Characteristics of the Drip-and-Ship Paradigm for Patients with Acute Ischemic Stroke in South Korea

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Background: Data on the drip-and-ship paradigm in Korea are limited. The present study aimed to evaluate the use of the drip-and-ship paradigm and the time delays and outcomes associated with the paradigm in Korea. *Methods:* We used data from the Clinical Research Center for Stroke-5 registry between January 2011 and March 2014. Among patients treated with tissue-type plasminogen activator (tPA), the use of the drip-and-ship paradigm was evaluated, and time delays and functional outcomes at 3 months were compared between patients treated with the paradigm and those treated directly at visits. *Results:* Among 1843 patients who met the eligibility criteria, 244 patients (13.2%) were treated with the drip-and-ship paradigm. Subsequent endovascular recanalization therapy was used in 509 patients (27.6%). The median time from symptom onset to groin puncture was greater in patients treated with the paradigm than in those treated directly at visits (305 versus 200 minutes, $P < .001$). In multivariate analysis, the risks of unfavorable functional outcomes and symptomatic intracranial hemorrhage were higher in

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patients treated with the paradigm than in those directly treated at visits (odds ratio [OR] 2.15; 95% confidence interval [CI], 1.50-3.08; $P < .001$ and OR 1.78; 95% CI, 1.02-3.12; $P = .041$, respectively). *Conclusions:* In Korea, the drip-and-ship paradigm was used in less than 15% of all patients treated with tPA. The use of the paradigm might cause an increase in the onset-to-groin puncture time. Additionally, clinical outcomes might be worse in patients treated with the paradigm than in those treated directly at visits. **Key Words:** Acute ischemic stroke—endovascular treatment—drip-and-ship—outcome assessment.

Introduction

In acute stroke patients, intravenous recombinant tissue-type plasminogen activator (tPA) administered within 4.5 hours after symptom onset has been shown to be effective for improving clinical outcomes.[1-4] Although the proportion of patients treated with tPA has increased in Korea, less than 10% of patients with acute ischemic stroke receive this treatment at present.[5,6] The drip-and-ship paradigm is one way to increase the use of tPA treatment among acute stroke patients at the regional level. In this paradigm, patients with acute ischemic stroke receive intravenous tPA at an outside hospital and are then transferred to comprehensive stroke centers (CSCs) for further management, such as post-thrombolysis neurointensive monitoring, endovascular recanalization therapy (ERT), and neurosurgical procedures.[7-9]

A previous study showed that regions with a high proportion of patients treated using the drip-and-ship paradigm had high rates of overall thrombolytic utilization.[10] The use of this paradigm has steadily increased in the United States, and it has been reported that 25% of patients are treated with the paradigm.[11] Recently, ERT using advanced devices has emerged as a new effective method for treating patients with acute ischemic stroke, in addition to intravenous tPA.[12-16] The use of the drip-and-ship paradigm could facilitate the use of ERT in patients with acute ischemic stroke because ERT is available at a limited number of centers.

However, the drip-and-ship paradigm may require additional evaluations, such as blood pressure monitoring and neurological assessment, and may result in complications, such as life-threatening hemorrhage during transport after infusion of tPA. A recent U.S. study suggested that in-hospital mortality and symptomatic intracranial bleeding might modestly increase with the use of the drip-and-ship paradigm.[11]

Most previous studies on the drip-and-ship paradigm were small-size studies or were based on a single regional center[17-20] and assessed patient outcomes only at discharge.[10,11,18,21] Additionally, most studies were from the United States, and only few studies have been reported from outside the United States.[17,22] The use of the drip-and-ship paradigm and the clinical characteristics and outcomes of patients treated with the paradigm vary according to the regional stroke care system.[10,11,17-19]

Data on the drip-and-ship paradigm in Korea are limited. The present study aimed to evaluate the use of the drip-and-ship paradigm and the time delays and outcomes associated with the paradigm in Korea.

Methods

Study Subjects

The present study used data from the Clinical Research Center for Stroke-5 (CRCS-5) registry, which is a web-based prospective, multicenter, nationwide registry of patients with acute ischemic stroke admitted to 14 academic centers in Korea as of July 2015 (http://www.stroke-crc.or.kr). The registry was designed to describe stroke statistics and quality of care in Korea and to aid in the implementation of quality indicators. The present study was approved by the institutional review boards of all participating centers. Detailed information on the structure, coverage, and case characteristics has been published previously.[23,24]

The present study analyzed the CRCS-5 registry between January 2011 and March 2014 to identify study subjects. The inclusion criteria were (1) 18 years of age or older, (2) evidence of acute ischemic stroke on neuroimaging, (3) arrival at the hospital within 6 hours from symptom onset, and (4) treatment with intravenous tPA either at the hospital or using the drip-and-ship paradigm. The exclusion criteria were (1) a prestroke modified Rankin Scale (mRS) score higher than 1, (2) unavailability of an mRS score at 3 months after the index stroke, and (3) treatment with tPA beyond 6 hours from symptom onset. The present study was approved by the institutional review board of Jeju National University Hospital.

Data Collection

We obtained the following information from the registry or by review of medical records for items that were missing or insufficient in the registry: (1) age, sex, prestroke mRS score, clear versus unclear onset, and onset-to-arrival time; (2) laboratory results (systolic and diastolic blood pressure at admission, and levels of glucose at