#### ORIGINAL RESEARCH

## Pulse Pressure and Other Cardiovascular Risk Factors Associated with Multiple Carotid Plaques in a Rural Chinese Population: A Population-Based Cross-Sectional Study

Chunxia Yan<sup>1</sup>, Juan Hao<sup>2</sup>, Xiaoqian Sun<sup>1</sup>, Yanan Ding<sup>1</sup>, Taofeng Tan<sup>2</sup>, Xiaoqian Yang<sup>1</sup>, Jun Tu<sup>2-4</sup>, Xianjia Ning<sup>2-4</sup>, Jinghua Wang <sup>2-4</sup>, Lingling Bai<sup>1</sup>

<sup>1</sup>Department of Neurology, Liaocheng People's Hospital, Liaocheng, Shandong Province, 252000, People's Republic of China; <sup>2</sup>Department of Neurology, Tianjin Medical University General Hospital, Tianjin, 300052, People's Republic of China; <sup>3</sup>Laboratory of Epidemiology, Tianjin Neurological Institute, Tianjin, 300052, People's Republic of China; <sup>4</sup>Tianjin Neurological Institute, Key Laboratory of Post-Neuroinjury Neuro-Repair and Regeneration in Central Nervous System, Ministry of Education and Tianjin City, Tianjin, 300052, People's Republic of China

Correspondence: Lingling Bai, Department of Neurology, Liaocheng People's Hospital, No. 67, Dongchang West Road, Liaocheng, Shandong Province, 252000, People's Republic of China, Tel +86 0635 8272374, Fax +86 0635 8212052, Email bailingling911@163.com

**Objective:** This study aimed to investigate the association between these Blood pressure (BP) components examined in this study, including systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP), and mean arterial pressure (MAP), with the presence of multiple carotid plaques in a low-income rural Chinese population.

**Methods:** This population-based cross-sectional study was conducted from April 2014 to January 2015, involving participants from the Tianjin Brain Study. Participants aged 45 years and older with diagnosed carotid plaques were included. Data on demographics, medical history, and lifestyle factors were collected through interviews and existing records. Blood pressure measurements were taken in a quiet room, following the standard procedures recommended by the American Hypertension Association (AHA), and ultrasono-graphic examinations were performed to identify and quantify carotid plaques. Multivariate logistic regression model was used to explore the association between blood pressure components and multiple plaques. The blood pressure component with a positive univariate analysis was included in different models, each adjusted for age, sex, body mass index (BMI), and the ratio of high-density lipoprotein cholesterol (HDL-C) to low-density lipoprotein cholesterol (LDL-C).

**Results:** The study found that 41.8% of participants had multiple carotid plaques, with a higher prevalence in men compared to women. Multivariate logistic regression analysis revealed that each 1-mmHg increase in systolic BP (SBP) was associated with a 0.9% increase in the prevalence of multiple carotid plaques (OR = 1.009; 95% CI 1.004–1.014; P < 0.001). Each 1-mmHg increase in pulse pressure (PP) was associated with a 1.2% increase (OR = 1.012; 95% CI 1.006–1.018; P < 0.001), and each 1-mmHg increase in mean arterial pressure (MAP) was associated with a 1.1% increase (OR = 1.011; 95% CI 1.003–1.019; P = 0.005). Participants with a history of hypertension had a significantly higher prevalence of multiple carotid plaques (OR = 1.554; 95% CI 1.135–2.127; P = 0.006). In addition, male sex, older age, and low BMI were all associated with a higher risk of multiple carotid plaques (P all< 0.05).

**Conclusion:** This study provides critical evidence on the relationship between BP components and multiple carotid plaques, with significant implications for patients, physicians, and society. By prioritizing BP management, particularly focusing on PP, which demonstrates the strongest association with carotid plaques, as well as targeting higher-risk populations such as males, older individuals, and those with low BMI, preventive measures against carotid atherosclerosis can be enhanced. This will ultimately contribute to better cardiovascular health outcomes and reduce the societal burden of stroke and related diseases.

Keywords: carotid plaques, blood pressure components, pulse pressure, hypertension, atherosclerosis

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### Introduction

Stroke is the second leading cause of disability and death worldwide, with its burden being particularly high in low- and middle-income countries.<sup>1</sup> In 2016, the global number of new stroke cases reached 13.7 million.<sup>1</sup> Carotid atherosclerosis, characterized by the formation of plaques in the carotid artery, is a significant contributor to stroke and other cardiovascular diseases.<sup>2</sup> Studies have shown that patients with a single carotid plaque are 1.82 times more likely to experience moderate to severe cerebral infarction compared to those without carotid plaques, while patients with multiple carotid plaques are 2.41 times more likely to suffer from moderate or severe cerebral infarction than those without carotid plaques.<sup>3</sup> The presence of multiple carotid plaques is strongly correlated with an increased risk of cardiovascular diseases, as it reflects a higher burden of atherosclerosis and a greater degree of arterial dysfunction. Therefore, early identification and management of multiple carotid plaques are critical for improving risk stratification, guiding preventive interventions, and reducing the incidence of cardiovascular events. The prevalence of carotid plaques globally was estimated at 21.1% among individuals aged 30–79 years in 2020, affecting approximately 815.76 million people.<sup>2</sup> As populations age, the incidence of carotid plaques and related complications are expected to rise.

