

# The prevalence of carotid plaque with different stability and its association with metabolic syndrome in China

## The Asymptomatic Polyvascular Abnormalities Community study

Anxin Wang, PhD<sup>a,b,c,d,e</sup>, Lingyun Wu, MD<sup>f</sup>, Xiaoxue Liu, MS<sup>g</sup>, Zhaoping Su, MS<sup>h</sup>, Yanxia Luo, PhD<sup>a,i</sup>, Shuohua Chen, MS<sup>k</sup>, Haibin Li, MS<sup>a,i</sup>, Xiangtong Liu, PhD<sup>a,i</sup>, Lixin Tao, PhD<sup>a,i</sup>, Jin Guo, PhD<sup>a,i</sup>, Feng Zhang, PhD<sup>a,i</sup>, Yibin Cao, MD<sup>j</sup>, Xingquan Zhao, MD, PhD<sup>b,c,d,e,\*</sup>, Shouling Wu, MD<sup>k</sup>, Xiuhua Guo, PhD<sup>a,i</sup>

### Abstract

Few studies have investigated the prevalence of carotid plaque with different stability in Chinese. As is well known, carotid atherosclerosis is tightly associated with metabolic syndrome (MetS); however, the data about the association between the presence of carotid plaque with different stability and MetS was limited. The aim of our study was to investigate the prevalence of carotid plaque with different stability and its potential association with MetS in general Chinese population.

The Asymptomatic Polyvascular Abnormalities Community study is a community-based study to investigate the epidemiology of asymptomatic polyvascular abnormalities in Chinese adults. A total of 5393 participants were finally eligible and included in this study. The carotid plaque and its stability were assessed using ultrasonography. The MetS was defined using the criteria from US National Cholesterol Education Program-Adult Treatment Panel III. Data were analyzed with multivariate logistic regression models.

Of the 5393 subjects, 1397 (25.9%) participants had stable carotid plaque, 1518 (28.1%) had unstable carotid plaque in participants, and 1456 (27.0%) had a MetS. MetS was, respectively, significantly associated with the prevalence of carotid plaque (odds ratio [OR]: 1.25; 95% confidence interval [CI]: 1.07, 1.47), stable carotid plaque (OR: 1.23; 95% CI: 1.02, 1.48), and unstable carotid plaque (OR: 1.27; 95% CI: 1.03, 1.56) after adjusting for age, gender, level of education, income, smoking, drinking, physical activity, body mass index, low-density lipoprotein, and high-sensitivity C-reactive protein. With the number of MetS components, the prevalence of carotid plaque, stable carotid plaque, and unstable carotid plaque significantly increased ( $P$  for trend <0.0001), respectively.

In summary, the prevalence of carotid plaque was 54.1%, stable carotid plaque was 25.9%, and unstable carotid plaque was 28.1%. Our study revealed that the prevalence of carotid plaque, stable carotid plaque, and unstable carotid plaque was, respectively, significantly associated with MetS in the general population.

**Abbreviations:** APAC = Asymptomatic Polyvascular Abnormalities Community, BMI = body mass index, BP = blood pressure, CI = confidence interval, HDL = high-density lipoprotein, hs-CRP = high-sensitive C-reactive protein, LDL = low-density lipoprotein, MetS = metabolic syndrome, OR = odds ratio, TC = total cholesterol, TG = triglycerides.

**Keywords:** carotid plaque, metabolic syndrome, stable carotid plaque, unstable carotid plaque

Editor: Helen Gharaei.

AW and LW contributed equally to this article.

The authors have no conflicts of interest to disclose.

<sup>a</sup> Department of Epidemiology and Health Statistics, School of Public Health, Capital Medical University, <sup>b</sup> Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, <sup>c</sup> China National Clinical Research Center for Neurological Diseases, <sup>d</sup> Center of Stroke, Beijing Institute for Brain Disorders, <sup>e</sup> Beijing Key Laboratory of Translational Medicine for Cerebrovascular Disease, Beijing, <sup>f</sup> North China University of Science and Technology, <sup>g</sup> Department of Cardiology, Tangshan People's Hospital, North China University of Science and Technology, Tangshan, <sup>h</sup> Department of Epidemiology and Health Statistics, Academy of Public Health and Management, Weifang Medical University, Weifang, <sup>i</sup> Beijing Municipal Key Laboratory of Clinical Epidemiology, Capital Medical University, Beijing, <sup>j</sup> Department of Neurology, Tangshan Gongren Hospital, <sup>k</sup> Department of Cardiology, Kailuan Hospital, North China University of Science and Technology, Tangshan, China.

\* Correspondence: Xiuhua Guo, Department of Epidemiology and Health Statistics, School of Public Health, Capital Medical University, Beijing 100069, China (e-mail: statguo@ccmu.edu.cn); Shouling Wu, Department of Cardiology, Kailuan Hospital, North China University of Science and Technology, Tangshan 063000, China (e-mail: drwusl@163.com); Xingquan Zhao, Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing 100050, China (e-mail: zxq@vip.163.com).

Copyright © 2016 the Author(s). Published by Wolters Kluwer Health, Inc. All rights reserved.

