

Perspective

# Intracranial artery stenosis: Current status of evaluation and treatment in China

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## Abstract

Intracranial artery stenosis (ICAS), a common cause of ischemic stroke, is a growing cause of concern in China. Recently, many epidemiological, etiological, pathophysiological, therapy, and diagnostic imaging studies have focused on ICAS, and guidelines and consensus on the diagnosis and treatment of ICAS have been published and updated by domestic experts. Such work is pivotal to our enhanced comprehension, diagnosis, and treatment of ICAS. In this review, we summarize the latest progress in the evaluation and treatment of ICAS in China.

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**Keywords:** Intracranial artery stenosis; Evaluation; Treatment

## Introduction

Stroke burden in China has increased over the last 30 years. Stroke is the leading cause of death in China. The incidence of ischemic stroke is estimated to be 69.6%, based on the Chinese intracranial atherosclerosis (CICAS) study,<sup>1</sup> and intracranial artery stenosis (ICAS) is estimated to account for 46.6% of all ischemic stroke cases.<sup>2</sup> Therefore, due attention should be paid to the problem.

Recently, many epidemiological, etiological, pathophysiological, therapy, and diagnostic imaging studies have focused on ICAS, and guidelines and consensus on the diagnosis and treatment of ICAS have been published or updated by Chinese experts.<sup>3–10</sup> Such work is fundamental to enhancing our understanding of ICAS, as well as improving the disease evaluation and treatment.

## Epidemiology

In China, ICAS is estimated to account for 33–50% of all stroke cases, and more than 50% of transient ischemic attacks (TIA), contrary to Caucasian patients who are prone to extracranial carotid stenosis.<sup>11–14</sup> Both angiographic and autopsy studies suggest that intracranial artery lesions demonstrate higher severity

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than extracranial artery lesions in Chinese patients, similar to Japanese patients but different from Caucasian patients.<sup>15,16</sup> It remains unclear why the occurrence and severity of extracranial and intracranial lesions differ, and requires further investigation. Recently, a large, prospective, multicenter, hospital-based, cohort study, the CICAS study, indicated that the prevalence of ICAS was 46.6% in Chinese patients, consistent with previous research by Hong Kong-based academics.<sup>2,12,13</sup> According to the CICAS study, patients with ICAS experience more severe stroke at admission, have longer hospital stays, and higher risk of recurrent stroke.<sup>2</sup> The recurrent stroke rate was only 5% in the CICAS study patients with 70–99% stenosis, and lower than previous trials (23% in the WASID study and 12.2% in the medical arm of the SAMMPRIS study).<sup>2,17–19</sup> However, the occurrence rate was exceptionally high among patients with severe stenosis and multiple risk factors.<sup>2,17–19</sup> Moreover, the CICAS study reported both a geographic and gender variation in the distribution of ICAS in China; higher rates were recorded in northern China and women aged >63 years.<sup>20</sup> Northern patients were more likely, than the southern patients, to have both intracranial and extracranial lesions, multiple intracranial atheroscleroses, and occlusive lesions, which may be explained by the higher number of risk factors observed in northern patients, such as diabetes mellitus, hyperlipidemia, family history of stroke, smoking, heavy drinking, hyperhomocysteinemia, and overweight.<sup>20</sup>

Contrary to symptomatic ICAS, asymptomatic ICAS is often ignored. Wong et al studied 590 asymptomatic villagers in central rural China, and found 41 individuals (6.9%) with ICAS.<sup>21</sup> However, when the investigators applied transcranial Doppler (TCD) to screen 3057 patients with no history of stroke or TIA but at least one vascular risk factor, including hypertension, diabetes, or hyperlipidemia, they found that 385 patients (12.6%) had middle cerebral artery (MCA) stenosis.<sup>22</sup> These data suggest that asymptomatic ICAS is not uncommon, especially in patients with vascular risk factors. Moreover, ICAS was most common in young Chinese patients with ischemic stroke, likely due to high exposure to hypertension, smoking, dyslipidemia, and diabetes.<sup>23,24</sup> Thus, more attention and further studies are required for these special subgroups.

## Etiology

Many studies indicate that vascular risk factors, including hypertension, diabetes mellitus, hyperlipidemia, family history of stroke and heart disorders,

smoking, heavy drinking, hyperhomocysteinemia, and overweight, are associated with ICAS.<sup>2,16,17,20–25</sup> However, there are some inconsistencies in the data. Unlike the CICAS study, most studies are limited by, for example, small sample sizes and single-center, retrospective designs. Moreover, several studies have attempted to explain the different distributions of extracranial and intracranial stenosis between Asians and Caucasians, with inconsistent conclusions.<sup>15,26–28</sup> Thus, well-designed epidemiological studies are required to provide more valuable clinical information for enhanced patient management.

## Evaluation of ICAS

The most widely used tools used for the diagnosis and assessment of ICAS include TCD, computed tomography angiography (CTA), magnetic resonance angiography (MRA), and digital subtraction angiography (DSA). However, whilst these techniques are able to measure arterial lumen stenosis, they cannot provide sufficient information on the characteristics of artery walls or plaques, or the status of collateral vessels and fractional flow, all of which play vital roles in predicting the risk of subsequent ischemic stroke.<sup>29</sup> More recent studies focus on atherosclerotic plaque morphology and hemodynamic assessment, and many new techniques, including high-resolution magnetic resonance imaging (HR-MRI), molecular imaging, intravascular ultrasound, and optical coherence tomography, have been developed.<sup>29</sup>

### HR-MRI

HR-MRI is a non-invasive and effective tool to depict the vessel wall and plaque components. Xu et al demonstrated that HR-MRI can clearly display the wall structure of MCA, compensate for the limitations of MRA, and help to detect atherosclerotic lesions not visible via MRA.<sup>30</sup> By comparing the vessel wall properties of symptomatic and asymptomatic MCA stenosis using HR-MRI, investigators have found that symptomatic MCA lesions have a larger wall area, greater remodeling ratio, higher prevalence of expansive remodeling, and lower prevalence of constrictive remodeling, suggesting a possible correlation between the MCA wall features and clinical manifestations.<sup>31</sup> Moreover, MCA plaques tend to be located in the ventral and inferior walls, opposing the penetrating arteries orifices, whilst symptomatic MCA stenosis is characterized by superior rather than inferior plaques, especially in patients with penetrating infarction.<sup>32</sup>

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