Association of Visceral Adiposity Index with Cardiovascular Disease in Postmenopausal Women: A Prospective Cohort Study Postprint

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Abstract

Background Cardiovascular disease represents a major threat to women's health, with postmenopausal women constituting a high-risk population. The decline in estrogen levels following menopause may promote visceral fat accumulation, which is closely associated with insulin resistance, chronic inflammatory responses, and lipid metabolism disorders, potentially increasing cardiovascular disease risk. However, research on the relationship between visceral adiposity indices and cardiovascular disease in postmenopausal women remains limited.

Objective To investigate the association between the Chinese Visceral Adiposity Index (CVAI) and cardiovascular disease in postmenopausal women, thereby informing preventive strategies.

Methods Using data from the China Health and Retirement Longitudinal Study (CHARLS) 2015–2020, we included 4,743 postmenopausal women aged $ $45 years without cardiovascular disease at baseline in 2015. Baseline CVAI served as the exposure factor, while incident cardiovascular disease in 2018 and 2020 constituted the outcome events. Cox proportional hazards regression models were employed to analyze the association between CVAI and cardiovascular disease, and restricted cubic spline (RCS) analysis was used to assess dose-response relationships.

Results By 2020, the incidence rates of cardiovascular disease, heart disease, and stroke among the 4,743 postmenopausal women were 20.2% (958/4,743), 13.6% (645/4,743), and 8.3% (393/4,743), respectively. Baseline CVAI quartiles were Q1: $ $84.78, Q2: (84.78–108.49], Q3: (108.49–132.01], and Q4: >132.01. After adjustment for confounding factors, Cox proportional hazards regression revealed that compared with the CVAI Q1 group, Q3 and Q4 groups showed increased risks of cardiovascular disease by 69% (HR=1.69, 95%CI=1.29–2.21) and 82% (HR=1.82, 95%CI=1.38–2.14), respectively; stroke risk increased by 76%

(HR=1.76, 95%CI=1.10–2.82) and 95% (HR=1.95, 95%CI=1.21–3.14), respectively; and heart disease risk increased by 57% (HR=1.57, 95%CI=1.14–2.15) and 68% (HR=1.68, 95%CI=1.21–2.33), respectively. RCS analysis demonstrated dose-response relationships between CVAI and the risks of cardiovascular disease, heart disease, and stroke (P<0.05). Subgroup analyses indicated that the association between CVAI and cardiovascular disease (CVD) risk was significant among postmenopausal women aged <65 years, $ $65 years, with BMI < 24.35 kg/m^{2}$, and in rural areas (P<0.05).

Conclusion Elevated CVAI significantly increases the risk of cardiovascular disease in postmenopausal women, particularly among those with lower BMI and in rural populations. Enhanced monitoring and management of visceral obesity in these subgroups is warranted to reduce cardiovascular disease risk.

Full Text

Preamble

Relationship between the Chinese Visceral Adipose Index and Cardiovascular Disease in Postmenopausal Women: A Prospective Cohort Study

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Abstract

Background: Cardiovascular disease (CVD) represents a major threat to women' s health, with postmenopausal women constituting a particularly high-risk population. The decline in estrogen levels following menopause may promote visceral fat accumulation, which is closely linked to insulin resistance, chronic inflammation, and lipid metabolism disorders, potentially increasing CVD risk. However, research on the relationship between visceral fat indices and CVD in postmenopausal women remains limited.

Objective: To explore the association between the Chinese visceral adipose index (CVAI) and cardiovascular disease in postmenopausal women, thereby informing prevention strategies for this high-risk group.

Methods: Using data from the China Health and Retirement Longitudinal Study (CHARLS) 2015–2020, we enrolled 4,743 postmenopausal women aged $ $45 years who were free of CVD at baseline in 2015. Baseline CVAI served as the exposure variable, while incident CVD events identified in 2018 and 2020

constituted the outcome. Cox proportional hazards regression models were employed to analyze the relationship between CVAI and CVD risk, and restricted cubic spline (RCS) analysis was used to evaluate dose-response relationships.

