Original Article

Association Between a Body Shape Index and Subclinical Carotid Atherosclerosis in Population Free of Cardiovascular and Cerebrovascular Diseases

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Aim: We used a dataset from a cross-sectional survey conducted in China to determine which of the anthropometric indices of obesity are important in terms of carotid atherosclerosis free of cardiovascular and cerebrovascular diseases.

Methods: A total of 5,245 participants who were volunteering for carotid ultrasound unit in this cross-sectional survey were included in the present analysis. All subjects were free of angina, myocardial infarction, heart failure and stroke, and cancer. A low-risk subgroup was defined as people free of hypertension, diabetes, and hyperlipidemia. All analyses based on logistic regression were gender-specific.

Results: The present study consisted of 2,501 males and 2,744 females, with 776 (31.03%) diagnosed as carotid artery plaque in males and 550 (20.04%) in females. Univariable analyses in unadjusted logistic model showed significant associations between disease presence and all central obesity indices. After adjusting for more variables, only a body shape index (ABSI) was associated with the presence of disease in both males and females. Moreover, stepwise regression approaches revealed that ABSI was always an independent determinant of the presence of subclinical carotid plaque. Multiple regression shows a linear and significant increase in the prevalence of atherosclerosis in males and females as ABSI decile levels increased. Similar results were obtained when the association between ABSI and carotid plaque was studied in this low-risk subgroup.

Conclusions: ABSI, as a novel anthropometric indicator compared with traditional indices, was found to have a closer relationship with subclinical carotid atherosclerosis, even in populations free of hypertension, diabetes, and hyperlipidemia.

Introduction

Atherosclerosis is a chronic progressive vascular disease, which is a dominant cause of cardiovascular and cerebrovascular diseases (CCVds) such as coronary heart disease and cerebral infarction[1, 2]. The process of atherosclerosis begins in adolescence. There is no typical clinical manifestation for a long time before the occurrence of CCVds; that is, it is in the risk stage of subclinical atherosclerosis. When the plaque develops and evolves into high-risk plaque phenotype, it may lead to cerebrovascular events[2]. Cerebral atherosclerosis and carotid atherosclerosis are serious stages of atherosclerosis development and are important risk factors of ischemic stroke. Stroke with cerebral and carotid artery stenosis is the main type of

severe disability and death[3]. A multicenter prospective study published in 2014 [4] pointed out that the prevalence of intracranial atherosclerosis in patients with acute cerebral ischemia within 7 days after symptoms was 46.6%. At the same time, compared with patients without intracranial stenosis, stroke patients with intracranial stenosis had more severe clinical manifestations, more hospitalization days, and more recurrence. Therefore, it is critically important to identify and control atherosclerosis earlier. In particular, patients with subclinical carotid atherosclerosis should be found as soon as possible.

Obesity is a chronic metabolic disease, which is widely believed to be independently associated with cardiovascular and cerebrovascular risk. Body mass index (BMI) has been widely used in the evaluation of obesity. However, there is no consensus on the relationship between BMI and the prevalence and prognosis of CCVds[5, 6]. BMI is not an appropriate indicator to assess fat distribution and diagnose visceral obesity; that is, it is unable to distinguish central obesity from systemic obesity. It is worth noting that central obesity seems more important to predict the risk of CCVds and deaths[7]. Waist circumference (WC, cm) is regarded as a simple physical measure to assess central obesity, but it does not take into account differences in height and overall body shape. Waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) have also been associated with increased arterial stiffness, but the relationship is not always significant[8-10]. A body shape index (ABSI) and the body roundness index (BRI) are newly developed anthropometric indices. Krakauer et al.[11] proposed ABSI in 2012, which combines height, BMI, and WC, and Thomas et al.[12] developed the BRI in 2013, which combines height and WC. Several studies[13-15] have raised the potential of these two indices to identify metabolic syndrome and cardiovascular health status; meanwhile, other studies[16-18] have looked at their association with atherosclerosis and subclinical vascular damage. However, these relationships have not been consistently recognized.

Aim

In this study, we aimed to explore the associations between obesity anthropometric indices and subclinical carotid atherosclerosis in rural adults in northwest China. Further, we analyzed whether this association persisted in populations at low risk of CCVds.

Methods

Study Design

This study was derived from a multi-stage sampling cross-sectional survey conducted in Jingyuan County, Ningxia Hui Autonomous Region, China, from January 2014 to April 2015 [19]. All the respondents had lived in Jingyuan County for more than 5 years and were at least 18 years old. Pregnant women and patients with mental illness were excluded. Participants underwent clinical interviews, laboratory analysis, and imaging studies. The study protocol, which conforms to the ethical guidelines of Helsinki Declaration, was approved by the ethics committee of the sixth people's hospital affiliated to Shanghai Jiao Tong University (approval no. 2014-18). All the subjects signed informed consent forms before the investigation.

This study includes residents between the ages of 18 and 80 who volunteered for carotid ultrasound unit. The main exclusion criteria in this study were known CCVds such as angina, myocardial infarction, heart failure and stroke, or cancer. At the same time, those who did not record gender, age (year), height (cm), weight (kg), WC (cm), hip circumference (HC, cm), systolic blood pressure (SBP, mmHg), diastolic blood pressure (DBP, mmHg), smoking status, and laboratory test results, such as fasting plasma glucose (FPG, mmol/L), serum total cholesterol (TC, mmol/L), serum total triglycerides (TG, mmol/L), high-density lipoprotein cholesterol (HDL-C, mmol/L), low-density lipoprotein cholesterol (LDL-C, mmol/L), and estimated glomerular filtration rate (eGFR, ml/min), were excluded.