BP components, such as SBP, DBP, PP, and MAP, play critical roles in the development and progression of atherosclerosis. Numerous studies have demonstrated that SBP is a major risk factor for carotid atherosclerosis, while the relationship between DBP and carotid plaque formation is less clear.<sup>4–6</sup> Additionally, there is growing evidence linking PP to early progression of carotid atherosclerosis.<sup>7–9</sup> The association between MAP and carotid plaques remains controversial, with some studies indicating a positive correlation while others do not.<sup>7–10</sup>

Despite significant research on the association between BP components and carotid plaques, there is limited understanding of how these BP components correlate with the presence of multiple carotid plaques, particularly in low-income populations.<sup>5</sup> Previous studies have primarily focused on single carotid plaques, and the potential differing impacts of BP components on multiple plaques have not been thoroughly explored. This gap highlights the need for more targeted research to understand the multifaceted relationship between BP components and multiple carotid plaques.

The primary objective of this study was to investigate the association between various BP components (SBP, DBP, PP, and MAP) and the presence of multiple carotid plaques in a rural Chinese population.

### **Methods**

### Participants and Study Design

This population-based cross-sectional study was conducted in Tianjin, China, between April 2014 and January 2015. Participants were selected from the Tianjin Brain Study, which began in 1985 and involved residents from 18 administrative villages in a Tianjin township. Approximately 95% of the participants were low-income farmers, with an average annual disposable income of less than \$1600 USD in 2014.<sup>11–14</sup> Inclusion criteria were residents aged 45 years or older with diagnosed carotid plaques. Exclusion criteria included individuals with a current or past history of cardio-vascular diseases (such as myocardial infarction, angina, and asymptomatic myocardial ischemia) or cerebrovascular diseases (including ischemic and hemorrhagic strokes).<sup>11</sup> This exclusion was implemented to reduce confounding effects from differing pathophysiological processes and treatments, minimize bias, and improve the overall reliability of the study results.

This study complies with the Declaration of Helsinki. The study protocol was approved by the Tianjin Medical University General Hospital Ethics Committee (IRB2018-100-01), and all participants provided written informed consent.

### Information Collection and Risk Factor Definitions

Demographic information, including sex, date of birth, and educational level, was collected based on existing records. Participants were categorized into four age groups: 45–54 years, 55–64 years, 65–74 years, and 75 years and older. Educational levels were divided into three groups: illiterate (no formal education), 1–6 years of education, and more than 6 years of education.

Medical histories, including the presence of diabetes mellitus, hypertension, coronary heart disease, stroke, and transient ischemic attacks, were obtained through self-reports or existing medical records. Lifestyle information, such as cigarette smoking and alcohol consumption, was collected through face-to-face interviews using structured questionnaires. Smoking status was categorized into never smoked, quit smoking, and current smoking, with cigarette smoking defined as smoking more than one cigarette per day for at least one year. Alcohol consumption was classified into never drank, quit drinking, and current drinking, defined as consuming more than 500 grams of alcohol per week for at least one year.

### Physical Examination

BP measurements were performed in a quiet room, following the American Hypertension Association's standard procedure. Participants were instructed to avoid smoking, alcohol consumption, drinking tea or coffee, or engaging in vigorous exercise within 30 minutes before the BP measurement. An electronic sphygmomanometer (HEM-741C; Omron, Tokyo, Japan) was used, and BP was measured with the participant seated, with the cuff positioned on the arm at heart level and adjusted to the arm circumference.

Two BP measurements were taken five minutes apart. If the difference between the readings was less than 10 mmHg for systolic BP (SBP) or 5 mmHg for diastolic BP (DBP), the average of the two readings was recorded. If the difference exceeded these limits or if the BP met the criterion for hypertension, two additional readings were taken after the participant rested for an additional 20 minutes. Hypertension was defined as an SBP of 140 mmHg or higher, a DBP of 90 mmHg or higher, or the use of antihypertensive medication. Pulse pressure (PP) was calculated as SBP minus DBP, and mean arterial pressure (MAP) was calculated as one-third SBP plus two-thirds DBP.

