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Chinese visceral adipose index is more closely associated with risk of arterial stiffness than traditional obesity indicators: a cohort study

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Abstract

Background The Chinese visceral adiposity index (CVAI) is a new index to evaluate visceral adipose tissue in the Chinese population. Arterial stiffness (AS) is a kind of degeneration of the large arteries, and obesity is an essential contributing factor to AS. Our study aimed to explore the longitudinal association between CVAI and the risk of AS and to compare the predictive power of CVAI, body mass index (BMI), and waist circumference (WC) for AS.

Methods Between 2010 and 2020, a total of 14,877 participants participating in at least two brachial-ankle pulse wave velocity (baPWV) measurements from the Kailuan study were included. The Cox proportional hazard regression models were performed to evaluate the longitudinal association between CVAI and the risk of AS. The area under the receiver operating characteristic (ROC) curve was calculated to compare the predictive power of CVAI, BMI, and WC for AS.

Results After adjusting for potential confounding factors, CVAI was significantly associated with the risk of AS. Compared with the first CVAI quartile, the hazard ratios (HR) and 95% CI of the second, third, and fourth quartiles were 1.30 (1.09–1.56), 1.37 (1.15–1.63), and 1.49 (1.24–1.78), respectively. The area under ROC curve of CVAI was 0.661, significantly higher than BMI (AUC: 0.582) and WC (AUC: 0.606).

Conclusion CVAI may be a reliable indicator to identify high-risk groups of AS in the Chinese general population, and the predictive power of CVAI for AS was better than BMI and WC.

Keywords Cohort study, CVAI, Arterial stiffness, Visceral adipose tissue, Obesity

Introduction

With the development of the social economy and the change in residents' lifestyles, the prevalence of cardiovascular diseases continues to rise. According to the Global Burden of Cardiovascular Diseases (CVD) and Risk Factors [1], in 2019, the global prevalence of cardiovascular diseases reached 523 million, with 18.6 million deaths attributed to it. In China, the number was 120 million, resulting in 4.58 million deaths from it [2]. CVD is a significant contributor to the global burden of disability-adjusted life years [3] and accounts for more than 50% of the economic losses incurred by non-communicable diseases. Arterial stiffness (AS) is a degenerative disease of the large arteries, characterized by breakage of elastic fibers, deposition of collagen, intimal fibrosis, and

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medial calcification [4, 5], resulting in decreased arterial elasticity and increased pulse pressure. Existing research indicates that AS can cause damage to organs such as the heart, brain, and kidneys. It can serve as an independent predictor for conditions like myocardial infarction, heart failure, stroke, and all-cause mortality [6–8]. AS is a long-term pathological process. Therefore, finding reliable and simple markers to identify patients in the early stages was enormously significant for preventing and delaying it.

Obesity is an essential risk factor for AS, and body mass index (BMI) and waist circumference (WC) are traditional indicators used to assess obesity. Some studies found a positive association between BMI and AS [9, 10], while others showed a negative or no association [11–13]. The inconsistent results may be attributed to the fact that BMI only reflects total body adipose but does not distinguish between lean body mass and adipose tissue. Two cross-sectional studies demonstrated that WC was more strongly associated with AS than BMI [14, 15]. However, WC only reflects the accumulation of abdominal adipose and can not distinguish between subcutaneous and visceral adipose tissue. Sun et al. reported a significantly positive association between visceral adipose tissue and AS [16]. Orr et al. also showed that the increased abdominal visceral adipose tissue was associated with increased AS [17]. The current methods for measuring visceral adipose tissue include nuclear magnetic resonance imaging (MRI) and computed tomography (CT). However, these methods have the drawbacks of high technical requirements, high costs, and potential radiation side effects, making them challenging to implement in large-scale epidemiological studies. On the basis of the visceral adiposity index (VAI), the Chinese visceral adiposity index (CVAI) was proposed in accordance with the characteristics of fat distribution in the Asian population, taking into consideration the factors of sex and age [18]. CVAI has been proven to be an independent predictor of CVD [19–21], but its association with AS remains unclear. Therefore, we used data from the Kailuan study [22] to explore the association between CVAI and AS measured by brachial-ankle pulse wave velocity (baPWV) from a longitudinal perspective and compared the predictive power of CVAI and traditional obesity indicators (BMI and WC) for AS.

Methods

Study population

The Kailuan Study was a cohort study (trial registration number: ChiCTR-TNRC-11001489) in the Kailuan community of Tangshan, China, which started in 2006. Detailed study design and procedures have been described in detail [23–25]. All participants underwent questionnaire assessments, physical examinations, and laboratory measurements and were followed biennially to update the aforementioned information. Since 2010, baPWV measurement has been added for some participants to assess the health status of blood vessel walls. In our study, participants were included and excluded according to the following criteria—inclusion criteria: (1) individuals with at least two baPWV measurements between 2010 and 2020; (2) individuals who participated in the first baPWV measurement at the same time as the current survey. Exclusion criteria: (1) individuals with missing baseline CVAI data; (2) individuals with baseline ankle-brachial index < 0.9; (3) individuals with a history of stroke, myocardial infarction, atrial fibrillation, or various cancers at baseline; (4) individuals with baseline baPWV ≥ 1800 cm/s. Finally, a total of 14,877 participants were included in our study (Fig. 1). Our study followed the Declaration of Helsinki and was approved by the Ethics Committee of Kailuan Medical Group. All participants agreed to participate in the Kailuan study and signed informed consent forms.

Data collection

Data from a standardized questionnaire was collected via face-to-face interviews. Information on socio-demographic factors (sex, age, and educational level, etc.), lifestyles (smoking status, alcohol consumption, physical activity, and salt intake, etc.), and medication history (antihypertensive drugs, antidiabetic drugs, antihyperlipidemic drugs, etc.) was included in the questionnaires. Smoking status and alcohol consumption were stratified into two levels: current and former or never. Current smoking or drinking was defined as consumption within the past year while quitting smoking or drinking was defined as abstaining for more than 1 year. Physical activity was stratified into three levels: low-intensity activity (< 10 min/week), moderate-intensity activity (10–80 min/week), and high-intensity activity (> 80 min/week). Salt intake was stratified into low, medium, and high. Education was stratified into two levels: high school graduation and below or college graduation and above.