Assessment of Physical Examination Indices and Blood Biochemical Parameters

Physical indicators were measured with participants in the fasted state, light clothing, and barefoot. Height and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively. WC was measured using an inelastic tape at the level of the midpoint between the top edge of iliac crest and the bottom edge of ribs to the nearest 1 cm. HC was measured horizontally at the greatest level of protrusion of the buttocks to the nearest 1 cm. Blood pressure was measured by using a standard cuff sphygmomanometer in the same arm for three times after the subjects sat quietly for 10 min, each time with an interval of 2 min. Then, take the average of the three readings. Subjects were seated and measured twice, 30 s apart. The average of the two measurements was taken as the blood pressure. eGFR were calculated according to Chronic Kidney Disease
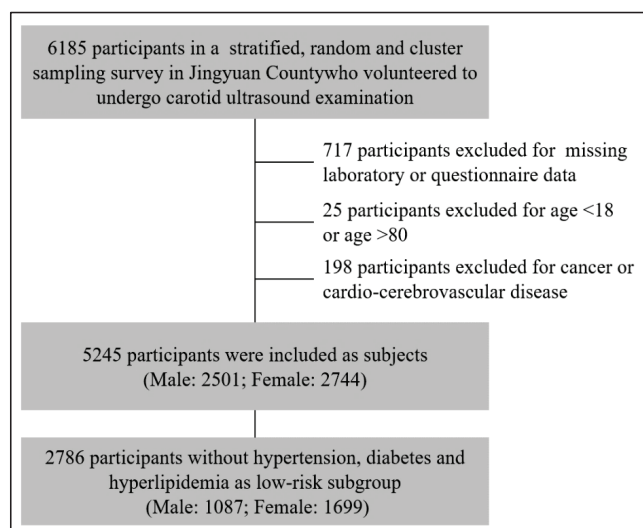
Fig. 1. The flowchart of study population inclusion and exclusion

Epidemiology Collaboration (CKD-EPI) formula[20].
BMI = weight/(height × height) (kg/m^2).
WHR = WC/HC × 100%. WHtR = WC/Height.

$$BRI = 364.2 - 365.5 \times \sqrt{1 - \left(\frac{WC}{2\pi}\right)^2 / (0.5 \times Height)^2}.$$

$$ABSI = WC / [BMI^{\frac{2}{3}} \times Height^{\frac{1}{2}}].$$

Venous blood was collected after 8 h of fasting for measurements of glucose and lipids using standard techniques. TC and TG were determined by oxidase method. HDL-C and LDL-C were measured by direct method.

Assessment of Atherosclerosis

Carotid color Doppler ultrasound was performed in all participants to assess the presence of carotid artery atherosclerotic (CAA) plaques. The presence of carotid plaques by ultrasound was assessed by cross-sectional sweep of bilateral common carotid artery, bilateral internal carotid artery extracranial segment, external carotid artery, and subclavian artery. Plaques were defined as an intravascular diffuse intima-media thickness greater than 1.5 mm, or a focal protrusion greater than 0.5 mm or 1/2 of the surrounding intima-media thickness[21]. The ultrasound examination was performed by an experienced, professional clinician and recorded and checked by another one. Finally, the two of them checked the results of the final images.

Definition of the CCVd-Free Population and the Low-Risk Subgroup

Participants in the study, who did not have angina, myocardial infarction, heart failure, or stroke,

were defined as CCVd-free population. The history of CCVds was confirmed by personal disease history, medication history, and surgical history in questionnaire. Within the CCVd-free population, we also defined a subgroup with low risk of CCVds, in which individuals were free of hypertension, diabetes, and hyperlipidemia **(Fig. 1)**. Hypertension was defined as a mean SBP ≥ 140 mm Hg or a mean DBP ≥ 90 mm Hg or use of antihypertensive medication; diabetes was defined as FPG ≥ 7 mmol/L; and hyperlipidemia was defined as an elevated level of TC (>200 mg/dL), LDL-C (≥ 4.1 mmol/L), or HDL-C (<1 mmol/L).

Statistics

The continuous variables of normal distribution or near normal distribution were described by mean and standard deviation ($\bar{x} \pm s$), and Student's *t*-test was used for comparison. The classification variables were described by the number of cases and composition ratio [n (%)], and the chi-square test (χ^2) was used for comparison. Binary logistic regression was used to evaluate the associations between anthropometric variables and carotid atherosclerosis. Adjustments were made for age in adjusted model 1 and for age, race, smoking status, SBP, LDL-C, FBG, and eGFR in adjusted model 2. Explanatory variables in adjusted models were selected from past literature[22-25], and race was also considered as an adjustment variable due to the different characteristics of Hui and Han[26, 27]. Odds ratios (ORs) and 95% confidence intervals (CI) were calculated. The ORs examined the change in odds per unit increase in variables, except for WHR, WHtR, and ABSI, which were scaled by a factor of 10

Table 1. The general demographic and clinical characteristics of the CCVd-Free population according to CAA