This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Medicine (2016) 95:34(e4619)

Received: 23 January 2016 / Received in final form: 6 July 2016 / Accepted: 27 July 2016

<http://dx.doi.org/10.1097/MD.0000000000004619>

## 1. Introduction

The presence of carotid plaque, a surrogate marker of subclinical atherosclerosis and a powerful predictor of vascular outcomes, can be visualized noninvasively in the arterial wall with the use of high-resolution ultrasound, and ultrasonic measurements are often used as a surrogate endpoint in epidemiological studies on cardiovascular and cerebrovascular disease. However, few studies have investigated the prevalence of carotid plaque with different stability in Chinese.

The metabolic syndrome (MetS) currently affects more and more adult population both in developed but especially in developing countries<sup>[1]</sup> and has become a major public-health challenge worldwide.<sup>[2–6]</sup> It is characterized by a cluster of several cardiovascular risk factors including abdominal obesity, atherogenic dyslipidemia (elevated triglycerides [TG] and low high-density lipoproteins [HDLs]), elevations of blood pressure (BP), and raised fasting plasma glucose.<sup>[7,8]</sup> Some significant studies have reported that MetS is associated with the progression of atherosclerosis<sup>[9]</sup> and has become a multiplex risk factor for cardiovascular disease.<sup>[10,11]</sup>

Previous studies have identified that there is a correlation between MetS and the presence of carotid plaque.<sup>[12,13]</sup> Northern Manhattan Study<sup>[14]</sup> investigated that MetS and its components were significantly associated with carotid plaque prevalence. However, the data about the association between the presence of carotid plaque with different stability and MetS was limited in general populations in China. Therefore, the aim of our study is to investigate the presence of carotid plaque with different stability and its potential association with MetS in a Chinese community-based cohort.

## 2. Materials and methods

### 2.1. Study population

The present cohort was from the Asymptomatic Polyvascular Abnormalities Community (APAC) study, a community-based, observational, prospective, long-term follow-up study, to investigate the epidemiology of asymptomatic polyvascular abnormalities in Chinese adults.<sup>[15]</sup> The detailed design and basic description of the APAC study have been published previously.<sup>[15–17]</sup> Briefly, a total of 5440 participants who provided the informed consent and completed the baseline survey were finally eligible and recruited in the APAC study. The Ethics Committee of the Ethics Committees of the Kailuan General Hospital and the Beijing Tiantan Hospital approved the study, and all participants signed written informed consent. Individuals were also informed of abnormal findings and recommended treatment.

### 2.2. Data collection

From the APAC study, 5393 participants with complete information regarding MetS and carotid plaque were analyzed in this study. All participants underwent questionnaire assessment, clinical examination, laboratory tests, and carotid duplex ultrasound examinations during the baseline survey. Structured interviews with a standardized questionnaire were performed by trained investigators. The questionnaire included questions on the demographic and socioeconomic background, level of education, self-reported income, smoking, drinking, physical activity, hypertension, diabetes mellitus, hyperlipidemia, coronary heart disease, previous stroke, and about the current

treatment of these diseases. Anthropometric indices included height, weight, and waist and hip circumference. Smoking was defined as at least 1 cigarette per day for more than 1 year. Drinking was defined as alcohol intake of at least 90 or 45 g of liquor per day for more than 1 year for men or women, respectively. Smoking or drinking cessation was regarded as only if it lasted for at least 1 year. The body mass index (BMI) was calculated as the ratio of body weight (kg) divided by the square of body height (m<sup>2</sup>). Fasting blood samples were biochemically examined for the concentration of glucose, HDL, low-density lipoproteins (LDLs), TG, total cholesterol (TC), and high-sensitive C-reactive protein (hs-CRP).

### 2.3. Definition of the metabolic syndrome

The MetS was defined using previously published criteria from US National Cholesterol Education Program-Adult Treatment Panel III. According to the definition proposed by the American Heart Association/National Heart, Lung, and Blood Institute, patients were considered to have MetS in the presence of  $\geq 3$  of the following criteria—central obesity: waist circumference  $>90$  cm for Chinese men,  $>80$  cm for Chinese women; a fasting triglyceride level  $\geq 150$  mg/dL (1.7 mmol/L); reduced HDL cholesterol:  $<40$  mg/dL (1.03 mmol/L) in men,  $<50$  mg/dL (1.29 mmol/L) in women; hypertension: systolic BP  $\geq 130$  mm Hg or diastolic  $\geq 85$  mm Hg or taking antihypertensive medication; and impaired fasting glucose: fasting glucose  $\geq 100$  mg/dL (5.6 mmol/L) or taking medication or previously diagnosed type 2 diabetes mellitus.

### 2.4. Assessment of carotid plaque

The complexity and advancement of carotid plaques were assessed by trained and certified sonographers using ultrasounds (Philips iU-22 ultrasound system, Philips Medical Systems, Bothell, WA). Bilateral carotid arteries were scanned with the beam focused on the near and far walls of the distal 2 cm of the common carotid artery proximal to its bifurcation. Both longitudinal and transverse images were obtained to extensively evaluate plaques. Carotid plaque was demonstrated as a thickness of 1.5 mm from the intima–lumen interface to the media–adventitia interface, or defined as a focal structure encroaching into the arterial lumen of at least 0.5 mm or 50% of the surrounding intima-media thickness value. In this study, stable carotid plaques have a uniform texture and present a smooth and regular surface, and plaques with high-level or homogeneous echoes. Whereas unstable carotid plaques were defined as plaques with incomplete fibrous cap or ulcerated plaques, and plaques with low-level or heterogeneous echoes.<sup>[18]</sup> Two independent operators reviewed the carotid ultrasound examination results, and the discrepancies between their evaluations were resolved by consensus.

