Recurrent Stroke, Myocardial Infarction, and Major Vascular Events during the First Year after Acute Ischemic Stroke: The Multicenter Prospective Observational Study about Recurrence and Its Determinants after Acute Ischemic Stroke I

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Background: Patients with acute ischemic stroke (AIS) are at high risk of subsequent vascular events. The aim of this study was to estimate rates of recurrent stroke, myocardial infarction (MI), and major vascular events during the first year after AIS in Korea. *Methods:* Through a multicenter stroke registry in Korea, 12,227 consecutive cases of AIS were identified between November 2010 and May 2013 and were followed up for recurrent stroke, MI, and major vascular events up to 1 year after stroke. *Results:* Cumulative 30-day, 90-day and 1-year rates were 2.7%, 3.9%, and 5.7% for recurrent stroke; .1%, .3%, and .5% for MI; and 8.1%, 10.6%, and 13.7% for major vascular events, indicating that the early period is at high risk of recurrent stroke and major vascular events. The risk of recurrent stroke

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was substantially higher than the risk of MI: 13.0 times at 90 days and 11.4 times at 1 year. Compared to those with small-vessel occlusion (SVO), those with ischemic stroke subtypes other than SVO had a higher risk of recurrent stroke as well as major vascular events. Other common independent predictors for recurrent stroke and major vascular events were diabetes and prior stroke history. *Conclusions:* During the first year after AIS, one in 18 had recurrent stroke and one in 7 major vascular events. More than two thirds of recurrent stroke and three quarters of major vascular events developed within 90 days in a Korean cohort of stroke patients. Better prevention strategies are required for high-risk patients during this high-risk period. **Key Words:** Ischemic stroke—myocardial infarction—recurrence—stroke subtype—vascular death—vascular event.

Stroke survivors are at high risk of subsequent vascular events including recurrent stroke, myocardial infarction (MI), and other vascular events. With the decline in stroke case-fatality rates,[1,2] subsequent vascular events after acute stroke would account for a greater share of the future stroke-related socioeconomic burden. To implement effective prevention strategies in a healthcare system, the risks of individual vascular events following acute ischemic stroke (AIS) and their predictors need to be elucidated.

Given the variation in the risk factor profiles, stroke subtypes, and incidence of individual vascular diseases,[3] the risks of individual subsequent vascular events in stroke survivors would vary across diverse ethnicities and geographic regions. However, most data were driven from Western populations.[4-9] Several Asian studies have reported the rates of recurrent stroke in patients with ischemic stroke, but have limitations of small sample size, single-center study, or selective enrollment of the study population in a clinical trial. In addition, the risks of vascular events other than recurrent stroke have not been well studied in Asian populations.[10-14]

To estimate the 1-year risk of recurrent stroke, MI, and major vascular events after AIS in Korea, we conducted the Multicenter Prospective Observational Study about Recurrence and Its Determinants after Acute Ischemic Stroke I. In addition, we explored the predictors of each vascular event.

Methods

Case Ascertainment and Clinical Data Collection

This was a prospective multicenter cohort study of 12 university hospitals or regional stroke centers participating in the Clinical Research Center for Stroke—5th division registry in South Korea. The detailed information on the Clinical Research Center for Stroke—5th division registry was published earlier.[15] We consecutively enrolled patients with AIS admitted within 7 days of onset from November 2010 to May 2013. For all patients, the diagnosis of AIS was confirmed by neuroimaging studies, and a cerebral ischemic event that lasted for less than 24 hours but had a relevant acute ischemic lesion on diffusion-weighted magnetic resonance imaging (DWI) was also included as an AIS. Data on demographics, stroke characteristics, vascular risk factors, etiological workup, and in-hospital management were prospectively collected in a web-based register with standardized protocols. Stroke subtypes were classified into 5 categories using a diagnostic algorithm modified from the Trial of Org 10172 in Acute Stroke Treatment classification system: (1) large-artery atherosclerosis (LAA), (2) small-vessel occlusion (SVO), (3) cardioembolism (CE), (4) stroke of other determined etiology (OD), and (5) stroke of undetermined etiology (UD).[16,17] The study was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2000. The study was approved by the institutional review boards of all the participating hospitals. Informed consent was obtained from subjects or their legally authorized representatives.

Outcome Event Assessment

Using a predefined protocol, we prospectively captured data on recurrent stroke, MI, and major vascular events during the first year after the index AIS by the review of medical records or telephone interview. Recurrent stroke included fatal and nonfatal ischemic and hemorrhagic strokes. Within 21 days of the index stroke, recurrent stroke was defined as a new neurological symptom/sign or any neurological worsening after a period of neurological stability or improvement lasting for 24 hours or more[7] and attributable to new discrete lesions on follow-up computed tomography or DWI. This event should not be attributable to edema, mass effect, brain shift syndrome, or hemorrhagic transformation of the index ischemic stroke and had to continue for 24 hours or more.[7] After 21 days from the index stroke, recurrent stroke was defined as suddenly developed focal neurological deficits attributable to occlusion or rupture of cerebral vessels and lasting for 24 hours or more. MI was defined as at least 2 of the following: symptoms of myocardial ischemia, enzyme changes indicative of MI, and electrocardiogram changes suggesting new ischemia.[4] MI included