

Intracranial Atherosclerosis in Chinese Young Adult Stroke Patients

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Background: Until now, intracranial atherosclerosis has been less well studied because of its rarity. We sought to investigate the prevalence and risk factors of intracranial atherosclerosis in Chinese young adult stroke patients. *Methods:* We retrospectively reviewed the medical records of consecutive young adult patients with first-ever ischemic stroke at our institution from May 2007 to May 2012. The demographic features and risk factors of intracranial large-artery atherosclerotic (LAA) stroke were analyzed by comparison with other stroke subtypes. *Results:* One hundred ninety-seven patients (age 39 ± 9 years, 127 male) were recruited. There were 81 (41%) patients with LAA stroke, including 68 (35%) strokes because of intracranial stenosis. Male gender ($P = .001$), dyslipidemia ($P = .015$), smoking ($P < .001$), hypertension ($P < .001$), hyperhomocysteinemia ($P = .003$), and family history of stroke ($P = .024$) were more common in patients with intracranial LAA stroke than with non-LAA stroke. A high percentage of patients with intracranial LAA stroke had multiple modifiable risk factors (ie, at least 2 of dyslipidemia, hypertension, diabetes mellitus, smoking, and hyperhomocysteinemia), much more than the patients with non-LAA stroke (82% versus 42%, $P < .001$). Simultaneous multiple modifiable risk factor exposure was the strongest “risk factor” for intracranial LAA stroke, with the adjusted odds ratio of 4.99. *Conclusions:* Intracranial atherosclerosis is highly prevalent in Chinese young stroke patients. Our results suggest that simultaneous exposure to multiple risk factors may contribute to the early development of intracranial atherosclerosis. **Key Words:** Intracranial atherosclerosis—ischemic stroke—risk factors—stroke in young adults.

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Introduction

In recent years, the prevalence of hospitalizations of acute ischemic stroke has gradually increased in young adults.¹ Although stroke in youth had overall better

outcome than in the elderly, it may cause death and severe disability.² The main clinical challenge in the management of a young stroke patient is to identify the cause of the stroke.

A number of studies have reported the risk factors and etiology of stroke in young adult patients.³⁻⁸ The most common risk factors were traditional atherogenic factors, such as dyslipidemia, smoking, and hypertension. However, large-artery atherosclerotic (LAA) stroke, one of the main causes in older stroke patients, was uncommon.^{3,4,7,9} In an analysis of 1008 consecutive young patients in Helsinki, Putaala et al⁹ reported an 8% prevalence of large-artery atherosclerosis among young adult stroke patients. Comparatively, cardioembolism (20%) and arterial dissection (15%) were reported to be the most frequent causes.⁹

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LAA stroke can be caused by extracranial and intracranial atherosclerosis. In Caucasian stroke patients, the prevalence of extracranial atherosclerosis is much higher than intracranial atherosclerosis.¹⁰ In Asians, Hispanics, and Africans, however, intracranial atherosclerosis is more common.^{10,11} Given Caucasians accounted for the highest proportion in previous studies on youth stroke, we hypothesize that the contribution of intracranial atherosclerosis to stroke may have been underestimated. Until now, little has been known about intracranial premature atherosclerosis because of its rarity. In this study, we investigated the prevalence and risk factors of intracranial LAA stroke in young adult Chinese patients, a population vulnerable to intracranial atherosclerosis.^{12,13}

Patients and Methods

This was a single-center retrospective study, approved by the local ethic authority. We reviewed the medical records of consecutive young adult patients with ischemic stroke in Peking Union Medical College Hospital from May 2007 to May 2012. Patients were enrolled if they had a first-ever ischemic stroke on admission and were aged 15-49 years at stroke onset. Patients were excluded if they had pure clinical transient ischemic attacks, stroke attributable to head trauma, ischemic lesions attributable to the complications of subarachnoid hemorrhage, angiography procedure, or major surgery.⁹