Height and weight were measured during the baseline survey, and body mass index (BMI) was calculated as weight (kg) divided by the square of height (m<sup>2</sup>). Participants were classified into three BMI categories: normal weight (18.5 kg/m<sup>2</sup>  $\leq$  BMI  $\leq$  24.0 kg/m<sup>2</sup>), overweight (24.0 kg/m<sup>2</sup>  $\leq$  BMI  $\leq$  28.0 kg/m<sup>2</sup>), and obesity (BMI  $\geq$  28.0 kg/m<sup>2</sup>).

### Laboratory Measurements

Fasting blood samples were collected and analyzed within two hours at the central laboratory of Tianjin Jizhou People's Hospital. The samples were used to measure fasting plasma glucose (FPG), total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) levels. Diabetes was defined as an FPG of 7.0 mmol/L or higher, or the use of insulin or oral hypoglycemic medication.

### Ultrasonography

A single professional technician performed all ultrasonographic examinations with a B-mode ultrasonography system (Terason 3000; Terason; Burlington, MA, USA) using a linear array transducer with a frequency range of 5–12 MHz. Carotid plaques were diagnosed based on one or more of the following criteria: (1) local carotid intima-media thickness (CIMT) > 1.5 mm, (2) localized protrusions of more than 0.5 mm into the lumen, or (3) local thickening of more than 50% of the surrounding CIMT.<sup>15</sup> Participants with at least two lesions were defined as having multiple carotid plaques.

### Statistical Analysis

All continuous variables are presented as means (standard deviations), and differences across groups were compared using Student's *t*-test. Categorical variables are presented as numbers (percentages), and between-group differences were analyzed using chi-squared tests. The chi-square test was used to assess the association between categorical variables (Gender, age group, hypertension group, etc) and the presence of multiple carotid plaques. The null hypothesis for each chi-square test was that there is no association between the categorical variable and the outcome, with statistical significance determined by a two-tailed p-value of less than 0.05. Multivariate logistic regression models were employed to evaluate the association between BP components and the presence of multiple carotid plaques, adjusting for age, sex, BMI, and HDL-C/LDL-C ratio. The dependent variable in the logistic regression model is the presence of multiple carotid plaques (presence or absence). The independent variables were blood pressure components (SBP, DBP, PP, MAP). In order to avoid potential collinearity between blood pressure components influencing the results, we analyzed the blood pressure independent variables with positive results after univariate analysis in different models. Each model

was adjusted for potential confounders, including age, sex, body mass index (BMI), and the ratio of high-density lipoprotein cholesterol (HDL-C) to low-density lipoprotein cholesterol (LDL-C).

Each logistic regression model can be represented as follows: Logit (Presence of multiple carotid plaques) =  $\beta 0 + \beta 1$ (blood pressure indicators) +  $\beta 2(Age) + \beta 3(Sex) + \beta 4(BMI) + \beta 5(HDL-C/LDL-C ratio).$ 

The results are presented as adjusted OR with 95% CI. A two-tailed P-value of less than 0.05 was considered statistically significant. All analyses were performed using SPSS for Windows (version 19.0; SPSS, Armonk, NY, USA).

### Results

### **Demographic Characteristics**

A total of 1574 participants aged 45 years and older with carotid plaques were included in this study; 49.7% were men. The average age of participants was 63.38 years (SD  $\pm$  9.49 years). More than 40% of the participants were between 55 and 64 years old. The mean years of formal education were 5.11 years, with 2.4% being low-weight, 41.0% overweight, and 22.3% obese. Among the participants, 24.0% were current smokers, and 14.7% were current alcohol drinkers. Furthermore, 77.1% of the participants had previously been diagnosed with hypertension, with 44.9% having grade 1 hypertension. The mean SBP, DBP, PP, and MAP levels were 151.58 mmHg, 87.32 mmHg, 64.26 mmHg, and 108.74 mmHg, respectively (Table 1).

