Nested Case-Control Study on Different Anthropometric Measurements and Stroke Risk (Postprint)

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Abstract

Background: With China' s socioeconomic development, the prevalence of overweight/obesity has increased significantly, becoming a major public health problem. Currently, commonly used obesity assessment indices such as body mass index (BMI) and waist circumference (WC) cannot distinguish between subcutaneous fat and visceral fat, while visceral fat is closely associated with chronic diseases. Therefore, studying the correlation between novel anthropometric indices and stroke risk is of great significance.

Objective: To explore the correlation of different anthropometric indices with stroke occurrence and their predictive ability for stroke risk, aiming to provide evidence for community-based chronic disease health management and cardiovascular and cerebrovascular disease surveillance.

Methods: Based on the Pudong New Area Chronic Disease and Risk Factors Surveillance Cohort Study Project, a nested case-control study design was adopted. Participants who attended on-site surveys in 2016 and 2019 were selected and followed up until December 31, 2023. Stroke patients were designated as the case group, and non-stroke participants as the control group. Uniformly designed epidemiological questionnaires were used to collect general demographic data, past medical history, family history, and major risk factors for related diseases. Physical examination and laboratory test indicators were collected. Logistic regression models and restricted cubic spline (RCS) regression models were used to analyze the association between different anthropometric indices and stroke, and receiver operating characteristic (ROC) curves were used to evaluate the predictive ability of different anthropometric indices for stroke, with pairwise comparisons performed using DeLong' s test.

Results: Among the 15,440 participants included in the analysis, 930 developed stroke. For each unit increase in BMI, WC, BRI, and CVAI, the risk of stroke increased by 3.8% (OR=1.038, 95%CI=1.017~1.058), 1.2% (OR=1.012, 95%CI=1.004~1.020), 10.6% (OR=1.106, 95%CI=1.042~1.174), and 0.5% (OR=1.005, 95%CI=1.003~1.007), respectively (P<0.05). The RCS regression model found linear dose-response relationships between BMI, WC, and BRI and stroke risk (P_{overall}<0.05, P_{nonlinear}>0.05), and a non-linear dose-response relationship between CVAI and stroke risk (P_{overall}<0.001, P_{nonlinear}=0.009). ROC curve results showed that CVAI' s ability to predict stroke risk (AUC=0.66) was superior to BMI (Z=-12.713, P<0.001), WC (Z=-13.512, P<0.001), and BRI (Z=-8.696, P<0.001).

Conclusion: BMI, WC, BRI, and CVAI are associated with stroke risk. CVAI is superior to BMI, WC, and BRI in predicting stroke risk and can be used as an applicable indicator for stroke risk. This also suggests that community-level chronic disease health management should adopt comprehensive management, with proper weight management and focused attention on the impact of visceral obesity.

Full Text

Preamble

Correlation between Anthropometric Indices and Stroke Risk: A Nested Case-Control Study

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Abstract

Background: With socioeconomic development in China, the prevalence of overweight/obesity has risen significantly, becoming a major public health issue. Currently, commonly used obesity indicators such as body mass index (BMI) and waist circumference (WC) cannot differentiate between subcutaneous and visceral fat, while visceral fat is closely associated with chronic diseases. Therefore, exploring the correlation between novel anthropometric indices and stroke risk holds significant importance.

Objective: To investigate the correlation between different anthropometric indices and stroke incidence and their predictive capacity for stroke risk, aiming to provide evidence for community-based chronic disease health management and cardiovascular/cerebrovascular disease surveillance.

Methods: Based on the Pudong New Area Chronic Disease and Risk Factors Surveillance Cohort Study Project, we conducted a nested case-control study involving participants from the 2016 and 2019 field surveys, with follow-up through December 31, 2023. Individuals who developed stroke during follow-up were assigned to the case group, while those without stroke served as controls. Standardized epidemiological questionnaires were used to collect demographic data, medical history, family history, and major risk factors. Physical and laboratory examination indicators were also recorded. Logistic regression and restricted cubic spline (RCS) regression models were applied to analyze the correlation between anthropometric indices and stroke. Receiver operating characteristic (ROC) curves were used to evaluate predictive performance, with pairwise comparisons conducted via DeLong' s test.

