Association of Chinese Visceral Adiposity Index and Its Dynamic Change With Risk of Carotid Plaque in a Large Cohort in China

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BACKGROUND: We aimed to evaluate the association between the Chinese visceral adiposity index (CVAI) and its dynamic change and risk of carotid plaque based on a large Chinese cohort.

METHODS AND RESULTS: This cohort included 23,522 participants aged 20 to 80 years without elevated carotid intima-media thickness and carotid plaque at baseline and who received at least 2 health checkups. CVAI was calculated at baseline and at every checkup. The dynamic change in CVAI was calculated by subtracting CVAI at baseline from that at the last follow-up. Cox proportional hazard regression model was used to estimate hazard ratios (HRs) and 95% CIs. The restricted cubic spline was applied to model the dose-response association between CVAI and carotid plaque risk. During the 82,621 person-years of follow-up, 5987 cases of carotid plaque developed (7.25/100 person-years). We observed a significant positive correlation between CVAI and carotid plaque risk (HR, 1.53; 95% CI, 1.48–1.59 [P < 0.001]) in a nonlinear dose-response pattern (P nonlinearity < 0.001). The sensitivity analyses further confirmed the robustness of the results. The association was significant in all subgroup analyses stratified by sex, hypertension, and fatty liver disease except for the diabetes subgroup. The association between CVAI and carotid plaque risk was much higher in men than in women. No significant association was identified between change in CVAI and carotid plaque risk.

CONCLUSIONS: CVAI was positively associated with carotid plaque risk in a nonlinear dose-response pattern in this study. Individuals should keep their CVAI within a normal level to prevent the development of carotid plaque.

Key Words: carotid plaque ■ Chinese visceral adiposity index ■ cohort study ■ dynamic change

Atherosclerosis is an inflammatory process that causes complex lesions or plaques to protrude into the arterial lumen.1 With the rupture and fragmentation embolization of the plaques, it can cause malignant cerebrovascular events and seriously threaten human health.2 Carotid plaque is a potential marker of atherosclerosis and can effectively predict the presence of atherosclerosis and cardiovascular events.3 It has been proposed that about one third of Chinese adults have carotid plaque, and its progression rate with age is more extreme than that of European countries.4 Therefore, it is urgent to identify effective tools to detect and intervene carotid plaque in advance to reduce the health burden of the population.

Studies have shown that visceral obesity is an independent risk factor for the increased risk of carotid atherosclerosis.5,6 Direct measurement of visceral obesity using imaging techniques is expensive and often not feasible in public health. Several clinical proxies are commonly used, such as body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR), and waist-to-height ratio (WHtR) to assess visceral obesity.

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However, these indicators can neither accurately distinguish between muscle and fat mass, nor between peripheral fat and abdominal fat, or are too sensitively influenced by height and weight, which could not effectively evaluate the body’s external morphology and internal tissue composition.

There is evidence of significant differences in body fat distribution between various ethnicities. Furthermore, the Asian population seems to be more inclined to visceral fat accumulation at lower BMIs, or myocardial infarction (n=63) at baseline were excluded from the current study. Finally, a total of 23,522 participants entered into this study. The institutional review board of the Xiaotangshan Hospital approved this study (No. 202006). Only routine health check information was used for data analysis, so the requirement for informed consent from participants was waived.

Carotid Ultrasound Assessment
The vascular ultrasonography examination was performed by experienced radiologists who had >3 years of experience in carotid ultrasound and were blinded to all clinical information using a 3.5-MHz transducer (logic Q700 MR, GE). Radiologists have unified training and diagnosis criteria and regular evaluation of the consistency of examination results among radiologists. The consistency of inspection results was typically evaluated every 3 months. For consistency assessments, all agreement rates were >95%, with the largest being 99.5%. Both sides of the internal carotid artery and common carotid artery were examined, and each side was measured 3 times. If the lesions on both sides were not consistent, the more serious side of the lesion prevailed. The recording frequency of ultrasonic images of the common carotid artery was 5 to 10 MHz, and the acquisition frequency of ultrasound images of the carotid bulb and proximal carotid artery was 9 MHz. The diastolic images were recorded on all ultrasound images to reduce cardiac cycle variability.