	Male			Female		
	CAA (N=776)	Non-CAA (N=1725)	p	CAA (N=550)	Non-CAA (N=2194)	p
Age (years)	58.23 ± 10.60	44.62 ± 11.78	<0.001	58.01 ± 9.27	42.51 ± 10.91	<0.001
Race[n(%)]			<0.001			<0.001
Han	227 (29.25)	348 (20.17)		181 (32.91)	450 (20.51)	
Hui	549 (70.75)	1377 (79.83)		369 (67.09)	1744 (79.49)	
Farmer[n(%)]			<0.001			<0.001
Yes	611 (78.74)	1168 (67.71)		486 (88.36)	1542 (70.28)	
No	165 (21.26)	557 (32.29)		64 (11.64)	652 (29.72)	
Smoking[n(%)]			<0.001			0.037
Yes	259 (33.38)	731 (42.38)		8 (1.45)	11 (0.50)	
No	517 (66.62)	994 (57.62)		542 (98.55)	2183 (99.50)	
SBP (mmHg)	126.00 ± 16.31	120.48 ± 14.71	<0.001	127.90 ± 17.08	116.64 ± 16.28	<0.001
DBP (mmHg)	82.55 ± 12.12	79.87 ± 11.03	<0.001	82.76 ± 12.12	77.07 ± 11.05	<0.001
FBG (mmol/l)	5.48 ± 1.35	5.30 ± 1.03	0.001	5.63 ± 1.63	5.27 ± 1.08	<0.001
TG (mmol/l)	1.42 ± 0.86	1.55 ± 1.15	0.001	1.47 ± 0.81	1.33 ± 0.94	<0.001
TC (mmol/l)	3.60 ± 0.67	3.47 ± 0.65	<0.001	3.82 ± 0.65	3.48 ± 0.64	<0.001
HDL-C (mmol/l)	1.17 ± 0.27	1.13 ± 0.26	0.002	1.33 ± 0.32	1.28 ± 0.27	<0.001
LDL-C (mmol/l)	2.51 ± 0.70	2.37 ± 0.64	<0.001	2.63 ± 0.64	2.33 ± 0.64	<0.001
eGFR (ml/min)	80.85 ± 10.92	88.21 ± 12.02	<0.001	71.99 ± 9.95	81.14 ± 11.29	<0.001
Height (cm)	164.30 ± 6.99	167.22 ± 6.91	<0.001	153.93 ± 6.11	157.56 ± 6.13	<0.001
Weight (kg)	64.22 ± 10.08	66.76 ± 10.45	<0.001	56.33 ± 9.64	58.60 ± 9.01	<0.001
WC (cm)	81.59 ± 9.00	80.50 ± 9.19	0.005	79.97 ± 10.03	76.13 ± 9.22	<0.001
HC (cm)	93.65 ± 6.19	93.75 ± 6.27	0.724	92.92 ± 7.25	92.26 ± 6.24	0.052
BMI (kg/m^2)	23.74 ± 3.05	23.84 ± 3.21	0.447	23.71 ± 3.42	23.59 ± 3.26	0.455
WHR	0.87 ± 0.07	0.86 ± 0.06	<0.001	0.86 ± 0.07	0.82 ± 0.07	<0.001
WHtR	0.50 ± 0.06	0.48 ± 0.06	<0.001	0.52 ± 0.07	0.48 ± 0.06	<0.001
ABSI	0.77 ± 0.07	0.75 ± 0.06	<0.001	0.78 ± 0.08	0.74 ± 0.07	<0.001
BRI	3.36 ± 1.08	3.09 ± 1.03	<0.001	3.83 ± 1.36	3.13 ± 1.16	<0.001

CAA, carotid artery atherosclerosis; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TG, serum total triglycerides; TC, serum total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; WC, waist circumference; HC, hip circumference; BMI, body mass index; WHR, waist-hip ratio; WHtR, waist-to-height ratio; ABSI, a body shape index; BRI, the body roundness index.

owing to its small range. Stepwise multiple regression analysis was used to evaluate the relationship among the factors. The incidence of carotid atherosclerosis plaque in each ABSI decile level and the OR compared with the first decile level were described graphically. All analyses were gender-specific due to differences in the incidence of carotid plaque between the genders. We used R 3.5.2 (for Windows, 64 bit) for statistical analysis. α =0.05 was considered the statistical significance level.

Results
Characterization of the CCVd-Free Population and the Low-Risk Subgroup

The physical examination indices and serum biomarkers of the CCVd-free population stratified by CAA are shown in **Table 1**. Our CCVd-free population consisted of 2,501 males and 2,744 females, with 776 (31.03%) diagnosed as CAA in males and 550 (20.04%) in females. In both males and females, all physical examination indices except for HC and BMI significantly differed according to atherosclerosis status. Meanwhile, significant differences were found in all serum biomarkers including blood glucose and blood lipids.

