

# Association Between Stroke Severity and 5-Year Mortality in Ischemic Stroke Patients with High-Grade Stenosis of Internal Carotid Artery

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**Background:** The clinical presentations and outcomes of patients with high-grade stenosis of internal carotid artery (ICA) are highly variable. We investigate the influence of different stroke severity on outcomes of ischemic stroke patients with high-grade stenosis of ipsilateral ICA. **Methods:** 372 acute first-ever ischemic stroke patients with high-grade stenosis (70%-99%) or occlusion of ipsilateral ICA were enrolled and followed up for 5 years. Stroke severities of the enrolled patients were grouped according to the Oxfordshire Community Stroke Project classification system as total anterior circulation infarcts (TACI) or non-TACI. Demographic features, vascular risk factors, comorbidities, and outcomes were compared between the 2 groups. **Results:** A total of 71 patients (19.1%) were presented with TACI. Of laboratory data, the values of white blood cell count and high-sensitivity C-reactive protein were significantly higher in patients with TACI ( $P = .008$  and  $P = .003$ , respectively). Of clinical course, the occurrence of initial impaired conscious, stroke-in-evolution, pneumonia, gastrointestinal bleeding, and urinary tract infection were significantly higher in patients with TACI. The prevalence of dependent functional status was higher in patients with TACI. Multivariate Cox regression revealed that TACI is a significant predictor of 5-year all-cause mortality in first-ever ischemic stroke patients with high-grade stenosis of ipsilateral ICA (HR [hazard ratio] = 3.66, 95% confidence interval = 2.23-6.00,  $P < .001$ ). **Conclusions:** TACI is associated with increased risk of 5-year mortality in ischemic stroke patients with high-grade stenosis of ipsilateral ICA. Intensive medical treatment for stroke prevention in patients with severe carotid artery stenosis is warranted.

**Key Words:** Internal carotid artery—Stenosis—Stroke outcome—Mortality—First-ever ischemic stroke—Carotid artery stenosis

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## Introduction

Atherosclerotic carotid artery stenosis is a well-recognized cause of cerebral ischemia. The prevalence of carotid artery stenosis ranges from 4% to 11%, and it increases with age and varies by race.<sup>1,2</sup> The clinical

features of carotid artery stenosis is highly variable, it ranges from completely asymptomatic to symptomatic, including minor stroke, severe disabling stroke, or even death.<sup>3</sup>

Patients with more severe luminal stenosis of carotid artery are at higher risk of stroke since more severe

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stenosis is associated with distal hemodynamic compromise.<sup>4-6</sup> Previous study also suggested that patients with greater than or equal to 50% stenosis of an intracranial internal carotid artery (ICA) have higher rate of 5-year mortality.<sup>7</sup> However, whether there are some factors that could predict the severity of ischemic stroke in patients with high-grade stenosis of ICA is still unknown. In addition, whether different stroke severity is associated with the long-term outcome of ischemic stroke patients with high-grade ICA stenosis remains unclear. To the best of our knowledge, the factors to predict stroke with higher severity in patient with high-grade ICA stenosis have not been investigated in previous studies.

As a result, the aims of this study were to explore: (1) the differences between ischemic stroke patients with high-grade ICA stenosis whom presented as total anterior circulation infarcts (TACI; severe stroke) and non-TACI (less severe stroke), which were grouped by the Oxfordshire Community Stroke Project classification system. (2) Whether TACI is an independent predictor of 5-year mortality in ischemic stroke patients with high-grade ICA stenosis.

## Materials and Methods

### *Study Patients*

All patients were selected from the Stroke Unit of the Department of Neurology at Kee-Lung Chang Gung Memorial Hospital from January 2007 to April 2012. The acute ischemic stroke was diagnosed according to the World Health Organization criteria, which was further confirmed by brain computed tomography or magnetic resonance imaging scan.<sup>8</sup> Only patients with first-ever ischemic stroke were enrolled, and individuals with either previous cerebral infarction, cerebral hemorrhage, or stroke of uncertain causes were excluded. Bilateral carotid duplex scanning was performed on admission within 7 days after acute stroke onset for evaluate the degree of ICA stenosis.

We recruited patients whose acute stroke symptoms that could be correlated with the territory of the unilateral ICA and the degree of ICA stenosis ranges from 70% to 99% or occlusion. Patients were excluded if they had (1) acute infarcts beyond the territory of the ipsilateral ICA (eg, stroke over posterior circulation or contralateral ICA); (2) received revascularization treatments. The clinical subtypes of ischemic stroke were rated according to the classification of the OSCP classification by 2 neurologists who independently looked at the history, conducted a physical examination, and assessed the patient's symptoms. The subtypes were partial anterior circulation infarcts, TACI, and lacunar infarcts.<sup>9</sup> Posterior circulation infarcts were excluded. Patients were divided into 2 groups according to the presentations of acute stroke were TACI or non-TACI (include partial anterior circulation infarcts and lacunar infarcts). This clinical study followed the

Declaration of Helsinki and was approved by the Medical Ethics Committee of Chang Gung Memorial Hospital, Taipei, Taiwan (IRB 201800689B0).

### *Clinical Assessments*

Comorbidities were identified after an in-depth review of the medical records, inclusive of personal history, physical examination, progress notes, discharge summaries, and consultations. Risk factors for cerebrovascular disease included hypertension, diabetes mellitus, hyperlipidemia, smoking, atrial fibrillation, valvular heart disease, coronary artery disease, and peripheral arterial diseases were recorded. Hypertension was defined as known hypertension diagnosed by a clinician, or systolic blood pressure >160 mm Hg and/or diastolic blood pressure >95 mm Hg on 2 different occasions, with the second measurement taken more than 5 days after the stroke.<sup>10,11</sup> Diabetes mellitus (DM) was diagnosed in patients with previously treated DM or in patients with fasting plasma glucose  $\geq 126$  mg/dL, a 2-hour value in the oral glucose tolerance test or a random plasma glucose concentration  $\geq 200$  mg/dL, in the presence of symptoms. Hyperlipidemia was defined as a fasting blood cholesterol level was  $\geq 200$  mg/dL and/or a triglyceride level was  $\geq 200$  mg/dL. Atrial fibrillation (AF) included paroxysmal AF and persistent AF identified by electrocardiography and/or 24-hour electrocardiography monitoring during admission. Cigarette smoking was defined as a current smoker or a smoker with cessation less than 5 years ago. Systematic assessments, including complete blood cell count, blood chemistry studies, lipid level, glycosylated hemoglobin, coagulation testing, urinalysis, chest X-ray, 12-lead electrocardiography, transcranial Doppler, trans-thoracic echocardiography, and head computed tomographic scan, were performed on all of the patients within 1 week after acute stroke onset. The scores of National Institutes of Health Stroke Scale, modified Rankin Scale,<sup>12</sup> and Barthel index were recorded at admission and upon discharge.

### *Cerebrovascular Assessments*

The high-grade stenosis of ICA (70%-99% stenosis or occlusion) was diagnosed by doppler study within 7 days after acute stroke onset. Brain magnetic resonance angiography was done when doppler study revealed 70% or greater stenosis over ICA within 10 days after acute stroke onset to confirm the ultrasound findings and to evaluate the infarction site.

### *Follow-Up*

Patients were followed-up for 5 years after initial assessment. The follow-up was conducted with clinical examinations at the first and the third month after first stroke and then every 3 months. New major medical

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