Carotid plaque was interpreted as the presence of focal wall thickening that was at least 0.5 mm, or 50% greater than that of the surrounding vessel wall.
or as a focal region with carotid intima-media thickness >1.5 mm that protrudes into the lumen, which was distinct from the adjacent boundary.\textsuperscript{11}

**Data Collection**

Information on demographic characteristics (eg, age and sex), lifestyles (eg, cigarette smoking and alcohol drinking), personal medical history, and use of medications were obtained at baseline and follow-up checkups for all participants by face-to-face standardized questionnaires interviews; anthropometry, clinical, and biochemical measures were collected by well-trained doctors and nurses. Height and weight were measured via standard methods with participants wearing light clothes without shoes. BMI was calculated by dividing weight (kg) by height squared (m\(^2\)). WC was measured twice at 1.0 cm horizontally above the navel as the participants exhaled with legs about 25- to 30-cm apart. WHR was calculated as WC divided by hip circumference. WHtR was calculated as WC divided by height. A body shape index (ABSI),\textsuperscript{12} lipid accumulation product (LAP),\textsuperscript{13} and visceral adiposity index (VAI)\textsuperscript{14} were calculated as follows, with triglyceride and high-density lipoprotein cholesterol (HDL-C) levels expressed as millimole per liter: ABSI=WC/(BMI\(^{2/3}\)×height\(^{1/2}\)); LAP=(WC−65)×triglycerides for men, LAP=(WC−58)×triglycerides for women; VAI=(WC/(36.58+(1.89×BMI)))×(triglycerides/0.81)\(^{-1}\) x(1.25/(HDL−C)) for women. Systolic and diastolic blood pressures were measured 3 times with a 30-second interval using an electronic sphygmomanometer (HEM-770AFuzzy, Omron) on the right arm of patients in a seated position at least 5 minutes of rest.

Overnight fasting blood samples were collected after at least 12-hour fasting and used to measure serum uric acid, serum alanine aminotransferase, and aspartate aminotransferase by an automated analyzer. Fasting plasma glucose was determined by the glucose dehydrogenase method (Merck). Serum levels of triglycerides, total cholesterol, HDL-C, and low-density lipoprotein cholesterol were detected by enzymatic colorimetry on the Roche Cobas C 710 automatic biochemical analyzer (Supplied by Beijing Barry Medical Equipment Co., Ltd). Estimated glomerular filtration rate was calculated as follows: (mL/min per 1.73 m\(^2\))=175×creatinine\(^{-1.234}\)×age\(^{-0.0179}\) (if women, x0.79), with creatinine level in mg/dL and age in years.\textsuperscript{15}

**Diabetes, Hypertension, and Fatty Liver Disease Definition**

Diabetes was defined with any of the following criteria: glycated hemoglobin ≥6.5%, fasting glucose level ≥126 mg/dL, 2-hour plasma glucose ≥200 mg/dL, or the use of antidiabetes medication according to the criteria of the American Diabetes Association.\textsuperscript{16} Hypertension was defined with any of the following criteria: (1) self-report of a physician’s diagnosis of hypertension, (2) use of antihypertensive medication during the past 2 weeks, or (3) systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure <90 mm Hg.\textsuperscript{17}

Individuals underwent abdominal ultrasonography at baseline and every follow-up examination. The diagnosis of fatty liver disease was the presence of at least 2 or 3 abnormal findings on abdominal ultrasonography: diffusely increased echogenicity (“bright”) liver with liver echogenicity greater than kidney or spleen, vascular blurring, and deep attenuation of the ultrasound signal.\textsuperscript{18}

**Chinese VAI**

CVAI was calculated using the sex-specific formulas previously described,\textsuperscript{9} with triglyceride and HDL-C levels expressed as millimole per liter. The visceral adiposity area was estimated by CVAI as follows:

For Men: CVAI = −267.93 + 0.68×age + 0.03×BMI + 4.00×WC + 22.00×log\(_{10}\)TG − 16.32×HDL−C.

For Women: CVAI = −187.32 + 1.71×age + 4.23×BMI + 1.12×WC + 39.76×log\(_{10}\)TG − 11.66×HDL−C.

