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# Clinical Study

# Pattern of cerebrovascular atherosclerotic stenosis in older Chinese patients with stroke

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#### ABSTRACT

The clinical pattern and angiographic distribution of cerebral atherosclerosis varies among different ethnic groups. This study was designed to identify the clinical background for intracranial and extracranial atherosclerotic stenosis in older eastern Chinese patients using digital subtraction angiography. We retrospectively reviewed the data collected from the Nanjing Stroke Registry Program, from January 2004 to March 2011. The analysis focused on the intracranial or extracranial location of stenosis in the anterior and posterior circulations. In total, records of 1041 patients were included in the study. Of these patients, 19.88% had intracranial carotid stenosis, 18.73% had stenosis in the extracranial vessels, and 33.33% had concurrent stenoses. A total of 2002 stenotic sites were detected in 749 patients. Among those patients with stenosis, a single stenosis was found in 170 (16.33%) and multiple stenoses were found in 579 (55.62%). The prevalence of intracranial stenosis in the single-stenosis group was 54.12%, while in the multiple-stenosis group it was 47.87% (p=0.127). A higher incidence of severe stenosis (70-99% blockage) and occlusion was found in the intracranial vessels than in the extracranial vessels (p=0.018). Older Chinese patients with atherosclerotic stenosis tend to have more intracranial stenoses.

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## 1. Introduction

In Asians, stroke incidence and mortality rates of stroke are higher than those in caucasians, even though the rate of coronary heart disease is lower in Asians. Intracranial and extracranial atherosclerosis is a common cause of ischemic stroke. In the past decade, racial and ethnic differences in the distribution of cervicocerebral atherosclerosis have been studied intensively. Atherosclerosis of the intracranial and extracranial cerebrovascular system is common in Asians. Methods used to diagnose cerebrovascular atherosclerosis include transcranial Doppler ultrasound (TCD), transcranial color-coded sonography, magnetic resonance angiography (MRA), computed tomographic angiography (CTA) and digital subtraction angiography (DSA). TCD and MRA have negative predictive values of 72-86% and positive predictive values of 36-66%. CTA has a negative predictive value of 84%. 1,2 DSA is considered to be the gold standard for confirmation of stenosis. Our unpublished data indicated that the prevalence of intracranial stenosis is greater in the Chinese population (especially in the Nanjing, Jiangsu area) than in Western populations. To test this hypothesis, we retrospectively reviewed the data from the Nanjing

Stroke Registry Program (NSRP). The characteristics and distribution of stenosis in patients with intracranial atherosclerotic disease (ICAD) and extracranial atherosclerotic disease (ECAD), and with disease located in the anterior and posterior circulation were investigated.

# 2. Patients and methods

# 2.1. Evaluation of atherosclerotic clinical backgrounds

Data were obtained from the NSRP, from January 2004 to March 2011. The NSRP was founded in July 2012 and is the first hospital-based stroke registry program conducted in mainland China. It is an ongoing, prospective observational project aiming at consecutively assembling demographic, clinical, neuroimaging and laboratory data of the registered patient.<sup>3</sup> All the patients were Han Chinese, without any known ancestors of other ethnic origins. 1041 patients (age >60 years) with symptoms or signs of an ischemic stroke related to atherosclerosis were included in this study. The male:female ratio was 749:292.

For all patients, we recorded clinical background data, such as age, gender, serum cholesterol level, serum glycated hemoglobin A1c (HbA1c) level, hypertension, smoking habits and alcohol consumption, and cerebrovascular infarct (CI) type. A diabetes mellitus (DM) diagnosis was based on a plasma glucose level

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≥11.1 mmol/L or a fasting plasma glucose level ≥7.0 mmol/L. Hypertension was defined as blood pressure needing to be controlled with antihypertensive agents, systolic blood pressure ≥140 mmHg, or diastolic blood pressure ≥90 mmHg on admission. Subjects were classified as smokers if they smoked at least a cigarette per day in the year before the study, and alcohol drinkers were defined as those who consumed at least 22 mg/day. Patients were excluded if they had moyamoya disease; vasculitis; stenosis or occlusion caused by trauma or dissection; subarachnoid hemorrhage, as depicted on CT scans; heart disease such as valvular defects of the heart or atrial fibrillation, which could lead to embolism; incomplete angiograms; multiple sclerosis; or mitochondrial encephalomyelopathy, lactic acidosis, and stroke-like episodes syndrome (MELAS).

