Drip-and-Ship Thrombolytic Therapy for Acute Ischemic Stroke

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Background: Neuroendovascular therapy is a common treatment for patients with acute ischemic stroke of the anterior circulation who fail to respond to recombinant tissue plasminogen activator. However, although most hospitals can provide recombinant tissue plasminogen activator therapy, many cannot perform neuroendovascular therapy. Thus, use of a drip-and-ship treatment-liaison system allowing recombinant tissue plasminogen activator-treated patients to be transferred to facilities offering neuroendovascular therapy is important. *Methods:* We retrospectively analyzed 16 drip-and-ship patients transferred to our hospital for additional neuroendovascular therapy after they received intravenous recombinant tissue plasminogen activator at prior hospitals between June 2009 and March 2017. *Results:* The mean patient age was 68 ± 17 years. Ten patients had cardiogenic embolism and 6 had atherothrombosis. Additional neuroendovascular therapy was performed in 14 patients. Median National Institute of Health Stroke Scale and diffusion-weighted image-Alberta Stroke Program Early Computed Tomography Scores before recombinant tissue plasminogen activator therapy were 14 and 8, respectively. Occluded or stenotic lesions of the cerebral arteries were detected by magnetic resonance angiography in the internal carotid artery (n = 4), middle cerebral artery (n = 10), and basilar artery (n = 3) (1 patient had tandem lesions). Mean intervals from onset-to-recombinant tissue plasminogen activator, recombinant tissue plasminogen activator-to-our hospital (door), door-to-puncture, and onset-to-recanalization were 166, 65, 32, and 334 minutes, respectively. No patients showed symptomatic intracranial hemorrhage. *Conclusions:* Magnetic resonance imaging/angiography performed in previous hospitals allows initiation of reperfusion therapy immediately after transfer. Thus, drip-and-ship plus neuroendovascular therapy is a safe and useful system for treatment of patients with acute infarcts. **Key Words:** Acute stroke—recombinant tissue plasminogen activator—endovascular therapy—drip and ship.

Introduction

Intravenous recombinant tissue-type plasminogen activator (rt-PA) therapy is the primary treatment option for patients having an acute ischemic stroke and is now an established standard therapy in terms of safety and efficacy.[1] However, a low recanalization rate was reported for intravenous rt-PA therapy when used in patients with major cerebral artery occlusion, particularly occlusion of the internal carotid artery and the proximal segment of the middle cerebral artery (MCA).[2] The efficacy of additional neuroendovascular treatment (NET) has been reported for cases failing to respond to rt-PA therapy, and

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use of NET is of high interest in Japan.[3] However, although most hospitals can provide intravenous rt-PA therapy, many are unable to provide NET. Thus, a cooperative treatment system, termed "Drip, ship, and retrieve (DS & R)" was proposed.[4] This system involves transporting patients that do not respond to intravenous rt-PA therapy to another facility capable of providing NET, and is widely used in Western countries.[5] Although DS & R has also been introduced in Japan, there are few reports of its efficacy.[6] Herein, we performed a retrospective clinical study of patients referred to our hospital for NET after having received intravenous rt-PA therapy at other hospitals.

Methods

Study Population and Design

This study involved 16 DS patients referred to our hospital to receive additional NET after having received intravenous rt-PA therapy at other facilities between June 2009 and March 2017. Patients were transferred to our hospital from 5 facilities. The following clinical data of the patients were retrospectively analyzed: age, gender, cerebral infarction type, history of ischemic stroke, risk factors for cerebral infarction, severity of stroke, diagnostic imaging findings, time course (onset-to-needle [rt-PA], O2N; needle-to-door [our hospital], N2D; door-to-puncture [D2P]; onset-to-recanalization [O2R]), clinical outcomes, and symptomatic intracranial hemorrhage [sICH]). The severity of stroke was assessed based on the National Institute of Health Stroke Scale (NIHSS) scores before rt-PA treatment and before NET. Diagnostic imaging findings were evaluated based on the diffusion-weighted image (DWI)-Alberta Stroke Program Early Computed Tomography Score (ASPECTS)[7] before rt-PA treatment, major cerebral arterial lesions revealed by magnetic resonance angiography (MRA), and ASPECTS before NET.[8] Clinical outcomes were evaluated using the modified Rankin Scale (mRS) at 3 months after NET treatment. Hypertension was judged to be present if the patient had a systolic blood pressure 140 mmHg or greater or a diastolic pressure 90 mmHg or greater at the time of discharge, or had been taking antihypertensive medication before the onset of cerebral infarction. Diabetes mellitus was judged to be present if the patient had a hemoglobin A1c Test 6.5% or greater (National Glycohemoglobin Standardization Program) or 6.1% or greater (Japan Diabetes Society), or had been taking oral hypoglycemic agents or receiving insulin therapy before the onset of cerebral infarction. Heart failure was judged to be present if the patient had any symptom of the New York Heart Association class II or higher upon admission or had a history of heart failure.