Participants were categorized into 4 groups based on the quartiles of CVAI: <49.63, 49.63 to 85.14, 85.14 to 116.12, and ≥116.12. The optimal cutoff value of CVAI was determined by the area under the receiver operating characteristic curve (cutoff value=86.229). The dynamic ΔCVAI was calculated by subtracting baseline CVAI from that of the previous follow-up. Participants were further classified by quintiles of ΔCVAI as follows: −9.429 to 4.000 (large decrease), −9.429 to 4.000 (large increase), −9.429 to 4.000 (moderate increase), and >4.000 (large increase).

**Statistical Analysis**

Baseline characteristics of the study participants are described based on the quartiles of CVAI. Numerical variables were reported as mean±SD, and categorical variables were expressed as frequency (percentage).

Person-years of follow-up were calculated from the date of the first entry visit to the date of the last confirmed follow-up, or the date of carotid plaque diagnosis. Three Cox proportional hazards models were established to assess the associations of CVAI and other adiposity indices (WHR, WHtR, LAP, ABSI, BMI,
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and VAI) with carotid plaque risk. The proportionality assumption was tested and verified. Hazard ratios (HRs) and 95% CIs were calculated in 3 models: model 1 was the crude model; model 2 was adjusted for sex, fasting plasma glucose, blood pressure information (systolic and diastolic), serum liver enzymes alanine aminotransferase and aspartate aminotransferase, estimated glomerular filtration rate, resting heart rate, lifestyle (cigarette smoking and alcohol drinking), and the medication history of hypolipidemic drugs and hypoglycemic drugs at baseline; and model 3 was further adjusted for white blood cell count at baseline. These covariates were included in the Cox models taking into account the univariate Cox regression results and their potential confounding effects between CVAI and carotid plaque risk. $P_{\text{trend}}$ was evaluated among baseline CVAI quartiles by imputing the median values for every quartile as continuous variables in Cox models. We also estimated the risk of carotid plaque associated with a 1-SD increase of CVAI. To describe the dose-response association between CVAI and incident carotid plaque, we used restricted cubic splines incorporated into the Cox models.

To assess the robustness of the results, sensitivity analysis was performed by removing individuals with carotid plaque that occurred during the first 2 years of follow-up. In addition, subgroup analyses were also performed by sex and personal medical history (eg, hypertension, diabetes, fatty liver disease, and medication history of hypoglycemic drugs). We performed crossover analyses in Cox model to evaluate CVAI and