Supplementary Table 1 shows the characteristics of the low-risk subgroup stratified by CAA. Similarly, all physical examination indices and serum biomarkers except for HC and BMI significantly differed according to atherosclerosis status in females. In males, there were no significant differences in BMI, HC,

Table 2 Correlations between obesity anthropometric indices with CAA in CCVd-Free population

	Unadjusted Model		Adjusted Model 1		Adjusted Model 2	
	OR(95%CI)	*p*	OR(95%CI)	*p*	OR(95%CI)	*p*
Male						
ABSI	1.58 (1.39, 1.81)	<0.001	1.31 (1.12, 1.53)	<0.001	1.29 (1.10, 1.51)	0.002
BRI	1.28 (1.18, 1.39)	<0.001	1.14 (1.04, 1.25)	0.006	1.09 (0.98, 1.20)	0.099
WHR	1.35 (1.19, 1.54)	<0.001	1.33 (1.14, 1.55)	<0.001	1.20 (1.02, 1.41)	0.025
WHtR	1.62 (1.39, 1.88)	<0.001	1.28 (1.07, 1.54)	0.007	1.17 (0.97, 1.42)	0.106
WC	1.01 (1.00, 1.02)	0.006	1.01 (1.00, 1.02)	0.028	1.01 (1.00, 1.02)	0.210
BMI	0.99 (0.96, 1.02)	0.455	1.00 (0.97, 1.03)	0.837	0.97 (0.94, 1.01)	0.149
Female						
ABSI	2.23 (1.96, 2.56)	<0.001	1.42 (1.21, 1.66)	<0.001	1.45 (1.24, 1.71)	<0.001
BRI	1.53 (1.42, 1.65)	<0.001	1.09 (0.99, 1.19)	0.063	1.10 (1.00, 1.21)	0.053
WHR	2.16 (1.88, 2.49)	<0.001	1.20 (1.01, 1.42)	0.033	1.17 (0.98, 1.39)	0.081
WHtR	2.36 (2.04, 2.74)	<0.001	1.18 (0.98, 1.41)	0.080	1.19 (0.98, 1.44)	0.072
WC	1.04 (1.03, 1.05)	<0.001	1.00 (0.99, 1.02)	0.471	1.00 (0.99, 1.02)	0.461
BMI	1.01 (0.98, 1.04)	0.442	0.95 (0.92, 0.99)	0.080	0.95 (0.91, 0.98)	0.003

Adjusted model 1: adjusted for age. Adjusted model 2: adjusted for age, race, smoking status, SBP, LDL-C, FBG and eGFR.
WHR, WHtR and ABSI were scaled by a factor of 10 owing to its small range.
CAA, carotid artery atherosclerosis; CCVd, cardiovascular and cerebrovascular diseases; ABSI, a body shape index; BRI, the body roundness index; WHR, waist-hip ratio; WHtR, waist-to-height ratio; WC, waist circumference; BMI, body mass index.

DBP, TG, and HDL-C between CAA and non-CAA populations.

Association Between ABSI and Subclinical Carotid Atherosclerosis

As shown in **Table 2**, we performed whether obesity indices that showed statistically significant differences above such as ABSI, BRI, WHR, WHtR, WC, and BMI are associated with CAA in CCVd-free population. Univariable analyses in unadjusted model showed significant associations between disease presence and all obesity indices except for BMI. In adjusted model 1, taking age into account, all central obesity indices were significantly associated with CAA in males, while only ABSI and WHR were in females. In adjusted model 2, after adjusting for more variables including age, race, smoking status, SBP, LDL-C, FBG, and eGFR, only ABSI was associated with the presence of disease in both males and females. BMI was statistically significant as a protective factor for CAA in females.

Moreover, stepwise regression approaches revealed that ABSI was always an independent determinant of the presence of subclinical carotid plaque in both males and females **(Table 3)**. Age, race, SBP, and eGFR were all associated with the presence of disease in both genders. Additional independent predictors included LDL-C in males and farmer in females.

The relationship between ABSI levels and atherosclerosis in CCVd-free population was illustrated in **Fig. 2**. The ABSI deciles of males and females were calculated separately to generate ten levels. As ABSI levels increased, there was a linear and significant increase in the prevalence of CAA in males, ranging from 19.60% in the lowest level to 43.43% in the highest level (*p* for trend <0.001). This progressive increase was also noted in females, with the prevalence of CAA ranging from 6.18% in the lowest level to 38.55% in the highest level (*p* for trend <0.001). Multivariate analysis showed that those with higher ABSI levels had a higher risk of suffering from carotid plaque than those in the lowest level group, which were the ninth and tenth decile levels for males and the fourth, seventh, eighth, ninth, and tenth decile levels for females. Compared with the lowest decile level, the OR of the highest decile level was 1.87 (95% CI 1.17–3.00, *p*=0.009) for males and 2.83 (95% CI 1.52–5.50, *p*=0.001) for females, respectively.

Association Between ABSI and Atherosclerosis in Low-Risk Subgroup

Individuals who were free of hypertension, diabetes, and hyperlipidemia were involved in low-risk subgroup. Similar results were obtained when the

Table 3. Multivariable logistic regression analyses for CAA in CCVd-Free population

	Estimate	SE	Z	OR(95%CI)	p
Male					
ABSI	0.2557	0.0802	3.19	1.29 (1.10, 1.51)	0.001
Age	0.1135	0.0062	18.27	1.12 (1.11, 1.13)	<0.001
Race(Hui)	-0.6504	0.1151	-5.65	0.52 (0.42, 0.65)	<0.001
SBP	0.0081	0.0033	2.48	1.01 (1.00, 1.01)	0.013
LDL-C	0.3734	0.0778	4.80	1.45 (1.25, 1.69)	<0.001
eGFR	0.0210	0.0060	3.52	1.02 (1.01, 1.03)	<0.001
Female					
ABSI	0.3573	0.0822	4.35	1.43 (1.22, 1.68)	<0.001
Age	0.1325	0.0082	16.18	1.14 (1.12, 1.16)	<0.001
Race(Hui)	-0.6836	0.1284	-5.32	0.50 (0.39, 0.65)	<0.001
Farmer(No)	-0.591	0.1651	-3.58	0.55 (0.40, 0.76)	<0.001
SBP	0.0141	0.0035	4.01	1.01 (1.01, 1.02)	<0.001
eGFR	0.0182	0.0074	2.48	1.02 (1.00, 1.03)	0.013