Results: By 2020, the incidence rates of CVD, heart disease, and stroke among the 4,743 postmenopausal women were 20.2% (958/4,743), 13.6% (645/4,743), and 8.3% (393/4,743), respectively. Baseline CVAI quartiles were Q1: $ $84.78, Q2: (84.78-108.49], Q3: (108.49-132.01], and Q4: >132.01. After adjusting for confounders, Cox regression showed that compared with the Q1 reference group, women in Q3 and Q4 had significantly elevated risks: CVD risk increased by 69% (HR=1.69, 95%CI=1.29-2.21) and 82% (HR=1.82, 95%CI=1.38-2.14); stroke risk increased by 76% (HR=1.76, 95%CI=1.10-2.82) and 95% (HR=1.95, 95%CI=1.21-3.14); and heart disease risk increased by 57% (HR=1.57, 95%CI=1.14-2.15) and 68% (HR=1.68, 95%CI=1.21-2.33), respectively. RCS analysis revealed linear dose-response relationships between CVAI and risks of CVD, heart disease, and stroke (P<0.05). Subgroup analyses showed that the association between CVAI and CVD risk remained significant in women aged <65 years, $ $65 years, those with BMI < 24.35 kg/m^{2}$, and rural residents (P<0.05).

Conclusion: Elevated CVAI significantly increases CVD risk in postmenopausal women, particularly among those with lower BMI and in rural populations. Targeted monitoring and management of visceral obesity in these high-risk subgroups are warranted to reduce CVD incidence.

Keywords: Cardiovascular diseases; Chinese visceral adipose index; Coronary disease; Stroke; Postmenopausal women

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Introduction

Cardiovascular disease (CVD) is a circulatory system disorder characterized by varying degrees of sclerosis in the heart and blood vessels (microvessels, veins, and arteries), accompanied by hypotension, arrhythmia, bradycardia, and cardiac arrest [1]. CVD primarily includes heart disease and stroke, featuring high incidence, mortality, and disease burden [2], and has been associated with cognitive decline, depression, and reduced quality of life in multiple studies [3-5], representing a serious public health threat. In 2019, the number of patients with CVD, coronary heart disease, and stroke in China reached 290 million, 11 million, and 13 million, respectively [6], with trends continuing to rise. The

standardized incidence of CVD is projected to reach 663.62 per 100,000 by 2050 [7].

The Chinese visceral adipose index (CVAI) is a population-specific indicator developed for Chinese individuals based on age, BMI, waist circumference, triglycerides, and high-density lipoprotein cholesterol, demonstrating high predictive value for CVD, hypertension, and diabetes [8-10]. Numerous studies have examined the relationship between CVAI and CVD, revealing significant associations [11-12]. However, most research has focused on middle-aged and older adults or the general population, with limited investigation of CVAI and CVD risk specifically in postmenopausal women. This population represents a unique group with significantly elevated CVD prevalence that has become the leading cause of death [13]. Postmenopausal women differ substantially from premenopausal women and the general population in physical and psychological characteristics, making existing findings potentially inapplicable. As population aging intensifies, the number of postmenopausal women in China reached 256 million in 2021 and is projected to grow to 280 million by 2030 [14]. Consequently, understanding the association between CVAI and CVD risk in this expanding population is urgently needed. This study utilizes CHARLS 2015–2020 data to explore the relationship between CVAI and CVD incidence in postmenopausal women, providing evidence for prevention strategies.

Methods

1.1 Study Population

Data were obtained from the China Health and Retirement Longitudinal Study (CHARLS) (http://charls.pku.edu.cn/), a nationally representative survey of adults aged $ $45 years covering 150 counties/districts across 30 provinces/municipalities. The survey includes comprehensive assessments of demographics, health status, and healthcare utilization. All participants provided written informed consent, and the study was approved by the Biomedical Ethics Review Committee of Peking University (IRB00001052-11015) [15]. We selected data from three survey waves (2015, 2018, and 2020), with 2015 serving as baseline. The final sample included 4,743 postmenopausal women after applying exclusion criteria: (1) age <45 years in 2015; (2) missing data on age, BMI, waist circumference, triglycerides, HDL cholesterol, stroke, or heart disease at baseline, or CVAI<0; (3) prevalent CVD (stroke or heart disease) at baseline; (4) not postmenopausal in 2015; and (5) absence from either 2018 or 2020 follow-up or missing CVD outcome data.

1.2 Variables

Exposure Factor: Baseline CVAI in 2015 served as the primary exposure. CVAI was calculated using the validated formula: CVAI = -187.32 + 1.71 ×

age + 4.23 × BMI + 1.12 × waist circumference + 39.76 × $\log_{10}$(triglycerides) - 11.66 × HDL cholesterol [8].

