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Clinical predictors for favorable outcomes from endovascular recanalization in wake-up stroke



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ABSTRACT

Background and purpose: Patients who have acute stroke symptoms present on awakening are ineligible for standard intravenous thrombolysis due to the unclear onset time of symptoms. Some of these wakeup stroke (WUS) patients may benefit from endovascular recanalization. This study aimed to evaluate clinical predictors of outcomes from endovascular recanalization in WUS patients.

Methods: Forty-one WUS patients with internal carotid (ICA) or middle cerebral artery (MCA) occlusion treated with endovascular recanalization were reviewed. Regression analysis was performed to measure clinical predictors of outcomes from endovascular recanalization in WUS patients.

Results: The mean initial NIHSS score was $16.41 \pm 4.96 (5-24)$. The mean symptom recognition-to-door time (SRDT) was $108.85 \pm 65.80 (19-230)$ min. Successful recanalization (TICl 2b-3) was achieved in 29 patients (70.7%). Thirty-four patients improved on NIHSS (amount 7.59 ± 4.84 , range; 1-17) at 7 days after recanalization. At 90 days after recanalization, a mRS of ≤ 2 was achieved in 19 patients (46.3%) and a mRS of ≤ 3 was achieved in 24 patients (58.5%). No symptomatic intracerebral hemorrhage occurred. Multivariate regression analysis identified SRDT (P = 0.019), successful recanalization (P = 0.013) were factors associated with an improvement of the NIHSS score. For a good functional outcome at 90 days, SRDT (P = 0.036) and initial NIHSS score (P = 0.016) were found to be significant predictors.

Conclusions: The results of this study suggest that the SRDT is an independent predictor of both an improvement of NIHSS score and a good functional outcome in endovascular recanalization for WUS patients.

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1. Introduction

Many studies on circadian variations of stroke onset have reported an early-morning peak occurrence of acute ischemic stroke. In particular, approximately 25% of patients with acute ischemic stroke experience neurologic deficits on awakening from sleep. In this wake-up stroke (WUS), the onset time of stroke symptoms is defined as the last-seen-normal (LSN) time before going to sleep which is often more than 4.5 h. Due to the uncertainty of actual onset time of stroke symptoms, WUS patients are usually ineligible for intravenous thrombolysis and are excluded from most clinical trials [1–6]. However, acute ischemic stroke may have developed shortly before awakening in a large

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proportion of WUS patients. Many recent studies have shown that clinical and early imaging characteristics of WUS patients are similar to those of patients with stroke of known onset [7–9]. Barreto et al. reported that thrombolysed patients with WUS had better clinical outcomes than non-thrombolysed patients with WUS [10]. Recent large randomized clinical trials showed that endovas-cular mechanical thrombectomy is an effective treatment modality for strokes with large artery occlusion. Also, several case studies have reported clinical outcomes of endovascular treatment for WUS patients [11,12]. The purpose of this study was to evaluate clinical predictors of outcomes from endovascular recanalization in WUS patients. In addition, we present here the baseline demographics, clinical characteristics, recanalization rates, complications, and clinical outcomes of WUS patients who were treated with endovascular recanalization.

2. Materials and methods

We retrospectively analyzed the interventional and clinical data of 41 WUS patients treated with endovascular recanalization in our stroke center between January 2012 and December 2015. Our institutional review board approved the collection of interventional and clinical data for this study. Informed consent was obtained from all patients or their legal representatives for endovascular recanalization. Our inclusion criteria for endovascular recanalization in WUS patients were the followings:

- (1) National Institute of Health Stroke Scale (NIHSS) score \geq 4.
- (2) Occlusion in M1 or M2 of middle cerebral artery and internal carotid artery on CT angiography or MR angiography.
- (3) Hypodensity of <1/3 in a territory of middle cerebral artery on initial CT.
- (4) Diffusion/perfusion mismatch of >50% and DWI lesion of <1/3 of MCA territory on MR imaging or CBV/TTP mismatch of >50% on CT perfusion.
- (5) Endovascular recanalization can be completed within 6 h from the recognition of stroke symptoms on awakening.