## 2.2. Digital subtraction angiography protocols

All patients were examined with a dynaCT angiography machine (Siemens Axiom Artis dTA, Siemens Healthcare, Munich, Germany) under local anesthesia. All images were evaluated by two experienced technicians who were blind to the clinical histories of the patients. In case of disagreement, a joint reading was performed to reach a consensus decision. In order to improve reproducibility of the results, extracranial vessel analysis was performed on a segmental basis, according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria, 4 and intracranial vessel analysis was performed according to the WASID trial criteria.<sup>5</sup> When a stenosis was present, it was categorized as mild (1-29% blockage), moderate (30-69% blockage), severe (70-99% blockage), or occlusion (100% blockage) depending on the degree of stenosis. Stenoses in the arteries of the anterior circulation were assigned to the common carotid artery (CCA), carotid bifurcation (CB), internal carotid arteries (ICA), anterior communicating artery (ACoA), anterior cerebral artery (ACA) or middle cerebral artery (MCA), and those of the posterior circulation were assigned to the vertebral artery (VA), basilar artery (BA), posterior cerebral artery (PCA) or posterior inferior cerebellar artery (PICA). In this study, we divided the intra- and extracranial vessels at the point where the internal carotid artery passes the inner dura, as Gorelick et al. previously suggested. We also defined the border in the posterior circulation as the point where the vertebral artery passes through the dura at the level of the foramen magnum. <sup>7</sup>

#### 2.3. Statistical analysis

Continuous variables with normal distribution were expressed as the mean  $\pm$  standard deviation. Categorical variables were presented as numbers and percentages. All statistical analyses were performed using the Statistical Package for the Social Sciences version 16.0 (SPSS Inc, Chicago, IL, USA). Mean values were compared using one-way analysis of variance (ANOVA). Unadjusted statistical analyses were performed using the chi-squared test (or Fisher's exact probability, if necessary) for dichotomous results. Two-sided p values <0.05 were considered significantly different. Multiple comparisons of significant differences within groups were analyzed using the chi-squared test with a modified  $\alpha$  value using the Bonferroni method.

#### 3. Results

The basic characteristics of the 1041 patients are summarized in Table 1. Among these, 749 patients had stenosis in their extracranial and/or intracranial arteries. In our cohort, there were more male patients (749) than female patients (292). The main common risk factors were hypertension (690, 66.28%) and diabetes mellitus (290, 27.86%). There were 207 (19.88%) patients with intracranial carotid stenoses only, 195 (18.73%) with stenosis in the extracranial vessels only, and 347 (33.33%) with stenoses both in intracranial and extracranial vessels. Of 1041 older Chinese stroke patients, 71.95% had vessel stenosis confirmed by DSA, and diabetes was a

**Table 1**Basic characteristics of the 1041 older Chinese stroke patients with cerebrovascular atherosclerotic stenoses

Characteristics	No stenosis ( <i>n</i> = 292)	Intracranial stenosis only $(n = 207)$	Extracranial stenosis only $(n = 195)$	Concurrent stenosis ( $n = 347$ )	р
Age, years ± SD	68.03 ± 5.35	68.04 ± 5.59	69.20 ± 5.99	69.26 ± 5.51	0.0013
Male sex, n (%)	209(71.58)	143(69.08)	139(71.28)	258(74.35)	0.8422
Risk factors, n (%	5)				
CHD	21(7.19)	11(5.31)	15(7.69)	25(7.20)	0.7814
Diabetes	69(23.63)	64(30.92)	50(25.64)	107(30.83)	0.1282
Hypertension	189(64.73)	129(63.32)	127(65.13)	245(70.61)	0.1879
Ever smoker	71(24.32)	51(24.64)	38 (19.49)	86(24.78)	0.5150
Drinking	34(11.64)	26(12.56)	23(11.79)	55(15.85)	0.3650
Hyperlipidemia	58(19.86)	51(24.64)	48(24.62)	103(29.68)	0.0420
Prior TIA	14(4.79)	8(3.86)	6(3.08)	16(4.61)	0.7888

CHD = coronary heart disease, TIA = transient ischemic attack, SD = standard deviation.

 Table 2

 Comparison of basic characteristics of patients with single compared to multiple cerebrovascular atherosclerotic stenoses

Characteristics	Patients with a single stenosis ( $n = 170$ )	Patients with multiple stenoses ( $n = 579$ )	Patients with no stenosis ( $n = 292$ )	p
Age, years ± SD	67.92 ± 5.55	69.20 ± 5.69	68.03 ± 5.35	0.0029
Male sex, n (%)	115 (67.65)	425 (73.40)	209 (71.58)	0.3354
Risk factors, n (%)				
CHD	6 (3.53)	45 (7.77)	21 (7.19)	0.1555
Diabetes	39 (22.94)	182 (31.43)	69 (23.63)	0.0156
Hypertension	102 (60.00)	399 (68.91)	189 (64.73)	0.0777
Ever smoker	36 (21.18)	139 (24.01)	71 (24.32)	0.7087
Drinking	20 (11.76)	84 (14.51)	34 (11.64)	0.4111
Hyperlipidemia	42 (24.71)	160 (27.63)	58 (19.86)	0.0436
Prior transient ischemic attack	2 (1.17)	28 (4.83)	14 (4.79)	0.0968

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