Risk Factors	Men	Women	Total
Total, n (%)	782 (49.7)	792 (50.3)	1574 (100)
Age, years, means±SD	64.18±9.71	62.59±9.20	63.38±9.49
Age group, n (%)			
45–54 years	125 (16.0)	156 (19.7)	281 (17.9)
55–64 years	323 (41.3)	361 (45.6)	684 (43.5)
65–74 years	208 (26.6)	182 (23.0)	390 (24.8)
≥75 years	126 (16.1)	93 (11.7)	219 (13.9)
Education, means±SD, years	6.13±3.24	4.10±3.57	5.11±3.57
Education group, n (%):			
0 years	79 (10.1)	239 (30.2)	318 (20.2)
I~6 years	390 (49.9)	369 (46.6)	759 (48.2)
≥ 7 years	313 (40.0)	184 (23.2)	497 (31.6)
Hypertension, n (%):			
No	172 (22.0)	189 (23.9)	361 (22.9)
Yes	610 (78.0)	603 (76.1)	1213 (77.1)
Degree of hypertension, n (%):			
Normal	219 (28.0)	244 (30.8)	463 (29.4)
Grade I	358 (45.8)	349 (44.1)	707 (44.9)
Grade 2	145 (18.5)	148 (18.7)	293 (18.6)
Grade 3	60 (7.7)	51 (6.4)	(7. )
Diabetes, n (%):			
No	641 (83.7)	622 (79.8)	1263 (80.2)
Yes	125 (16.3)	157 (20.2)	282 (19.8)
Smoking status, n (%):			
Never smoking	368 (47.1)	753 (95.1)	1121 (71.2)
Abandon smoking	70 (9.0)	5 (0.6)	75 (4.8)
Smoking	344 (44.0)	34 (4.3)	378 (24.0)
Alcohol consumption, n (%):			
Never drinking	532 (68.0)	779 (98.4)	3  (8 . )
Abandon drinking	31 (4.0)	0 (0)	31 (2.2)
Drinking	219 (28.0)	13 (1.6)	232 (16.6)

 Table I The Demographic Characteristic and Risk Factors in This Population by Sex

(Continued)

Risk Factors	Men	Women	Total
SBP, mmHg, means±SD	151.62±22.51	151.55±23.97	151.58±23.25
DBP, mmHg, means±SD	88.20±11.51	86.44±11.55	87.32±11.56
PP, mmHg, means±SD	63.41±18.36	65.11±19.19	64.26±18.80
MAP, mmHg, means±SD	109.34±13.50	108.14±14.09	108.74±13.81
BMI, Kg/m², means±SD	25.02±3.38	25.67±3.96	25.35±3.70
BMI group, n (%):			
Low-weight	21 (2.7)	17 (2.1)	38 (2.4)
Normal	280 (35.8)	259 (32.7)	539 (34.2)
Overweight	332 (42.5)	314 (39.6)	646 (41.0)
Obesity	149 (19.1)	202 (25.5)	351 (22.3)
Central obesity, n (%):			
No	718 (92.1)	343 (43.4)	1061 (67.5)
Yes	62 (7.9)	448 (56.6)	510 (32.5)
FPG, mmol/L, means±SD	5.99±1.53	6.18±2.08	6.09±1.83
TC, mmol/L, means±SD	4.72±1.01	5.25±1.21	4.99±1.15
TG, mmol/L, means±SD	1.57±1.03	1.94±1.19	1.76±1.13
HDL, mmol/L, means±SD	1.40±0.44	1.50±0.45	1.45±0.45
LDL, mmol/L, means±SD	2.90±1.34	3.24±1.51	3.07±1.44
HDL/LDL, means±SD	0.58±0.35	0.58±0.51	0.58±0.44

Table I (Continued).

### Factors Associated with Multiple Carotid Plaques in the Univariate Analysis

Table 2 shows that 41.8% of the participants had multiple carotid plaques, with a higher prevalence in men (46.2%) compared to women (37.5%). Univariate analysis indicated that significantly higher proportions of men, the elderly, the underweight, and participants with a low educational level had multiple carotid plaques (all P < 0.05) compared to other groups. The prevalence of multiple plaques was positively correlated with age (P < 0.001) and inversely correlated with BMI (P = 0.003) and the HDL-C/LDL-C ratio (P < 0.001; Table 3).

Risk Factors	Multiple Carotid Plaques Group	Single Carotid Plaque Group	χ²/t	Ρ
Total	658 (41.8)	916 (58.2)	_	
Sex, n (%):			12.140	<0.001
Men	361 (46.2)	421 (53.8)		
Women	297 (37.5)	495 (62.5)		
Age group, n (%):			77.399	<0.001
45–54 years	69 (24.6)	212 (75.4)		
55–64 years	278 (40.6)	406 (59.4)		
65–74 years	184 (47.2)	206 (52.8)		
≥75 years	127 (58.0)	92 (42.0)		
Education group, n (%):			11.337	0.001
0 years	153 (48.1)	165 (51.9)		
I~6 years	324 (42.7)	435 (57.3)		
≥ 7 years	181 (36.4)	316 (63.6)		
Hypertension, n (%):			9.922	0.002
No	125 (34.6)	236 (65.4)		
Yes	533 (43.9)	680 (56.1)		

**Table 2** The Prevalence of Multiple Carotid Plaques by Demographical Characteristics and Risk Factors forAll Participants in This Study

(Continued)