| Table 1. Characteristics at Baseline by Follow-Up Outcomes |
|-------------------------------------------------------------|
| **Baseline characteristics**                                   |
| **CVAI quartiles**                                            |
| **Quartile 1** | **Quartile 2** | **Quartile 3** | **Quartile 4** | **P for trend** |
| No. of participants | 5712 | 5921 | 5988 | 5901 |  |
| Women, No. (%) | 4674 (81.83) | 3208 (54.18) | 1663 (27.77) | 620 (10.51) | <0.001 |
| Age, y | 34.87±8.49 | 42.34±9.06 | 45.53±10.17 | 47.62±11.26 | <0.001 |
| Height, m | 162.95±6.93 | 165.35±7.87 | 168.20±7.81 | 171.16±7.15 | <0.001 |
| Weight, kg | 56.80±6.77 | 66.03±7.34 | 73.72±7.85 | 84.63±10.32 | <0.001 |
| BMI, kg/m² | 21.38±2.06 | 24.14±2.06 | 26.05±2.17 | 28.85±2.77 | <0.001 |
| Hip circumference, cm | 91.10±4.37 | 94.90±4.19 | 97.70±4.40 | 102.31±5.34 | <0.001 |
| WC, cm | 71.69±5.19 | 80.77±4.40 | 87.58±3.93 | 96.63±6.05 | <0.001 |
| Resting heart rate, beats per min | 76.75±10.2 | 75.62±9.79 | 75.84±9.59 | 77.32±10.09 | <0.001 |
| UA, μmol/L | 265.13±62.73 | 307.66±75.43 | 354.23±78.68 | 387.86±80.39 | <0.001 |
| TC, mmol/L | 4.45±0.80 | 4.81±0.87 | 5.04±0.92 | 5.10±0.97 | <0.001 |
| Triglycerides, mmol/L | 0.84±0.37 | 1.27±0.67 | 1.83±1.20 | 2.61±2.04 | <0.001 |
| LDL-C, mmol/L | 2.57±0.65 | 2.96±0.71 | 3.16±0.74 | 3.14±0.76 | <0.001 |
| HDL-C, mmol/L | 1.60±0.34 | 1.42±0.32 | 1.29±0.27 | 1.17±0.24 | <0.001 |
| eGFR, mL/min per 1.73 m² | 60.06±19.09 | 65.78±22.83 | 72.86±21.81 | 78.46±20.00 | <0.001 |
| ALT, U/L | 15.46±10.03 | 20.88±15.14 | 26.72±18.42 | 34.21±29.07 | <0.001 |
| AST, U/L | 18.27±5.86 | 20.43±8.72 | 22.46±10.59 | 24.55±12.94 | <0.001 |
| FPG, mmol/L | 4.98±0.47 | 5.25±0.81 | 5.54±1.10 | 5.90±1.42 | <0.001 |
| SBP, mm Hg | 108.41±11.76 | 115.96±13.90 | 121.52±14.1 | 127.31±14.78 | <0.001 |
| DBP, mm Hg | 67.18±7.97 | 73.14±9.16 | 77.61±9.39 | 81.52±9.70 | <0.001 |
| WBC count, 10³/L | 5.72±3.60 | 5.96±4.51 | 6.20±3.13 | 6.59±2.09 | <0.001 |
| Cigarette smoking, No. (%) | 866 (15.16) | 1621 (27.38) | 2501 (41.77) | 2988 (50.64) | <0.001 |
| Alcohol drinking, No. (%) | 1050 (18.38) | 2095 (35.38) | 3072 (51.30) | 3640 (61.68) | <0.001 |
| Hypertension, No. (%) | 126 (2.21) | 251 (41.77) | 179 (28.76) | 368 (61.17) | <0.001 |
| Diabetes, No. (%) | 33 (0.58) | 176 (2.97) | 441 (7.36) | 857 (14.18) | <0.001 |
| Fatty liver, No. (%) | 146 (2.56) | 1123 (18.97) | 2741 (45.77) | 4487 (76.04) | <0.001 |
| Hypolipidemic drugs, No. (%) | 3 (0.05) | 15 (0.25) | 25 (0.42) | 47 (0.80) | <0.001 |
| Hypoglycemic drugs, No. (%) | 5 (0.09) | 26 (0.44) | 50 (0.84) | 69 (1.17) | <0.001 |

Values are expressed as mean±SD unless otherwise indicated. ALT indicates alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CVAI, Chinese visceral adiposity index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; UA, uric acid; WBC, white blood cell; and WC, waist circumference.
During the 82,621 person-years of follow-up, a total of 42.66±10.92 years, and 10,165 (43.21%) were women. The mean age of the study population was... 

RESULTS 

Baseline Information 

The mean age of the study population was 42.66±10.92 years, and 10,165 (43.21%) were women. During the 82,621 person-years of follow-up, a total of 5987 patients developed carotid plaque, with an incidence rate of 7.25 per 100 person-years. The baseline characteristics by quartiles of CVAI are shown in Table 1. With increasing CVAI quartiles (from quartile 1 to quartile 4), participants were older and had a higher level of BMI, hip circumference, WC, resting heart rate, uric acid, total cholesterol, triglycerides, low-density lipoprotein cholesterol, estimated glomerular filtration rate, alanine aminotransferase, aspartate aminotransferase, fasting plasma glucose, systolic blood pressure, diastolic blood pressure, and white blood cell count; and a lower level of HDL-C. In addition, there was an increased proportion of participants who smoked cigarettes and drank alcohol; had hypertension, diabetes, or fatty liver disease; and revealed a medication history of hypolipidemic drugs and hypoglycemic drugs (all \( P_{trend} <0.001 \)).