ABSI, a body shape index; SBP, systolic blood pressure; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate. ABSI were scaled by a factor of 10 owing to its small range.
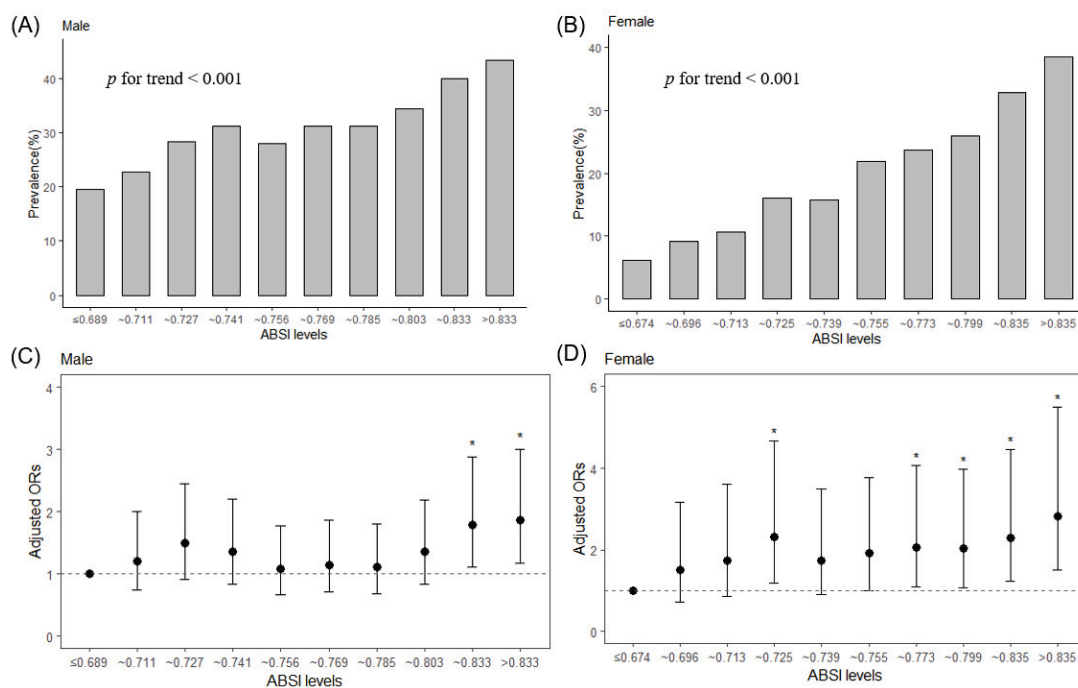

Fig. 2. Prevalence and adjusted odds ratios for the association of CAA with ABSI decile levels for both men and women in CCVd-free population

(A) As ABSI decile levels rise, there is a linear and significant increase in the prevalence of CAA in males, ranging from 19.60% in the lowest level to 43.43% in the highest decile level ($p<0.001$). (B) A similar pattern is observed for females, with the prevalence of CAA ranging from 6.18% in the lowest level to 38.55% in the highest level ($p<0.001$). (C and D) Adjusted odds ratios for the association of CAA with ABSI decile levels for males and females, respectively. Compared with the lowest decile level, the OR of the highest decile level was 1.87 (95% CI 1.17–3.00, $p=0.009$) for males and 2.83 (95% CI 1.52–5.50, $p=0.001$) for females, respectively.
*means the OR compared with the first decile level were statistical significance ($p<0.05$).
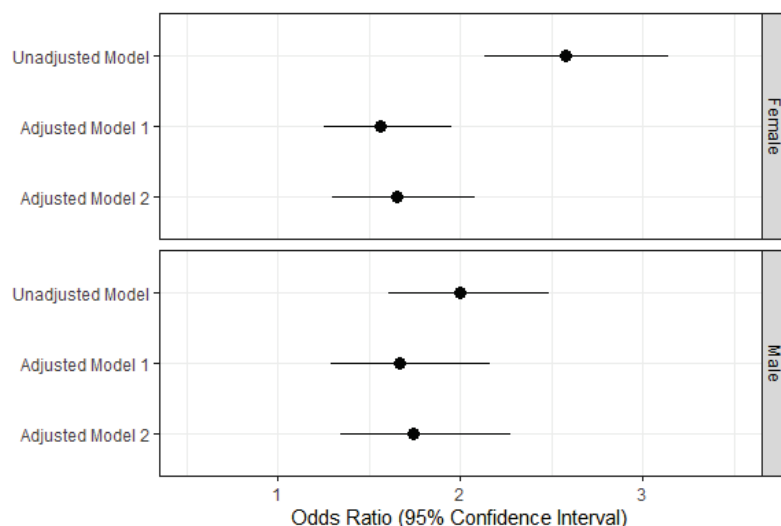The lowest decile served as the reference category. Vertical bars represent 95 percent confidence intervals.

