# Outcomes after Tissue Plasminogen Activator Administration under the Drip and Ship Paradigm May Differ According to the Regional Stroke Care System

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The drip and ship paradigm for stroke patients enhances the rate of using intravenous tissue plasminogen activator (IVT) in community hospitals. The safety and outcomes of patients treated with IVT for acute ischemic stroke (AIS) under the drip and ship paradigm were compared with patients directly treated at a comprehensive stroke center in the Busan metropolitan area of Korea. This was a retrospective study of patients with AIS treated with IVT between January 2009 and January 2012. Information on patients' baseline characteristics, neuroimaging, symptomatic intracerebral hemorrhage (sICH), and outcome 90 days after using IVT was obtained from our stroke registry. We surveyed stroke neurologists regarding their pattern of post-thrombolysis care. During the observation periods, we selected 317 patients using IVT. Among these, 239 patients received IVT at our stroke center, and 78 were treated at 21 community hospitals under the drip and ship paradigm. Initial neurologic deficits and the size of ischemic lesions on magnetic resonance imaging were much more severe in patients treated with IVT under the drip and ship paradigm compared with patients treated at our comprehensive stroke center. The prevalence of a poor outcome (modified Rankin Scale score 3-6) 90 days after IVT was much higher in patients treated with the drip and ship paradigm than in those treated at our comprehensive stroke center. Regarding the occurrence of sICH, there was no significant difference between the 2 groups. The clinical characteristics and outcomes after using IVT under the drip and ship paradigm may differ greatly among stroke care systems. **Key Words:** Thrombolysis—stroke—drip and ship—outcomes.


## Introduction

Intravenous tissue plasminogen activator (IVT) is the standard treatment for patients with acute ischemic stroke (AIS) within the first 4.5 hours after symptom onset.[1,2] In Korea, only 6% of patients with AIS who were eligible received IVT in 2010.[3] Several factors are involved in the lower than expected therapeutic rate in Korea. First, many hospitals lack a stroke specialist who can aid in the timely treatment with IVT. Second, many emergency physicians are concerned about administering tissue plasminogen activator (t-PA) in a setting without a stroke team or appropriate neurologic and neurosurgical resources equipped to handle the complications of t-PA. To overcome these problems, when treatment with IVT is recommended, patients are initially treated at the community hospital and then transferred to a facility with Neurology and Neurosurgery staff available for continuation of care. This method of administering t-PA to stroke patients has

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been termed "drip and ship."[4] Several previous reports have shown that the drip and ship approach has similar safety and outcome compared with direct treatment in a stroke center.[5,6] However, this notion may differ greatly according to the stroke care system in each country. For example, in a stroke care system with common protocols for IVT in which patients are treated at an outlying hospital using a telestroke consultation with a stroke neurologist from a regional stroke center, there may not be any differences in stroke severity and outcome in patients treated outside the hospital compared with those treated in a stroke center. However, in our metropolitan area, a neurologist at each hospital determines patient eligibility for IVT, and selected cases are then transferred to the regional stroke center because of a lack of facilities for further intensive care.

Therefore, we hypothesized that patients with more severe neurologic deficits may be transferred to a regional comprehensive stroke center under the drip and ship paradigm in the Busan metropolitan area in Korea. Under this hypothesis, we compared the prevalence of symptomatic intracerebral hemorrhages (sICHs) and the 90-day outcome after thrombolysis between our comprehensive stroke center and community hospitals using the drip and ship paradigm.

## *Subjects and Methods*

Our hospital is a tertiary teaching hospital located in the Busan metropolitan area (size 765.64 $km^2$, population: ~4 million). Our stroke center is a regional comprehensive stroke center supported by the Korean government in the Busan metropolitan area. When the comprehensive stroke center opened, an 8-bed stroke care unit was installed for the care of acute stroke patients. This unit contains a telemetry system for the monitoring of blood pressure, pulse, respiration, and oxygenation. A multidisciplinary group developed stroke care pathways to guide the evaluation and treatment of each stroke subtype. Stroke treatment was generally administered according to a well-organized team approach, for example, intravenous thrombolysis, endovascular treatment, hemicraniectomy, and carotid endarterectomy.

Our strategy for using IVT is based on magnetic resonance imaging (MRI) in principle. Our door to image time is maintained within 20 minutes. In 2009, we implemented a hotline system in conjunction with the Korean Emergency Medical Information System (119 and 1339) for prehospital notification. The primary role of the Korean Emergency Medical Information System is to connect a patient needing an emergency or operation in a community hospital with the appropriate available hospital.

This was a retrospective observational study that was approved by our institutional review board. For the purpose of this study, we identified AIS patients with intravenous thrombolytic treatment between January 2009 and December 2012 from our stroke registry. We excluded patients who were not evaluated by MRI in the emergency room or were transferred to our stroke center more than 8 hours after their stroke onset from other hospitals under the drip and ship paradigm.

### *Clinical Assessment and Outcome Measures*

Stroke severity at baseline, as measured by the National Institutes of Health Stroke Scale (NIHSS), was recorded. The primary end point was a poor outcome at 90 days (modified Rankin Scale [mRS] score $> 2$). Trained study nurses assessed the mRS at 90 days by telephone interview, with the patients or his or her next of kin or by hospital chart review. Outcome mRS values after 3 months were dichotomized into good outcome and poor outcome for independence (mRS score 0-2 versus 3-6). sICH was defined as intracerebral hemorrhage detected by computed tomography or MRI associated with a neurologic decline of 4 points or more in the NIHSS score.[2]

### *Measurement of Ischemic Size on MRI*

All included patients underwent MRI (1.5 T, Signa EchoSpeed Superconducting Imaging System; General Electric Medical Systems, Milwaukee, WI). Images included T1, axial fluid-attenuated inversion recovery, 3-dimensional time-of-flight magnetic resonance angiography, axial diffusion-weighted imaging (DWI), and axial perfusion-weighted imaging. DWI was performed using echo planar imaging techniques. The DWI lesion volume was determined by manually tracing the edge of the hyperintense signal on each slice of the trace DWI scans. The area of a region of interest was multiplied by the section thickness plus the intersection gap and then summed to give the lesion volume.

### *Survey for Protocols of Care and Transferring after Administering IVT*

We retrospectively surveyed stroke neurologists who have transferred patients to our stroke center about the care system after thrombolysis during the observation period as follows: Were more than 50% of patients treated at their center after administering IVT? What was the most important reason for transferring patients to our comprehensive stroke center after administering IVT?

### *Statistical Analysis*

The statistical significance of intergroup differences was assessed using the chi-square test for categorical variables. Continuous variables were expressed as the mean and standard deviation. *P* values less than .05 were considered statistically significant.