Uniformly trained researchers measured the height, weight, and WC of the participants. Height was measured with a tape measure, accurate to 0.1 cm. Weight was measured with a calibrated bench scale, accurate to 0.1 kg. BMI was calculated as weight (kg) divided by height squared (m^2). BMI was stratified into three levels: normal: BMI < 24.0 kg/m^2, overweight: 24.0 $kg/m^2 \leq$ BMI < 28.0 kg/m^2, and general obesity: BMI ≥ 28.0 kg/m^2. WC was measured with a dedicated measuring tape, and the measurement unit was in centimeters (cm). WC was stratified into two levels: normal: WC < 90 cm in men or WC < 85 cm in women, and central obesity: WC ≥ 90 cm in men or WC ≥ 85 cm in

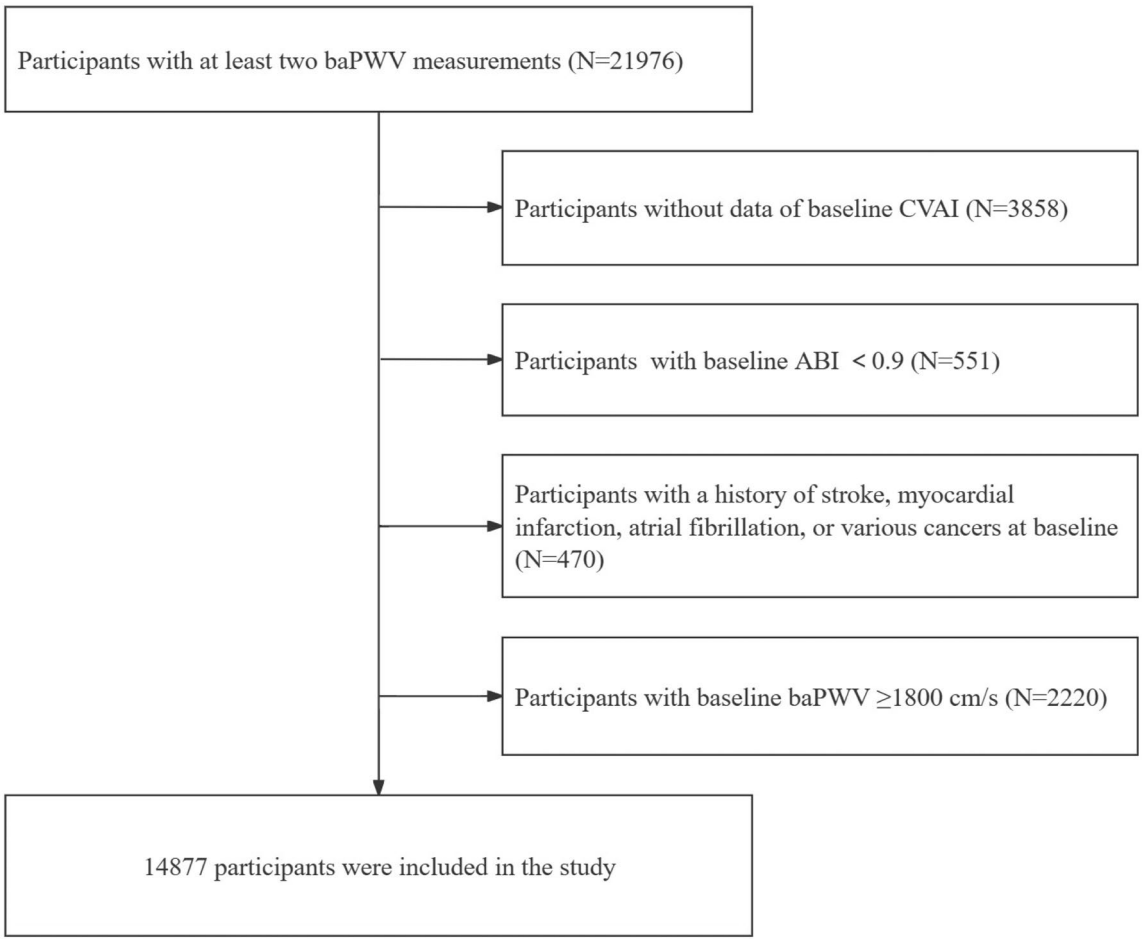


Fig. 1 Flow diagram for participants included in the study. *CVAI* Chinese visceral adipose index, *baPWV* brachial-ankle pulse wave velocity, *ABI* ankle-brachial index

women. Blood pressure was measured by a mercury sphygmomanometer in a sitting position. Three consecutive measurements were taken, and the average of systolic blood pressure (SBP) and diastolic blood pressure (DBP) was recorded as the measurement result. Since 2014, blood pressure has been measured by a HEM-8102A electronic sphygmomanometer manufactured by Omron (Dalian, China) Co., LTD. Mean arterial pressure (MAP) was defined as 1/3 * SBP + 2/3 * DBP. Hypertension was defined as SBP ≥ 140 mmHg or DBP ≥ 90 mmHg, and/or the use of antihypertensive drugs, and/or a self-reported history of hypertension.

Participants fasting for more than 8 h had fasting venous blood collected in the morning on the day of the physical examination. Biochemical parameters including fasting blood glucose (FBG), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), serum uric acid (SUA), and high-sensitivity C-reactive protein (hs-CRP) were measured on the Hitachi 747 auto-analyzer (Hitachi, Tokyo, Japan). The instruments used in all hospitals were of the same model, calibrated uniformly, reagents purchased uniformly, and medical staff trained uniformly. Diabetes was defined as FBG ≥ 7.0 mmol/L, and/or the use of antidiabetic drugs, and/or self-reported history of diabetes. HDL-C and TG levels were measured by the direct test and the enzymatic colorimetric method, respectively. CVAIs were calculated as follows:

Male: $CVAI = -267.93 + 0.68 \times age\ (years) + 0.03 \times BMI\ (kg/m^2) + 4.00 \times WC\ (cm) + 22.00 \times log10\ TG\ (mmol/L) - 16.32 \times HDL\text{-}C\ (mmol/L)$;

Female: $CVAI = -187.32 + 1.71 \times age\ (years) + 4.23 \times BMI\ (kg/m^2) + 1.12 \times WC\ (cm) + 39.76 \times log10\ TG\ (mmol/L) - 11.66 \times HDL\text{-}C\ (mmol/L)$.