Risk Factors	Multiple Carotid Plaques	Single Carotid Plaque	$\chi^2/t$	Р
	Group	Group		
Degree of hypertension, n (%):			15.051	< 0.001
Normal	167 (36.1)	396 (63.9)		
Grade I	291 (41.2)	416 (58.8)		
Grade 2	145 (49.5)	148 (50.5)		
Grade 3	55 (49.5)	56 (50.5)		
Diabetes, n (%):			0.033	0.856
No	530 (42.0)	733 (58.0)		
Yes	120 (42.6)	162 (57.4)		
Smoking status, n (%):			1.493	0.526
Never smoking	461 (41.1)	660 (58.9)		
Abandon smoking	36 (48.0)	39 (52.0)		
Smoking	161 (42.6)	217 (57.4)		
Alcohol consumption, n (%):			0.188	0.664
Never drinking	546 (41.6)	765 (58.4)		
Abandon drinking	11 (35.5)	20 (64.5)		
Drinking	101 (43.5)	131 (56.5)		
BMI group, n (%):			7.138	0.008
Low-weight	20 (52.6)	18 (47.4)		
Normal	240 (44.5)	299 (55.5)		
Overweight	270 (41.8)	376 (58.2)		
Obesity	128 (36.5)	223 (63.5)		
Central obesity, n (%):			1.262	0.261
No	454 (42.8)	607 (57.2)		
Yes	203 (39.8)	307 (60.2)		

#### Table 2 (Continued).

**Table 3** The Differences in Measurements of Risk Factors Between Multiple Carotid Plaques

 Group and Single Carotid Plaque Group in This Population

Measurements (means±SD)	Multiple Carotid Plaques Group	Single Carotid Plaque Group	χ²/t	Р
SBP, mmHg	155.25±24.18	148.95±22.20	-5.532	<0.001
DBP, mmHg	87.48±11.97	87.24±1.26	-0.301	0.764
PP, mmHg	67.83±19.59	61.70±17.78	-6.356	<0.001
MAP, mmHg	110.03±14.32	107.81±13.36	-3.120	0.002
Age, year	65.69±9.31	61.72±9.27	-8.368	<0.001
BMI, Kg/m <sup>2</sup>	25.02±3.57	25.58±3.77	2.939	0.003
FPG, mmol/L	6.17±2.03	6.03±1.67	-1.443	0.149
TC, mmol/L	5.05±1.14	4.95±1.15	-1.657	0.098
TG, mmol/L	1.73±1.11	1.78±1.14	0.806	0.421
HDL, mmol/L	1.43±0.42	1.47±0.46	1.546	0.122
LDL, mmol/L	3.14±1.40	3.02±1.46	-1.690	0.091
HDL /LDL, mmol/L	0.53±0.30	0.61±0.51	3.296	<0.001

# Association of BP Components with Multiple Carotid Plaques in the Univariate Analysis

Univariate analysis revealed a significantly higher prevalence of multiple carotid plaques among participants previously diagnosed with hypertension (P = 0.002) and those with higher grades of hypertension (P < 0.001). Additionally, the prevalence of multiple plaques increased with higher SBP (P < 0.001), PP (P < 0.001), and MAP (P = 0.002) (Table 4).

BP Components	Multiple Carotid Plaques Group	Single Carotid Plaque Group	$\chi^2/t$	Р
Hypertension, n (%):			9.922	0.002
No	125 (34.6)	236 (65.4)		
Yes	533 (43.9)	680 (56.1)		
Degree of hypertension, n (%):			15.051	< 0.001
Normal	167 (36.1)	396 (63.9)		
Grade I	291 (41.2)	416 (58.8)		
Grade 2	145 (49.5)	148 (50.5)		
Grade 3	55 (49.5)	56 (50.5)		
SBP, mmHg, means±SD	155.25±24.18	148.95±22.20	-5.532	<0.001
DBP, mmHg, means±SD	87.48±11.97	87.24±1.26	-0.301	0.764
PP, mmHg, means±SD	67.83±19.59	61.70±17.78	-6.356	<0.001
MAP, mmHg, means±SD	110.03±14.32	107.81±13.36	-3.120	0.002

Table 4 Association of Blood Pressure Components with Multiple Carotid Plaques in the Univariate Analysis

# Association of BP Components with Multiple Carotid Plaques in the Multivariate Analysis

Table 5 presents the multivariate logistic regression analysis results, showing the association between BP components and multiple carotid plaques after adjusting for age, sex, BMI, and HDL-C/LDL-C ratio. Statistically significant correlations were observed between multiple carotid plaques and a history of hypertension (OR = 1.343; 95% CI 1.031–1.749; P = 0.029), grade 2 hypertension (OR = 1.554; 95% CI 1.135–2.127; P = 0.006), SBP (OR = 1.009; 95% CI 1.004–1.014; P < 0.001), PP (OR = 1.012; 95% CI 1.006–1.018; P < 0.001), and MAP (OR = 1.011; 95% CI 1.003–1.019; P = 0.005). In all models of hypertension, women had a lower risk of developing multiple carotid plaques (all P<0.05). In both the SBP and MAP models, BMI was negatively correlated with the risk of multiple carotid plaques (both P<0.05).