The flow of management of DS patients until NET at our hospital is shown in Figure 1. The Institutional Review Board of Saitama Medical University International Medical Center approved this study protocol (No. 17-016).

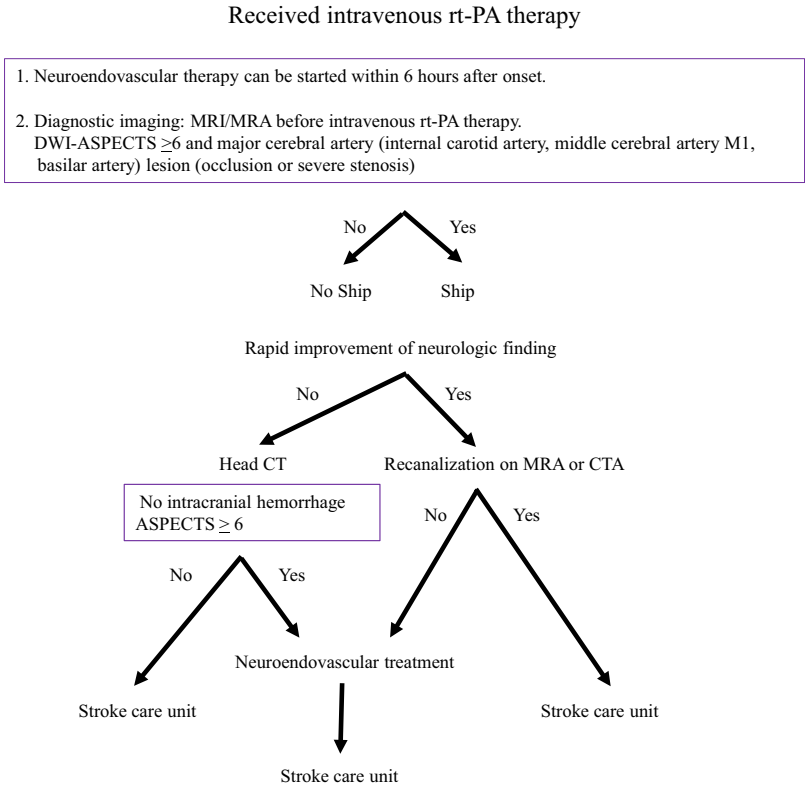

Figure 1. *Flow of management of DS patients until neuroendovascular treatment (NET) at our hospital. In our department, neuroendovascular therapy is started within 6 hours after stroke onset. Magnetic resonance angiography (MRA)-diffusion-weighted image (DWI) mismatch-positive patients who had a DWI-Alberta Stroke Program Early Computed Tomography Score (ASPECTS) ≥6 and occlusion or severe stenosis of the major artery (internal carotid artery, middle cerebral artery M1, basilar artery) found by magnetic resonance imaging/angiography (MRI/MRA) before intravenous tissue-type plasminogen activator therapy are transported to our hospital. Before patient arrival, steps to prepare for NET are performed with close communication between physicians involved in NET, nurses, and radiation technologists. If the symptoms of the patient improve rapidly after arrival, head MRA or computed tomography (CT) angiography is performed to check for recanalization. If rapid improvement is not seen, head CT scan is performed upon arrival to check for intracranial hemorrhage and to evaluate the infarction size, and NET is then performed.*