compared to BMI, body roundness index (BRI), and WWI, they discovered that RFM has the strongest correlation with HF events [28]. The RFM score is a more reliable and consistent obesity measure than BMI for determining CAD severity, according to Efe et al. [14]. Corrêa et al. also found that RFM could identify excessive obesity more accurately than BMI in a cross-sectional study on 81 young men [29]. Kobo et al. carried out an observational cohort study on 20,167 participants, and their findings revealed that RFM exhibited superior predictive capabilities for various dyslipidemias and metabolic syndrome (MetS), compared to BMI [30]. Another Dutch study showed that RFM was significantly correlated with T2DM than traditional indicators like BMI, WC, and WHR [15]. Thus, RFM can more accurately assess stroke-related risk factors.

This study effectively exhibited the complex correlation between obesity and stroke. With a 2% increase in the odds of stroke for every unit increase in RFM, these results suggested that focusing on RFM levels may help prevent the onset and recurrence of stroke. The present study also found that the association between RFM and stroke differed significantly by age and BMI, maintaining a positive correlation in the 20–59 years or BMI 25–29 kg/m² groups. This may be due to the more active metabolic state of the young and middle-aged population, which is more sensitive to elevated RFM and is prone to triggering metabolic stress responses such as insulin resistance and elevated blood pressure. Early signs of these responses are key components of stroke risk factors, such as MetS and hypertension [31, 32]. Additionally, young and middle-aged populations typically face greater life stress and unhealthy lifestyles (e.g., unbalanced diets and physical inactivity) [33], which may contribute to elevated RFM and increase the likelihood of stroke. Adopting healthy lifestyle habits significantly reduces the risk of cardiovascular disease and stroke in obese individuals [23, 34]. Notably, the association between RFM and stroke in the BMI ≥ 30 kg/m² group was not as significant as in the BMI 25–29 kg/m² group, possibly because individuals in the latter group are not as concerned about their health status as those in the former. Due to the chronic state of obesity in the BMI ≥ 30 kg/m² group, individuals within this category may have adopted more extensive preventive measures (such as pharmacological interventions, dietary modifications, and physical exercise), potentially mitigating the impact of elevated RFM on the odds of stroke to some extent. Moreover, there may be additional confounding factors (e.g., comorbidities, medication use, etc.) in the BMI ≥ 30 kg/m² population that could influence the relationship between RFM and stroke. Thus, RFM may be a potential indicator of stroke prevention or management in people aged 20–59 years or with a BMI of 25–29 kg/m^2.

The relationship between RFM and stroke can be explained by several potential mechanisms. Firstly, enhanced RFM induces fat tissue malfunction and releases numerous pro-inflammatory cytokines, such as interleukin-6 (IL-6), leptin, lipocalin, and tumor necrosis factor-alpha (TNF-alpha). All these factors induce chronic low-level inflammation. Elevation of pro-inflammatory cytokines causes vascular endothelial dysfunction, insulin resistance, atherosclerosis [35–37], and generation of reactive oxygen species (ROS) [38]. Excessive ROS production can trigger oxidative stress, disrupt cellular signaling, damage DNA, lipids and proteins, lead to inflammation and apoptosis [39], and increase the risk of atherosclerosis [40]. Secondly, elevated ROS decreases nitric oxide (NO) bioavailability, and the vasculature-protecting perivascular adipose tissue (PVAT) is transformed into a source of pro-inflammatory factors. This leads to an endothelin-1/NO imbalance. Vessels undergo structural and functional damage due to the action of pro-inflammatory factors released by PVAT and their own oxidative stress, triggering endothelial dysfunction and thus increasing the risk of atherosclerosis and thrombosis [41]. Furthermore, abdominal fat accumulation causes adipocytes to release excessive free fatty acids (FFAs) and inflammatory mediators. These mediators interfere with the normal physiological functions of insulin, particularly mechanisms that impede insulin-induced NO release via endothelial cells, thereby affecting the dilation of skeletal muscle vasculature. Subsequently, this elicits insulin resistance, affects glucose metabolism, exacerbates FFA circulation, promotes systemic inflammatory responses, and significantly elevates the risks of CVDs [42–45]. Additionally, obesity elevates very low-density lipoprotein cholesterol, triglycerides, and total cholesterol levels, enhances the formation of numerous small low-density lipoprotein particles, and reduces high-density lipoprotein cholesterol levels. These dyslipidemic conditions represent crucial risk factors for atherosclerosis [46]. Moreover, obesity increases blood volume, cardiac output, and systemic vascular resistance. These changes can lead to higher blood pressure, adversely affect cardiac function [47]. In summary, RFM increases the odds of stroke in several ways by causing CVD and metabolic disorders, affecting vascular structure and function, and increasing the odds of other associated factors.

Strengths and limitations

This study's strength lies in the NHANES data, which used stratified multi-stage probability sampling to ensure its representativeness and reliability. In order to enhance results' generalizability, this study stratified analyses across several subgroups and adjusted exposure and outcome-related variables to obtain a more precise correlation between RFM and stroke. Nonetheless, the present study has a few limitations. Firstly, the inclusion criteria for stroke were solely based on self-reported stroke history, rather than on clinical diagnoses. Moreover, there was no detailed information about stroke's specific subtypes. Secondly, although this study adjusted for several confounding variables, it could not determine whether the observed relationships were affected by other confounding factors. Lastly, the study population included U.S. adults only and might not accurately reflect the situation in other topographical regions. Therefore, further studies are necessary to verify the applicability of the results of this study.

Conclusion

The findings of this study demonstrate a significant positive correlation between RFM and stroke, underscoring the potential benefits of stroke prevention through the management of RFM values. Since the results of the current study do not establish causality, further prospective studies are needed to confirm the association between RFM and stroke.

Abbreviations

RFM	relative fat mass
NHANES	National Health and Nutrition Examination Survey
BMI	body mass index
CVD	cardiovascular disease
WC	waist circumference
T2DM	type 2 diabetes mellitus
CAD	coronary artery disease
NCHS	National Center for Health Statistics
MCQ	Medical Condition Questionnaire
MEC	Mobile Examination Center
PIR	Poverty Income Ratio
SD	standard deviation
OR	odds ratio
CI	confidence interval
HF	heart failure
AF	atrial fibrillation
DXA	dual-energy X-ray absorptiometry
BRI	body roundness index
WWI	weight-adjusted waist index
MetS	metabolic syndrome
WHR	waist-to-hip ratio
IL-6	interleukin 6
TNF-alpha	tumor necrosis factor-alpha
ROS	reactive oxygen species
NO	nitric oxide
PVAT	perivascular adipose tissue
FFAs	free fatty acids
U.S.	United States

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Author contributions

YZ and CW designed the study. CH, JJ, YZ and HC collected the data. YZ analyzed the data. YZ and CH drafted the manuscript. YZ and WC revised the manuscript. All authors contributed to the article and approved the submitted version.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Ethical statement.

The portions of this study involving human participants, human materials, or human data were conducted in accordance with the Declaration of Helsinki and were approved by the NCHS Ethics Review Board. The participants provided their written informed consent to participate in this study.

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