Study Outcomes: Incident CVD was determined based on affirmative responses to either: "Has a doctor ever told you that you had a heart condition (such as myocardial infarction, coronary heart disease, angina, congestive heart failure, or other heart diseases)?" or "Has a doctor ever told you that you had a stroke (including cerebral infarction or hemorrhage)?" Heart disease and stroke were analyzed separately as secondary outcomes to examine potential differential associations with CVAI.

Covariates: Based on previous research, we included sociodemographic, lifestyle, and health status variables: age, education level, marital status, residence (urban/rural), hypertension, self-rated health, sleep duration, smoking status, alcohol consumption, cognitive function, and life satisfaction.

1.3 Statistical Analysis

All analyses were performed using R version 4.3.3. Continuous variables were presented as mean ± standard deviation, and categorical variables as frequencies (%). Group comparisons used ^{2} tests or trend ^{2} tests. CVAI was categorized into quartiles (Q1–Q4) for primary analysis. Cox proportional hazards regression models were employed to calculate hazard ratios (HR) and 95% confidence intervals (CI) for associations between CVAI quartiles and risks of CVD, heart disease, and stroke. CVAI was also modeled as a continuous variable using restricted cubic spline (RCS) analysis to evaluate dose-response relationships. The significance level was set at α=0.05.

Results

2.1 Baseline Characteristics

The 4,743 postmenopausal women had a mean age of (62.3$±8.6)$yearsandmeanCVAIof$(108.83±$36.11) at baseline. CVAI quartile cutoffs were Q1: $ $84.78, Q2: (84.78–108.49], Q3: (108.49–132.01], and Q4: >132.01. Significant differences across CVAI groups were observed for age, marital status, residence, hypertension prevalence, BMI, cognitive function, self-rated health, and alcohol consumption (P<0.05), while education level, sleep duration, smoking, and life satisfaction showed no significant differences (P>0.05) .

2.2 Incident Outcomes

Over 5 years of follow-up (total 21,957 person-years, mean 4.62 years per participant), the incidence of CVD was 20.2% (958/4,743), heart disease 13.6% (645/4,743), and stroke 8.3% (393/4,743). Incidence rates across CVAI quartiles demonstrated clear gradients: CVD rates were 12.9% (96/742), 16.8%

(210/1,249), 21.4% (313/1,463), and 26.3% (339/1,289) for Q1–Q4, respectively; heart disease rates were 9.8% (73/742), 12.6% (157/1,249), 14.0% (204/1,463), and 18.1% (233/1,289); and stroke rates were 4.2% (31/742), 6.3% (78/1,249), 8.6% (126/1,463), and 12.3% (158/1,289). Trend ^{2} tests confirmed that risks of CVD (^{2} trend=64.21, P<0.001), heart disease (^{2} trend=30.46, P<0.001), and stroke (^{2} trend=50.28, P<0.001) increased significantly with higher CVAI.

2.3 Association between CVAI and CVD Risk

Multivariable Cox regression analyses with CVD, heart disease, and stroke as outcomes, CVAI quartiles as exposure, and years as the time variable revealed consistent dose-dependent associations (P trend<0.001 for all outcomes). In Model 1 (unadjusted), CVAI Q3 and Q4 showed elevated heart disease risk compared with Q1 (P<0.05), while Q2–Q4 showed elevated stroke and CVD risk (P<0.05). Model 2 adjusted for age, education, marital status, and residence, with Q3 and Q4 remaining significantly associated with increased risks of all three outcomes (P<0.05). Model 3 additionally adjusted for hypertension, self-rated health, sleep duration, smoking, alcohol consumption, cognitive function, and life satisfaction, confirming that Q3 and Q4 were associated with significantly higher risks of heart disease, stroke, and CVD compared with Q1 (P<0.05) .

2.4 Dose-Response Relationship

Modeling CVAI as a continuous variable in RCS analysis revealed linear dose-response relationships with CVD, heart disease, and stroke risk after adjusting for confounders (P for overall<0.05, P for nonlinear>0.05). The risk of all three outcomes increased progressively with higher CVAI levels [Figure 1: see original paper].

2.5 Subgroup Analysis

Stratified analyses by age, BMI, and residence showed that CVAI was significantly associated with CVD, heart disease, and stroke risks in women aged <65 years, those with BMI<24.35 kg/m^2, and rural residents (P<0.05). In women aged $ $65 years, CVAI elevation was associated only with CVD risk (P<0.05). In urban residents, CVAI was associated only with heart disease risk (P<0.05) .