Results: Among 15,440 study subjects included in the analysis, 930 developed stroke. For every one-unit increase in BMI, WC, body roundness index (BRI), and Chinese visceral adiposity index (CVAI), stroke risk increased by 3.8% (OR=1.038, 95%CI=1.017-1.058), 1.2% (OR=1.012, 95%CI=1.004-1.020), 10.6% (OR=1.106, 95%CI=1.042-1.174), and 0.5% (OR=1.005, 95%CI=1.003-1.007), respectively ($P<0.05$). The RCS regression model showed a linear dose-response relationship between BMI, WC, and BRI with stroke risk (P-total<0.05, P-non-linear>0.05), and a non-linear dose-response relationship between CVAI and stroke risk (P-total<0.001, P-non-linear=0.009). ROC curve results indicated that CVAI had the best predictive ability for stroke risk (AUC=0.66), outperforming BMI (Z=-12.713, $P<0.001$), WC (Z=-13.512, $P<0.001$), and BRI (Z=-8.696, $P<0.001$).

Conclusion: BMI, WC, BRI, and CVAI are correlated with stroke risk. CVAI is superior to BMI, WC, and BRI in predicting stroke risk and can serve as an applicable indicator. These findings underscore the need for comprehensive chronic disease management in community health programs, emphasizing weight control and the impact of visceral obesity.

Keywords: Stroke; Visceral fat; Nested case-control study; Logistic regression model; Risk prediction

Introduction

With China' s rapid economic and social development, significant changes have occurred in people' s lifestyles, dietary patterns, and habits, leading to a marked increase in overweight and obesity prevalence. Studies project that by 2030, the combined prevalence of overweight/obesity among Chinese adults will reach 65%, representing a major public health challenge. The World Health Organization recognizes obesity as a disease, and research demonstrates that overweight and obesity are associated with increased risks of coronary heart disease, stroke, diabetes, and other chronic conditions. Currently, China primarily uses body mass index (BMI) to diagnose overweight/obesity and waist circumference (WC) to diagnose central obesity. However, these indices cannot distinguish between subcutaneous and visceral fat, and evidence confirms that visceral fat is a risk factor for multiple chronic diseases. Consequently, researchers have proposed novel anthropometric indices in recent years, including body roundness index (BRI), visceral adiposity index (VAI), Chinese visceral adiposity index (CVAI), lipid accumulation product (LAP), and cardiometabolic index (CMI), providing new directions for exploring associations between visceral fat and chronic disease development and for formulating community-based chronic disease prevention strategies. This nested case-control study investigates the correlations between BMI, WC, BRI, VAI, CVAI, LAP, CMI and stroke risk, aiming to identify optimal predictors of stroke and provide evidence for community chronic disease health management, cardiovascular/cerebrovascular disease surveillance, and stroke prevention.

Methods

1.1 Study Subjects

Based on the Pudong New Area Chronic Disease and Risk Factors Surveillance Cohort Study Project, we employed a nested case-control design. Participants from the 2016 and 2019 field surveys were selected and followed up through December 31, 2023. Individuals who developed stroke during follow-up constituted the case group, while those without stroke served as controls. Subjects with missing physical examination or laboratory data, or for whom chronic disease status could not be determined, were excluded. The final analysis included 15,440 subjects, comprising 930 cases and 14,510 controls. This study was approved by the Ethics Committee of Shanghai Pudong New Area Center for Disease Control and Prevention (Ethics No.: PDCDCLL-20220718-001), and all participants provided informed consent.

