

Prevalence of carotid artery stenosis in Chinese patients with angina pectoris

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Background: The prevalence of carotid artery stenosis (CAS) in Chinese patients with angina pectoris is unknown.

Methods: The study population consisted of 989 consecutive patients who were scheduled to undergo nonemergent coronary angiography for suspicion of coronary artery disease (CAD) because of angina pectoris between January 2013 and December 2014. All patients underwent carotid ultrasonography to screen for CAS within one month before or after coronary angiography. We defined cases with 0–50%, 50%–70%, and >70% stenosis as mild, moderate, and severe stenosis, respectively.

Results: CAD was presented in 853 patients (86.2%) of whom 191 patients (19.3%) had 1-vessel disease, 246 patients (24.9%) had 2-vessel disease and 416 patients (42.1%) had 3-vessel disease; left main trunk stenosis present in 137 patients (13.9%). In carotid ultrasonography, the prevalence of mild, moderate, and severe stenosis as well as that of total occlusion of the carotid artery was 54.5%, 13%, 4.7% and 0.8%, respectively. Significant CAS (>50% stenosis and total occlusion) was present in 10.3%, 13.9%, 19.9% and 22.8% of patients with 0-vessel, 1-vessel, 2-vessel and 3-vessel CAD. The severity of CAS was directly correlated ($r=0.194$, $P<0.001$) with the extent of CAD. The independent predictors of severe CAS and total carotid artery occlusion were increased age, male sex, hypertension, diabetes mellitus, hyperhomocysteinemia, a previous history of stroke and 3-vessel CAD.

Conclusions: The prevalence of CAS was not rare in China when compared with that in western countries, and the presence of CAS was weakly correlated with the extent of CAD. Screening for CAS should be recommended in Chinese patients with CAD, especially in those with one or more CAS-associated risk factors.

Keywords: Coronary artery disease (CAD); carotid artery stenosis (CAS); Chinese

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Introduction

In China, stroke has surpassed cardiovascular disease as the leading cause of death and adult disability (1). Carotid artery atherosclerotic stenosis is an important cause of stroke worldwide (2). Unlike in western countries, patients in China and other Asian countries predominantly exhibit intracranial atherosclerotic stenosis (3-5), whereas those in western countries are more likely to experience extracranial carotid artery stenosis (CAS) (6). However, recent studies have shown that significant extracranial CAS is not uncommon in Asian populations (7,8). The rising prevalence of extracranial carotid and vertebral artery disease was noted in a Chinese population (9) and may due to lifestyle changes in an effort to adopt western habits.

Atherosclerosis is a systemic disorder that can involve multiple arterial beds (10). The association between CAS and coronary artery disease (CAD) has been widely reported (11-13). Approximately 8% to 14% of patients undergoing myocardial revascularization because of CAD have significant CAS (14), and 28% of patients in western countries who are candidates for carotid endarterectomy because of CAS have significant CAD (15). However, until now, few studies have determined the prevalence of CAS in Chinese patients with angina pectoris.

We performed carotid ultrasonography, which is the first choice for imaging in carotid stenosis screening (16), in consecutive patients undergoing nonemergent coronary artery angiography. We investigated the prevalence and severity of CAS in a Chinese patient population with angina pectoris to identify the risk factors associated with CAS.

Materials and methods

Study population

The study population consisted of 989 consecutive patients with angina pectoris who were scheduled to undergo nonemergent coronary angiography for suspicion of CAD between January 2013 and December 2014 at our hospital. Patients who were making their initial visits to the clinic and patients with previous percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) histories were enrolled. Patients who did not undergo coronary angiography and carotid ultrasonography within a month before or after coronary angiography were also excluded. The study procedures were in accordance with institutional guidelines. All data were collected retrospectively. The

study was approved by the institutional ethics committee of our hospital.

Associated risk factors

The risk factor variables evaluated in the study included age, sex, body mass index (BMI), hypertension, hyperlipidemia, diabetes mellitus, chronic kidney insufficiency, smoking, hyperhomocysteinemia, history of stroke, history of myocardial infarction and previous PCI or CABG.

Hypertension was defined as any history of hypertension or if the subject's blood pressure exceeded 140 mmHg in systole or 90 mmHg in diastole according to at least two measurements performed in the hospital. Hyperlipidemia was defined as a fasting serum total cholesterol of >200 mg/dL, triglyceride concentration of >150 mg/dL, low-density lipoprotein cholesterol concentration of >140 mg/dL, high-density lipoprotein cholesterol concentration of <40 mg/dL or documented hyperlipidemia requiring lipid-lowering drug therapy. Diabetes mellitus was defined as a requirement for diabetes medication or a repeated fasting plasma glucose level exceeding 126 mg/dL or 200 mg/dL 2 hours after eating. Chronic kidney insufficiency was defined as evidence of renal damage or a glomerular filtration rate of <60 mL/min/1.73 m². Smoking was defined as if the patient smoked >1 cigarette per day for more than 6 months or had quit smoking for less than 2 years. Hyperhomocysteinemia was defined as a serum homocysteine concentration of >15 umol/L.