Outcomes assessment

We used baPWV to assess the AS of participants, and the baPWV was measured by a PB-203RPEIII networked AS measurement device produced by Omron Healthcare

(China) Co., LTD. Participants should refrain from smoking and consuming alcoholic or caffeinated beverages and rest adequately to achieve the optimal state before measurements. Binding of the instrument cuff was performed by an experienced researcher. The detailed operations and principles can be found in the literature [26]. BaPWV was measured twice, with a 5-min interval, and the second measurement was taken as the final result. The higher values on the left and right sides were used for the analysis in our study. According to the previous study, baPWV ≥ 1800 cm/s was considered as AS [27].

Statistical analyses

Baseline characteristics were expressed as mean ± standard deviation (SD), median with interquartile range, or frequency with percentage, as appropriate. Comparisons between groups were performed by analysis of variance (ANOVA), Kruskal–Wallis test, or chi-square test.

The person-time of follow-up for each participant was determined from the date when the first baPWV was measured to either the date of AS onset, death, or the end of the follow-up in this study (December 31, 2020), whichever occurred first. The Cox proportional hazard regression models were performed to evaluate hazard ratios (HR) and 95% confidence intervals (CI) for AS across the CVAI quartiles. The proportional hazards assumption was satisfied by checking the Schoenfeld residual plots. Three Cox proportional hazards regression models were developed: Model 1, adjusted for sex and age; Model 2, adjusted for variables in model 1 plus education, smoking, alcohol drinking, physical activity, salt intake, LDL-c, SUA, Hs-CRP, MAP and FBG; Model 3: adjusted for variables in model 2 plus hypertensive drugs, hypoglycaemic drugs, and lipid-lowering drugs. Subgroup analyses were employed according to sex, age, smoking status, alcohol consumption, hypertension, and diabetes. The restricted cubic spline (RCS) with 3 knots defined at the 25th, 50th, and 75th percentiles of CVAI was used to evaluate the dose–response relationship between CVAI and the risk of AS.

The receiver operating characteristic (ROC) curve was established, and the area under the ROC curve (AUC) was calculated to compare the predictive power of CVAI, BMI, and WC for AS. The best CVAI, BMI, and WC cutoff values were calculated based on the Youden Index.

Three sensitivity analyses were performed to test the robustness of our findings. Firstly, the primary analysis was repeated after excluding participants with medication usage to minimize the impact of medication. Secondly, the Fine-Gray competing risk model was performed by considering death as a competing risk event. Lastly, to avoid potential measurement bias, the primary analysis was repeated to exclude participants who attended two baPWV measurements (N = 8095).

All data processing and analysis were performed using SAS, version 9.4 (SAS Institute Inc., Cary, NC), and a two-tailed P value < 0.05 was considered statistically significant.

Results

Baseline characteristics

The baseline characteristics of the participants were presented by the CVAI quartiles (Table 1). MAP, FBG, TG, BMI, WC, SUA, and Hs-CRP of the participants in the highest CVAI quartile were significantly higher than those in the lowest CVAI quartile. In addition, participants in the highest CVAI quartile had a higher proportion of males, individuals aged ≥ 45, current smoking, current alcohol drinking, diabetes, hypertension, and medication usage.

Association of CVAI and the risk of AS

In a median follow-up spanning 5.96 years (IQR: 3.83–9.04 years), after 2.8 ± 1.2 measurements of baPWV, 1902 out of 14,877 participants (12.8%) developed AS. We developed three Cox proportional hazard regression models to evaluate the association between CVAI and the risk of AS (Table 2). Relative to that of the first CVAI quartile, in model 3, the adjusted HR of the second, third, and fourth CVAI quartile were 1.30 (1.09–1.56), 1.37 (1.15–1.63), and 1.49 (1.24–1.78), respectively. The risk of AS increased by 9% for each SD increase in CVAI (HR = 1.09, 95% CI 1.03–1.15). Kaplan–Meier curves showed significant differences (P < 0.001 for the log-rank test) in the risk of AS among baseline CVAI quartiles (Fig. 2). The restricted cubic spline revealed a nonlinear relationship between CVAI and the risk of AS (P nonlinearity < 0.001) (Fig. 3). However, neither BMI nor WC was significantly associated with the risk of AS (Supplement Tables 1 and 2).

Subgroup analyses

To verify the stability of the association between CVAI and the risk of AS, subgroup analyses were conducted stratified by sex, age, smoking status, alcohol consumption, hypertension, and diabetes (Fig. 4). CVAI was significantly associated with the risk of AS in women, those aged ≥ 45, former or never smokers (drinkers), and those without hypertension or diabetes (P < 0.05). Sex, age, smoking status, alcohol consumption, and chronic diseases all significantly modified the association between CVAI and the risk of AS (P for multiplicative interaction < 0.01).

Table 1 Baseline characteristics of the participants according to baseline CVAI quartiles