1.2 Data Collection

1.2.1 Questionnaire Survey A standardized epidemiological questionnaire was administered by trained investigators to collect data on demographics, medical history, family history, and major disease risk factors.

1.2.2 Physical and Laboratory Examinations Trained investigators used calibrated equipment to measure height, weight, waist circumference, hip circumference, and blood pressure. Laboratory tests included homocysteine (Hcy), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), C-reactive protein (CRP), fasting plasma glucose (FPG), 2-hour postprandial glucose (2-hPG), and glycated hemoglobin (HbA1c).

1.2.3 Definitions and Diagnostic Criteria

1. **Hypertension:** Diagnosed by secondary or higher-level hospitals, or defined as systolic blood pressure (SBP) $ $140 mmHg and/or diastolic blood pressure (DBP) $ $90 mmHg on three separate occasions without antihypertensive medication (1 mmHg=0.133 kPa).
2. **Diabetes:** Diagnosed by secondary or higher-level hospitals, or defined as FPG $ $7.0 mmol/L or 2-hPG $ $11.1 mmol/L (venous plasma glucose).
3. **Stroke:** Self-reported during surveys or identified from Pudong New Area secondary or higher-level hospital data with ICD-10 codes I60-I64 (I60-I62: hemorrhagic stroke; I63: ischemic stroke/cerebral infarction; I64: unspecified stroke).
4. **Dyslipidemia:** Self-reported or based on blood samples meeting the Chinese Guidelines for Prevention and Treatment of Dyslipidemia in Adults (2016 revision): TC $ $6.22 mmol/L, TG $ $2.26 mmol/L, LDL-C $ $4.14 mmol/L, or HDL-C $ $1.04 mmol/L without lipid-lowering medication.
5. **Coronary Heart Disease:** Self-reported or diagnosed by secondary or higher-level hospitals.
6. **BMI:** BMI = weight (kg) / height (m)^2.
7. **BRI:** BRI = 364.2 - 365.5 × √{1 - [waist circumference (m) / (2π)]^2 × [0.5 × height (m)]^2}.
8. **VAI:** For men: VAI = {[waist circumference (cm)] / [39.68 + (1.88 × BMI)]} × (TG/1.03) × (1.31/HDL-C). For women: VAI = {[waist circumference (cm)] / [36.58 + (1.89 × BMI)]} × (TG/0.81) × (1.52/HDL-C).
9. **CVAI:** For men: CVAI = -267.93 + 0.68 × age + 0.03 × BMI + 4.00 × waist circumference (cm) + 22.0 × log(TG) - 16.32 × HDL-C. For women: CVAI = -187.32 + 1.71 × age + 4.23 × BMI + 1.12 × waist circumference (cm) + 39.76 × log(TG) - 11.66 × HDL-C.
10. **LAP:** For men: LAP = [waist circumference (cm) - 65] × TG. For women: LAP = [waist circumference (cm) - 58] × TG.
11. **CMI:** CMI = (TG/HDL-C) × WHtR, where WHtR (waist-to-height ratio) = waist circumference (cm) / height (cm). TG and HDL-C units are mmol/L.
12. **Marital Status:** Dichotomized as married versus other (including widowed/divorced/unmarried).
13. **Education Level:** Dichotomized as below junior high school versus junior high school and above.
14. **Sedentary Lifestyle:** Defined as total sitting time $ $6 hours/day.

15. **Smoking History:** Defined as having smoked at least one cigarette daily for six consecutive months.
16. **Overweight/Obesity:** 24 kg/m^2 $\leq$ BMI <28 kg/m^2 as overweight; BMI $ 28kg/m^{2}$ as obesity. For this study, subjects were grouped as BMI <18 kg/m^2, 18 $\leq$ BMI <24 kg/m^2, and BMI $ 24kg/m^{2}$.
17. **Triglyceride-Glucose Index (TyG):** TyG = ln[(TG × FPG)/2], with TG and FPG in mg/dL.