### 2.5. Statistical analysis

The participants were divided into 2 groups according to the presence of carotid plaque. The subgroup of participants with carotid plaque presenting stable carotid and unstable carotid plaque were further analyzed. Continuous variables were described by mean  $\pm$  standard deviation or median with interquartile range. Categorical variables were expressed as proportions. We used the analysis of variance (ANOVA) test for nonpaired samples of normally distributed parameters and the

**Table 1**  
**Baseline characteristics.**

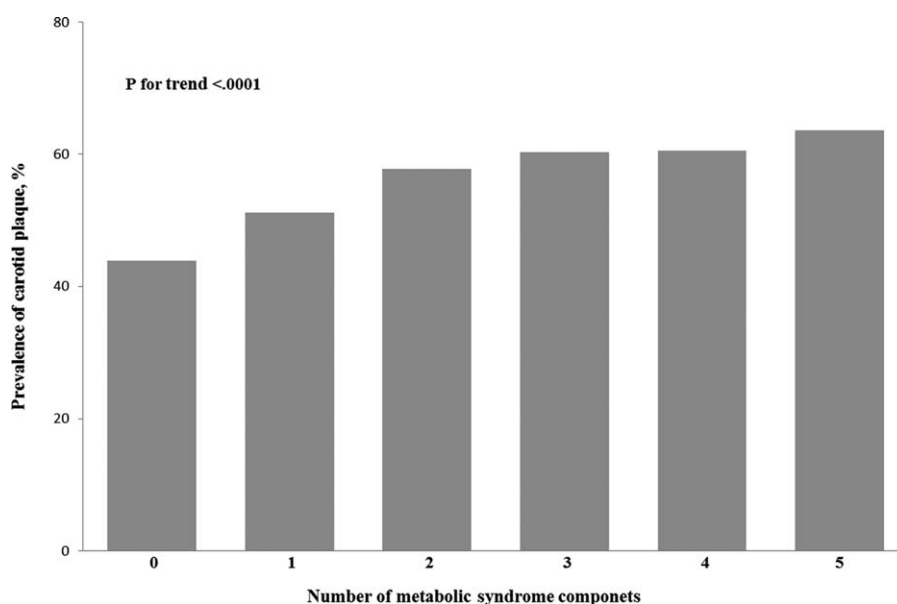
Characteristics	No carotid plaque	Carotid plaque		P
		Stable carotid plaque	Unstable carotid plaque	
No. of subjects	2478	1397	1518	
Age, y	49.4 ± 7.8	56.5 ± 11.2	63.4 ± 12.5	<0.001
Male, n (%)	1148 (46.3)	925 (66.2)	1157 (76.2)	<0.001
Education, n (%)				<0.001
Illiteracy/primary school	163 (6.6)	185 (13.2)	310 (20.4)	
Middle school	1146 (46.2)	613 (43.9)	614 (40.4)	
High school or higher	1169 (47.2)	599 (42.9)	594 (39.1)	
Income, n (%)				<0.001
<¥ 1000	625 (25.2)	325 (23.3)	342 (22.5)	
¥ 1000–3000	1683 (67.9)	925 (66.2)	952 (62.7)	
≥¥ 3000	170 (6.9)	147 (10.5)	224 (14.8)	
Smoking, n (%)				<0.001
Never	1754 (70.8)	803 (57.5)	815 (53.7)	
Former	78 (3.2)	90 (6.4)	135 (8.9)	
Current	646 (26.1)	504 (36.1)	568 (37.4)	
Drinking, n (%)				<0.001
Never	1774 (71.6)	864 (61.8)	890 (58.6)	
Former	19 (0.8)	22 (1.6)	42 (2.8)	
Current	685 (27.6)	511 (36.6)	586 (38.6)	
Physical activity, n (%)				<0.001
Inactive	1071 (43.2)	569 (40.7)	519 (34.2)	
Moderately active	699 (28.2)	324 (23.2)	350 (23.1)	
Very active	708 (28.6)	504 (36.1)	649 (42.7)	
Body mass index, kg/m <sup>2</sup>	25.0 ± 3.3	24.9 ± 3.2	24.8 ± 3.2	0.71
LDL cholesterol, mmol/L	2.6 ± 0.7	2.7 ± 0.7	2.7 ± 0.8	<0.001
hs-CRP	1.7 ± 3.1	2.3 ± 4.9	2.7 ± 5.3	<0.001
Waist circumference, cm	84.8 ± 9.8	87.0 ± 9.5	87.4 ± 9.4	<0.001
TG, mmol/L	1.6 ± 1.3	1.8 ± 1.5	1.7 ± 1.4	<0.001
TC, mmol/L	4.9 ± 0.9	5.1 ± 1.0	5.3 ± 1.1	<0.001
HDL cholesterol, mmol/L	1.6 ± 0.5	1.6 ± 0.4	1.6 ± 0.5	<0.001
SBP, mm Hg	125.1 ± 17.8	134.2 ± 19.8	138.5 ± 20.7	<0.001
DBP, mm Hg	82.0 ± 10.9	84.1 ± 11.0	83.0 ± 11.3	<0.001
Fasting plasma glucose, mmol/L	5.4 ± 1.2	5.7 ± 1.7	5.8 ± 1.7	<0.001
MetS, n (%)	575 (23.2)	426 (30.5)	455 (30.0)	<0.001
MetS components, n (%)				
Central obesity	1328 (53.6)	754 (54.0)	780 (51.4)	0.30
Raised TG	769 (31.0)	499 (35.7)	491 (32.4)	0.01
Reduced HDL cholesterol	278 (11.2)	170 (12.2)	160 (10.5)	0.38
Raised BP	796 (32.1)	660 (47.2)	815 (53.7)	<0.001
Raised fasting plasma glucose	702 (28.3)	493 (35.3)	582 (38.3)	<0.001
No. of MetS components (%)				<0.001
0 MetS comp	585 (23.6)	222 (15.9)	235 (15.5)	
1 MetS comp	712 (28.7)	365 (26.1)	382 (25.2)	
2 MetS comp	606 (24.5)	384 (27.5)	446 (29.4)	
3 MetS comp	375 (15.1)	282 (20.2)	287 (18.9)	
4 MetS comp	176 (7.1)	123 (8.8)	147 (9.7)	
5 MetS comp	24 (1.0)	21 (1.5)	21 (1.4)	

