Symptomatic Steno-occlusion of Cerebral Arteries and Subsequent Ischemic Events in Patients with Acute Ischemic Stroke

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Background: We aimed to assess the impact of symptomatic steno-occlusion (SYSO) of cerebral arteries and its characteristics on subsequent ischemic event (SIE) in patients with acute ischemic stroke. *Methods:* Using a prospective stroke registry database, we identified consecutive patients with ischemic stroke who were hospitalized within 48 hours of symptom onset. SYSO denoted significant stenosis or occlusion of major cerebral arteries with ischemic lesions at the corresponding arterial territories and was characterized by its location and severity. Primary outcome was SIE that was defined as ischemic progression or recurrence within 1 year. *Results:* In total, 1546 patients (age, 67.4 ± 13.0 years; median National Institutes of Health Stroke Scale score, 4) were enrolled in this study. The cumulative risk of SIE was 14.5% at 7 days, 14.9% at 14 days, 15.5% at 90 days, and 16.9% at 1 year. Patients with SYSO had significantly higher SIE rates compared with those without SYSO

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(23.0% versus 11.6%). Of the characteristics of SYSO, the location, not the severity, was significantly associated with SIE ($P < .001$ and $P = .186$, respectively). Multiple (adjusted hazard ratio, 5.85; 95% confidence interval, 1.81-18.85), intracranial internal carotid artery (ICA) (3.54; 1.21-8.21), and extracranial ICA SYSO (2.88; 1.01-8.21) raised the risk of SIE. *Conclusions:* Subsequent cerebral ischemic events (progression or recurrence) after an acute ischemic stroke occur mostly within several days of stroke onset and is associated with the location, but not the severity, of symptomatic steno-occlusion of cerebral arteries. **Key Words:** Ischemia—stroke—stenosis—occlusion—prognosis.

Introduction

Detection of symptomatic steno-occlusion (SYSO) of cerebral arteries is essential for appropriate therapeutic decisions in patients with ischemic stroke.[1] At the hyperacute stage of ischemic stroke, a major treatment target is to achieve reperfusion of cerebral arteries with SYSO, to prevent irreversible damage to the penumbra.[2] With newly introduced reperfusion modalities, good outcomes can be achieved for more patients.[3,4]

The question of whether clinicians should intervene in cases of SYSO beyond the hyperacute stage remains unresolved because of uncertainties regarding the efficacy of, and indications for, late-stage intervention. Clinical trials for carotid endarterectomy have clearly demonstrated beneficial effects of late-stage intervention in preventing recurrence in patients with symptomatic stenosis.[5] However, stenting for symptomatic stenosis of major intracranial cerebral arteries has not been shown to be superior to medical treatment because of, at least partly, high periprocedural risk.[6,7] If patients with a high risk for subsequent stroke could be identified, then the high periprocedural risk of the stenting procedure might be outweighed by the potential benefits in such patients.

Factors contributing to stroke recurrence are diverse, but location and severity of SYSO should be considered, and elapsed time after stroke onset is also regarded as an important factor.[8-11] Overall, about 50% of 1-year recurrences occur within the first 90 days of stroke onset, and the first few weeks after onset are considered as the period of maximum risk.[9] In this context, assessment of risk according to SYSO characteristics with consideration of elapsed time from stroke onset might be essential for predicting recurrence accurately; however, such comprehensive studies have not yet been conducted.[8,10]

The present study aimed to observe subsequent cerebral ischemic events during the first year after stroke and assess the effects of SYSO and its characteristics on these events. Because ischemic progression is another important cause of neurologic deterioration and it is difficult to differentiate it from recurrence at the acute stage,[11,12] we compositely captured ischemic progression and recurrence and combined them as a single outcome variable called "subsequent ischemic event (SIE)."

Methods

Standard Protocol Approval and Patient Consent

This study was approved by the local Institutional Review Board with a waiver of informed consent because of its retrospective nature and minimal risk to participants.

Subjects and Data Collection

Between July 2007 and December 2010, a consecutive series of patients who were admitted at the Seoul National University Bundang Hospital because of acute ischemic stroke within 48 hours of symptom onset were identified using a prospective stroke registry database.[13] We excluded patients who did not undergo angiographic evaluation at presentation.

For enrolled study subjects, we collected data on demographics, stroke characteristics, vascular risk factors, diagnostic workup, and in-hospital management directly from the registry database or by reviewing the electronic medical records.[14] Investigated vascular risk factors were hypertension, diabetes mellitus, dyslipidemia, smoking, cardiac sources of cerebral embolism including atrial fibrillation,[15] and history of stroke. Stroke characteristics included baseline stroke severity assessed by the National Institutes of Health Stroke Scale (NIHSS) score, elapsed time from stroke onset to arrival, and stroke subtype (Trial of Org 10172 in Acute Stroke Treatment classification[16]). Regarding in-hospital management, revascularization treatment and its modalities and antithrombotic medications at discharge were considered.

Assessments of SYSO

Experienced stroke neurologists (N.K. and J.K.) assessed the existence of SYSO and its characteristics. SYSO was defined as a significant stenosis or occlusion of major cerebral arteries with relevant ischemic lesions in their corresponding arterial territories, and SYSO