1.2.4 Quality Control Quality control was implemented throughout the study. Trained medical professionals conducted the surveys using calibrated instruments. Questionnaires were reviewed daily by designated personnel. Telephone follow-ups and audio recording reviews were performed for 20% of participants, achieving a 95% concordance rate. Data were centrally managed and standardized to create the Pudong New Area Chronic Disease and Risk Factors Database. Laboratory testing was performed by technicians from a Shanghai Clinical Laboratory Accreditation-qualified facility.

1.3 Statistical Analysis

R version 4.4.3 was used for statistical analysis with a significance level of α=0.05. Categorical data were described using percentages (%) and analyzed using chi-square tests. Quantitative data were tested for normality. Lipid profiles, glucose indices, blood pressure, TyG, Hcy, and anthropometric indices were non-normally distributed and described as median (P25, P75), with Mann-Whitney U tests used for group comparisons. Logistic regression models analyzed associations between anthropometric indices and stroke, calculating odds ratios (OR) with 95% confidence intervals (CI). RCS regression models explored non-linear relationships; P-total<0.05 and P-non-linear<0.05 indicated non-linear dose-response relationships. ROC curves evaluated predictive performance, with area under the curve (AUC) calculated and pairwise comparisons performed using DeLong' s test.

Results

2.1 Baseline Characteristics

The cohort included 15,440 subjects (14,510 without stroke, 930 with stroke) with a median age of 59.0 (49.0, 66.0) years and more females than males. Cases and controls differed significantly in age, marital status, education level, hypertension, diabetes, dyslipidemia, and coronary heart disease (P<0.05), but not in smoking history, gender, or sedentary lifestyle (P>0.05). The case group had higher TG, TC, LDL-C, FPG, 2-hPG, HbA1c, systolic blood pressure, and diastolic blood pressure, but lower HDL-C and CRP (P<0.05). During follow-up, 621 deaths occurred, including 53 attributed to stroke.

2.2 Comparison of Anthropometric Indices and Laboratory Findings

The case group showed significantly higher levels of TyG, Hcy, BMI, WC, BRI, VAI, CVAI, LAP, and CMI compared to controls (P<0.001) .

2.3 Logistic Regression Analysis of Anthropometric Indices and Stroke Risk

Using stroke occurrence as the dependent variable (0=no stroke, 1=stroke) and anthropometric indices as independent variables (continuous), univariate logistic regression showed associations between BMI, WC, BRI, VAI, CVAI, LAP, CMI and stroke (P<0.001). After adjusting for age, gender, hypertension, diabetes, coronary heart disease, dyslipidemia, education, marital status, smoking, sedentary lifestyle, TyG, and Hcy, multivariate analysis revealed that each one-unit increase in BMI, WC, BRI, and CVAI increased stroke risk by 3.8%, 1.2%, 10.6%, and 0.5%, respectively (P<0.05) .

RCS regression showed significant associations between BMI, WC, BRI, and CVAI with stroke risk. BMI, WC, and BRI demonstrated linear dose-response relationships, with stroke risk increasing as levels rose. CVAI showed a non-linear dose-response relationship (P-total<0.001, P-non-linear=0.009). No statistically significant associations were observed for VAI, LAP, or CMI (P-total>0.05) [Figure 1: see original paper].

2.4 ROC Curve Analysis for Stroke Risk Prediction

ROC curve analysis evaluated the predictive accuracy of anthropometric indices for stroke risk. CVAI demonstrated the highest predictive value (AUC=0.66), significantly outperforming BRI, BMI, and WC (all P<0.001). The optimal cutoff point for CVAI was 97.367, with sensitivity of 0.48 and specificity of 0.75. BRI' s AUC was greater than those of BMI and WC (P<0.001), while BMI and WC did not differ significantly (P=0.758) [Figure 2: see original paper], , .