BP = blood pressure, DBP = diastolic blood pressure, HDL = high-density lipoprotein, hs-CRP = high-sensitive C-reactive protein, LDL = low-density lipoprotein, MetS = metabolic syndrome, SBP = systolic blood pressure, TC = total cholesterol, TG = triglycerides.

Kruskal–Wallis test for nonparametric variables. The  $\chi^2$  or Fisher exact test was used for categorical variables.

The Chi-square trend test was used to test the trends of the prevalence of carotid plaque, stable carotid plaque, and unstable carotid plaque with increasing number of components of MetS. Odds ratios (ORs) and 95% confidence intervals (CIs) for the associations of MetS or the number of MetS components with carotid plaque, stable carotid plaque, and unstable carotid plaque were calculated using 3 multivariate logistic regression models. Model 1 adjusted for age and gender; model 2 adjusted for as model 1 plus level of education, income, smoking,

drinking, and physical activity; and model 3 adjusted for as model 2 plus BMI, LDL, and hs-CRP. For each model, a trend test was performed after the number of MetS components was entered into the model and treated as a continuous variable. A multivariate stepwise logistic regression was also used to identify the associations between MetS and carotid plaque, stable carotid plaque, unstable carotid plaque all other variables in the model 3. Two-tailed *P* values less than 0.05 were taken to be statistically significant. All statistical analyses were carried out with SAS Version 9.4 software (SAS Institute Inc., Cary, NC).



**Figure 1.** Prevalence (95% confidence interval) of carotid plaque stratified by the number of metabolic syndrome components in the Asymptomatic Polyvascular Abnormalities in Community Study (unadjusted data).