Baseline CVAI and Its Dynamic Change 

With Risk of Carotid Plaque 

Figure 1 showed that the risk of carotid plaque increased among the quartiles of CVAI. The risk of carotid plaque was increased with the increasing quartiles of CVAI in all 3 Cox regression models. In model 3, CVAI was significantly associated with carotid plaque risk comparing quartile 2 and quartile 3 and quartile 4 with quartile 1, with corresponding HRs and 95% CIs of 2.22 (1.97–2.51), 3.36 (2.98–3.80), and 4.00 (3.52–4.54), respectively (Figure 1). In the sensitivity analysis, by excluding participants who developed carotid intima-media thickness or carotid plaque in the first 2 years of follow-up, the associations remained significant (Figure 1). However, there was no significant association between ΔCVAI and carotid plaque risk (Table 2).

Restricted cubic splines showed a nonlinear dose-response association between the baseline CVAI and carotid plaque risk (\( P_{\text{nonlinearity}}<0.001 \)), and the risk of incident carotid plaque was >1.00 when CVAI was >85.868 (Figure 2). The risk of incident carotid plaque increased by 53% per 1-SD increase in baseline CVAI (HR, 1.53; 95% CI, 1.48–1.59) after adjusting for sex, fasting plasma glucose, systolic blood pressure, diastolic blood pressure, and white blood cell count; and a lower level of HDL-C. In addition, there was an increased proportion of participants who smoked cigarettes and drank alcohol; had hypertension, diabetes, or fatty liver disease; and revealed a medication history of hypolipidemic drugs and hypoglycemic drugs at baseline; and model 3 was further adjusted for white blood cell count at baseline. HR indicates hazard ratio.
Association Between CVAI and Carotid Plaque Risk

**Table 2. Association Between Dynamic ΔCVAI and Risk of Carotid Plaque**

| Model          | ΔCVAI quintiles | Per-SD increase | P for trend | ΔCVAI cutoff | P for trend |
|----------------|-----------------|-----------------|-------------|--------------|-------------|
| Model 1        | Reference        | 1.04 (0.95–1.13) | 0.98 (0.97–1.01) | 0.98 (0.96–1.01) | 0.98 (0.96–1.01) |
| Model 2        | Reference        | 0.97 (0.89–1.05) | 0.94 (0.86–1.02) | 0.94 (0.86–1.02) | 0.94 (0.86–1.02) |
| Model 3        | Reference        | 1.00 (0.98–1.03) | 1.00 (0.98–1.03) | 1.00 (0.98–1.03) | 1.00 (0.98–1.03) |

**Figure 2. Nonlinear association between Chinese visceral adiposity index (CVAI) and the risk of carotid plaque.**
Data are hazard ratios (HRs; solid line) and 95% CIs (gray area) from Cox proportional hazard regression analysis with restricted cubic splines. Adjusted for sex, fasting plasma glucose, systolic blood pressure, diastolic blood pressure, alanine aminotransferase, aspartate aminotransferase, uric acid, estimated glomerular filtration rate, resting heart rate, cigarette smoking, alcohol drinking, medication history of hypolipidemic drugs and hypoglycemic drugs, and white blood cell count at baseline.

Subgroup Analyses

In the subgroup analyses stratified by sex, the associations between CVAI and carotid plaque risk were both significant in men and women, and the HR was larger in men than in women (in model 3, for men: HR, 4.14 [95% CI, 3.36–5.12]; for women: HR, 2.92 [95% CI, 2.42–3.53]). For a 1-SD increase in CVAI, the association between CVAI and carotid plaque risk remained significant in model 3 (Figure 1). As shown in Figure 1, either in the overall analysis or in the sensitivity analysis of model 3, compared with CVAI ≤86.229, CVAI >86.229 could significantly increase carotid plaque risk (for overall analysis: HR, 1.94 [95% CI, 1.81–2.08]; for sensitivity analysis: HR, 1.95 [95% CI, 1.79–2.12]).
Table 3. Interaction Between CVAI Level and Diabetes Status on Risk of Carotid Plaque

| CVAI level | Diabetes status | Interaction |
|------------|----------------|-------------|
|            | No diabetes    | Diabetes    | HR (95% CI) | P value |
| **Model 1**|                |             |             |         |
| Low CVAI   | Reference      | 3.82 (3.11–4.68) | 0.42 (0.34–0.53) | <0.001 |
| High CVAI  | 2.65 (2.49–2.81) | 4.26 (3.89–4.67) |             |         |
| **Model 2**|                |             |             |         |
| Low CVAI   | Reference      | 3.09 (2.51–3.80) | 0.42 (0.38–0.47) | <0.001 |
| High CVAI  | 2.07 (1.93–2.22) | 2.99 (2.70–3.32) |             |         |
| **Model 3**|                |             |             |         |
| Low CVAI   | Reference      | 3.09 (2.51–3.80) | 0.42 (0.38–0.47) | <0.001 |
| High CVAI  | 2.07 (1.93–2.22) | 2.99 (2.70–3.32) |             |         |