Discussion

Stroke represents a major cause of mortality and disability globally and in China, constituting a significant public health challenge. Evidence confirms obesity as an independent risk factor for stroke, primarily through its contribution to hypertension, dyslipidemia, and diabetes—established stroke risk factors. This study compared seven anthropometric indices and found that after adjusting for confounders, BMI, WC, BRI, and CVAI were positively associated with stroke risk, with BMI, WC, and BRI showing linear dose-response relationships and CVAI demonstrating a non-linear relationship.

BMI is commonly used in China to evaluate obesity and investigate its relationship with various diseases. Consistent with our findings, domestic and international studies show stroke risk increases with BMI, mainly due to obesity-related metabolic abnormalities. However, some research indicates an inverse relationship between BMI and mortality/recurrence risk in ischemic stroke. WC is widely used to assess central obesity due to its simplicity, and most studies confirm its association with increased stroke risk. However, WC primarily reflects abdominal fat accumulation rather than visceral fat specifically, highlighting limitations of both BMI and WC in distinguishing between subcutaneous and visceral adiposity.

Multiple studies confirm visceral fat as a risk factor for chronic diseases. Visceral adipocytes are larger than subcutaneous adipocytes, richly vascularized, less insulin-sensitive, and more metabolically active, producing free fatty acids, adipokines, and inflammatory markers closely linked to type 2 diabetes, coronary heart disease, and stroke. This study introduced five novel indices—BRI, VAI, CVAI, LAP, and CMI—to explore visceral fat' s relationship with stroke risk.

BRI, derived from eccentricity theory by Thomas et al., is a geometric model based on height and waist circumference that estimates visceral fat content, with higher values indicating greater visceral fat accumulation. Most studies, including ours, confirm BRI' s positive association with stroke. CVAI, developed by Chinese researchers considering Chinese body fat distribution characteristics, incorporates age, WC, BMI, TG, and HDL-C to reflect adipose tissue dysfunction and cardiometabolic risk. Studies demonstrate CVAI' s superior value over BMI and WC in assessing metabolic risk. Our RCS analysis revealed a non-linear dose-response relationship between CVAI and stroke after confounder adjustment, consistent with some but not all previous research using CHARLS data—differences likely attributable to metabolic heterogeneity across populations and unadjusted factors.

ROC analysis of the four indices associated with stroke in our multivariate model showed CVAI had the best predictive performance (AUC=0.66). Chinese scholars have similarly found CVAI' s diagnostic efficacy superior to VAI, WC, and BMI for coronary heart disease with metabolic syndrome. Although CVAI showed the highest AUC in our study, its sensitivity was modest, possibly due to population structure and model selection. Future studies could employ machine learning methods like neural networks or random forests to develop more stable predictive models.

Other visceral fat indices—VAI, LAP, and CMI—consider height, waist circumference, weight, TG, HDL-C, and sex effects on fat distribution, with studies confirming their associations with stroke risk. Our study found higher VAI, LAP, and CMI levels in cases and associations in univariate analysis, but no statistical significance after multivariate adjustment. These composite indices assess both fat distribution and metabolic risk. Our population' s characteristics—more females, older age structure—may have created differential fat distribution patterns across sexes and ages, while underlying diseases and complex interactions among confounders may have obscured associations. Future research should target specific populations and optimize study designs.

In conclusion, BMI, WC, BRI, and CVAI correlate with stroke risk, with CVAI demonstrating superior predictive performance and serving as an applicable risk indicator. Community-based chronic disease management should adopt comprehensive strategies addressing obesity and dyslipidemia. Study limitations include lack of consideration for stroke recurrence and insufficient hemorrhagic stroke cases (n=51) to examine subtype-specific associations. Future prospective cohort studies with larger samples, dynamic anthropometric measurements, and optimized designs are needed to further explore visceral fat indices' impact on stroke and inform more effective chronic disease prevention strategies.

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