Characteristics	Total (n = 14,877)	CVAI				*P* value
		Q1 (n = 3719)	Q2 (n = 3721)	Q3 (n = 3718)	Q4 (n = 3719)	
Age (year, mean [SD])	44.89 ± 11.57	39.71 ± 9.62	44.39 ± 11.00	46.75 ± 11.35	48.72 ± 12.15	< 0.001
Age ≥ 45 (year, mean [%])	7508 (50.47)	996 (26.78)	1848 (49.66)	2202 (59.23)	2462 (66.20)	< 0.001
Gender (n [%])						< 0.001
Female	4857 (32.65)	2207 (59.34)	1354 (36.39)	799 (21.49)	497 (13.36)	
Male	10,020 (67.35)	1512 (40.66)	2367 (63.61)	2919 (78.51)	3222 (86.64)	
HDL-C (mmol/L, mean [SD])	1.49 ± 0.42	1.70 ± 0.46	1.54 ± 0.40	1.40 ± 0.36	1.32 ± 0.35	< 0.001
LDL-C (mmol/L, mean [SD])	2.69 ± 0.76	2.40 ± 0.70	2.71 ± 0.72	2.81 ± 0.75	2.85 ± 0.79	< 0.001
TG (mmol/L, median [IQR])	1.24 (0.84–1.95)	0.81 (0.62–1.10)	1.13 (0.83–1.57)	1.49 (1.04–2.18)	1.91 (1.30–2.97)	< 0.001
SUA (μmol/L, mean [SD])	306.30 ± 96.53	262.10 ± 80.46	297.17 ± 89.65	322.72 ± 94.12	343.23 ± 101.19	< 0.001
hs-CRP (mg/L, median [IQR])	1.05 (0.46–2.20)	0.70 (0.30–1.50)	1.00 (0.48–2.00)	1.10 (0.50–2.30)	1.50 (0.70–3.07)	< 0.001
FBG (mmol/L, mean [SD])	5.47 ± 1.30	5.05 ± 0.75	5.37 ± 1.08	5.61 ± 1.48	5.85 ± 1.58	< 0.001
SBP (mmHg, mean [SD])	126.17 ± 16.57	116.11 ± 14.66	124.62 ± 14.95	129.66 ± 15.27	134.28 ± 15.66	< 0.001
DBP (mmHg, mean [SD])	80.69 ± 10.48	75.07 ± 9.25	79.54 ± 9.50	82.50 ± 9.83	85.67 ± 10.28	< 0.001
MAP (mmHg, mean [SD])	95.84 ± 11.65	88.72 ± 10.28	94.55 ± 10.44	98.21 ± 10.69	101.86 ± 10.96	< 0.001
BMI (kg/m^2, mean [SD])	24.85 ± 3.38	21.79 ± 2.22	24.10 ± 2.31	25.60 ± 2.47	27.91 ± 3.06	< 0.001
WC (cm, mean [SD])	85.48 ± 9.85	74.44 ± 6.25	82.45 ± 4.51	87.94 ± 4.02	97.08 ± 6.39	< 0.001
baPWV (cm/s, mean [SD])	1374.12 ± 196.79	1255.61 ± 183.39	1362.92 ± 181.87	1419.01 ± 180.89	1458.94 ± 179.21	< 0.001
Current smoker, n (%)	5026 (33.78)	742 (19.95)	1198 (32.20)	1457 (39.19)	1629 (43.80)	< 0.001
Current alcohol use, n (%)	4729 (31.79)	720 (19.36)	1139 (30.61)	1369 (36.82)	1501 (40.36)	< 0.001
College graduation and above (n [%])	3413 (22.94)	1260 (33.88)	825 (22.17)	671 (18.05)	657 (17.67)	< 0.001
Physical activity (n [%])						< 0.001
Low intensity	5763 (38.74)	1402 (37.70)	1441 (38.73)	1446 (38.89)	1474 (39.63)	
Moderate intensity	7438 (50.00)	1988 (53.46)	1885 (50.66)	1820 (48.95)	1745 (46.92)	
High intensity	1676 (11.27)	329 (8.85)	395 (10.62)	452 (12.16)	500 (13.44)	
Salt intake (n [%])						< 0.001
Low salt intake	2278 (15.31)	599 (16.11)	570 (15.32)	550 (14.79)	559 (15.03)	
Medium salt intake	11,217 (75.40)	2858 (76.85)	2827 (75.97)	2818 (75.79)	2714 (72.98)	
High salt intake	1382 (9.29)	262 (7.04)	324 (8.71)	350 (9.41)	446 (11.99)	
Hypertension (n [%])	4628 (31.11)	404 (10.86)	883 (23.73)	1372 (36.90)	1969 (52.94)	< 0.001
Diabetes (n [%])	1161 (7.80)	54 (1.45)	186 (5.00)	339 (9.12)	582 (15.65)	< 0.001
Hypotensive drugs (n [%])	978 (6.57)	59 (1.59)	148 (3.98)	257 (6.91)	514 (13.82)	< 0.001
Hypoglycaemic drugs (n [%])	283 (1.90)	9 (0.24)	46 (1.24)	85 (2.29)	143 (3.85)	< 0.001
Lipid-lowing treatment (n [%])	89 (0.60)	8 (0.22)	13 (0.35)	20 (0.54)	48 (1.29)	< 0.001

CVAI Chinese visceral adipose index, *Q* quartiles, *HDL-C* high-density lipoprotein, *LDL-C* low-density lipoprotein, *TG* triglyceride, *SUA* serum uric acid, *hs-CRP* high-sensitivity C-reactive protein, *FBG* fasting blood glucose, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *MAP* mean arterial blood pressure, *BMI* body mass index, *WC* waist circumference, *baPWV* brachial-ankle pulse wave velocity

Receiver operating characteristic curve analysis

The ROC curve analysis was performed to compare the predictive power of CVAI, BMI, and WC for AS. The ROC curve analysis identified that CVAI had the highest accuracy in predicting AS (Fig. 5). The area under the ROC curve of CVAI was approximately 0.7, while for BMI and WC, the areas were 0.582 and 0.606 (Table 3), respectively, indicating that CVAI had relatively higher discriminatory power for AS compared to BMI and WC. The Youden index of CVAI for predicting AS was 0.241, higher than that of BMI (Youden index: 0.121) and WC (Youden index: 0.154). The best cut-off value of CVAI for predicting AS was 92.18.

