Poor Hypertension Control and Longer Transport Times Are Associated with Worse Outcome in Drip-and-Ship Stroke Patients

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Background: The "drip-and-ship" paradigm is an important treatment modality for acute ischemic stroke (AIS) patients who do not have immediate access to a comprehensive stroke center (CSC). Intravenous thrombolysis is initiated at a primary stroke center followed by expeditious transfer to a CSC. We sought to determine factors associated with poor outcomes in drip-and-ship AIS patients transferred to a CSC. *Methods:* This study is a retrospective analysis of 130 consecutive drip-and-ship patients transferred by ambulance to a single CSC between July 2012 and June 2014. Multiple patient and transport factors were analyzed. Transport blood pressure (BP) control was considered inadequate if the systolic BP was greater than 180 mmHg and/or diastolic BP was greater than 105 mmHg upon CSC arrival. Poor patient outcome was defined as discharge to hospice or expiry, a discharge modified Rankin Scale (mRS) score higher than 2, or symptomatic intracerebral hemorrhage (ICH). *Results:* There was a significant association between inadequate BP control upon CSC arrival and in-hospital mortality or discharge to hospice ($P < .0007$). Arrival BP was not associated with the risk of post-thrombolysis symptomatic ICH. Longer transport time was significantly associated with a poorer mRS score at discharge ($P < .0174$) and death ($P < .0351$). *Conclusions:* Post-thrombolysis BP guideline violations and longer transport times during drip-and-ship transfers were significantly associated with poor outcome. Guidelines for strict transport BP management and alternative modes of transfer for longer-distance transports may be warranted. **Key Words:** Ischemic stroke—drip and ship—endovascular therapy—thrombolysis—acute therapy.

Introduction

Stroke is a major health concern in the United States, affecting more than 795,000 people each year.[1] On average, every 4 minutes a person dies from a stroke, making it the fifth leading cause of death.[2] The current mainstay treatment for acute ischemic stroke (AIS) is the administration of intravenous recombinant tissue plasminogen activator (IV-rtPA) within a 3.0- to 4.5-hour window from the last known well time. IV-rtPA was first approved by the Food and Drug Administration in 1996 for the treatment of AIS.[3,4] However, IV-rtPA still has a low frequency of use due to the narrow time frame for administration and the concern for hemorrhagic complications. For patients with large-vessel occlusions, endovascular stroke therapy, especially with the newer stent retriever devices, has been shown in numerous, recent randomized controlled trials to improve patient outcome.[5-9] The technical

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complexity and equipment requirements of these procedures and the postoperative management of these patients necessitate their performance at comprehensive stroke centers (CSCs). In the drip-and-ship paradigm, IV-rtPA is initiated at a local community hospital or primary stroke center, and then the patient is rapidly transferred to a CSC, often while the recombinant tissue plasminogen activator is still infusing. Previous studies have explored drip-and-ship paradigm safety in smaller populations.[10] The purpose of the present study is to assess factors associated with poor outcome in a larger drip-and-ship population transported by ambulance within a major metropolitan area.

Materials and Methods

A retrospective observational study was performed, following institutional review board approval, on a consecutive series of AIS patients treated by the drip-and-ship paradigm and transported by ambulance to a single CSC within a large stroke care network in the New York metropolitan area between July 2012 and June 2014. All patients were treated within the standard 0- to 3-hour or extended 3.0- to 4.5-hour time window with intravenous thrombolysis (IVT) using eligibility criteria based on national guidelines.[11] The patients were received by the CSC from 16 referring hospitals varying in size and distance from the accepting facility. Interfacility distances ranged from 3 to 35 mi, and primary hospital sizes varied from 103 to 827 beds. All interfacility transports were conducted by the receiving health system's emergency medical service (EMS), ensuring consistent patient transfer protocols.

Data were gathered from the CSC's "Get With the Guidelines" database. Compiled data points included patient demographics and the presence of standard vascular risk factors, initial National Institutes of Health Stroke Scale (NIHSS) at the transferring facility, NIHSS score and blood pressure (BP) upon CSC arrival, transport duration, symptomatic intracerebral hemorrhage (ICH), discharge modified Rankin Scale (mRS) score, and discharge status.

The initial NIHSS score was used to determine the severity of the neurological deficit and was obtained in the documentation from the transferring facility. Patients whose initial NIHSS score was not available were excluded from the study. Patients with a systolic BP greater than 180 mmHg or a diastolic BP greater than 105 mmHg during transport or upon CSC arrival were considered to have a BP guideline violation. Transportation time between the referring and accepting facility was recorded using ambulance run sheets. The mRS score was determined using the vascular neurology attending progress notes, as well as notes from the rehabilitation team including occupational, speech, and physical therapists. Symptomatic ICH was defined as an ICH detected by CT or MRI associated with a neurological decline of 4 points or higher in the NIHSS score as documented in the vascular neurology attending notes. Poor patient outcome was defined as discharge to hospice or in-hospital death, a discharge mRS score higher than 2, and symptomatic ICH.

For statistical analysis, the association between each outcome and each categorical variable was examined using the chi-square test, or the Fisher exact test, as appropriate. The association between each outcome and each continuous variable was determined using logistic regression. A P value less than .05 was considered statistically significant. The statistical analysis was performed using SAS Version 9.3 (SAS Institute Inc., Cary, NC) software.

Results

A total of 123 drip-and-ship patients were confirmed to have an ischemic stroke (7 stroke mimics were excluded from the analysis). BP at CSC arrival was available for 120 patients, defining the final cohort. The mean age of the cohort was 62.7 years (range: 24-100 years). Mean outside hospital NIHSS score was 12.5 (range: 0-32). The mean CSC admission NIHSS score was 11.0 (range: 0-28). The mean BP upon CSC arrival was 143.3/77.8 mmHg (systolic range: 90-200 mmHg/diastolic range: 44-112 mmHg). The mean mRS score at discharge was 2.8. Transport times were available for 83 of 123 confirmed drip-and-ship AIS patients. The mean transport time to the CSC was 21.6 minutes (range: 4-51 minutes).

There was a significant association between BP upon CSC arrival and discharge status (Fisher exact test, $P < .0007$). Seven out of 15 (46.7%) patients with BP guideline violation on CSC arrival expired or were discharged to hospice, compared to 9 of 105 (8.6%) patients without BP guideline violations. Symptomatic ICH frequency was not significantly different between groups, being observed in 1 of 15 (6.7%) patients with BP violations compared to 10 of 105 (9.5%) patients without BP parameter violations. Eleven of 15 (73.3%) patients with BP violations had a discharge mRS score higher than 2, compared to 54 of 103 (52.4%) patients without BP parameter violation (not significant).

Transport time was also significantly associated with discharge status ($P < .0351$). Subjects with longer transport times were more likely to die or be discharged to hospice (odds ratio [OR]: 1.07, 95% confidence interval [CI]: 1.01-1.15). For every 1-minute increase in transport time, the odds of dying or discharge to hospice were increased by 7%. For every 5-minute increase in transport time, the odds were increased by 42% (OR for 5 minutes: 1.42, 95% CI: 1.03-1.97). There was also a significant association between the mRS score at discharge and transport time ($P < .0174$). Patients with longer transport times were more likely to have mRS scores of 3-6 (OR: 1.06, 95% CI: 1.01-1.11). For every 1-minute increase in transport time, the odds of having an mRS score of 3-6 increased by 6%. For every 5-minute increase in transport time, the odds