Model	BP Components	Reference	OR (95% CI)	Р	Interaction P-value
Model I	Hypertension	No	1.343(1.031, 1.749)	0.029	
	Women	Men	0.751 (0.609, 0.924)	0.007	0.960
	HDL-C/LDL-C		1.056 (0.987, 1.131)	0.114	0.371
	BMI		0.971 (0.943, 1.001)	0.060	0.120
	Age groups	45–54 years			0.499
	55–64 years		1.981 (1.439, 2.729)	<0.001	
	65–74 years		2.446 (1.726, 3.465)	<0.001	
	≥75 years		3.693 (2.473, 5.516)	<0.001	
Model 2	Degree of hypertension	Normal			
	Grade I		1.142(0.884, 1.475)	0.309	
	Grade 2		1.554(1.135, 2.127)	0.006	
	Grade 3		1.497(0.963, 2.327)	0.073	
	Women	Men	0.749 (0.608, 0.922)	0.007	0.584
	HDL-C/LDL-C		1.063 (0.993, 1.139)	0.973	0.145
	BMI		0.973 (0.944, 1.002)	0.071	0.206

**Table 5** Association of Blood Pressure Components with Multiple Carotid Plaques in theMultivariate Analysis

(Continued)

Model	BP Components	Reference	OR (95% CI)	Р	Interaction
	-				P-value
	Age groups	45–54 years			0.685
	55–64 years		2.016 (1.464, 2.775)	<0.001	
	65–74 years		2.475 (1.748, 3.504)	<0.001	
	≥75 years		3.644 (2.438, 5.445)	<0.001	
Model 3	SED			<0.001	
i lodel 5	Women	Men	0.740 (0.601 0.912)	0.001	0.271
		i ien	1 059 (0 989 1 134)	0.005	<0.001
	RMI		0.970 (0.941 0.999)	0.101	0.458
		45–54 vears		0.011	0.731
	55-64 years	10 0 1 years	1.927 (1.398, 2.656)	<0.001	0.751
	65-74 years		2.303 (1.621, 3.271)	<0.001	
	≥75 years		3.272 (2.172, 4.928)	<0.001	
Model 4	PP		1.012(1.006, 1.018)	<0.001	
	Women	Men	0.718 (0.582, 0.886)	0.002	0.125
	HDL-C/LDL-C		1.059 (0.989, 1.134)	0.101	0.296
	BMI		0.975 (0.947, 1.004)	0.092	0.257
	Age groups	45–54 years			0.115
	55–64 years		1.868 (1.353, 2.579)	<0.001	
	65–74 years		2.153 (1.505, 3.080)	<0.001	
	≥75 years		2.933 (1.914, 4.495)	<0.001	
Model 5	MAP		1.011(1.003–1.019)	0.005	
	Women	Men	0.757 (0.614, 0.933)	0.009	0.590
	HDL-C/LDL-C		1.059 (0.989, 1.134)	0.099	-
	BMI		0.970 (0.941, 1.000)	0.047	0.721
	Age groups	45–54 years			0.258
	55–64 years		2.014 (1.464, 2.770)	<0.001	
	65–74 years		2.506 (1.773, 3.542)	<0.001	
	≥75 years		3.779 (2.541, 5.619)	<0.001	

 Table 5 (Continued).

Notes: Model 1–5 analysis adjusted by age, sex, BMI and HDL-C/LDL-C.

However, no significant associations were observed between grade 1 or grade 3 hypertension and multiple carotid plaques in Model 2. These results suggest that higher SBP, PP, and MAP levels are independently associated with an increased prevalence of multiple carotid plaques. The strongest correlation was observed with PP, indicating the importance of monitoring this BP component in clinical practice to prevent carotid atherosclerosis progression.

### Interaction Analysis

The interaction analysis of blood pressure components and other covariates in the multivariate analysis model with the risk of multiple carotid plaque discovery showed that there was a significant interaction between the ratio of SBP to HDL-C/HDL-C and the incidence of multiple carotid plaque in the SBP model (P<0.001). No significant interaction was found in the other models (all P>0.05).