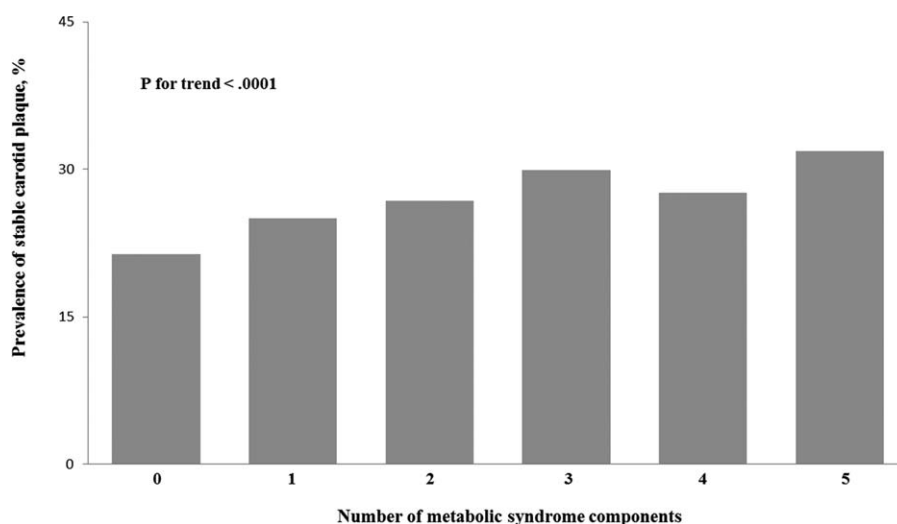
### 3. Results

#### 3.1. Patient characteristics

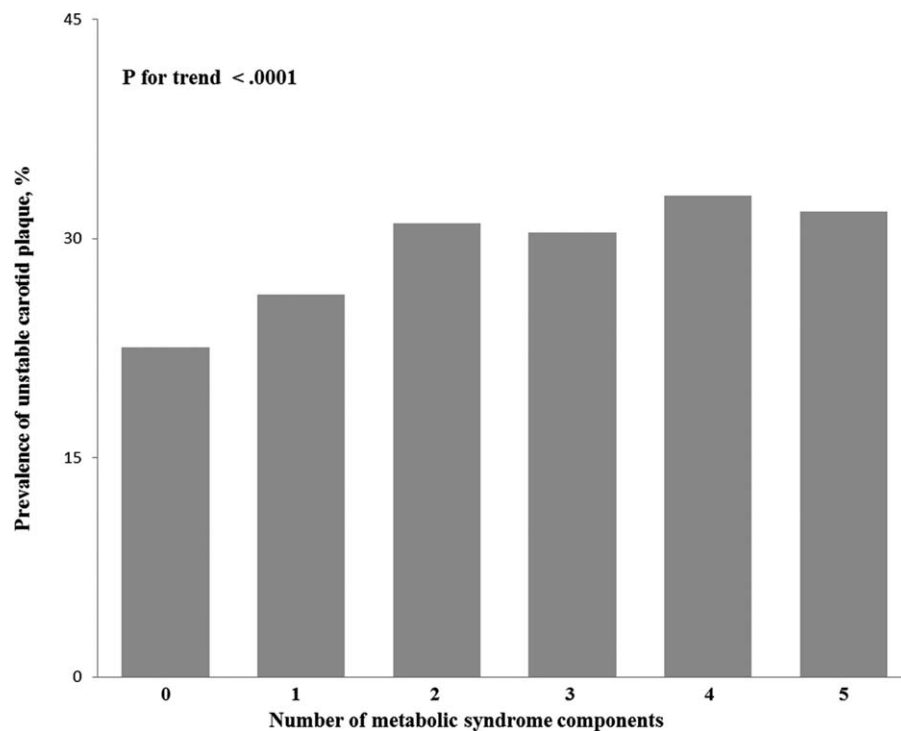
Baseline characteristics of the 3 groups included in the study were presented in Table 1. Out of 5393 study participants, stable carotid plaque was detected in 1397 (25.9%) participants, unstable carotid plaque in 1518 (28.1%) individuals, and 1456 (27.0%) study participants had a MetS. There was statistically significant difference between the 3 groups in the following factors: age, gender, level of education, level of income, smoking, drinking, physical activity, blood concentration of LDL, hs-CRP, TG, TC, HDL, fasting plasma glucose, waist circumference, higher systolic BP, and diastolic BP (all  $P < 0.05$ ). There was no significant difference between the 3 groups in BMI ( $P = 0.71$ ). The frequency of raised TG, elevated arterial BP, raised fasting plasma

glucose concentration and the degree of MetS were significantly different in the 3 groups (Table 1) (Figs. 1–3). The prevalence of carotid plaque increased significantly ( $P < 0.0001$ ) from 43.9% (95% CI: 0.41, 0.47) in the subgroup without any MetS component to 51.2% (95% CI: 0.49, 0.54) in the subgroup with 1 component of MetS, to 57.8% (95% CI: 0.55, 0.60) in the subgroup with 2 components, and to 63.6% (95% CI: 0.51, 0.75) in the subgroup with 5 components of MetS (Fig. 1).

In the multivariate logistic regression analysis, MetS was, respectively, significantly associated with the prevalence of carotid plaque (OR: 1.25; 95% CI: 1.07, 1.47), stable carotid plaque (OR: 1.23; 95% CI: 1.02, 1.48), and unstable carotid plaque (OR: 1.27; 95% CI: 1.03, 1.56) after adjusting for age,



**Figure 2.** Prevalence (95% confidence interval) of unstable and stable plaque stratified by the number of metabolic syndrome components in the Asymptomatic Polyvascular Abnormalities in Community Study (unadjusted data).



**Figure 3.** Prevalence (95% confidence interval) of unstable carotid plaque stratified by the number of metabolic syndrome components in the Asymptomatic Polyvascular Abnormalities in Community Study (unadjusted data).

gender, level of education, income, smoking, drinking, physical activity, BMI, blood concentration of LDL, and hs-CRP (Table 2). Using the subgroup with 0 MetS component as baseline, the ORs for the associations between the subgroups with 1, 2, 3, 4, and 5 MetS components and carotid plaque were 1.33 (95% CI: 1.09, 1.62), 1.57 (95% CI: 1.28, 1.93), 1.82 (95% CI: 1.44, 2.30), 1.96 (95% CI: 1.47, 2.62), and 2.46 (95% CI: 1.36, 4.47), respectively. The ORs for the associations between the subgroups with 1, 2, 3, 4, and 5 MetS components and stable carotid plaque were 1.38 (95% CI: 1.10, 1.73), 1.52 (95% CI: 1.20, 1.93), 1.87 (95% CI: 1.43, 2.46), 1.87 (95% CI: 1.43, 2.46), and 2.29 (95% CI: 1.16, 4.52), respectively. The ORs for the associations between the subgroups with 1, 2, 3, 4, and 5 MetS components and unstable carotid plaque were 1.30 (95% CI: 0.99, 1.69), 1.66 (95% CI: 1.27, 2.19), 1.69 (95% CI: 1.24, 2.30), 2.42 (95% CI: 1.68, 3.48), and 2.4695 (95% CI: 1.43, 6.09), respectively (model 3).

In this multivariate model, the prevalence of carotid plaque including stable carotid plaque and unstable carotid plaque

increased significantly ( $P$  for trend  $<0.0001$ ) with the number of MetS components. The same held true for the 2 other models of the multivariate analysis (Table 3).