CVAI indicates Chinese visceral adiposity index; HR<sub>interaction</sub>, the combination effect of CVAI and diabetes on the risk of carotid plaque; and HR<sub>1</sub>, the interaction effect of CVAI and diabetes on the risk of carotid plaque.

1 Model 1 was the crude model.

2 Model 2 was adjusted for sex, fasting plasma glucose, systolic blood pressure, diastolic blood pressure, alanine aminotransferase, aspartate aminotransferase, uric acid, estimated glomerular filtration rate, resting heart rate, cigarette smoking, alcohol drinking, and medication history of hypolipidemic drugs and hypoglycemic drugs at baseline.

3 Model 3 was further adjusted for white blood cell count at baseline.

Figure 3. Forest plot of the association between baseline Chinese visceral adiposity index (CVAI) and risk of carotid plaque stratified according to disease status.

Model 1 was the crude model; model 2 was adjusted for sex, fasting plasma glucose, systolic blood pressure, diastolic blood pressure, alanine aminotransferase, aspartate aminotransferase, uric acid, estimated glomerular filtration rate, resting heart rate, cigarette smoking, alcohol drinking, and medication history of hypolipidemic drugs and hypoglycemic drugs at baseline; and model 3 was further adjusted for white blood cell count at baseline. *P* values < 0.025 were considered statistically significant.
HR of carotid plaque risk in men was also stronger than that in women (in model 3, for men: HR, 2.15 [95% CI, 1.99–2.33]; for women: HR, 1.33 [95% CI, 1.28–1.39]). A similar pattern was also observed when comparing CVAI >86.229 with CVAI ≤86.229 (Figure 1).

As shown in Figure 3, in the subgroup analyses stratified by hypertension and fatty liver disease, the association between CVAI and carotid plaque risk remained significant in all subgroups. In the subgroup analysis stratified by diabetes, the positive correlation between CVAI and carotid plaque risk was highly significant in the nondiabetes subgroup in all 3 models (in model 3, quartile 4 versus quartile 1: HR, 4.21 [95% CI, 3.69–4.80]; quartile 3 versus quartile 1: HR, 3.41 [95% CI, 3.01–3.86]; quartile 2 versus quartile 1: HR, 2.19 [95% CI, 1.94–2.48]). However, this association became nonsignificant in the diabetic population (Figure 3).

We also conducted a multiplicative interaction test and observed an antagonistic interaction effect between CVAI and diabetes status in all 3 models (in model 3: HR, 0.42 [95% CI, 0.38–0.47]; P<0.001) (Table 3). We further conducted subgroup analysis by the medication history of hypoglycemic drugs in the diabetic group and found a significant positive correlation between CVAI and carotid plaque risk in the group without a medication history of hypoglycemic drugs, with no significant linear trend (in model 3, quartile 4 versus quartile 1: HR, 2.29 [95% CI, 1.06–4.92]; quartile 3 versus quartile 1: HR, 2.30 [95% CI, 1.07–4.93]; quartile 2 versus quartile 1: HR, 2.31 [95% CI, 1.05–5.05]) (Table 4). However, no significant correlation was observed in the subgroup of patients with a medication history of hypoglycemic drugs.

