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Opinion paper

Factors associated with early dramatic recovery following successful recanalization of occluded artery by endovascular treatment in anterior circulation stroke

Dae-Hyun Kim^{a,b,*}, Hyun-Wook Nah^{a,b}, Hyun-Seok Park^a, Jae-Hyung Choi^a, Myung-Jin Kang^a, Jae-Kwan Cha^{a,b}

^a Busan-Ulsan Regional Cardiocerebrovascular Center, Dong-A University Hospital, Busan, Republic of Korea

^b Department of Neurology, College of Medicine, Dong-A University, Busan, Republic of Korea

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ABSTRACT

Endovascular treatment (EVT) significantly increases the recanalization rate and improves functional outcomes in acute ischemic stroke. However, despite successful recanalization by EVT, some stroke patients demonstrate no early dramatic recovery (EDR). We assessed factors associated with EDR following recanalization by EVT. We included subjects with anterior circulation stroke treated with EVT who met the following criteria: Thrombolysis in Cerebral Ischemia scores (TICI) 2b–3 after EVT, lesion volume <70 mL as seen on the pre-treatment diffusion-weighted imaging (DWI) scan and a baseline NIHSS score ≥ 6 . EDR was defined as a ≥ 8 -point reduction in the NIHSS score, or NIHSS score of 0 or 1 measured 24 h following treatment. Multivariate regression analyses were performed to identify the predictors associated with EDR. Of the 102 patients (mean age, 64.3 years; median National Institutes of Health Stroke Scale score, 14), EDR was achieved in 39 patients (38.2%). The median DWI lesion volume was 12 mL (interquartile range, 5–25 mL). Median onset-to-recanalization time in these patients was 320 min (interquartile range, 270–415 min). Logistic regression analysis identified a higher initial NIHSS score (OR 1.17, 95% CI 1.03–1.33, $P = 0.016$) and shorter time from onset to recanalization (OR 0.99, 95% CI 0.986–0.997, $P = 0.003$), to be independently associated with EDR. In the setting of pretreatment DWI lesion volume <70 mL, a higher initial NIHSS score and faster time from onset to recanalization may be important predictors of EDR following successful EVT.

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1. Introduction

Successful arterial recanalization is critical in order to achieve favorable outcomes after thrombolytic therapy in acute ischemic stroke [1]. However, large-vessel occlusion is resistant to intravenous thrombolysis and often does not lead to rapid recanalization on its own. Several recent randomized controlled trials have demonstrated that endovascular treatment (EVT) significantly increases the rate of successful recanalization and provides good functional outcomes [2]. The success rates of recanalization using newer thrombectomy devices were 86% in EXTEND-IA [3] and 88% in SWIFT PRIME [4]. EVT is recommended for patients with a large artery occlusion when treatment can be initiated within 6 h of the onset of symptoms [5].

A subset of patients treated with intravenous thrombolytic therapy shows an early dramatic recovery (EDR) within 24 h, which is also referred to as “major neurological improvement,” “rapid neurological recovery” and “early neurological improvement” [6,7]. Approximately 24–33% of acute stroke patients reveal an EDR in response to intravenous recombinant tissue plasminogen activator (rtPA) therapy [6–9]. EDR was associated with better long-term outcome [6,7].

We expected that more EDRs would be achieved through EVT, given that EVT using new thrombectomy devices or intra-arterial thrombolysis allows successful recanalization in patients with acute cerebral artery occlusion. However, despite successful recanalization following EVT, not all patients show EDR and treatment response is often unpredictable.

The predictors of EDR in patients with successful recanalization by EVT have not been sufficiently identified. Therefore, we aimed to evaluate the factors associated with EDR following successful recanalization by EVT in patients with anterior circulation infarction.

* Corresponding author at: Department of Neurology, College of Medicine, Dong-A University, 1, 3-ga Dongdaesin-dong, Seo-gu, Busan 602-715, Republic of Korea.
E-mail address: kdh6542@hanmail.net (D.-H. Kim).

2. Materials and methods

We reviewed prospectively registered, consecutive patients with acute ischemic stroke who received endovascular revascularization between January 2007 and July 2015 at the Dong-A University Hospital.

During this study period, magnetic resonance imaging (MRI) was systematically implemented as the first-line diagnostic work-up in our center. When patients with acute ischemic stroke who presented to the center within 4.5 h after the onset of stroke were eligible for thrombolytic therapy, they were treated with the rtPA (dose: 0.6 or 0.9 mg per kilogram of body weight). EVT was performed in addition to intravenous rt-PA when magnetic resonance angiography revealed a large arterial occlusion. Some patients with arterial occlusion who were not eligible for intravenous rt-PA directly underwent EVT. The EVT eligibility of patients with a large artery occlusion was determined by stroke physician. The EVT procedure included the intra-arterial thrombolysis, use of mechanical thrombectomy or aspiration device, and stent placement. Prior to receiving the approval for mechanical intervention devices and intracranial stenting in our country, the EVT comprised only intra-arterial urokinase administration. Following this, the neuro-interventionists decided on the use of mechanical devices, such as the Solitaire stent retriever device or the Penumbra or both, as recanalization techniques, or extra/intracranial stenting. If two methods were used, a final method used was chosen as representative.