### Discussion

The primary objective of this study was to investigate the association between various BP components, which including SBP, DBP, PP, and MAP, and the presence of multiple carotid plaques in a rural Chinese population. This study aimed to provide insights into the impact of BP components on carotid atherosclerosis, particularly in a low-income demographic. We observed that 41.8% of the participants had multiple carotid plaques. This prevalence was notably higher in men

compared to women. There was a significant positive association between the presence of multiple carotid plaques and higher levels of SBP, PP, and MAP. Specifically, PP showed the strongest correlation, with each 1-mmHg increase in PP being associated with a 1.2% increase in the prevalence of multiple carotid plaques. Participants with a history of hypertension had a significantly higher prevalence of multiple carotid plaques compared to normotensive individuals. Notably, grade 2 hypertension was significantly associated with multiple carotid plaques, while no significant associations were observed for grades 1 and 3 hypertension. In addition, male sex, older age, and low BMI were all associated with a higher risk of multiple carotid plaques.

The prevalence of multiple carotid plaques has been previously investigated. The Tromsø (Norway) study reported that 44.5% of stroke-free individuals aged 55–74 years had carotid plaques, and 36.7% of these participants had multiple plaques.<sup>16</sup> Similarly, the China Stroke Primary Prevention Trial (CSPPT) found that 41.8% of hypertensive individuals aged 45–75 years had carotid plaques, with 54.5% of them having multiple plaques.<sup>17,18</sup> In our study, 41.8% of participants aged  $\geq$ 45 years with carotid plaques had multiple plaques, and among hypertensive participants, the prevalence was 43.9%. Differences in demographic characteristics such as age and education level may account for the variance in prevalence across studies. While the age and race of our study population were similar to those in the CSPPT study, the proportion of participants with multiple carotid plaques in our study (43.9%) was lower than in the CSPPT study (54.5%). Further investigation is needed to understand these differences.

Hypertension is a well-established independent risk factor for carotid plaques. A 7-year prospective cohort study found that individuals with elevated baseline BP levels were more likely to develop carotid plaques by the end of the study period (adjusted hazard ratio [HR], 1.52; 95% CI, 1.02–2.26).<sup>7</sup> The China Kadoorie Biobank study indicated that plaque prevalence was twice as high in participants with SBP  $\geq$ 160 mmHg compared to those with SBP <120 mmHg (44% vs 22%), even after adjusting for age, sex, and region.<sup>19</sup> The Rotterdam Study demonstrated that SBP was independently correlated with a higher plaque burden in women and that hypertension was strongly related to intraplaque hemorrhage and calcification.<sup>6,20</sup> The European Carotid Surgery Trial found that SBP was positively associated with plaque ulceration (OR, 1.66; 95% CI, 1.05–2.62; P = 0.02), while DBP was not.<sup>21</sup>

Despite these findings, few studies have specifically examined the relationship between hypertension and the presence of multiple carotid plaques. Our study found a positive association between a history of hypertension, the degree of hypertension, and SBP with multiple carotid plaques. The constituent ratio of multiple carotid plaques in hypertensive participants was 1.343 times higher than that in normotensive participants. No association was observed between DBP and the presence of multiple carotid plaques. These results suggest that multiple carotid plaques may share similar risk factors with carotid plaque progression, potentially due to vascular shear-related damage caused by hypertension. Increased pressure and the proliferation of vascular cells in hypertensive individuals may promote the progression of atherosclerosis.<sup>22,23</sup>

Elevated PP levels are known to correlate with the progression of coronary atherosclerosis,<sup>24,25</sup> and the relationship between PP and carotid atherosclerosis is becoming increasingly clear. An Italian cross-sectional study found a significant correlation between CIMT and PP in post-menopausal women.<sup>26</sup> The Étude du Vieillissement Artériel (EVA) study in France also reported a positive association between baseline CIMT and PP.<sup>9</sup> A 4-year follow-up confirmed that higher PP levels were linked to CIMT progression and that higher CIMT was linked to PP widening.<sup>9</sup> Additionally, a 7-year prospective cohort study found that higher PP levels were associated with an increased incidence of carotid plaque (adjusted HR, 1.15; 95% CI, 0.76–1.75) in women after adjusting for confounders.<sup>7</sup> The European Carotid Surgery Trial identified PP as a reliable independent predictor of ulceration in symptomatic carotid plaque patients.<sup>21</sup>

Our study adds to this body of evidence by showing that PP is positively correlated with multiple carotid plaques. The constituent ratio of multiple carotid plaques increased by 1.2% for every 1-mmHg increase in PP. Elevated PP levels can induce endothelial dysfunction and promote monocyte adhesion to endothelial cells, contributing to plaque development. As atherosclerosis progresses, it further increases PP by altering the cellular matrix of the vascular wall and reducing its elasticity, creating a vicious cycle.<sup>9,27–29</sup>

The association between MAP and carotid plaque formation remains unclear. A 7-year prospective cohort study from China found that higher MAP was linked to an increased incidence of carotid plaque (adjusted HR, 1.44; 95% CI, 1.00–2.08) in women after adjusting for confounders.<sup>7</sup> However, a hospital-based retrospective cohort study found no association between MAP and carotid plaques (P > 0.05).<sup>30</sup> The European Carotid Surgery Trial also reported no

correlation between MAP and ulceration of symptomatic carotid plaques.<sup>21</sup> Our study found that MAP was positively correlated with multiple carotid plaques, with the constituent ratio increasing by 1.1% for each 1-mmHg increase in MAP. Further research is needed to clarify the role of MAP in carotid plaque formation.