Sensitivity analysis

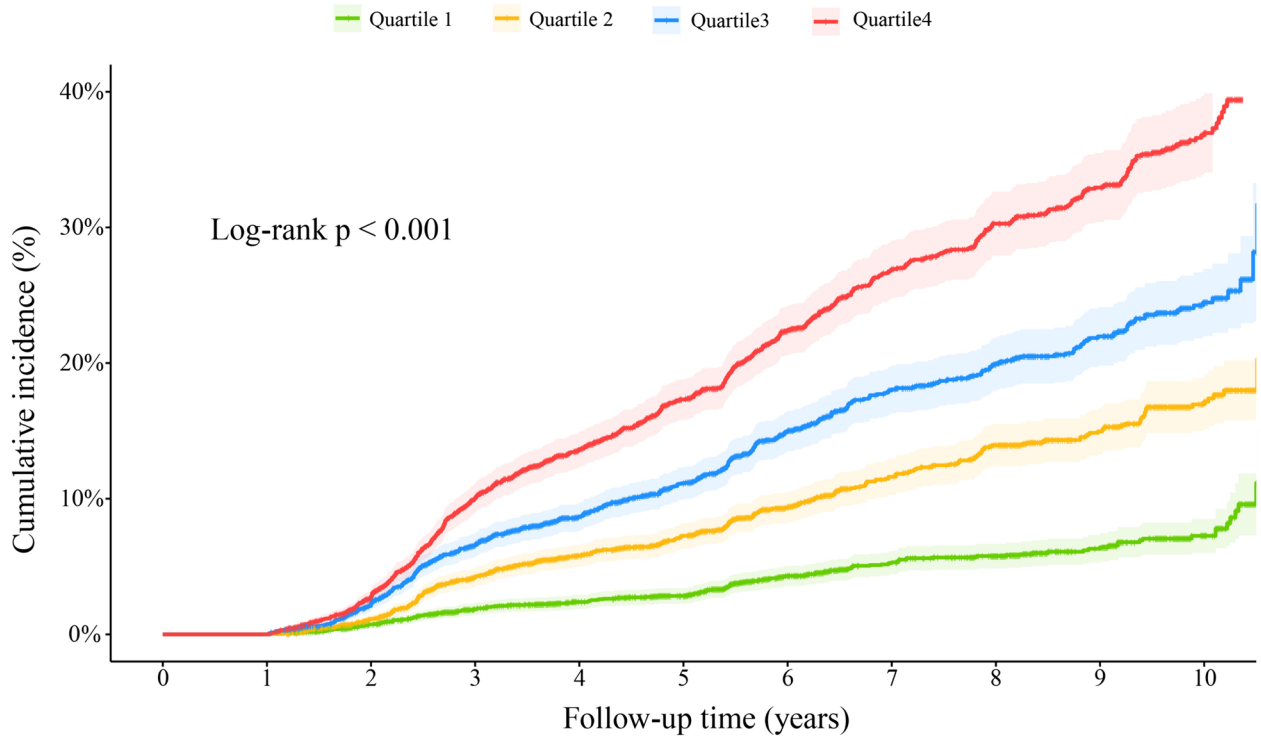
In sensitivity analyses that excluded participants with medication history at baseline (Supplement Table 3) and the competing risk model was used to account for death (Supplement Table 4), findings for the association of CVAI and the risk of AS were not appreciably altered compared with our primary analyses. The baseline characteristics were similar for participants who attended at

Table 2 Association of BMI with the risk of arterial stiffness

Characteristics	CVAI, HR (95% CI)				
	Q1	Q2	Q3	Q4	CVAI, per SD
Arterial stiffness					
Cases /n	184/3719	385/3721	528/3718	805/3719	
Incident rate, per 1000 person-years	7.22	16.22	23.89	35.79	
Model 1	1.00	1.72 (1.44–2.05)	2.24 (1.88–2.66)	3.03 (2.56–3.59)	1.35 (1.28–1.42)
Model 2	1.00	1.31 (1.09–1.56)	1.37 (1.15–1.64)	1.52 (1.28–1.82)	1.10 (1.04–1.16)
Model 3	1.00	1.30 (1.09–1.56)	1.37 (1.15–1.63)	1.49 (1.24–1.78)	1.09 (1.03–1.15)

Model 1: adjusted for sex and age; Model 2: adjusted for variables in model 1 plus education level, smoking status, alcohol consumption, physical activity, salt intake, LDL-C, SUA, hs-CRP, MAP, and FBG; Model 3: adjusted for variables in model 2 plus hypertensive drugs, hypoglycaemic drugs, and lipid-lowering drugs

CVAI Chinese visceral adipose index, *HR* hazard ratio, *CI* confidence interval, *Q* quartiles, *SD* standard deviation



Quartile 1	3719	3719	3580	3338	2945	2746	2297	1993	1683	899	468
Quartile 2	3721	3721	3572	3285	2785	2544	1888	1431	1275	934	504
Quartile 3	3718	3718	3500	3150	2609	2320	1554	1149	1041	870	459
Quartile 4	3719	3719	3457	3047	2607	2292	1647	1287	1172	1035	542

Fig. 2 Kaplan–Meier estimates of the cumulative incidence of arterial stiffness by baseline CVAI quartiles

least three baPWV measurements (Supplement Table 5) and at least two baPWV measurements. In addition, the association between CVAI and the risk of AS among participants with at least three baPWV measurements was also similar to the core results (Supplement Table 6).

Discussion

In this large cohort study, we identified the following: (1) increased CVAI was a risk factor for AS; (2) the association between CVAI and the risk of AS was age- and sex-dependent; (3) the ROC curve analysis

