

A Fall in Systolic Blood Pressure 24 Hours after Thrombolysis for Acute Ischemic Stroke Is Associated with Early Neurological Recovery

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Background: Outcomes are worse in patients who underwent thrombolysis for acute ischemic stroke (AIS) with persistent hypertension. The objective of this study is to investigate whether fall in systolic blood pressure (SBP) has any relationship with neurological outcome 24 hours after thrombolysis, after adjusting for potentially confounding factors. *Methods:* Retrospective analysis of a single-center database of consecutive thrombolysis cases for AIS. Multivariate regression analysis was used to explore the relationship between fall in SBP and reduction in National Institutes of Health Stroke Scale (NIHSS) score 24 hours after thrombolysis. Other potentially confounding predictor variables used in the model were SBP on thrombolysis, blood glucose level on thrombolysis, NIHSS score on thrombolysis, administration of antihypertensive medications, and the time to thrombolysis after symptom onset. *Results:* A fall in SBP 24 hours after thrombolysis is independently associated with greater improvement in NIHSS score 24 hours after thrombolysis (coefficient .051, 95% confidence interval .023-.078, $P < .001$). Thus, a reduction of 10 mmHg in SBP after 24 hours is associated with a .51 point reduction in the NIHSS score. *Conclusions:* Restoration of SBP toward normal limits after thrombolysis for AIS is associated with greater early neurological improvement. **Key Words:** Blood pressure—cerebral infarction—hypertension—ischemic stroke—rtPA—thrombolysis—tPA.

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Introduction

Appropriate administration of intravenous thrombolysis with recombinant tissue plasminogen activator (tPA) improves outcomes after acute ischemic stroke (AIS).¹⁻³ The benefit of tPA is attributable to lysis of the occlusive thrombus and reperfusion of ischemic but not yet infarcted brain tissue.⁴ Recanalization of occluded vessels is correlated with early clinical improvement and this benefit is sustained at 3 months.^{5,6} Its benefit is strongly time dependent due to reperfusion of tissue before infarction and is only clinically effective when given within 4.5-5.0 hours following symptom onset.^{5,7}

The relationship between blood pressure and clinical outcome in patients treated with tPA is complex. The majority of patients will demonstrate increased blood pressure in response to AIS.⁸ High admission systolic blood pressure (SBP) is associated with poorer outcome in patients who are not treated with tPA.^{9,10}

Elevated blood pressure before or after thrombolysis is associated with an increased risk of intracranial hemorrhage.^{11,12} For this reason, the original National Institute of Neurological Disorders and Stroke (NINDS) trial used similar blood pressure eligibility and management algorithms to those in the early dose-finding trials which had low incidence of symptomatic intracranial hemorrhage (SICH).¹³ These criteria are now used in clinical practice.

Prethrombolysis elevated SBP is associated with improved leptomeningeal collateral circulation,⁴ which may be a physiological response to improve perfusion to the ischemic penumbra. However, 3-month outcomes were inversely associated with prethrombolysis SBP in the same study.⁴

In patients treated with intravenous tPA, favorable outcome was inversely associated with the maximum, mean, and variation in post-thrombolysis blood pressure over 24 hours.⁹ Ahmed et al¹⁴ showed that the association between post-thrombolysis SBP and mortality and independence at 3 months is U-shaped, with the most favorable outcome associated with SBP between 141 and 150 mmHg. However, the association of SBP with SICH being linear with lower SBP associated with lower risk of SICH.

Mattle et al¹⁵ showed that in patients treated with intra-arterial tPA, early reduction in SBP is associated with early recanalization. Furthermore, early recanalization was associated with improved outcome at 3 months. However, there was no association between the absolute blood pressure decline and outcome. Delgado-Mederos et al¹⁶ showed in patients treated with intravenous tPA that early recanalization was associated with a fall in SBP. Delgado-Mederos et al did not find any association between early recanalization and outcome for absolute values of blood pressure, but showed that early clinical improvement was associated with reduced blood pressure variability following tPA administration.

In the present study, we aimed to assess whether reduction in blood pressure 24 hours following intravenous administration of tPA is associated with improved early neurological recovery as assessed by early improvement in National Institutes of Health Stroke Scale (NIHSS), after adjusting for potentially confounding factors.

Methods

Population

All patients who were transferred to the Imperial College Healthcare NHS Trust (ICHNT, London, United Kingdom) hyperacute stroke unit and consequently underwent thrombolysis for presumed AIS between October 1, 2011, and June 30, 2015, inclusive, were included. Cases of thrombectomy, later confirmed nonstroke diagnoses (after review of imaging, including magnetic resonance imaging, where performed, and clinical presentation), and death within 24 hours were excluded from the present study.

Clinical Parameters

All patients undergoing thrombolysis for presumed AIS were initially assessed by a stroke physician, and underwent brain computed tomography to exclude hemorrhage or other pathology. The NIHSS score was completed on admission and 24 hours following administration of tPA. Blood pressure recordings were made on admission and following thrombolysis to monitor response. Patients with persistent elevation of blood pressure higher than 185/105 mmHg before thrombolysis were treated with intravenous labetalol to reduce blood pressure to below this level. Blood pressure elevations following thrombolysis were treated with both intravenous (labetalol) and oral antihypertensives (amlodipine) as clinically appropriate. Blood glucose level was recorded at initial assessment.

Statistical Analysis and Confounding Variables

Statistical analysis was performed using Stata 14 (StataCorp LP, College Station, TX). Summary statistics are offered as percentages, medians and interquartile ranges. Multivariate regression analysis was used to explore the relationship between fall in SBP over the 24 hours after thrombolysis (predictor variable) with reduction in NIHSS score 24 hours after thrombolysis (dependent variable).

Other potentially confounding predictor variables used in the model were SBP on thrombolysis, blood glucose level (millimole per liter) on thrombolysis, NIHSS score on thrombolysis (points), administration of antihypertensive medications (dichotomized as received antihypertensives or did not), and the time to thrombolysis after symptom onset (minutes). Age was not considered to be a confounding variable as previous studies have demonstrated that tPA is as effective in those over 80 years compared to those under.⁷

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