Definition of CAD

Nonemergent coronary angiography to investigate CAD was performed with a commercially available machine (Allura Xper FD20, Phillips) by standard techniques. The percentage of diameter stenosis was calculated by quantitative coronary angiography with an automated coronary analysis system (DCI-S, Phillips Medical System). CAD was defined as a lumen diameter stenosis of >50% in at least one major coronary artery (left anterior descending artery, left circumflex artery, right coronary artery or grafting vessel in patients with previous CABG). CAD was also considered present if the stenosis existed in some major branches (e.g., marginal or diagonal arteries) of the major coronary artery as mentioned above. According to the number of diseased vessels, each patient was classified into 1 of the following 4 groups: group 1, patients with 0-vessel disease; group 2, patients with 1-vessel disease; group 3, patients with 2-vessel disease; and group 4, patients with

Table 1 Demographic and clinical features

Characteristics	No. (%)
No. of patients	989
Male/female	627/362
Age [range]	63.4±10.5 [32-91]
Body mass index	25.8±3.4
Hypertension	673 (68.0)
Hyperlipidemia	547 (55.3)
Diabetes mellitus	410 (41.5)
Current smoking	224 (22.6)
Hyperhomocysteinemia	314 (31.7)
Previous MI	174 (17.6)
Previous stroke	194 (19.6)
Prior PCI	274 (27.7)
Prior CABG	24 (2.4)
Chronic renal insufficiency	48 (4.9)
Stable angina pectoris	326 (33.0)
Unstable angina pectoris	663 (67.0)
Left main trunk involved	137 (13.9)
0-vessel disease	136 (13.8)
1-vessel disease	191 (19.3)
2-vessel disease	246 (24.9)
3-vessel disease	416 (42.1)

3-vessel disease or left main trunk disease with right coronary artery disease.

Definition of CAS

CAS was investigated by carotid duplex ultrasound scanning using a commercially available machine (SSA-660A, Toshiba) with a 10-MHz linear array transducer. The sonography technician was experienced and blinded to clinical and coronary angiographic data. The sites of the extracranial measurements included the common carotid artery, bifurcation and internal carotid artery. The intima-media thickness, lumen diameter and the diameter of atherosclerotic plaque were also measured. The carotid stenosis was evaluated by the maximum percentage of diameter reduction recorded by B-mode ultrasound, by peak systolic velocity (PSV) and by peak diastolic velocity per Doppler. The maximum stenosis was defined as the greatest stenosis observed in the common carotid artery, bifurcation and internal carotid artery either on the

right or left. Patients were classified into the following five categories: normal (carotid arteries with no signs of atherosclerotic lesion, no plaque and normal intima-media thickness); mild CAS (stenosis diameter <50% and PSV <125 cm/s); moderate CAS (stenosis diameter 50% to 70% and PSV between 125 and 230 cm/s); severe CAS (stenosis diameter >70% and PSV >230 cm/s); and total occlusion (PSV of 0). We defined cases of moderate CAS, severe CAS and total occlusion to be significant CAS.

Statistical analysis

Continuous variables are presented as the mean ± SD. A two-sided unpaired *t*-test was performed for continuous variables, and the chi-square test or Fisher's exact test was used to analyze discrete variables. Spearman correlation was used to evaluate the relationship between CAS severity and CAD extent. Multivariate stepwise logistic regression analysis was applied to detect independent predictors of significant CAS. Data analysis was performed using SPSS version 22 (SPSS Inc., Chicago, IL, USA). A *P* value of <0.05 was considered statistically significant.

Results

The final study population consisted of 989 consecutive patients (627 men; mean age 63.4±10.5 years, range 32 to 91 years), and the demographic and clinical features of the patient cohort are presented in *Table 1*.

