

Predictors of Symptomatic Intracranial Hemorrhage after Endovascular Therapy in Acute Ischemic Stroke with Large Vessel Occlusion

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Background: The symptomatic intracranial hemorrhage (SICH) is a serious complication of endovascular therapy (EVT) in acute ischemic stroke (AIS) with large vessel occlusion. We aimed to clarify the predictors of SICH after EVT in patients with internal carotid artery (ICA) or proximal M1 segment of middle cerebral artery occlusions. *Methods:* Among 1442 AIS patients with large vessel occlusion admitted within 24 hours after onset between July 2010 and June 2011, 226 patients with ICA or proximal M1 occlusions were treated with EVT. SICH was defined as any type of intracranial hemorrhage with a decline in the National Institutes of Health Stroke Scale (NIHSS) score ≥ 4 . *Results:* Of the 226 patients, 204 with sufficient data were analyzed. SICH was observed in 10 patients (4.9%). Baseline NIHSS score (22 versus 17), serum glucose level (206 mg/dL versus 140 mg/dL), and prior antiplatelet therapy (60.0% versus 21.7%) were significantly higher in patients with SICH than in those without (all $P < .01$). With receiver operating characteristic analyses, the optimal cutoff values for predicting SICH were NIHSS score ≥ 19 and serum glucose ≥ 160 mg/dL. In multivariate analysis, glucose level ≥ 160 mg/dL (odds ratio: 11.89; 95% confidence interval [CI]: 2.79-65.08), prior antiplatelet therapy (odds ratio: 8.03; 95% CI: 1.83-41.70), and NIHSS score ≥ 19 (odds ratio: 7.78; 95% CI: 1.63-59.44) were independent predictors of SICH. *Conclusion:* Hyperglycemia, prior antiplatelet therapy, and high baseline NIHSS score were associated with SICH after EVT in AIS patients with ICA or proximal M1 occlusions. **Key Words:** Acute ischemic stroke—large vessel occlusion—endovascular therapy—symptomatic intracranial hemorrhage—hyperglycemia—antiplatelet therapy. © 2016 National Stroke Association. Published by Elsevier Inc. All rights reserved.

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Introduction

Recently, evidence was established that endovascular therapy (EVT) was effective in acute ischemic stroke (AIS) patients with large vessel occlusion in anterior circulation.¹⁻⁵ In patients with internal carotid artery (ICA) or middle cerebral artery M1 occlusions within 6 hours from the onset, EVT, in addition to best medical treatment including intravenous tissue plasminogen activator (IV t-PA), improves functional outcome. Because the recanalization rate by IV t-PA is low in patients with ICA occlusion^{6,7} or M1 occlusion of residual length <5 mm,⁸ early recanalization with EVT is especially expected to improve the prognosis in these patients.

Randomized trials showed that EVT, in addition to best medical treatment, did not increase the rate of symptomatic intracranial hemorrhage (SICH). However, once SICH occurs, it has a serious impact on clinical outcome. SICH was reported to be associated with worse functional outcome and mortality after EVT.⁹

Although several predictors of SICH after EVT have been reported,⁹⁻¹² these have not been clarified in patients with acute ICA or proximal M1 occlusions. A better understanding of SICH would lead to improved treatment strategy of EVT and better outcome in patients with severe AIS.

Aim

The present study aimed to clarify predictors of SICH after EVT in patients with acute ICA or proximal M1 occlusions.

Methods

Patients

In the Recovery by Endovascular Salvage for Cerebral Ultra-acute Embolism (RESCUE)-Japan Registry, 1442 AIS patients with large vessel occlusions who were admitted to 84 participating medical centers within 24 hours after the onset were registered between July 1, 2010 and June 30, 2011. The details of the study design and main analysis have been reported previously.¹³ In this study, we evaluated 714 patients who had ICA or proximal M1 occlusions. Proximal M1 occlusion was defined as residual M1 length <5 mm on initial vascular image using magnetic resonance angiography (MRA).⁸ Among 714 patients with ICA or proximal M1 occlusions, 226 patients treated with EVT were included in this study. Study procedures were reviewed and approved by local ethics committees.

Clinical Data

Blood pressure and the National Institutes of Health Stroke Scale (NIHSS) scores were evaluated, and blood collection to measure laboratory data was performed on admission. Neuroimaging studies with magnetic resonance

imaging (MRI) and MRA at baseline were used for detection of ischemic lesion and large vessel occlusion. The expanse of ischemic lesion was evaluated using the Alberta Stroke Program Early CT Score¹⁴ on diffusion-weighted image.

Treatment

IV t-PA was performed in accordance with the Japanese standard protocol at the study period (.6 mg/kg dose, 10% bolus, 90% continuously infused over 60 minutes). IV t-PA failed or ineligible patients were treated with EVT, including clot removal, clot aspiration, balloon angioplasty, stenting, mechanical clot disruption, and intra-arterial thrombolysis. Devices of EVT were chosen by the site neurointerventionalist. The use of Penumbra system® (Penumbra Inc., Alameda, CA, USA) and stent retrievers was not approved in Japan during this study period. Reperfusion of the occluded artery was evaluated on final angiography and classified according to the modified thrombolysis in cerebral infarction grade.¹⁵ Successful reperfusion was defined as modified thrombolysis in cerebral infarction grade 2b or 3.

Evaluation of SICH

Intracranial hemorrhage was evaluated on follow-up computed tomography (CT) or MRI at 24 ± 8 hours after the onset or at the time of clinical deterioration within 24 hours. SICH was defined according to the Second European-Australasian Acute Stroke Study (ECASS 2) definition as any type of hemorrhagic infarction (HI) or parenchymal hemorrhage (PH) associated with a decline in NIHSS score ≥ 4 within 24 hours. All imaging data, including MRI, CT, and angiography, were evaluated in each institution.

Statistical Analysis

Statistical analyses were performed using JMP version 10 (SAS Institute, Inc, Cary, NC). Baseline characteristics were compared between patients with and without SICH using Pearson χ^2 test or Fisher exact test for categorical variables, Student *t*-test for continuous variables, and Mann-Whitney *U*-test for ordinal variables. $P < .05$ was regarded as statistically significant. Receiver operating characteristic analysis was used to evaluate the optimal cutoff value for predicting SICH. Variables with $P < .10$ were entered into the multivariate logistic regression model to determine predictors of SICH.

Results

Of the 226 patients with acute ICA or proximal M1 occlusions who were treated by EVT, 204 patients with sufficient data were analyzed. The mean age was 70.7 ± 12.8 years, 60.8% were men, and the median NIHSS score was 17.5 (interquartile range: 13-22). As for devices of EVT,

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