Among the patients with acute ischemic stroke who underwent EVT, we identified subjects who met the following criteria: 1) the patients suffered an anterior circulation infarction with complete occlusion of the internal carotid artery or the middle cerebral artery and 2) they underwent recanalization with Thrombolysis in Cerebral Ischemia (TICI) grade 2b–3 following EVT. We excluded patients with an initial National Institutes of Health Stroke Scale (NIHSS) score <6 upon considering acute treatment guidelines [5], and patients with pretreatment diffusion weighted imaging (DWI) lesion volume ≥ 70 mL given the reduced possibility of benefit derived from reperfusion therapy [10].

NIHSS recordings were collected at admission and at 24 h after the initiation of treatment. EDR was predefined as an improvement of ≥ 8 points on the NIHSS, or an NIHSS score of 0 or 1 at 24 h [6,11] after the initiation of treatment. The functional outcome was assessed with the modified Rankin scale (mRS) at 3 months, and patients were grouped based on favorable (mRS score 0–2) and unfavorable (mRS score 3–6) outcomes.

The site of the artery occlusion was categorized as the internal carotid artery (isolated or in tandem with the middle cerebral artery), or isolated middle cerebral arteries M1 and M2. The recanalization status after EVT was classified according to the TICI grade [12], with successful recanalization being as TICI grade 2b–3 [13]. The TICI grade was assessed by two members of the staff (H.P. and D.K.). The onset-to-recanalization time was defined as the time from the onset of stroke symptoms to the termination of the procedure in patients with technically successful reperfusion.

The DWI lesion volume was determined by manually tracing the edge of the hyperintense signal in each frame of the DWI images scans. The region of interest was multiplied by the section thickness plus the intersection gap, and then summed across the frames to obtain the total lesion volume. Symptomatic intracerebral hemorrhage was defined as any sign of hemorrhage on computed tomography or MRI scans at 24 h, which was associated with clinical deterioration as indicated by an NIHSS score that is 4 points greater than the baseline [14].

2.1. Statistical analysis

The patients characteristics are presented as mean \pm standard deviation or median (interquartile range [IQR]) for continuous variables and as frequency and proportions for categorical variables. Univariate associations between categorical variables were investigated using the χ^2 or Fisher's exact tests, as appropriate. Continuous and ordinal variables were compared using the Student's *t* test (normal distribution) or the Mann-Whitney *U* test (skewed distribution). A two-sided *P* value <0.05 was used to designate statistically significant.

In order to determine the factors associated with EDR following successful recanalization, the demographics and clinical data were compared between patients with and without EDR.

Multinomial logistic regression was performed to estimate the adjusted odds ratios (ORs) of each variable for the prediction of EDR. To avoid variable selection caused by spurious correlations, only the variables showing an association with EDR ($p < 0.2$) in the univariate analysis were included as potential factors associated with EDR in the multivariate logistic regression model.

3. Results

During the study period, 262 consecutive patients with acute ischemic stroke were treated with EVT. Sixty-three patients had a posterior circulation stroke. Of the 199 patients with an occlusion of the internal carotid or the middle cerebral arteries, 125 patients (62.8%) had a TICI score $\geq 2b$. Twenty-three patients were not eligible because of either contraindication to MRI at admission ($N = 9$), a DWI lesion volume >70 mL ($N = 9$), or an NIHSS score ≤ 5 ($N = 5$). Finally, 102 patients met the eligibility criteria for the present study (Fig. 1).

Of the 102 study subjects, 38.2% were female. The mean age (mean \pm SD) of the sample was 64.3 ± 10.4 years, while the median NIHSS score at admission was 14 (interquartile range [IQR]: 10–17). The median DWI lesion volume was 12 mL (IQR, 5–25 mL), while the median onset-to-recanalization time was 320 min (IQR, 270–415 min). Thirty-nine patients (38.2%) showed EDR at 24 h following EVT.

Univariate analysis revealed that there was statistically significant difference ($p = 0.014$) in the number of patients with a baseline NIHSS score ≥ 12 between the groups of patients with and without EDR (79.5% vs 55.6%). The onset-to-recanalization time

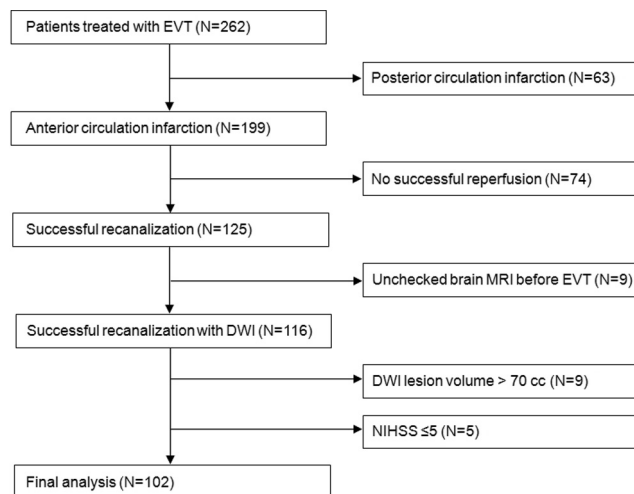


Fig. 1. Schematic description of the patient selection process. EVT, endovascular treatment; DWI, diffusion-weighted imaging.

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