Discussion

This prospective cohort study examined the association between CVAI and CVD risk in postmenopausal women using nationally representative data. The incidence rates of CVD (20.2%), heart disease (13.6%), and stroke (8.3%) exceeded those reported for the general middle-aged and older population (14.31%,

10.74%, and 4.71%, respectively) [16], likely reflecting the combined effects of estrogen deficiency [13] and accumulated CVD risk factors [17] in this population. Estrogen enhances vascular tone and inhibits atherosclerosis development; its decline after menopause reduces vascular protection and increases CVD risk [18]. Additionally, postmenopausal women experience metabolic abnormalities including dyslipidemia, altered fat distribution, elevated blood pressure, and insulin resistance, with significant increases in total cholesterol, triglycerides, and total cholesterol/HDL ratios, all established CVD risk factors [13,19-20].

Multivariable Cox regression demonstrated a positive association between CVAI and CVD risk, with RCS analysis confirming linear dose-response relationships. Compared with Q1, women in Q3 and Q4 faced significantly elevated risks of CVD, heart disease, and stroke ($P<0.05$), consistent with previous findings [11,21]. This association may be mediated by harmful substances released from abdominal adipose tissue. Increased visceral fat induces production of inflammatory cytokines and oxidized low-density lipoprotein [21], promotes insulin resistance and metabolic syndrome [22], and disrupts endothelial function, thereby increasing CVD risk. Furthermore, abdominal fat accumulation may disrupt the leptin-adiponectin balance; increased leptin or decreased adiponectin can induce oxidative stress and endothelial damage [23]. Visceral adiposity also contributes to hypertension, hyperglycemia, and dyslipidemia—established CVD risk factors [24].

Subgroup analyses revealed that the association between CVAI and CVD was particularly pronounced in women aged <65 years, those with lower BMI, and rural residents, suggesting heterogeneous pathophysiological mechanisms across populations. In age-stratified analysis, CVAI showed stronger predictive value in younger postmenopausal women. The "cumulative effect" theory may explain this phenomenon: older individuals often have multiple cardiovascular risk factors, and the accumulation of non-metabolic risks (e.g., arterial stiffness, chronic inflammation) may mask CVAI' s independent effect. In contrast, younger populations with fewer age-related confounders may more directly reflect the pathological impact of visceral fat [25-26]. The significant association in women $ $65 years may relate to age-related vascular degeneration.

The strong association observed in lower-BMI individuals is particularly noteworthy. While obesity is traditionally considered a major CVD risk factor, our findings support the "metabolically obese normal weight" (MONW) hypothesis, which posits that metabolic status rather than BMI determines obesity-related risks. MONW individuals may have normal BMI but abnormal visceral fat distribution, leading to insulin resistance and metabolic dysregulation. Their reduced metabolic compensatory capacity may render them more susceptible to lipotoxicity, oxidative stress, and endothelial damage from equivalent visceral fat accumulation, resulting in CVD risks comparable to or exceeding those of obese individuals [27]. Conversely, some higher-BMI individuals without metabolic abnormalities may not experience increased CVD risk.

The pronounced association in rural populations highlights health inequities.

Rural areas typically have limited healthcare resources, lower health literacy, and less favorable dietary patterns, predisposing residents to visceral adiposity with inadequate early intervention. Once metabolic abnormalities develop, delayed treatment may accelerate cardiovascular damage [28-29]. Urban residents, with better healthcare access and health awareness, utilize health screening services more frequently, enabling early intervention that may mitigate CVAI' s detrimental effects [30]. The association between CVAI and heart disease in urban populations may reflect combined effects of air pollution and psychosocial stress.

This study has several limitations. First, as an observational design, we could not directly measure molecular markers such as leptin and adiponectin, limiting mechanistic insights. Second, we did not capture CVAI trajectories over time, precluding analysis of how changes in CVAI relate to CVD risk. Future research should incorporate biomarker studies and longitudinal CVAI tracking to elucidate underlying mechanisms more comprehensively.

In conclusion, elevated CVAI is positively associated with increased CVD risk in postmenopausal women, particularly among those with lower BMI and in rural settings. Primary prevention strategies for CVD in postmenopausal women should monitor CVAI levels, with enhanced surveillance and management of visceral obesity in these high-risk subgroups to reduce CVD incidence.

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Author Contributions: FAN Zhuanzhuan conceptualized and designed the study, performed data analysis, and drafted the manuscript. LI Wenting collected and organized data and revised the manuscript. MA Guoliang supervised quality control, reviewed the manuscript, and provided overall oversight.

Conflict of Interest Statement: The authors declare no conflicts of interest.

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Note: Figure translations are in progress. See original paper for figures.