### Baseline Adiposity Indices and Risk of Carotid Plaque

Carotid plaque risk was significantly increased with the increasing quartiles of WHR, WhtR, LAP, ABSI, BMI, and VAI in all 3 Cox regression models, except for the nonsignificant association between ABSI and BMI and carotid plaque risk comparing quartile 2 with the reference. Carotid plaque risk was also increased with per-SD increase in WHR, WhtR, LAP, ABSI, BMI, and VAI, except that the association between VAI and LAP and risk of incident carotid plaque became weakly statistically significant in the sensitivity analyses. The corresponding HRs for carotid plaque with per-SD increase in model 3 were 1.12 (95% CI, 1.07–1.17) and 1.10 (95% CI, 1.04–1.16) for WHR, 1.08 (95% CI, 1.02–1.15) and 1.11 (95% CI, 1.03–1.19) for WhtR, 1.02 (95% CI, 1.00–1.05) and 1.01 (95% CI, 0.98–1.04) for LAP, 1.03 (95% CI, 1.00–1.06) and 1.03 (95% CI, 1.00–1.07) for ABSI, 1.06 (95% CI, 1.03–1.09) and 1.08 (95% CI, 1.04–1.13)
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![Image](https://example.com/image.png)

**Figure 4.** Forest plot of the association between baseline adiposity indices level and risk of carotid plaque.

Model 1 was the crude model; model 2 was adjusted for sex, fasting plasma glucose, systolic blood pressure, diastolic blood pressure, alanine aminotransferase, aspartate aminotransferase, uric acid, estimated glomerular filtration rate, resting heart rate, cigarette smoking, alcohol drinking, and medication history of hypolipidemic drugs and hypoglycemic drugs at baseline; and model 3 was further adjusted for white blood cell count at baseline. ABSI indicates a body shape index; BMI, body mass index; LAP, lipid accumulation product; VAI, visceral adiposity index; WHR, waist-to-hip ratio; and WHtR, waist-to-height ratio.

for BMI, and 1.03 (95% CI, 1.00–1.05) and 1.02 (95% CI, 0.99–1.05) for VAI in overall analyses and sensitivity analyses, respectively (Figure 4).

We constructed 2 receiver operating characteristic curves to compare the predictive efficacy of CVAI and other adiposity indices, and CVAI and its constituent indices on the risk of carotid plaque. The receiver operating characteristic curves and AUCs for CVAI, WHR, WHtR, LAP, ABSI, BMI, VAI, WC, triglycerides, and HDL-C for predicting carotid plaque risk were shown in Figure 5. The corresponding AUCs were 0.710 (95% CI, 0.563–0.764) for CVAI, 0.675 (95% CI, 0.575–0.691) for WHR, 0.658 (95% CI, 0.481–0.762) for WHtR, 0.656 (95% CI, 0.496–0.747) for LAP, 0.641 (95% CI, 0.552–0.657) for ABSI, 0.614 (95% CI, 0.407–0.780) for BMI, and 0.609 (95% CI, 0.480–0.691) for VAI (Figure 5A). The corresponding AUCs were 0.655 (95% CI, 0.518–0.724) for WC, 0.638 (95% CI, 0.481–0.733) for
for triglycerides, and 0.544 (95% CI, 0.436–0.645) for HDL-C, respectively (Figure 5B). The AUC of CVAI was the largest among all of the adiposity indices (P<0.001).

DISCUSSION

In this cohort study, we observed a positive correlation between CVAI and carotid plaque risk in a non-linear dose-response pattern. The association remained significant in all subgroup analyses stratified by sex, hypertension, and fatty liver disease except for in the diabetes subgroup. The association between CVAI and carotid plaque risk was much higher in men than in women. The sensitivity analysis excluding individuals who developed carotid plaque within the first 2 years further confirmed the robustness of the results.

Previous studies have shown that abdominal obesity and adipose tissue dysfunction were closely related to cardiovascular disease. The accumulation of abdominal fat can independently increase the risk of cardiovascular disease, and fat cells may mechanically promote the increased vascular stiffness in obesity. Furthermore, a retrospective study also found that CVAI was significantly higher in patients with carotid atherosclerosis and was associated with a 39% higher risk of carotid atherosclerosis. Adipose tissue is an active endocrine and paracrine organ that releases a large number of cytokines and bioactive mediators, such as leptin, adiponectin, interleukin 6, and tumor necrosis factor-α, which may influence blood flow and promote atherosclerosis.