Fig. 3. Correlations between ABSI and CAA in low-risk subgroup

Adjusted model 1: adjusted for age. Adjusted model 2: adjusted for age, race, smoking status, SBP, LDL-C, FBG, and eGFR.

association between ABSI and carotid plaque was studied in this low-risk subgroup **(Fig. 3)**. In all models for both males and females, ABSI consistently represented a risk factor for CAA. Meanwhile, as ABSI levels increased, there was also a linear and significant increase in the prevalence of atherosclerosis (*p* for trend < 0.001 for both males and females) that was revealed in **Fig. 4**. The ORs for the highest deciles in males and females were 5.02 (95% CI 2.18–12.41, *p* < 0.001) and 3.34 (95% CI 1.37–9.26, *p* = 0.012), respectively. **Supplementary Table 2** displayed adjusted ORs for the association of CAA with ABSI grouped by smoking and eGFR. In the non-smoking subgroup of low-risk individuals, the ORs were 1.82 (1.32~2.52) for males and 1.6 (1.27~2.01) for females. Similar results were observed in subgroups with normal renal function (eGFR ≥ 60 ml/min). What's more, ABSI still associated with CAA in a low-risk group without smoking and kidney diseases, with ORs of 1.9 (1.37, 2.66) for males and 1.58 (1.25, 2.01) for females.

Discussion

Cerebrovascular disease has the characteristics of high morbidity, mortality, and disability, which has brought a heavy burden of public health[28]. Acute ischemic stroke is the most common type of stroke, accounting for about 70% to 80% of all strokes[29]. Approximately 20% of all strokes are attributable to thromboembolism due to atherosclerotic disease[30]. It is generally believed that people can reduce the risk of CCVds and complications by preventing and treating

obesity. Guidelines recommend BMI and WC as valid indicators of obesity[31, 32]; however, a number of studies have indicated that they may not be accurate measures of body fatness distribution[33]. To overcome the limitations of traditional obesity indicators, previous studies have developed new indicators such as WHR, WHtR, ABSI, and BRI to measure central obesity. Results reported in this study support the role of ABSI, rather than other indicators, as an independent risk factor for the weight loss due to sarcopenia with age subclinical carotid atherosclerosis in adults, even in people with low risk of CCVds, which is defined as those without hypertension, diabetes, and hyperlipidemia.

Obesity is often seen as a risk factor for many diseases. BMI is the most commonly used parameter of generalized obesity, but not of central obesity[33]. There is no consensus on the relationship between BMI and carotid plaque[34]. Similar to the findings of atherosclerosis from Salari *et al.*[35] and Geraci *et al.*[36], in the present study, BMI showed no statistically significant correlation with the presence of subclinical carotid atherosclerosis in unadjusted model in females and all models in males. Brodsky *et al.*[37] and Tang *et al.*[16] suggested BMI as a protective factor for atherosclerosis, and we also found this relationship after multivariate adjustment in females. A number of studies have suggested an irrelevant or negative association between BMI and cerebrovascular disease and its complications, which is reported as the "obesity paradox"[38]. Several hypotheses have been proposed to explain it, including the inability of BMI to recognize visceral fat deposition[39], the possibility that
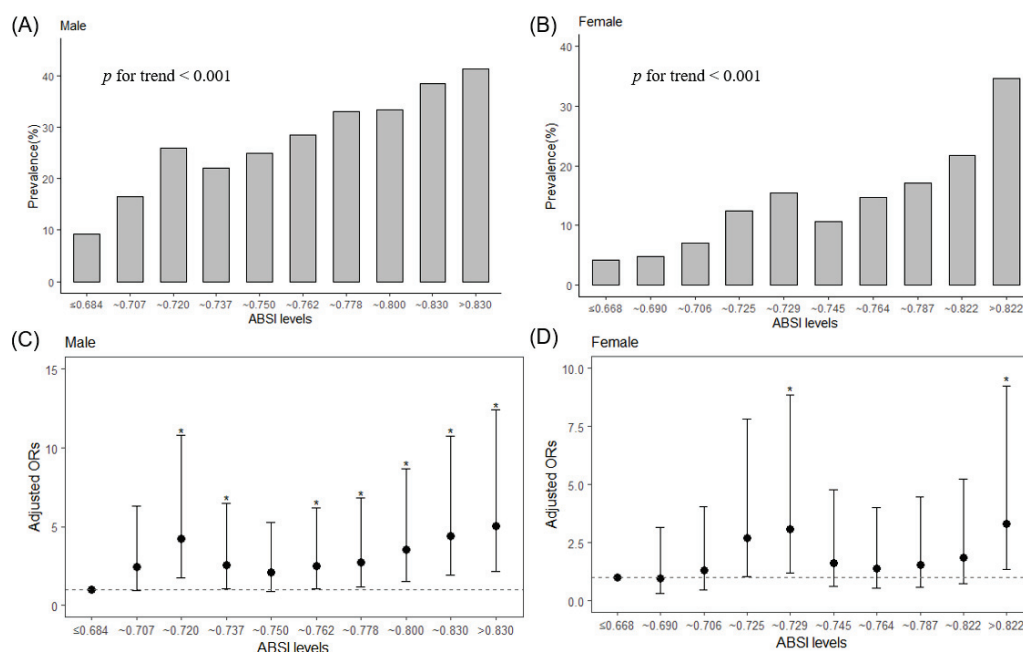
Fig. 4. Prevalence and adjusted odds ratios for the association of CAA with ABSI decile levels for both men and women in low-risk subgroup

(A and B) As ABSI decile levels rise, there is a linear and significant increase in the prevalence of CAA in both males and females ($p < 0.001$). (C and D) Adjusted odds ratios for the association of CAA with ABSI decile levels for males and females, respectively. Compared with the lowest decile level, the ORs for the highest deciles in males and females were 5.02 (95% CI 2.18–12.41, $p < 0.001$) and 3.34 (95% CI 1.37–9.26, $p = 0.012$), respectively.