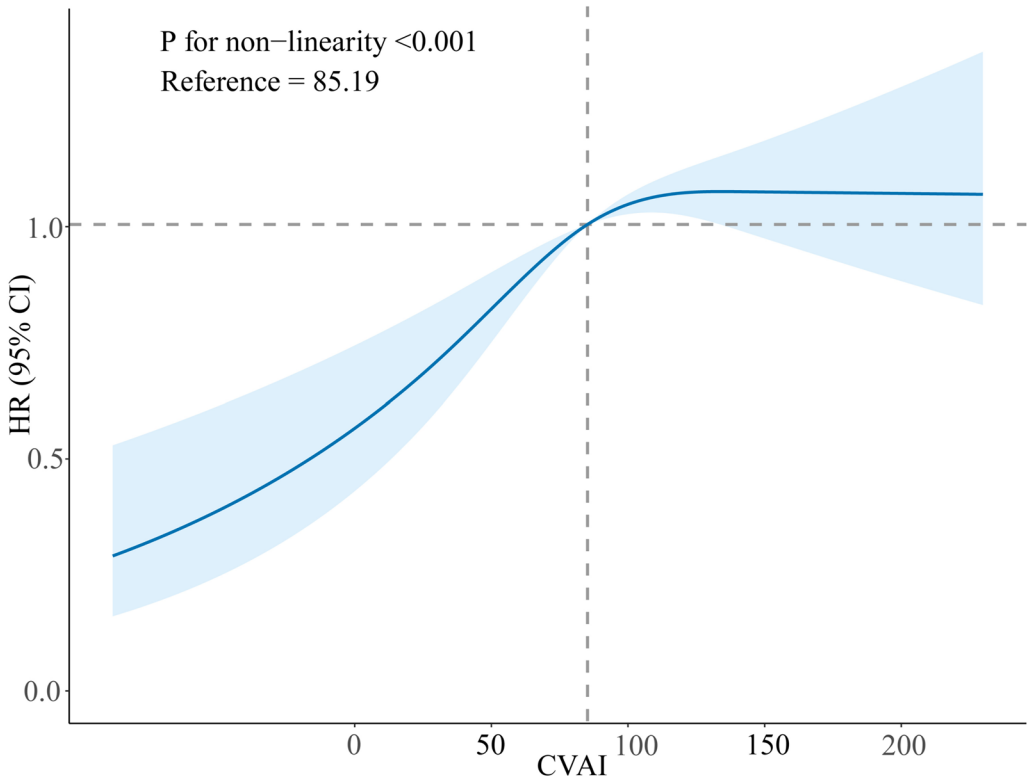


Fig. 3 The dose–response relationship of CVAI and the risk of arterial stiffness. Data were fitted using a Cox regression model of the restricted cubic spline with 3 knots at the 25th, 50th, and 75th percentiles of baseline CVAI. The reference point was the median of the CVAI in the 14,877 participants. The solid line represented point estimation on the association of CVAI and the risk of arterial stiffness, and the shaded portion represented 95% CI estimation. Covariates in the model included sex, age, education level, smoking status, alcohol consumption, physical activity, salt intake, LDL-C, SUA, hs-CRP, MAP, FBG, hypertensive drugs, hypoglycaemic drugs, and lipid-lowering drugs. *CVAI* Chinese visceral adipose index, *HR* hazard ratio, *CI* confidence interval

identified that CVAI was the best predictor of AS compared with BMI and WC.

We found that increased CVAI was a risk factor for AS. The risk of AS in the highest CVAI quartile increased by 49% compared with the lowest CVAI quartile. This association still persisted even after adjustment for traditional risk factors of AS and medications that had potential influences on AS. In addition, our study also manifested a nonlinear association between CVAI and the risk of AS. The risk of arterial stiffness increased with the rise of CVAI when CVAI < 133. Although there has been no previous research exploring the association between CVAI and AS, a cross-sectional study reported VAI was a risk factor for AS in the elderly in China [28]. The risk of AS prevalence in the highest VAI tertile increased by 323% compared with the lowest VAI tertile. The association between VAI and baPWV was nonlinear. BaPWV increased with the rise of VAI when VAI < 2.10, but the association between VAI and baPWV was insignificant when VAI ≥ 2.10. To the best of our knowledge, our study is the first to reveal that increased CVAI was a risk factor for AS in a full population, including all age groups.

The association between CVAI and the risk of AS showed sex dependency. Subgroup analysis revealed that the strength of the association between women's CVAI and the risk of AS was more significant than that for men. The HR for the highest quartile of CVAI in women was 2.30 (95% CI 1.27–4.18). Zuo et al. found a linear association between BMI and AS in Chinese women but was not observed in men [29]. Scuteri et al. reported that the association between BMI, WC, and AS was stronger in Western women than in men [30]. Wohlfahrt et al. adopted the method of repeated measurements to assess obesity and long-term longitudinal changes of ventricular stiffness and identified the significant association between WC and increased left ventricular end-systolic stiffness in women but not in men [31]. Our study showed that increased CVAI had a more pronounced impact on AS in women.

It should be noted that we identified a significant association between CVAI and the risk of AS in middle-aged

