# Does Large Vessel Occlusion Affect Clinical Outcome in Stroke with Mild Neurologic Deficits after Intravenous Thrombolysis?

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*Background:* Large vessel occlusion (LVO) is associated with poor functional outcome in acute ischemic stroke. Given the uncertainty whether LVO has the same significance in mild and severe stroke, we compared functional outcomes after intravenous thrombolysis, based on severity and LVO. *Methods:* Ischemic stroke patients were thrombolyzed in less than 4.5 hours after onset between 2007 and 2013. LVO was defined as occlusion of one of the following arteries: internal carotid, middle cerebral (M1/M2), anterior cerebral (A1), posterior cerebral (P1), basilar, or vertebral (V4) arteries on prethrombolysis computed tomography angiography. Mild stroke was defined as baseline National Institutes of Health Stroke Scale (NIHSS) score 0-6. Favorable outcome was defined as modified Rankin Scale (mRS) score 0-1 at 3 months or equal to the prestroke mRS. *Results:* There were 175 acute stroke patients, median age 74 years (interquartile range [IQR], 64-83), median baseline NIHSS = 11 (IQR, 5-16), and 63 of 175 patients (36%) with mild stroke. LVO was associated with worse outcome in severe stroke (age-adjusted odds ratio [OR] of favorable outcome, .42; 95% confidence interval [CI], .19-.93; $P = .033$) and mortality (age-adjusted OR, 3.52; 95% CI, 1.08-11.48; $P = .037$). Although the difference in favorable outcome between mild stroke patients with and without LVO was not significant (55.6% vs. 74.1%, $P = .262$; age-adjusted OR of favorable outcome, .42; 95% CI, .1-1.84; $P = .251$), the similarity of effects across both subgroups cannot be excluded (LVO-by-stroke severity interaction test, $P = .906$). *Conclusions:* LVO is associated with worse functional outcome and mortality in severe stroke after intravenous thrombolysis. Although significant association between LVO and outcome in mild stroke was not found, there were similar effects on outcome and a larger study might well confirm a relationship. **Key Words:** Ischemic stroke—mild stroke—intravenous thrombolysis—CT angiography—modified Rankin Scale.


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Received April 10, 2014; revision received June 28, 2014; accepted July 11, 2014.

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This study was supported by projects of National Natural Science Foundation of China (NSFC 81220108008, NSFC 81171099).

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1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2014.07.018

## Introduction

Intravenous tissue plasminogen activator (IV tPA) leads to improved functional outcomes for patients with acute ischemic stroke.[1-4] Of patients who receive IV tPA within 3 hours of symptom onset, 61.1% have a favorable outcome,[2] and of those who receive IV tPA within 4.5 hours of stroke onset, 52.4% have a favorable outcome.[3] Large vessel occlusion (LVO) is associated with poor outcome in acute stroke,[5] and IV tPA leads to successful recanalization in only 21.3% of acute stroke patients with LVO.[6] The effect of IV tPA diminishes in the setting of large clot burden.[6-8] Successful recanalization at 2 hours after tissue plasminogen activator is achieved in only 6% of patients with terminal internal carotid artery (ICA) occlusion,[9] and only 18% of patients in this group achieve a favorable outcome.[9]

Up to half of acute stroke patients in the United States have mild neurologic deficit, defined by a National Institutes of Health Stroke Scale (NIHSS) less than 6.[10] Patients with low NIHSS scores were excluded from tPA treatment in randomized clinical trials, for example, National Institute of Neurological Disorders and Stroke recombinant tissue plasminogen activator stroke trial (NIHSS $\leq$5 exclusion)[1] and European Cooperative Acute Stroke Study III trial (NIHSS $<$5 exclusion).[3] Current guidelines for acute ischemic stroke management from the American Heart Association/American Stroke Association state that the use of IV tPA in patients with mild stroke remains controversial and may be considered.[11] However, approximately one third of patients who did not receive IV tPA because of mild or rapidly improving stroke symptoms have a poor outcome.[5,12-14] It is important to examine the reasons behind poor outcome in mild stroke. It has been postulated that LVO exerts a negative effect on outcomes in mild stroke.[5,15]

The aim of our study was to investigate the effects of LVO in stroke patients with mild and severe deficits treated with IV tPA. We hypothesized that there will be different LVO effects on outcomes in stroke patients with mild and severe neurologic deficits.

## Methods

### *Patients*

Clinical and demographic details of acute ischemic stroke patients who presented and were treated with IV tPA at Royal Melbourne Hospital within 4.5 hours after stroke onset, between December 2007 and February 2013, were prospectively recorded in a database. Patients with acute ischemic stroke meeting clinical and noncontrast computed tomography (CT) eligibility criteria were administered .9 mg/kg IV tPA within 4.5 hours after onset of symptoms. We included only those patients who had received computed tomography angiography (CTA) before thrombolysis. The following parameters were included: (1) demographics (age and sex); (2) vascular risk factors (such as hypertension, diabetes, hypercholesterolemia, atrial fibrillation, smoking, and ischemic heart disease); (3) previous stroke history; (4) baseline NIHSS score; (5) onset to treatment time; (6) CTA before tPA; (7) CT/magnetic resonance imaging after tPA; and (8) modified Rankin Scale (mRS) prestroke and 3 months. Mild neurologic deficit was defined as baseline NIHSS score 0-6 and severe neurological deficit as baseline NIHSS score greater than or equal to 7.[16] Patients eventually diagnosed with stroke mimics[17] and those patients who received IV tPA plus intra-arterial (IA) therapy were excluded from the analysis. The study was approved by our institutional human research ethics committee.

### *Imaging Assessment*

From December 2007, CTA was routinely performed in acute ischemic stroke patients before IV tPA at Royal Melbourne Hospital, unless contraindicated (eg, renal impairment or known contrast allergy). All patients underwent CT or magnetic resonance imaging scan approximately 24 hours after IV tPA to assess hemorrhagic transformation and extent of infarction. Symptomatic intracerebral hemorrhage (sICH) was defined as blood at any site in the brain associated with clinical deterioration, resulting in greater than or equal to 4 point increase in the NIHSS score.[18] LVO was defined by proximal vessel occlusion in any of the following arteries[5]: ICA, middle cerebral artery (M1 and M2 segment), anterior cerebral artery (A1 segment), V4 segment of vertebral artery, basilar artery, and posterior cerebral artery (P1 segment). LVO was assessed on CTA image by 2 independent experienced stroke neurologists (W.Z., B.Y.). LVO was considered relevant only if the site of occlusion correlated with acute ischemic stroke symptoms.

### *Outcome*

The primary outcome was mRS score at 3 months. Favorable outcome was defined as mRS 0-1 at 3 months or equal to prestroke mRS.[19,20] Secondary outcomes were mortality at 3 months and sICH after IV tPA treatment.

### *Statistical Analysis*

Statistical analysis was performed using Stata (v13IC; StataCorp, College Station, TX). Continuous variables were expressed as mean values $\pm$ standard deviation or median values (interquartile range [IQR]) depending on the nature of the underlying distribution. Differences between groups were assessed using the Student $t$ test or Mann–Whitney $U$ test for continuous variables and the chi-square test or Fisher exact test for categorical variables. Multivariable logistic regression analysis was