#### 4. Discussion

In our population-based study, the prevalence of carotid plaque was 54.1%, stable carotid plaque was 25.9%, and unstable carotid plaque was 28.1%. The prevalence of carotid plaque, stable carotid plaque, and unstable carotid plaque was independently associated with both presence of the MetS and the number of components. Further, study participants with 5 MetS components had higher risk of carotid plaque, stable carotid plaque, and unstable carotid plaque than participants with 0 MetS component.

Previous hospital-based studies revealed that patients with an acute cardiovascular event were more likely to have unstable plaque in the arteries compared with patients without acute cardiovascular events.<sup>[19–22]</sup> One of above studies showed that

**Table 2**  
**Associations between MetS presence and plaques.**

Plaques	Model 1 <sup>*</sup>		Model 2 <sup>†</sup>		Model 3 <sup>‡</sup>	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
Carotid plaque	1.22 (1.06–1.41)	$<0.01$	1.21 (1.05–1.40)	0.01	1.25 (1.07–1.47)	$<0.01$
Stable carotid plaque	1.19 (1.01–1.40)	0.03	1.18 (1.00–1.40)	0.04	1.23 (1.02–1.48)	0.03
Unstable carotid plaque	1.26 (1.05–1.51)	0.01	1.24 (1.03–1.48)	0.02	1.27 (1.03–1.56)	0.02

CI = confidence interval, OR = odds ratio.

<sup>\*</sup> Adjusted for age (years) and gender.

<sup>†</sup> Adjusted for as model 1 plus level of education, income, smoking, drinking, and amount of physical activity.

<sup>‡</sup> Adjusted for as model 2 plus body mass index, and serum concentrations of low-density lipoprotein cholesterol and high-sensitivity C-reactive protein.

**Table 3****Associations between the components of MetS presence and plaques.**

Plaques	No. of MetS components	Model 1*	Model 2†	Model 3‡
		OR (95% CI)	OR (95% CI)	OR (95% CI)
Carotid plaque	0	Reference	Reference	Reference
	1	1.25 (1.04–1.52)	1.26 (1.04–1.53)	1.33 (1.09–1.62)
	2	1.41 (1.17–1.71)	1.42 (1.18–1.72)	1.57 (1.28–1.93)
	3	1.59 (1.30–1.96)	1.59 (1.29–1.96)	1.82 (1.44–2.30)
	4	1.69 (1.31–2.19)	1.67 (1.29–2.16)	1.96 (1.47–2.62)
	5	1.90 (1.08–3.37)	1.92 (1.08–3.41)	2.46 (1.36–4.47)
	<i>P</i> for trend	<0.001	<0.001	<0.001
Stable carotid plaque	0	Reference	Reference	Reference
	1	1.30 (1.05–1.62)	1.31 (1.05–1.63)	1.38 (1.10–1.73)
	2	1.36 (1.09–1.69)	1.37 (1.10–1.71)	1.52 (1.20–1.93)
	3	1.62 (1.28–2.05)	1.62 (1.28–2.05)	1.87 (1.43–2.46)
	4	1.53 (1.14–2.06)	1.52 (1.12–2.05)	1.74 (1.24–2.43)
	5	1.74 (0.91–3.36)	1.79 (0.93–3.45)	2.29 (1.16–4.52)
	<i>P</i> for trend	<0.01	<0.01	<0.01
Unstable carotid plaque	0	Reference	Reference	Reference
	1	1.18 (0.91–1.52)	1.20 (0.93–1.56)	1.30 (0.99–1.69)
	2	1.50 (1.17–1.94)	1.50 (1.16–1.94)	1.66 (1.27–2.19)
	3	1.51 (1.15–1.99)	1.50 (1.14–1.98)	1.69 (1.24–2.30)
	4	2.05 (1.49–2.84)	2.00 (1.45–2.78)	2.42 (1.68–3.48)
	5	2.29 (1.14–4.61)	2.35 (1.17–4.74)	2.95 (1.43–6.09)
	<i>P</i> for trend	<0.001	<0.001	<0.001

CI = confidence interval, MetS = metabolic syndrome, OR = odds ratios.

\* Adjusted for age (years) and gender.

† Adjusted for as model 1 plus level of education, income, smoking, drinking, and amount of physical activity.

‡ Adjusted for as model 2 plus body mass index, and serum concentrations of low-density lipoprotein cholesterol and high-sensitivity C-reactive protein.

the prevalence of unstable carotid plaque in patients with an acute coronary event was 43% and those without an acute coronary event was 15%. In a European study, a certain percentage of patients with asymptomatic carotid stenosis have an unstable carotid plaque, which 78% patients had stable plaque and 22% unstable one.<sup>[23]</sup> The presence of carotid plaque with different stability in general population was almost lower than community studies. As a Japanese general population study showed that the prevalence of carotid plaque was 20.0%,<sup>[24]</sup> which is commonly underestimated with the reason that participants were without antihypertensive medications whose BP were less than 140/90 mm Hg. Our research results were as similar as the finding of a small sample Chinese cross-section study, which included 116 stroke-free participants and investigated that the prevalence of carotid plaque was 62.9%, stable carotid plaque was 27.6%, and unstable carotid plaque was 35.3%.<sup>[25]</sup>

These findings are further extended by a number of studies, which have shown both presence of MetS and its components<sup>[13,26,27]</sup> to be significantly associated with carotid plaque, with increasing number of MetS components being associated with increased carotid plaque prevalence.<sup>[28]</sup> The same findings have shown that individual components are the driving force behind the association between MetS and progression of plaque (>5% increase in percent atheroma volume) and not the binary presence of the syndrome itself.<sup>[29]</sup> As well as few studies investigated, we further reported the association between MetS and the presence of carotid plaque with different stability in Chinese. We report that there is a strong association between MetS and its components and both stable carotid plaque and unstable carotid plaque.