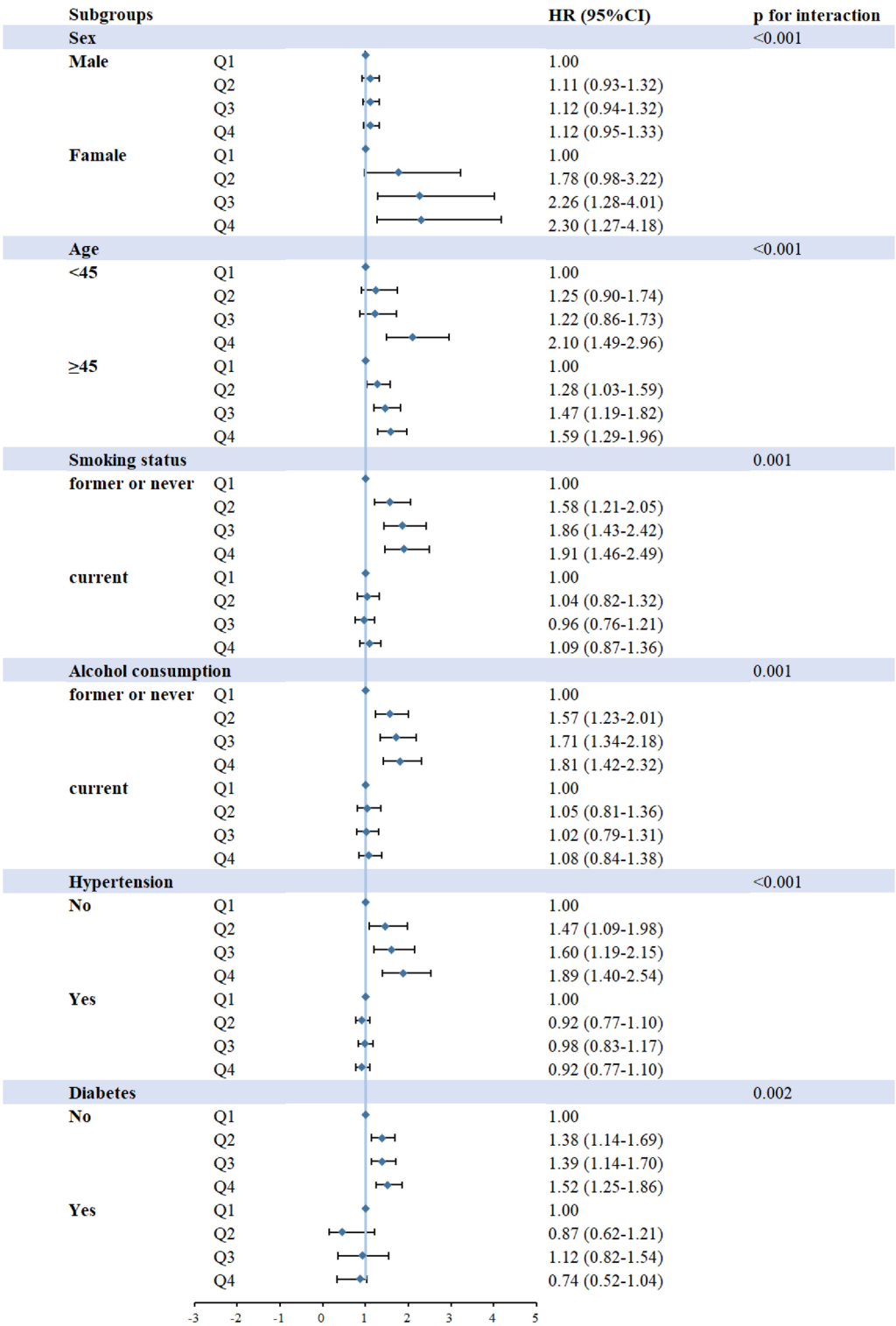


Fig. 4 The association of CVAI and the risk of arterial stiffness in different subgroups. Each subgroup was adjusted for sex, age, education level, smoking status, alcohol consumption, physical activity, salt intake, LDL-C, SUA, hs-CRP, MAP, FBG, hypertensive drugs, hypoglycaemic drugs, and lipid-lowering drugs. *Q* quartiles, *HR* hazard ratio, *CI* confidence interval

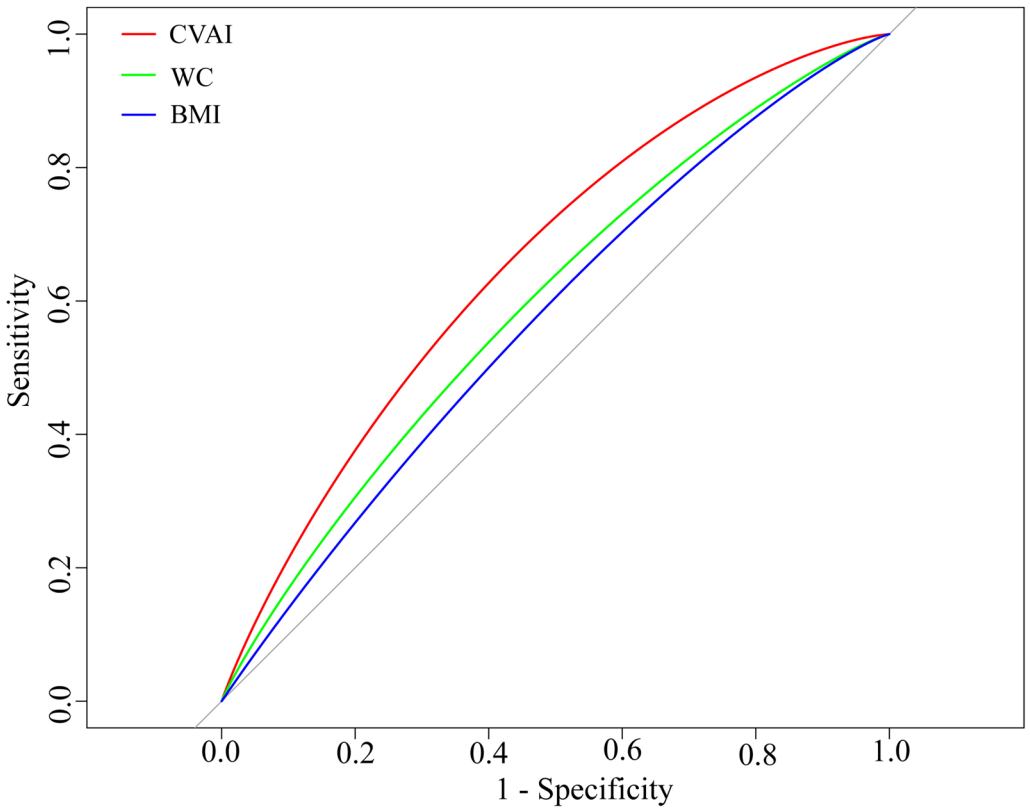


Fig. 5 The ROC curves for the CVAI, BMI, and WC to diagnose arterial stiffness. Significant differences in the AUC for each obesity index were compared with the method of the DeLong test. *CVAI* Chinese visceral adipose index, *BMI* body mass index, *WC* waist circumference

Table 3 Predictive power of CVAI, BMI, and WC for arterial stiffness

	AUC (95% CI)	Cut-off	Sensitivity and specificity, %	Youden index	*P* for comparison
CVAI	0.661 (0.648–0.673)	92.18	0.648/0.593	0.241	Ref
WC	0.606 (0.593–0.620)	84.39	0.676/0.478	0.154	< 0.001
BMI	0.582 (0.569–0.595)	24.35	0.629/0.492	0.121	< 0.001

CVAI Chinese visceral adipose index, *BMI* body mass index, *WC* waist circumference, *AUC* area under the curve, *CI* confidence interval

and older elderly participants, and the HR of the highest CVAI quartile was 1.59 (95% CI 1.29–1.96), compared to the lowest CVAI quartile. At present, many studies have generated results that are consistent with our study. The Whitehall II study in the UK reported significant associations between BMI, WC, body fat percentage, and increased AS in the late middle-aged population [32]. The ARIC study in the US showed significant associations between BMI, WC, body fat percentage, and increased ventricular-arterial stiffness in older adults [33]. However, there were variations in the association between obesity and AS in young individuals across different studies. A cross-sectional study involving 1306 participants based on the FLEMENGHO study found a higher BMI was closely associated with increased AS in middle-aged and elderly women, but this association was not present in young women [34]. Another cross-sectional study involving 186 young individuals and 177 middle-aged and elderly individuals found insignificant differences in the association between BMI, WC, and AS in young and middle-aged/elderly populations [35]. The inconsistent measurement methods of AS may cause the differences in the results of the above studies. Based on a large-scale cohort, we identified that increased CVAI in middle-aged and elderly individuals leads to a more pronounced AS than young ones.