*means the OR compared with the first decile level were statistical significance ($p < 0.05$).

The lowest decile served as the reference category. Vertical bars represent 95 percent confidence intervals.

endothelial function may remain normal in individuals with a high BMI[40], and the weight loss due to sarcopenia with age[41].

Previous studies have indicated that abdominal obesity seems more strongly associated with carotid atherosclerosis than general obesity[8, 42, 43]. As a traditional anthropometric parameter of central obesity, WC has been suggested as an alternative to BMI[32]. However, our study found that WC could not be an appropriate indicator to predict subclinical carotid atherosclerosis. WC does not take into account that the distribution of abdominal fat is inconsistent among people of the same abdominal circumference and different heights. Moreover, WHR and WHtR, the commonly used parameters of central obesity based on WC, are suitable for diagnosing central obesity and have better predictive value for obesity-related disease than WC[44]. Our findings support that WHR was weakly significantly associated with subclinical carotid atherosclerosis only in the men. In the women, WHR was negatively associated with subclinical carotid atherosclerosis. WHtR was not statistically significant for both men and women.

Thomas *et al.*[12] developed the BRI combining

height and WC. BRI was claimed to be a better predictor of visceral fat than BMI and WC; however, the findings of studies about the relationship between BRI and atherosclerosis are not consistent. Li G *et al.*[18] found that BRI have a close relationship with arterial stiffness in overweight and obesity people. In other studies, BRI was not or only had a weak association with atherosclerosis or arterial stiffness after adjusting for covariates[36, 45]. In this study, BRI did not show a better predictive power than traditional indicators in predicting subclinical carotid atherosclerosis.

ABSI, a novel proposed obesity indicator, was also positively associated with visceral fat[11]. The findings of previous studies suggested that ABSI appears to reflect visceral adiposity independently of BMI and significantly correlate with arterial stiffness in adults[45, 46] and subjects with type 2 diabetes[47]. The arterial stiffness of these studies was mostly represented by the mean ba-PWV. Moreover, Geraci G *et al.*[36] and Nimkuntod P *et al.*[48] have concentrated on carotid atherosclerosis and presented that ABSI was closely associated with carotid plaques. In these two studies, the relationship between ABSI and carotid

plaques was explored in perimenopausal and menopausal women and in patients with arterial hypertension, respectively. Therefore, we attempted to elucidate the relationship between ABSI and subclinical carotid plaques in a larger adult population. At the present study, ABSI was independently associated with CAA in both males and females of adult population without CCVds. Furthermore, it is worth noting that ABSI also showed an independent association with CAA in males and females in a low-risk subgroup who was free of hypertension, diabetes, and hyperlipidemia of CCVd-free population. These results suggested that ABSI may be convenient and useful to apply as simple assessment indicator for CAA risk in adult population without CCVds. It is believed that ABSI can identify visceral fat and thus predict the occurrence and development of CAA and other CCVds[11]. Recent studies[49, 50] indicated that ABSI may represent not only be a marker of visceral obesity but also an index of muscle mass. Cho *et al.*[51] expressed that ABSI is a useful clinical approach to identify sarcopenia. The accumulation of fat in the abdomen can stimulate muscle protein breakdown and inhibit protein synthesis through an inflammatory response[52]. Aging and a sedentary lifestyle may lead to loss of muscle mass and, at the same time, promote abdominal fat deposition[53]. The interaction of these two mechanisms may represent a vicious cycle leading to the occurrence and adverse outcomes of cardiovascular and cerebrovascular diseases[50].

It is known that age, SBP, and eGFR are important risk factors for atherosclerosis[22-24], which we confirmed in stepwise multivariate regressions in both males and females. LDL-C is also commonly regarded as an independent risk factor for CAA[25], and we demonstrated such association in multivariate regression in males. LDL-C showed a "scissor-shaped" pattern between genders, rising with age in females but remaining stable or even declining in males[54]. Although attempts have been made to explain sex differences by studying the role of sex hormones in metabolism and inflammation, studies that directly compare the mechanisms and factors of plaque between genders are limited and require stronger explanations[55].

In our study, Hui nationality was protectively associated with CAA. Previous studies have also shown significant differences in the prevalence of stroke and atherosclerosis between Hui and Han populations[26]. The influence of race on atherosclerosis may be caused by the difference of pathogenic genes, living habits, and the composition of chronic diseases between Hui and Han[26, 27]. Moreover, farmer was founded as a risk factor for CAA in females in the present study. Wang X *et al.*[56] also reported that prevalence of CAA was higher among participants living in rural areas than in urban areas in China. This may be due to the lower education level and poor eating habits of rural residents[56, 57]. M Rosvall *et al.*[58] noted that women with low education levels and low occupational status had a higher risk of carotid artery stenosis. Although possible mechanisms have been reported, more precisely designed studies are needed in the future.

This work was the first study to examine the relationship between obesity anthropometric indices and CAA in a predominantly ethnic minority population in western China. Jingyuan County in Ningxia is a region with a majority of ethnic minorities and a unique dietary structure and lifestyle. The prevalence of diabetes in this region is lower than the average level in China, but the prevalence of obesity, hypertension, and hypertriglyceridemia are higher[19]. Our results demonstrate a high prevalence of subclinical carotid plaque in both males and females. These indicate a potential burden of stroke among the population in this region. Therefore, our work may help in understanding the association between central obesity indices, especially ABSI, and subclinical carotid atherosclerosis and aid in more effective community and clinical management.