Previous studies have shown a higher risk of developing carotid plaque in men, older age, and high BMI.<sup>31–34</sup> Our study also confirms that female sex and advanced age are risk factors for multiple carotid plaques, which may be related to the protective effect of estrogen on female blood vessels and the increase in age-induced inflammatory response and total matrix metalloproteinase-9.<sup>35,36</sup> However, this study found that low BMI is a risk factor for multiple carotid plaques, which may be related to the unique characteristics of our study population, including the rural setting and lifestyle factors, which warrant further investigation. Additionally, the study found a significant interaction between the ratio of SBP to HDL-C and the incidence of multiple carotid plaques. This finding is consistent with previous hypotheses suggesting that hypertension-induced damage to the vascular endothelium, combined with lipid deposition, contributes to the development of atherosclerosis.<sup>37</sup> These findings emphasize the complex interplay between blood pressure, lipid metabolism, and vascular health in the pathogenesis of carotid atherosclerosis and underline the importance of managing both BP components and lipid profiles to reduce cardiovascular risk.

There were several limitations in the present study. First, this study is a cross-sectional study, which restricts the ability to establish causality between BP components and the presence of multiple carotid plaques. This means that observed associations may be influenced by unmeasured confounding factors and temporal relationships cannot be determined. Future research should employ a longitudinal study design, tracking changes in BP components and carotid plaque development over time. This approach would provide a causality and the progression of atherosclerosis. Second, the study population was limited to a rural, low-income Chinese demographic, which may limit the generalizability of the findings to other populations. Results may not be applicable to urban populations, different socioeconomic groups, or other ethnicities, potentially limiting the broader applicability of the findings. Expanding future studies to include a more diverse population sample, encompassing urban, higher-income, and different ethnic groups, would enhance the generalizability of the results and provide a more comprehensive understanding of the relationships between BP components and carotid plaques. Third, potential for measurement errors exists due to reliance on self-reported data and single-time-point measurements for BP and other variables. Measurement errors and biases from self-reported data could affect the accuracy of the associations observed, potentially leading to misclassification or underestimation of the true relationships. Incorporating multiple BP measurements over time and utilizing more objective data collection methods, such as wearable BP monitors and detailed, validated questionnaires for lifestyle factors, would help to reduce measurement errors and provide more accurate and reliable data. Finally, the study may be affected by unmeasured confounding factors such as genetic predispositions, dietary habits, and other lifestyle factors that were not controlled for. These unmeasured confounders could influence the observed associations, making it difficult to isolate the effects of BP components on multiple carotid plaques. Future studies would collect comprehensive data on potential confounders and use advanced statistical techniques to adjust for these variables. Detailed assessments of diet, physical activity, medication use, and genetic factors would help to control for these confounders and provide a more accurate analysis of the relationships between BP components and carotid plaques.

### Conclusion

This study highlights the significant associations between blood pressure components, including SBP, DBP, PP, and MAP, and the presence of multiple carotid plaques in a rural Chinese population. In addition to blood pressure, factors such as age, gender, and BMI were found to be crucial in determining the risk of carotid atherosclerosis. Our findings also reveal a significant interaction between SBP and HDL-C ratio, suggesting the combined impact of hypertension and lipid metabolism on vascular health. These results emphasize the importance of early detection and comprehensive management of both blood pressure and lipid levels, particularly in higher-risk populations, to reduce the burden of cardiovascular diseases.

### **Abbreviations**

SBP, systolic BP; DBP, diastolic BP; PP, pulse pressure; MAP, mean arterial pressure; BMI, body mass index; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; CIMT, carotid intima-media thickness; CSPPT, China Stroke Primary Prevention Trial; EVA, Étude du Vieillissement Artériel.

### **Data Sharing Statement**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

### **Ethics Approval and Consent to Participate**

The research protocol was approved by the Tianjin Medical University General Hospital Ethics Committee (IRB2018-100-01) and all participants provided written informed consent. Our study complies with the Declaration of Helsinki.

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### **Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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### Disclosure

The authors declare no conflict of interest.

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