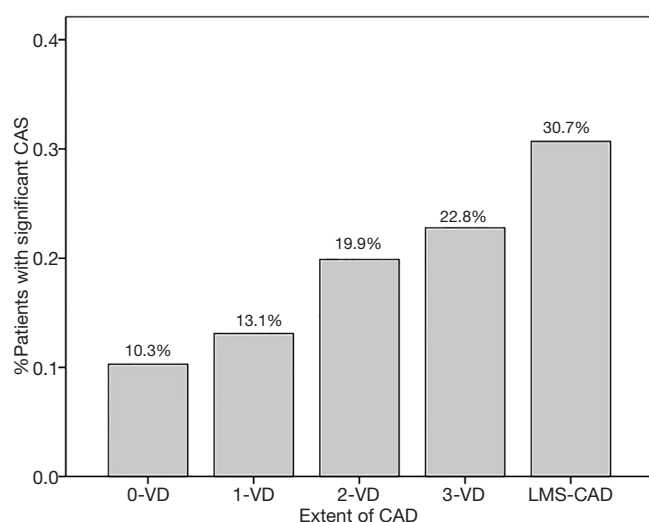
In the entire study population, CAD was present in 853 patients (86.2%) of whom 191 patients (19.3%) had 1-vessel disease, 246 patients (24.9%) had 2-vessel disease and 416 patients (42.1%) had 3-vessel disease. Left main trunk stenosis was present in 137 patients (13.9%). In carotid ultrasonography, 267 patients (27%) had patent carotid arteries without any evidence of atherosclerosis. The prevalence of mild, moderate, and severe stenosis as well as that of total occlusion of the carotid artery was 54.5%, 13%, 4.7% and 0.8%, respectively. Significant CAS (>50% stenosis diameter and total occlusion) was present in 10.3%, 13.1%, 19.9%, 22.8% and 30.7% of patients with 0-vessel, 1-vessel, 2-vessel, 3-vessel and left main trunk involved CAD, respectively (*Table 2*). There was a stepwise increase in the number of patients with significant CAS among patients with increasing severity of CAD (*Figure 1*). The severity of CAS was weakly correlated (*r*=0.194, *P*<0.001) with the extent of CAD.

The incidence of significant CAS was higher in patients

Table 2 Incidence of CAS severity by degree of CAD severity

CAD	CAS			
	Normal	Mild	Moderate	Severe and total occlusion
0-vessel	53 (39.0)	69 (50.7)	11 (8.1)	3 (2.2)
1-vessel	71 (37.2)	95 (49.7)	18 (9.4)	7 (3.7)
2-vessel	64 (26.0)	133 (54.1)	40 (16.3)	9 (3.7)
3-vessel	79 (19.0)	242 (58.2)	60 (14.4)	35 (8.4)
Left main trunk involvement	24 (17.5)	71 (51.8)	29 (21.2)	13 (9.5)

CAS, carotid artery stenosis; CAD, coronary artery disease.

**Figure 1** Distribution of significant CAS according to the extent of CAD. CAS, carotid artery stenosis; CAD, coronary artery disease.

with left main trunk involvement than in the study population as a whole (30.7% vs. 18.5%, $P < 0.001$).

A forward stepwise logistic regression was applied to identify factors that were associated with CAS. The results of this analysis are presented in *Table 3*. The independent predictors of severe CAS and total carotid artery occlusion were increased age, male sex, hypertension, diabetes mellitus, hyperhomocysteinemia, a previous history of stroke and 3-vessel CAD.

Discussion

Our principle finding was that the prevalence of CAS was not rare in China compared with that in western countries, and the presence of CAS was weakly correlated with the extent of CAD. Furthermore, age, male sex, hypertension,

diabetes mellitus, hyperhomocysteinemia, a previous history of stroke, and 3-vessel CAD were independently related to the presence of severe CAS and total carotid artery occlusion.

The different prevalence rates of CAS between western and Asian countries have been reported in many studies (4,6,8,17). A magnetic resonance angiography study (4) in Chinese stroke patients showed that extracranial CAS was less frequent in Chinese patients than in patients from western countries (14% compared with 30% to 60% in western patients), whereas intracranial lesions were more common (46.6%). In the 1990s, Shi (18) reported that the incidence of clinically significant extracranial CAS was 3% in Chinese elderly patients without CAD. The incidence of extracranial CAS has increased in the past few decades in Asian countries. In 2005, Tanimoto *et al.* (19) reported that the incidence of CAS was 7% in patients without CAD in a Japanese population. Our study showed that CAS was present in 10.3% of patients without CAD. The reported prevalence of CAS in western countries has ranged from 2% to 18% among the patients studied (15). Thus, the prevalence of CAS in our cohort was comparable with those reported in western populations, which may be due to lifestyle changes in China that favor western habits. Another possible explanation for the increased prevalence of CAS in China may be improved diagnostic techniques and screening frequencies compared with those of western countries.