Recanalization for the occluded artery was attempted using the Penumbra system (Penumbra Inc., Alameda, CA, USA), the Wingspan stent (Boston Scientific, Natick, MA, USA), the Solitaire device (ev3, Irvine, CA, USA), or the Carotid Wallstent (Boston Scientific, Natick, MA, USA). We analyzed data of patients including age, gender, vascular risk factors, the site of occlusion, the time interval between LSN and symptom recognition on awakening, the time interval between symptom recognition and door, the time interval between door and recanalization. Hemorrhagic events on followup CT were classified according to the European Cooperative Acute Stroke Study (ECASS) II classification [13]. For determination of the subtype of ischemic stroke, the TOAST (Trial of ORG 10172 in Acute Stroke Treatment) criteria were used [14]. Neurologic status was evaluated with the NIHSS at admission and at 7 days after recanalization. Results of recanalization were measured using the Thrombolysis in Cerebral Infarction (TICI) grade (graded as 0 for no perfusion, 1 for penetration with minimal perfusion, 2a for partial perfusion with only partial filling, 2b for partial perfusion with complete filling but the filling is slower than normal, and 3 for complete perfusion). Successful recanalization was defined as the TICI grade of 2b-3. Safety was assessed on the basis of symptomatic intracerebral hemorrhage (SICH), defined as any intracerebral hemorrhage associated with a >4 points increase on the NIHSS score. Functional outcome was measured by a modified Rankin Scale (mRS) score at 90 days after recanalization. Good functional outcome was defined as the mRS score of 0-2.

2.1. Statistics

Data are summarized using descriptive statistics: frequency and percentage for categorical variables and the mean ± SD (standard deviation) with the range for continuous variables. Univariate binary logistic regression analysis was performed for the effect of independent variables on a good functional outcome (mRS ≤ 2) and successful recanalization (TICI 2b-3). Individual variables that were found to be significant in univariate analysis were used in multivariate regression analysis. The effect of independent variables on improved NIHSS scores was analyzed using the univariate and multivariate linear regression, and the statistically significant variables were selected in a backward elimination manner with 0.05 used as the cut off for removal. To check the multicollinearity problem, the variance inflation factor (VIF) was also estimated. VIF quantified the severity of multicollinearity in an ordinary least squares regression analysis. Hair et al. suggest variance inflation factors (VIF) less than 10 are indicative of inconsequential collinearity [15]. All statistical analyses were performed using SPSS (version 21.0; SPSS Inc., Chicago, IL, USA). A p value of less than 0.05 was considered statistically significant.

3. Results

A total of 41 patients (23 men and 18 women, mean age (68.2 ± 9.08) were included in this study. Among them, there were 15 patients in the large-artery atherosclerosis group, 23 patients in the cardioembolism group, and 3 patients in the undetermined etiology group. All patients were treated with endovascular recanalization (Penumbra: 5, Solitaire: 7, Wingspan stent: 10, Wallstent: 3, Penumbra and Wingspan stent: 9, Penumbra and Solitaire: 2, Solitaire and Wingspan stent: 1, Penumbra and Wallstent: 1, Solitaire and Wallstent: 1, Wingspan stent and Wallstent: 2). The mean initial NIHSS score was 16.41 ± 4.96 (range 5–24). There were 11 patients with an occlusion of the proximal ICA (left: 6, right: 5), 4 patients with an occlusion of the distal ICA (left: 4), 5 patients with T occlusion (left: 4, right: 1), 17 patients with an occlusion of the M1 segment of MCA (left: 8, right: 9), and 4 patients with an occlusion of the M2 segment of MCA (left: 3, right: 1). The mean LSN-to-symptom recognition time was 338.90 ± 100.03 (range 210-540) min. The mean symptom recognition-to-door time (SRDT) was 108.85 ± 65.80 (range 19-230) min. The mean door-to-recanalization time was 167.00 ± 45.37 (range 77–250) min. The mean symptom recognition-to-recanalization time was 276 ± 59 (range 155-351) min. The mean LSN-to-recanalization time was 615 ± 119 (range 370-880) min (Table 1). Successful recanalization (TICI 2b-3) was achieved in 29 patients (70.7%, TICI 2b: 11, TICI 3: 18). The mean

Table	1				

Demographics and clinical characteristics.

	N = 41 (%)	Mean ± SD (minmax.)
Male gender	23 (56.1)	
Age, years		68.20 ± 9.08 (47-81)
LSN to SR time, minutes		338.90 ± 100.03 (210-540)
SR to door time, minutes		108.85 ± 65.80 (19-230)
Door to recanalization time,		167.00 ± 45.37 (77-250)
minutes		
Initial NIHSS score		16.41 ± 4.96 (5-24)
AF	22 (53.7)	
DM	10 (24.4)	
Hyperlipidemia	9 (22.0)	
Hypertension	30 (73.2)	
Smoking	18 (43.9)	

Abbreviations: LSN, last seen normal; SR, symptom recognition; NIHSS, National Institutes of Health Stroke Scale; AF, atrial fibrillation; DM, diabetes mellitus.

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