There was also a notable association between CVAI and the risk of AS in participants considered relatively

healthy, excluding those with hypertension and diabetes in our study. Compared to the lowest CVAI quartile, the HR of the highest CVAI quartile in non-hypertension and non-diabetes groups were 1.89 (95% CI 1.40–2.54) and 1.52 (95% CI 1.25–1.86), respectively. The increased CVAI may be a risk factor for AS in relatively healthy individuals. Another possible reason was both hypertensive and diabetic participants were highly homogeneous as high-risk groups for AS, resulting in the insignificance of the effect of CVAI.

It is worth noting that in the analysis of this study, we found an insignificant association between BMI, WC, and the risk of AS. Currently, the association between BMI, WC, and AS is inconsistent in different studies. Li et al. reported positive associations between BMI, WC, and the risk of AS prevalence in overweight and obese participants in China [35]. On the other hand, several prior studies had reached opposite conclusions, which suggested there was no strong association between them. In a cohort study with 30 years of follow-up, the association between the long-term burden of BMI from childhood to adulthood and AS was insignificant [36]. A cross-sectional study based on the MARK study reported an insignificant association between WC and AS [37]. Kim et al. found an insignificant association between increased WC and increased AS in different age groups and both sexes [38]. Our findings, along with previous studies, suggested that BMI and WC may not be reliable indicators for AS.

The ROC curve analysis found BMI and WC had lower predictive power for AS than CVAI. Zhang et al. also showed BMI and WC had low predictive power for AS [39]. Our study identified that CVAI may be a more accurate predictor of AS compared to traditional obesity indicators such as BMI and WC.

Our observational study could not explore the mechanism of the association between CVAI and AS. However, based on previous studies, the mechanisms may include: (1) the accumulation of visceral adipose tissue led to an increase in components of the Renin–Angiotensin–Aldosterone System (RAAS). Renin hydrolyzed angiotensinogen to produce angiotensin I, which was then converted to angiotensin II by the action of angiotensin-converting enzyme. Angiotensin II enhanced renal sodium reabsorption and vasoconstriction, leading to an increase in blood pressure. Aldosterone induced an osteogenic phenotype of vascular smooth muscle cells, vascular inflammation, and gene expression profiles at the vascular levels, ultimately contributing to calcification and stiffness of the vascular wall [40]; (2) two inflammatory factors, including tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), were secreted by macrophages infiltrating adipose tissue. In obesity, IL-6 was mainly produced by visceral adipose tissue [41]. Accumulation of visceral adipose tissue increased the release of TNF-α and IL-6, causing vascular remodeling and endothelial dysfunction [42]; (3) the visceral adipose tissue accumulation promoted the secretion of adipokines, with most being pro-inflammatory adipokines, including leptin, resistin, and visfatin. High levels of leptin cause vascular inflammation [43]. Resistin promotes the proliferation and migration of vascular smooth muscle cells, leading to endothelial dysfunction [44]. Visfatin increased oxidative stress [45], the production of matrix metalloproteinases (such as MMP-9) [46], and collagen deposition. Adiponectin was one of the few anti-inflammatory and protective adipokines. Adiponectin protects endothelial function by inhibiting the proliferation of vascular smooth muscle cells induced by resistin [44]. However, the accumulation of visceral adipose tissue reduced the secretion of adiponectin, diminishing its protective effects on blood vessels.

The strength of our study was the confirmation of new-onset AS in a large cohort by performing and repeating baPWV measurements. In addition, we evaluated the participants' visceral adipose tissue by CVAI instead of VAI. There were significant differences in visceral adipose tissue between different ethnic groups [47], and VAI developed for Caucasians may not be suitable for Chinese populations [48]. CVAI has been reported to be positively associated with visceral adipose tissue as assessed by CT [19]. However, our study had several limitations: (1) although many confounding factors were adjusted, there may still be some unmeasured or residual confounding factors. (2) The participants in our study were all from the Kailuan community, which may be consistent in some aspects. Therefore, whether the results could be generalized to other populations remains to be determined. (3) Our study did not use CT or MRI to measure the actual content of participants' visceral adipose tissue, which prevented us from verifying whether CVAI was consistent with the actual content of visceral adipose tissue. (4) As a long-term cohort study, bias due to loss of follow-up inevitably existed. However, sensitivity analysis identified that the association between CVAI and the risk of AS in participants with at least three baPWV measurements still persisted.

Conclusions

CVAI may be a valuable obesity indicator for identifying individuals at high risk of AS in the Chinese population. In public health practice, reducing the accumulation of visceral adipose tissue could be an intervention to prevent AS. This hypothesis needed to be confirmed by a large-scale randomized clinical trial.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13098-024-01436-3.

Supplementary Material 1.

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Author contributions
Conceptualization, H.S. and S.W.; methodology, H.S.; software, H.S.; validation, S.W. and Y.W.; formal analysis, H.S.; data curation, Y.T. and H.W.; writing—original draft preparation, H.S.; writing—review and editing, C.Z. and L.L.; supervision, S.C., S.W. and Y.W. All authors have read and agreed to the published version of the manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The project protocol was approved by the ethics committee of Ethics Committee of the Kailuan Medical Group and was by the guidelines of the Helsinki Declaration, and all study individuals in this project signed an informed consent form at enrollment.

Consent for publication
If the manuscript is accepted, we approve it for publication in Diabetology and Metabolic Syndrome.

Competing interests
The authors declare no competing interests.

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