As suggested in a previous study,<sup>[30]</sup> hypertension and larger waist circumference were MetS components associated with

atherosclerosis. One early study reported that hypertension was also identified to be an important MetS component associated with a higher prevalence of carotid plaque, as well as impaired fasting glucose.<sup>[31]</sup> A majority of evidence shows that long-term elevations of BP accelerate collagen synthesis, arterial smooth muscle hypertrophy and hyperplasia, and atherosclerosis, thus increasing the development of carotid plaque.<sup>[32]</sup> Abdominal obesity also have been suggested as a risk factor for accelerated atherosclerosis.<sup>[33]</sup> Visceral obesity is often accompanied by impaired glucose tolerance, hyperlipidemia, and hypertension, whereas such complications are comparatively rare in subcutaneous obesity.<sup>[34]</sup> Visceral fat accumulation is closely associated with the various components of MetS.<sup>[35]</sup> The finding of our study was consistent with the previous study, which was reported that MetS can predict the unstable plaque.<sup>[36]</sup> In addition, we further investigated that the components of MetS were strongly associated with unstable carotid plaque. As high-risk atheromatous plaque, unstable carotid plaque consists of lipid-rich atheromatous core, thin fibrous cap with macrophage and lymphocyte infiltration, decreased smooth muscle cell content, and extensive remodeling of the arterial wall.<sup>[37]</sup> HDL can remove excess cholesterol from the foam cells of the evolving atherosclerotic plaque and return it to the liver.<sup>[38]</sup> Patients with low concentrations of HDL cholesterol might have a high risk of plaque rupture and thrombus formation, which can lead to ischemic cerebrovascular diseases, because of the disruption of plaque.

Our study had some limitations. First, as mentioned earlier, this is a cross-sectional study so we cannot draw a causal inference which usually has to be found in a longitudinal investigation. Our findings only can conclude on an association between MetS and carotid plaque, while the causal association of MetS with carotid plaque will be tested in the follow-up study.

Second, the assessment of carotid plaque with ultrasonography may be less reliable than magnetic resonance angiography or other forms of angiography. However, as an accepted method for screening carotid plaque, ultrasonography is widely used in a general population. Third, residual confounding factors could not completely be excluded, even though a stratified random sampling method was used to reduce inclusion bias. Although a stratified random sampling method by age and gender according to the data of the Chinese National Census from 2010 was used, the population in our study may not have been representative for the general population of China.

In summary, the prevalence of carotid plaque was 54.1%, stable carotid plaque was 25.9%, and unstable carotid plaque was 28.1%. The community-based study revealed that the prevalence of carotid plaque, stable carotid plaque, and unstable carotid plaque was, respectively, significantly associated with MetS.

## Acknowledgments

We thank all the participants of the APAC study for their invaluable contributions. We declare no conflicts of interest.