This study has some limitations. First, this study cannot establish a cause-effect relationship due to its cross-sectional design. Second, our study is based on participants who lived in a predominantly ethnic minority county in western China. Caution is needed when applying the results of our study to other regions and ethnics.

Conclusion

In summary, ABSI, as a novel anthropometric indicator compared with traditional indices, was found to have a closer relationship with subclinical carotid plaque in rural adults in northwest China, even in populations free of hypertension, diabetes, and hyperlipidemia. In addition, the role of this association in prospective plaque development and unstable plaque subtypes deserves further investigation.

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The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author Contributions

Xiaotian Ma performed statistical analysis, and wrote the manuscript. Lihong Chen contributed to standardised the database and interpreted the data. Wenchao Hu interpreted the data and edited the manuscript. Lanjie He contributed to the conception of the study and reviewed the manuscript.

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Supplementary Table 1. The general demographic and clinical characteristics of the low-risk subgroup according to CAA

	Male			Female		
	CAA (N=297)	Non-CAA (N=790)	*p*	CAA (N=242)	Non-CAA (N=1457)	*p*
Age (years)	58.73±10.77	43.34±12.07	<0.001	56.60±9.04	40.59±10.58	<0.001
Race[*n*(%)]			0.037			<0.001
Han	82 (27.61)	169 (21.39)		79 (32.64)	314 (21.55)	
Hui	215 (72.39)	621 (78.61)		163 (67.36)	1143 (78.45)	
Farmer[*n*(%)]			<0.001			<0.001
Yes	245 (82.49)	573 (72.53)		214 (88.43)	1003 (68.84)	
No	52 (17.51)	217 (27.47)		28 (11.57)	454 (31.16)	
Smoking[*n*(%)]			0.004			0.027
Yes	97 (32.66)	335 (42.41)		5 (2.07)	8 (0.55)	
No	200 (67.34)	455 (57.59)		237 (97.93)	1449 (99.45)	
SBP (mmHg)	116.12±10.79	114.39±10.82	0.019	118.00±11.64	111.02±11.48	<0.001
DBP (mmHg)	74.85±7.53	74.60±7.30	0.636	75.00±7.04	72.91±7.20	<0.001
FBG (mmol/l)	5.27±0.55	5.12±0.51	<0.001	5.26±0.55	5.12±0.49	<0.001
TG (mmol/l)	1.18±0.63	1.24±0.76	0.19	1.31±0.60	1.13±0.60	<0.001
TC (mmol/l)	3.55±0.59	3.43±0.57	0.005	3.81±0.62	3.41±0.57	<0.001
HDLC (mmol/l)	1.29±0.22	1.26±0.21	0.074	1.39±0.28	1.34±0.24	0.014
LDLC (mmol/l)	2.40±0.59	2.28±0.58	0.002	2.58±0.62	2.25±0.58	<0.001
eGFR (ml/min)	81.50±11.09	89.70±12.12	<0.001	74.33±9.77	82.78±10.93	<0.001
Height (cm)	163.43±6.97	167.05±6.83	<0.001	153.82±5.94	157.63±6.11	<0.001
Weight (kg)	60.70±9.30	63.75±9.33	<0.001	54.08±8.82	57.09±8.42	<0.001
WC (cm)	79.08±7.98	77.43±8.34	0.003	77.90±10.65	74.02±8.39	<0.001
HC (cm)	91.90±5.76	91.82±5.76	0.834	91.98±7.77	91.06±5.73	0.081
BMI (kg/m^2)	22.65±2.61	22.83±2.99	0.336	22.79±3.05	22.96±3.01	0.425
WHR	0.86±0.06	0.84±0.06	<0.001	0.84±0.07	0.81±0.06	<0.001
WHtR	0.48±0.05	0.46±0.05	<0.001	0.51±0.07	0.47±0.06	<0.001
ABSI	0.78±0.07	0.75±0.06	<0.001	0.78±0.09	0.73±0.06	<0.001
BRI	3.11±0.89	2.76±0.92	<0.001	3.58±1.45	2.88±1.03	<0.001

CAA, carotid artery atherosclerosis; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TG, serum total triglycerides; TC, serum total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; WC, waist circumference; HC, hip circumference; BMI, body mass index; WHR, waist-hip ratio; WHtR, waist-to-height ratio; ABSI, a body shape index; BRI, the body roundness index.

Supplementary Table 2. Adjusted ORs for the association of CAA with ABSI grouped by smoking and eGFR

	Male		Female	
	OR(95%CI)	*p*	OR(95%CI)	*p*
Smoking[*n*(%)]				
Yes	1.60 (1.01, 2.57)	0.046	-	-
No	1.82 (1.32, 2.52)	<0.001	1.60 (1.27, 2.01)	<0.001
eGFR (ml/min)				
<60	-	-	2.14 (0.87, 6.03)	0.114
60~89	1.78 (1.30, 2.45)	<0.001	1.43 (1.11, 1.84)	0.006
>90	1.73 (1.02, 2.91)	0.039	4.32 (2.16, 11.02)	<0.001

The number of subgroups is too small to fit the regression equation, which is expressed by "-".
eGFR, estimated glomerular filtration rate.