Intravenous Thrombolysis for Acute Ischemic Stroke due to Cervical Internal Carotid Artery Occlusion

Leonard L. L. Yeo, MBBS, MRCP,* Wan Yee Kong, MBBS,* Prakash Paliwal, MBBS,*
Hock L. Teoh, MBchB,* Raymond C. Seet, MBBS,*† Derek Soon, PhD,*
Rahul Rathakrishnan, MBBS,* Venetia Ong, BDS,* Tsong-Hai Lee, MBBS,‡§
Ho-Fai Wong, MBBS,§‖ Bernard P. L. Chan, MBBS,* Wee Kheng Leow, PhD,¶
Cheng Yuan, PhD,¶ Eric Ting, MBBS,# Anil Gopinathan, MBBS,#
Benjamin Y. Q. Tan, MBBS,* and Vijay K. Sharma, MBBS*†

Background: Internal carotid artery (ICA) occlusions are poorly responsive to intravenous thrombolysis with tissue plasminogen activator (IV-tPA) in acute ischemic stroke (AIS). Most study populations have combined intracranial and extracranial ICA occlusions for analysis; few have studied purely cervical ICA occlusions. We evaluated AIS patients with acute cervical ICA occlusion treated with IV-tPA to identify predictors of outcomes. *Methods:* We studied 550 consecutive patients with AIS who received IV-tPA and identified 100 with pure acute cervical ICA occlusion. We evaluated the associations of vascular risk factors, National Institutes of Health Stroke Scale (NIHSS) score, and leptomeningeal collateral vessel status via 3 different grading systems, with functional recovery at 90 days, mortality, recanalization of the primary occlusion, and symptomatic intracranial hemorrhage (SICH). Modified Rankin Scale score 0-1 was defined as an excellent outcome. *Results:* The 100 patients had mean age of 67.8 (range 32-96) and median NIHSS score of 19 (range 4-33). Excellent outcomes were observed in 27% of the patients, SICH in 8%, and mortality in 21%. Up to 54% of the patients achieved recanalization at 24 hours. On ordinal regression, good collaterals showed a significant shift in favorable outcomes by Maas, Tan, or ASPECTS collateral grading systems. On multivariate analysis, good collaterals also showed reduced mortality (OR .721, 95% CI .588-.888, $P = .002$) and a trend to less SICH (OR .81, 95% CI .65-1.007, $P = .058$). Interestingly, faster treatment was also associated with favorable functional recovery (OR 1.028 per minute, 95% CI 1.010-1.047, $P = .001$). *Conclusions:* Improved outcomes are seen in patients with early acute cervical ICA occlusion and better collateral circulation. This could be a valuable biomarker for

Introduction

The major aim of intravenous thrombolysis with tissue plasminogen activator (IV-tPA) in acute ischemic stroke (AIS) is to achieve recanalization of the occluded intracranial artery, which in turn is an important predictor of favorable clinical outcome.[1,2] Various studies have proven that the IV-tPA-induced recanalization rates vary with the site of arterial occlusion.[1-4] Systemic thrombolysis with IV-tPA continues to be the primary standard of care.[4] Although endovascular therapy is an effective modality in patients who fail to achieve arterial recanalization with IV-tPA, the techniques are resource intensive and not widely available.[5]

Thrombotic occlusion of the internal carotid artery (ICA) is associated with large infarct size and poor functional outcome.[6] Studies on isolated ICA occlusions are scarce, tend to combine intracranial and cervical ICA occlusions, and can reach contrasting conclusions.[7-9] Only few studies have focused on the response to IV-tPA in patients with primary acute occlusion of cervical ICA.[10-12] These disparate populations may have different hemodynamic properties and response to IV-tPA.[8] We identified AIS patients with primary occlusion of cervical ICA from our thrombolysis cohort and analyzed them for the determinants of functional outcome. We hypothesize that there are factors that may be associated with better outcomes with IV-tPA treatment in this group.

Methods

Consecutive patients treated between 2010 and 2014 were included. All AIS patients presenting within the thrombolysis window of 4.5 hours undergo noncontrast computed tomography (CT) of the brain and CT angiography (CTA) of the cervico-cranial arterial tree. We identified all patients with primary occlusion of cervical ICA on the prethrombolysis CTA. Patients with primary intracranial ICA occlusions, tandem lesions, carotid-L occlusions, and carotid-T occlusions (n = 27) were excluded. However, as the CTA scans did not have a delayed phase, we were unable to absolutely rule out these lesions. All patients received a standard dose of IV-tPA (.9 mg/kg body weight). Further details of the inclusion and exclusion criteria are provided in the Supplementary section.

Data for demographic characteristics and vascular risk factors such as hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, and smoking were then extracted from the registry. Systemic blood pressure values were recorded for all patients at presentation and at 24 hours after thrombolysis. AIS subtypes were determined by using the TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification.[13] The National Institutes of Health Stroke Scale (NIHSS) scores were recorded for all cases by credentialed neurologists before IV-tPA bolus, at 2 hours, and 24 hours after treatment initiation.

CTA was repeated at 24 hours. Scans were performed on a 64-slice multidetector helical scanner (Philips Inc, Cleveland, OH, USA) and images were acquired with 70 mL bolus injection of contrast. Scan parameters were as follows: slice thickness 1 mm; no slice gap; field of view 200 mm; matrix 512 × 512, and mAs 230-250. Coverage was from the base of skull to the vertex and the source images were reformatted into 3-mm-thick axial, coronal, and sagittal projections. CTA images were independently reviewed by 2 experienced neuroradiologists using maximum intensity projections in the axial planes. They were blinded to the patients' clinical status, outcome, or results of other neuroimaging modalities.

The recanalization status was determined by arterial occlusive lesion grading, with grades 2 and 3 considered as "recanalized" whereas grades 0 and 1 were classified as an "occluded" artery.[14] The leptomeningeal collateral status on the prethrombolysis CTA was assessed by 3 predefined criteria—Maas, Tan, and ASPECTS collaterals, which have been previously described.[15-19]

Functional outcome was assessed by the modified Rankin Scale (mRS) at 3 months. An mRS score of 0-1 represented a favorable functional outcome. Symptomatic intracranial hemorrhage (SICH) was defined as the presence of new blood on the follow-up CT scan that was associated with an increase in NIHSS by 4 points or more.[20,21]

Statistical Analysis

We present the numerical variables as mean and standard deviation (SD) or median and range. Categorical variables are presented as percentages. Numerical predictors were assessed by using independent-samples t-test or Mann–Whitney U-test where applicable. Categorical variables were evaluated using Pearson chi-square test or Fisher exact test where applicable. Variables that were found to have a significant association ($P < .05$) were entered into the multivariable model using backward stepwise selection procedure to perform logistic regression for determining the independent predictors of mortality and SICH. In addition, the association of the various collateral grading with 3-month functional outcome was also