We identified 212 potential candidates. Fifteen patients were excluded: 1 with pure transient ischemic attacks, 3 with subarachnoid hemorrhage, 2 with postoperation stroke, 1 with brain trauma, 1 with central nervous system leukemia, 2 with undefined diagnosis after discharge, and 5 with insufficient or missing medical records. A total of 197 patients were finally included for analysis. All patients underwent a wide range of blood tests, a chest x-ray, electrocardiogram, and cranial computed tomography (CT), and/or magnetic resonance imaging (MRI) (Supplement Table 1). Cerebrovascular imaging was performed in 179 (91%) patients, including angiography (digital subtraction, CT angiography, or magnetic resonance angiography) in 159 (81%) patients, and ultrasound examination (carotid duplex and transcranial Doppler) in 160 (81%) patients. A transthoracic echocardiogram was performed in 131 (67%) patients. To confirm potential cardiac arrhythmia, 24-hour Holter was performed in 11 patients. Twenty-two (11.2%) patients received agitated saline contrast transcranial Doppler test for screening cardiac right-to-left shunts, and 3 of them also underwent transesophageal echocardiography. On the basis of these evaluations, stroke subtypes were classified according to the Trial of Org 10172 in Acute Stroke Treatment criteria: (1) small-vessel occlusion; (2) large-artery atherosclerosis; (3) cardioembolism; (4) stroke of other determined etiology; and (5) stroke of undetermined etiology.¹⁴ The diag-

nostic criterion applied for the definition of stroke risk factors, including non-modifiable (age, gender, and family history), well-documented and modifiable (dyslipidemia, smoking, hypertension, diabetes, etc.), and less well-documented and potentially modifiable (migraine, oral contraceptive, etc.) factors,⁹ are shown in Supplement Table 1.

In young adult patients with intracranial artery stenosis, nonatherosclerosis cause is a concern. The technique of high-resolution MRI (HR-MRI) has been recently developed, which is helpful for identifying the etiology of intracranial stenosis.^{15,16} In this study, in addition to other diagnostic test results, HR-MRI findings were available for 19 patients (13 male, age 37 ± 6 years) with clinically diagnosed intracranial LAA stenosis. To testify the accuracy of the clinical diagnosis, vessel wall images of these patients were reviewed. The existence of a plaque was confirmed if eccentric wall thickening was identified.¹⁵⁻¹⁷

The Pearson chi-square test was used to compare categorical variables across groups, and the Student *t* test was used to compare means of quantitative data. Logistic regression analysis was used to evaluate possible confounding effects such as age, gender, and common risk factors (including dyslipidemia, smoking, diabetes mellitus, hypertension, hyperhomocysteinemia, and family history of stroke) on stroke subtypes. All statistical analysis used SPSS Statistics 17.0 for Windows (SPSS, Inc., Chicago, IL). Two-sided values of $P < .05$ were considered statistically significant.

Results

There were 127 men and 70 women (age 39 ± 9 years). For patients aged less than 30 years, the ratio of males to females was nearly 1:1, whereas for those aged 30-49 years, males tremendously outnumbered females (2.1:1). The mean time between the admission and onset of stroke was 18 ± 40 days, and the average National Institutes of Health Stroke Scale score for all patients was 4 ± 5 . Frequencies of risk factors are presented in Supplement Table 2. The most common risk factor was dyslipidemia (57%), followed by cigarette smoking (45%) and hypertension (41%).

Large-artery atherosclerosis (81 patients, 41%) was the most frequent identified cause of stroke. In these patients, 11 were diagnosed by angiography (magnetic resonance angiography, CT angiography, or digital subtraction angiography), 67 by both angiography and ultrasound examinations, and 3 by only ultrasound examinations. Males more likely have this subtype than females (50% versus 24%, $P < .001$). There were 68 patients with intracranial stenosis, 5 with extracranial stenosis, and 8 with tandem extracranial and intracranial stenosis.

Cardioembolic stroke was diagnosed in 18 (9.1%) patients, of whom 6 were thought to have a stroke associated with cardiac right-to-left shunts. A total of 31 patients had

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