Xia et al promoted CVAI as a simple clinical index composed of age, WC, triglycerides, HDL-C, and BMI, which was easily available in clinical practice to reflect visceral fat mass. A Chinese prospective cohort study also found that the visceral obesity rate estimated by CVAI was more predictive of the occurrence of prediabetes and diabetes than the traditional estimates of obesity such as BMI and WC. In addition, we also tried to analyze the impact of ΔCVAI on carotid plaque risk during the observation period, but we did not find a significant correction between the dynamic change of CVAI and carotid plaque risk. In brief, our results supported CVAI as a reliable and promising marker of carotid plaque.
The association between CVAI and carotid plaque risk. In patients without diabetes, increased CVAI was strongly related to larger adverse risk of carotid plaque, but, in patients with diabetes, this association became weaker and not statistically significant. We also observed an antagonistic interaction between the abdominal adiposity index CVAI and diabetes, which may weaken the impact of CVAI on carotid plaque formation. Further stratified analyses according to the medication history of hypoglycemic drugs found that there was a significant positive correlation between CVAI and carotid plaque risk in the subgroup without hypoglycemic drug use. However, there were no significant results in the other subgroup. There are several possible explanations. First, the small sample size (n=1487) in the diabetes subgroup may explain the nonsignificant results. Second, patients with diabetes may have blood glucose control (such as using hypoglycemic drugs) and changed their lifestyle and dietary habits during the follow-up period, which may affect the association between CVAI and carotid plaque risk. Third, as diabetes is accompanied by glucose regulation disorders, patients’ risk of vascular disease may be more related to the variability in glycemic control, which could explain our results in this subgroup.

Evidence supports that the risk of diabetes was affected by plasma concentrations of different adipokines, and the mechanism in the healthy population and patients with atherosclerosis was different. Interestingly, our results also show that the risk of carotid plaque affected by the abdominal adiposity index CVAI was different in patients with diabetes and those without diabetes. Proinflammatory resistin was reported to be positively correlated with insulin sensitivity. However, in patients with atherosclerosis, the plasma level of resistin was increased, and the positive correlation between resistin and insulin sensitivity was weakened. Taken together, patients with diabetes may be able to reverse their carotid plaque risk caused by abdominal obesity by changing certain lifestyle or dietary habits or trying to keep their glucose levels steady.

Previous studies reported that CVAI was superior to BMI, WC, WHR, WHtR, VAI, ABSI, and LAP for diagnosing diabetic kidney disease, hypertension, diabetes, and prediabetes. Similar results were also observed in our analyses that the AUC of CVAI was the largest among all of the adiposity indices in predicting the risk of incidence of carotid plaque. CVAI, as a comprehensive index, includes many well-known carotid plaque risk factors, such as BMI, WC, triglycerides, and HDL-C. Compared with these single indicators, CVAI also presented the largest AUC.

BMI, WC, ABSI, WHR, and WHtR are typically recommended as indicators of general obesity or as measures of abdominal obesity but still have limitations in distinguishing subcutaneous adipose tissue from visceral fat. VAI and LAP were also cardiometabolic risk indices, with similar correlations but with relatively less strength. These results suggest that CVAI may be better than other adiposity indices at identifying carotid plaque risk.

This cohort study has many advantages, including the prospective design, large sample size, and adjustment for multiple potential confounding factors. Limitations should also be considered. First, we did not use imaging methods to quantitatively assess abdominal fat to further validate our results. Second, the CVAI values of 5901 participants were missing because of missing values of WC, triglycerides, or HDL-C. However, we used multiple imputation methods to fill in the missing data to reduce bias. Third, although we adjusted for many covariates, there is still the possibility of residual confounding, such as dietary intake and psychological factors. Finally, all of the participants in this study were selected from ongoing health checkups of highly educated employees, and, therefore, their education level may be higher than that of general Chinese citizens and their awareness of disease and prevention may also be stronger. In addition, Beijing has better health care resources, and the diagnosis rate of diseases may be higher than that of other regions. Moreover, with the rapid development of Beijing’s economy, residents’ diets and lifestyles are unique compared with other regions. All of the above may limit the generalizability of these findings.

CONCLUSIONS
The CVAI was a useful and applicable indicator for predicting carotid plaque risk for both sexes, individuals with and without hypertension and fatty liver disease, and individuals without diabetes. The association between CVAI and risk of carotid plaque was in a nonlinear pattern. Individuals should keep their CVAI within a normal level to prevent carotid plaque.

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Disclosures

None.
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