Predictors of Infarct Growth after Endovascular Therapy for Acute Ischemic Stroke

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Background: Intra-arterial (IA) thrombectomy for acute ischemic stroke has an excellent recanalization rate but variable outcomes. The core infarct also grows at a variable rate despite recanalization. We aim to study the factors that are associated with infarct growth after IA therapy. *Methods:* We reviewed the hyperacute ischemic stroke imaging database at Cleveland Clinic for those undergoing endovascular thrombectomy of anterior circulation from 2009 to 2012. Patients with both pretreatment and follow-up magnetic resonance imaging were included. Seventy-six patients were stratified into quartiles by infarct volume growth from initial to follow-up diffusion-weighted imaging (DWI) measure by a region of interest demarcation. *Results:* The median infarct growth of each quartile was .6 cm^3 (no-growth group), 13.8, 37, and 160.2 cm^3 (large-growth group). Pretreatment stroke severity was comparable among groups. Compared with the no-growth group, the large-growth group had larger initial infarct defined by computed tomography (CT) Alberta Stroke Program Early CT score (median 10 versus 8, $P = .032$) and DWI volume (mean 13.8 versus 29.2 cm^3, $P = .034$), lack of full collateral vessels on CT angiography (36.8% versus 0%, $P = .003$), and a lower recanalization rate (thrombolysis in cerebral infarction ≥2b, $P = .044$). The increase in infarct growth is associated with decrease in favorable outcomes defined by a modified Rankin Scale score of 0-2 at 30 days: 57.9%, 42.1%, 21.1%, and 5.3%, respectively ($P < .001$). DWI reversal was observed in 11 of 76 patients, translating to 82% favorable outcome. *Conclusions:* Infarct evolution after endovascular thrombectomy is associated with an outcome. DWI reversal or no growth translated to a favorable outcome. Small initial ischemic core, good collateral support, and better recanalization grades predict the smaller infarct growth and favorable outcome after endovascular thrombectomy. **Key Words:** ischemic stroke—mechanical thrombectomy—outcome—MRI.

Introduction

One goal of acute stroke treatment is to restore blood flow and salvage the penumbral ischemic tissue. DEFUSE 2 study showed that time to treatment might not be an absolute factor affecting the outcome.[1] It seems that some patients lose neurons at a high rate and that even very early reperfusion may not provide benefit. In contrast, there seems to be a subgroup of stroke patients in whom irreversible ischemic injury evolves over many hours.[2] The factors affecting infarct growth remain unclear.

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Intra-arterial (IA) mechanical thrombectomy for acute stroke has an excellent recanalization rate but variable outcomes.[1,3] This is also reflected in the variability in the infarct growth despite arterial recanalization and reperfusion. The goal of this study was to investigate the factors associated with diffusion-weighted imaging (DWI) infarct lesion regression and evolution, as well as the relationship between infarct evolution and functional outcome after IA therapy.

Methods

Data were abstracted from Cleveland Clinic Hyperacute Ischemic stroke Database stored in Research Electronic Data Capture, a secure, web-based application approved by Institutional Review Board of Cleveland Clinic.[4] The prospective database included demographic, clinical, radiographic, and endovascular therapy information for ischemic stroke patients undergoing acute mechanical thrombectomy at Cleveland Clinic. Data from 2010 to 2012 were reviewed. Patients with occlusion at internal carotid artery, middle cerebral artery, and middle cerebral artery M2 branches, with both initial magnetic resonance imaging (MRI) and after IA therapy MRI in 2-5 days were included. Patients with acute strokes attributable to posterior circulation or incomplete medical record were excluded. At the discretion of the treating physicians, single or multiple combination modalities of stent retriever (Trevo; Stryker, Kalamazoo, Michigan or Solitaire; EV3, Irvine, California), Penumbra aspiration system (Penumbra, Alameda, California), Merci retrieval device (Stryker), IA thrombolysis, or angioplasty was used to restore blood flow. IA tissue plasminogen activator or glycoprotein IIb/IIIa inhibitors were also administered at the discretion of the treating interventionalists.

Stroke onset was determined as the time patient was last seen well. Stroke severity was measured by the National Institutes of Health Stroke Scale (NIHSS) score on admission and discharge. Major neurologic improvement was defined as the NIHSS score of 0-1 on discharge or when the NIHSS score improved by 8 points or greater.[5] Functional outcome was measured by a modified Rankin Scale (mRS) score at 30 days. Favorable outcome was defined as the mRS score of 0-2.[6]

Vascular neurologists (S.M., J.A., Y.T., and E.C.) blinded to clinical information reviewed the radiographic images. Computed tomography (CT) and CT angiography (CTA) images were analyzed for Alberta Stroke Program Early CT score,[7-9] infarct volume, and arterial occlusion location. Collateral vessels on single time-frame CTA were graded on maximal intensity projection imaging as follows: 0, no collaterals; 1, less than 50% of expected territory; 2, more than 50% of expected territory; and 3, full collaterals.[10,11]

Infarct volume on DWI sequence was measured by manually outlining the area of abnormal signal intensity on each DWI slice and then multiplying by slice thickness. Infarct growth was defined as and calculated by subtracting initial DWI volume (core infarct) from the follow-up DWI that was performed within 2-5 days after the IA therapy. Fluid-attenuated inversion recovery hyperintense vessel sign (FHVS) was classified based on the location: none; within Sylvian fissure; to temporoparietal junction; and high cortical. Perfusion images were processed using commercial software on a workstation by the vendor (Siemens, Erlangen, Germany). Arterial input function was derived from the M1 artery or branch on the opposite hemisphere to the largest diffusion abnormality.[12] Mean transit time and time-to-peak (TTP) maps were used to detect the ischemic penumbra as previously have been used.[13]

Intracranial arterial recanalization was determined by digital subtraction angiography by interventionalists (M.S.H., F.H., G.T.) blinded to the clinical outcome using the thrombolysis in cerebral infarction (TICI) grade[14]: 0, no perfusion; 1, perfusion past the initial obstruction, but limited distal branch filling with little or slow distal perfusion; 2a, perfusion of less than one half of the vascular distribution of the occluded artery (eg, filling and perfusion through one M2 division); 2b, perfusion of one half or greater of the vascular distribution of the occluded artery (eg, filling and perfusion through two or more M2 divisions); 3, full perfusion with filling of all distal branches.

Statistical Analysis

The patients were stratified into quartiles of infarct growth. When a trend was observed among the quartiles, the statistical analysis was performed to compare the first and fourth quartiles. The data were analyzed using JMP 10.0 (SAS Inc, Cary, North Carolina). Chi-square or fisher exact test was used for categorical variables. An analysis of variance was used for continuous variables. Wilcoxon test was performed for nonparametric variables. Logistic regression was used to identify the predictors for infarct evolving between the first quartile and the combination of the last three quartiles. A P value of less than .05 was considered statistically significant.

Results

During the study period, 97 consecutive patients had IA therapy for acute stroke because of anterior circulation large vessel occlusion. Among them 76 (78%) patients had complete record and were included in this analysis. Figure 1 illustrates the initial infarct volume and growth for each patient in the order of infarct growth. The patients were stratified into quartiles based on the range of infarct growth: no growth (−19.1 to 4.2 cm^3), small growth (4.8-25.8 cm^3), moderate growth (26.5-68.5 cm^3), and large growth (77.6-314.5 cm^3). Median infarct growth in each group was .6, 13.8, 37, and 160.2 cm^3 in each group. Fourteen percent (11 of 76) of patients had DWI