Atherosclerosis can affect both the coronary artery and the carotid artery. Concurrent CAS and CAD are frequently detected in clinical practice (20). Autopsy studies (21) and clinical studies (15) have demonstrated a strong correlation between the extent of CAD and CAS. Ciccone (22) reported that the left ventricular mass index (LVMI) and the severity of CAD were positively related to the carotid intima media thickness in an Italian patient population. However, the

Table 3 Multivariate correlates of significant CAS

Variables	Mild CAS		Moderate CAS		Severe CAS or total occlusion	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Age	1.051 (1.032–1.069)	<0.001	1.105 (1.076–1.134)	<0.001	1.083 (1.044–1.122)	<0.001
BMI	1.033 (0.984–1.084)	0.192	1.017 (0.946–1.092)	0.651	0.956 (0.865–1.058)	0.387
Male	1.030 (0.711–1.493)	0.875	1.674 (0.970–2.888)	0.064	2.321 (1.033–5.218)	0.042
Hypertension	1.413 (1.007–1.981)	0.045	2.148 (1.253–3.683)	0.005	3.711 (1.557–8.846)	0.003
Hyperlipidemia	1.528 (1.108–2.107)	0.010	1.184 (0.740–1.893)	0.481	1.687 (0.843–3.179)	0.146
Diabetes mellitus	1.171 (0.841–1.632)	0.349	1.510 (0.934–2.441)	0.092	2.436 (1.255–4.729)	0.009
Post-stroke	1.365 (0.867–2.150)	0.180	1.424 (0.780–2.597)	0.250	3.074 (1.491–6.336)	0.002
Post-MI	1.339 (0.822–2.180)	0.242	1.184 (0.610–2.298)	0.617	1.137 (0.441–2.935)	0.790
CKD	2.880 (0.842–9.850)	0.092	1.323 (0.302–5.797)	0.711	2.293 (0.500–10.516)	0.286
Hyperhomocysteinemia	1.540 (1.047–2.266)	0.280	2.778 (1.665–4.637)	<0.001	5.445 (2.734–10.843)	<0.001
Previous PCI or CABG	1.893 (1.258–2.849)	0.002	2.836 (1.639–4.906)	<0.001	1.298 (0.583–2.890)	0.523
Left main trunk involved	1.149 (0.662–1.995)	0.621	2.131 (1.171–4.240)	0.031	1.742 (0.416–4.235)	0.221
Normal or nonobstructive CAD	1.00 (reference)	–	1.00 (reference)	–	1.00 (reference)	–
1-vessel CAD	1.195 (0.717–1.992)	0.494	1.477 (0.599–3.643)	0.397	2.243 (0.514–9.778)	0.282
2-vessel CAD	1.507 (0.908–2.499)	0.113	2.620 (1.142–6.012)	0.023	1.992 (0.472–8.403)	0.348
3-vessel CAD	2.393 (1.459–3.923)	0.010	3.264 (1.432–7.438)	0.005	5.811 (1.526–22.125)	0.010
Current smoker	1.141 (0.759–1.715)	0.526	1.157 (0.640–2.193)	0.629	1.594 (0.753–3.375)	0.223

CAS, carotid artery stenosis; OR, odds ratio; CI, confidence interval; CAD, coronary artery disease.

prevalence of CAS in Chinese patients with angina pectoris has not been well evaluated. In our study, the prevalence of significant CAS was 18.5% in patients with angina pectoris, and the severity of CAS was weakly correlated with the extent of CAD.

It has been reported (23) that soft carotid plaque with large necrotic core may be predictive of increased risk for neurological events, and heavily calcified plaque may be indicative of a high risk of coronary events. The presence of CAS in patients with CAD is associated with apparently higher perioperative stroke if the patient requires heart surgery (24,25). During coronary revascularization, neurological complication is the leading cause of mortality and disability (25,26). Thus, to decrease the neurological complication rate, Ascher *et al.* (27) indicated that carotid screening is recommended for patients undergoing open heart surgery who are over 60-year-old or less than 60-year-old but have risk factors for CAS.

It has been reported that carotid screening may be cost-effective in patients for whom the prevalence of severe CAS exceeds 4.5% (27). Age and sex may influence the detection of early markers of atherosclerosis (28).

CAS screening seems insufficient in China because the prevalence of CAS was assumed to be low in these patients. In our study population, the prevalence of severe CAS reached 5.5% and increased age, male sex, hypertension, diabetes mellitus, hyperhomocysteinemia, a previous history of stroke and 3-vessel CAD were identified as predictors of concomitant CAS. Therefore, we recommend that screening for CAS should be carried out in Chinese patients with angina pectoris, especially those with the risk factors mentioned above.

There may be limitations to our study. First, this is a retrospective study, and all limitations inherent in any retrospective study may also exist here. Second, the enrolled patients were referred for coronary angiography because of angina pectoris. Thus, our findings are relevant only to this particular group of patients and may not be applicable to the general population. Third, compared with selective intra-arterial digital subtraction angiography, color duplex sonography has an overall sensitivity of 91% to 95% and a specificity of 86% to 97% (16), and therefore, false positive or negative results may be present in the CAS screening data reported here.

Conclusions

In conclusion, the prevalence of CAS was not rare in China compared with western countries, and the presence of CAS was weakly correlated with the extent of CAD. CAS screening is recommended in Chinese patients with CAD, especially in those with one or more CAS-associated risk factors.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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