## References

- Grundy SM. Metabolic syndrome pandemic. *Arterioscler Thromb Vasc Biol* 2008;28:629–36.
- Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet* 2005;365:1415–28.
- Danaei G, Finucane MM, Lin JK, et al. National, regional, and global trends in systolic blood pressure since 1980: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5.4 million participants. *Lancet* 2011;377:568–77.
- Farzadfar F, Finucane MM, Danaei G, et al. National, regional, and global trends in serum total cholesterol since 1980: systematic analysis of health examination surveys and epidemiological studies with 321 country-years and 3.0 million participants. *Lancet* 2011;377:578–86.
- Finucane MM, Stevens GA, Cowan MJ, et al. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *Lancet* 2011;377:557–67.
- Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;380:2095–128.
- Alberti KG, Zimmet P, Shaw J. Metabolic syndrome—a new world-wide definition. A consensus statement from the International Diabetes Federation. *Diabet Med* 2006;23:469–80.
- Novo S, Balbarini A, Belch JJ, et al. The metabolic syndrome: definition, diagnosis and management. *Int Angiol* 2008;27:220–31.
- Jung JM, Young Kwon D, Han C, et al. Metabolic syndrome and early carotid atherosclerosis in the elderly. *J Atheroscler Thromb* 2014;21:435–44.
- Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. *Circulation* 2005;112:2735–52.
- Grundy SM. Metabolic syndrome: a multiplex cardiovascular risk factor. *J Clin Endocrinol Metab* 2007;92:399–404.
- Vaudo G, Marchesi S, Siepi D, et al. Metabolic syndrome and preclinical atherosclerosis: focus on femoral arteries. *Metabolism* 2007;56:541–6.
- Hassinen M, Komulainen P, Lakka TA, et al. Metabolic syndrome and the progression of carotid intima-media thickness in elderly women. *Arch Intern Med* 2006;166:444–9.
- Rundek T, White H, Boden-Albala B, et al. The metabolic syndrome and subclinical carotid atherosclerosis: the Northern Manhattan Study. *J Cardiometab Syndr* 2007;2:24–9.
- Zhou Y, Li Y, Xu L, et al. Asymptomatic Polyvascular Abnormalities in Community (APAC) study in China: objectives, design and baseline characteristics. *PLoS One* 2013;8:e84685.
- Wang A, Liu X, Guo X, et al. Resting heart rate and risk of hypertension: results of the Kailuan cohort study. *J Hypertens* 2014;32:1600–5; discussion 1605.
- Wang A, Wu J, Zhou Y, et al. Measures of adiposity and risk of stroke in China: a result from the Kailuan study. *PLoS One* 2013;8:e61665.
- Sztajzel R. Ultrasonographic assessment of the morphological characteristics of the carotid plaque. *Swiss Med Wkly* 2005;135:635–43.
- Goldstein JA, Demetriou D, Grines CL, et al. Multiple complex coronary plaques in patients with acute myocardial infarction. *N Engl J Med* 2000;343:915–22.
- Rossi A, Franceschini L, Fusaro M, et al. Carotid atherosclerotic plaque instability in patients with acute myocardial infarction. *Int J Cardiol* 2006;111:263–6.
- Peeters W, Hellings WE, de Kleijn DP, et al. Carotid atherosclerotic plaques stabilize after stroke: insights into the natural process of atherosclerotic plaque stabilization. *Arterioscler Thromb Vasc Biol* 2009;29:128–33.
- Tegos TJ, Sohail M, Sabetai MM, et al. Echomorphologic and histopathologic characteristics of unstable carotid plaques. *AJNR Am J Neuroradiol* 2000;21:1937–44.
- Milosevic D, Pasternak J, Popovic V, et al. The analysis of the connection between plaque morphology of asymptomatic carotid stenosis and ischemic brain lesions. *Vojnosanit Pregl* 2013;70:993–8.
- Ishizaka N, Ishizaka Y, Hashimoto H, et al. Metabolic syndrome may not associate with carotid plaque in subjects with optimal, normal, or high-normal blood pressure. *Hypertension* 2006;48:411–7.
- Tan C, Liu Y, Li W, et al. Associations of matrix metalloproteinase-9 and monocyte chemoattractant protein-1 concentrations with carotid atherosclerosis, based on measurements of plaque and intima-media thickness. *Atherosclerosis* 2014;232:199–203.
- Pollex RL, Al-Shali KZ, House AA, et al. Relationship of the metabolic syndrome to carotid ultrasound traits. *Cardiovasc Ultrasound* 2006;4:28.
- Empana JP, Zureik M, Garipey J, et al. The metabolic syndrome and the carotid artery structure in noninstitutionalized elderly subjects: the three-city study. *Stroke* 2007;38:893–9.
- Herder M, Arntzen KA, Johnsen SH, et al. The metabolic syndrome and progression of carotid atherosclerosis over 13 years. The Tromso study. *Cardiovasc Diabetol* 2012;11:77.
- Bayturan O, Tuzcu EM, Lavoie A, et al. The metabolic syndrome, its component risk factors, and progression of coronary atherosclerosis. *Arch Intern Med* 2010;170:478–84.
- Della-Morte D, Gardener H, Denaro F, et al. Metabolic syndrome increases carotid artery stiffness: the Northern Manhattan Study. *Int J Stroke* 2010;5:138–44.
- Stehouwer CD, Henry RM, Ferreira I. Arterial stiffness in diabetes and the metabolic syndrome: a pathway to cardiovascular disease. *Diabetologia* 2008;51:527–39.
- Arnett DK, Boland LL, Evans GW, et al. Hypertension and arterial stiffness: the Atherosclerosis Risk in Communities Study. *ARIC Investigators. Am J Hypertens* 2000;13:317–23.
- Sutton-Tyrrell K, Newman A, Simonsick EM, et al. Aortic stiffness is associated with visceral adiposity in older adults enrolled in the study of health, aging, and body composition. *Hypertension* 2001;38:429–33.
- Okura T, Watanabe S, Kurata M, et al. Long-term effects of angiotensin II receptor blockade with valsartan on carotid arterial stiffness and hemodynamic alterations in patients with essential hypertension. *Clin Exp Hypertens* 2008;30:415–22.
- Godia EC, Madhok R, Pittman J, et al. Carotid artery distensibility: a reliability study. *J Ultrasound Med* 2007;26:1157–65.
- Lee MG, Jeong MH, Kim DH, et al. Can metabolic syndrome predict the vulnerable plaque in patients with stable angina pectoris? Virtual histology-intravascular ultrasound analysis. *J Cardiol* 2012;59:266–74.
- Schaar JA, Muller JE, Falk E, et al. Terminology for high-risk and vulnerable coronary artery plaques. Report of a meeting on the vulnerable plaque, June 17 and 18, 2003, Santorini, Greece. *Eur Heart J* 2004;25:1077–82.
- Barter PJ, Nicholls S, Rye KA, et al. Antiinflammatory properties of HDL. *Circ Res* 2004;95:764–72.