

Original Paper

## Factors Associated with Unsuccessful Recanalization in Mechanical Thrombectomy for Acute Ischemic Stroke

Toshiaki Goda<sup>a</sup> Naoki Oyama<sup>a</sup> Takaya Kitano<sup>a, b</sup> Takanori Iwamoto<sup>a</sup>  
Shinji Yamashita<sup>a</sup> Hiroki Takai<sup>c</sup> Shunji Matsubara<sup>c</sup> Masaaki Uno<sup>c</sup>  
Yoshiki Yagita<sup>a</sup>

<sup>a</sup>Department of Stroke Medicine, Kawasaki Medical School, Okayama, Japan;

<sup>b</sup>Department of Neurology, Osaka University Graduate School of Medicine, Osaka, Japan;

<sup>c</sup>Department of Neurosurgery, Kawasaki Medical School, Okayama, Japan

### Keywords

Acute ischemic stroke · Mechanical thrombectomy · Unsuccessful recanalization

### Abstract

**Introduction:** Mechanical thrombectomy (MT) for acute ischemic stroke has become a standard therapy, and the recanalization rate has significantly improved. However, some cases of unsuccessful recanalization still occur. We aimed to clarify patient factors associated with unsuccessful recanalization after MT for acute ischemic stroke. **Methods:** This was a single-center, retrospective study of 119 consecutive patients with anterior circulation acute ischemic stroke who underwent MT at our hospital between April 2015 and March 2019. Successful recanalization after MT was defined as modified Treatment in Cerebral Ischemia (mTICI) grade 2b or 3, and unsuccessful recanalization was defined as mTICI grades 0–2a. Several factors were analyzed to assess their effect on recanalization rates. **Results:** Successful recanalization was achieved in 88 patients (73.9%). The univariate analysis showed that female sex (38.6 vs. 67.7%,  $p = 0.007$ ), a history of hypertension (53.4 vs. 83.9%,  $p = 0.003$ ), and a longer time from groin puncture to recanalization (median 75 vs. 124 min,  $p < 0.001$ ) were significantly associated with unsuccessful recanalization. The multivariate analysis confirmed that female sex (OR 3.18; 95% CI 1.12–9.02,  $p = 0.030$ ), a history of hypertension (OR 4.84; 95% CI 1.32–17.8,  $p = 0.018$ ), M2–3 occlusion (OR 4.26; 95% CI 1.36–13.3,  $p = 0.013$ ), and the time from groin puncture to recanalization (per 10-min increase, OR 1.22; 95% CI 1.09–1.37,  $p < 0.001$ ) were independently associated with unsuccessful recanalization. **Conclusion:** Female sex and a history of hypertension might be predictors of unsuccessful recanalization after MT for anterior circulation acute ischemic stroke. Further studies are needed to fully evaluate predictors of recanalization.

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Toshiaki Goda  
Department of Stroke Medicine, Kawasaki Medical School  
Matsushima 577  
Kurashiki, Okayama 701-0192 (Japan)  
E-Mail to4aki.5da.takaraduka@gmail.com

## Introduction

Mechanical thrombectomy (MT) has become a standard therapy for acute ischemic stroke with large vessel occlusion [1]. Recanalization of modified Treatment in Cerebral Ischemia (mTICI) 2b or 3 is significantly associated with a good clinical outcome [2], and the recommended target angiographic end point for technical success is mTICI 2b or 3 [3]. With the continued development of devices for MT, such as the stent retriever and aspiration catheter, the recanalization rate has significantly improved, reaching approximately 80% in recent trials [1, 4]. However, unsuccessful recanalization may still occur.

In previous reports, more proximal occlusions, such as those in the internal carotid artery (ICA) and M1 segment of the middle cerebral artery (MCA), was associated with successful recanalization [5, 6]. Other studies have revealed that an erythrocyte-rich thrombus, appearing as a hyperdense signal on computed tomography or a low-intensity signal (known as a susceptibility vessel sign) on T2\*gradient echo magnetic resonance imaging, predicts successful recanalization [7–9]. Conversely, difficult anatomical access [10, 11] and intracranial atherosclerotic stenosis [9, 12] have been reported to be associated with unsuccessful recanalization. However, patient background factors associated with successful or unsuccessful recanalization remain unknown.

Identifying background factors associated with unsuccessful recanalization is important for improving MT treatment strategies. Furthermore, if these factors are modifiable, appropriate management before the onset of stroke might increase the possibility of successful recanalization in patients with large vessel occlusion. In this study, we aimed to clarify patient factors associated with unsuccessful recanalization in MT for acute ischemic stroke.

## Methods

This was a single-center, retrospective study of 119 consecutive patients with anterior circulation acute ischemic stroke who underwent MT at our hospital between April 2015 and March 2019. Successful recanalization after MT was defined as mTICI grade 2b or 3, and unsuccessful recanalization was defined as mTICI grade 0–2a. Several factors were analyzed to assess their effect on recanalization rates, including: sex, risk factors (history of cerebral infarction/transient ischemic attack, coronary artery disease, hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, and smoking [past and current]), antiplatelet agents and anticoagulants before the onset of stroke, BMI on admission, prestroke modified Rankin Scale, initial National Institute of Health Stroke Scale score, Alberta Stroke Program Early Computed Tomography Score for Diffusion-Weighted Imaging including deep white matter lesions [13], occluded vessels (common carotid artery, ICA, and M1–3 segment of the MCA), whether intravenous thrombolysis with a recombinant tissue plasminogen activator was performed, thrombectomy procedure, time from stroke onset to admission, time from admission to groin puncture, time from groin puncture to recanalization, and stroke subtype based on Trial of ORG 10172 in Acute Stroke Treatment criteria [14].

Hypertension was defined as the presence of a positive history or drug treatment, or persistent elevation of systolic ( $\geq 140$  mm Hg) or diastolic blood pressure ( $\geq 90$  mm Hg). Dyslipidemia was defined as current drug treatment, or a serum triglyceride level  $\geq 150$  mg/dL, a low-density lipoprotein cholesterol level  $\geq 140$  mg/dL, or a high-density lipoprotein cholesterol level  $\leq 40$  mg/dL. Diabetes mellitus was defined as the presence of a positive history or drug treatment, or fasting blood glucose  $\geq 126$  mg/dL, or random blood glucose  $\geq 200$  mg/dL. MT was performed using a stent retriever and/or a direct aspiration first pass

technique with the Penumbra system (Penumbra, Alameda, CA, USA) as the first choice. Devices were selected at the discretion of each operator. All clinical information was retrospectively collected from medical records.

### Statistical Analysis

Differences between groups were tested using Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous variables. To assess the independent contribution of each variable, we performed a multiple logistic regression analysis. A backward stepwise regression model including all variables was used, and OR and 95% CI were calculated. Variables that remained significant ( $p < 0.05$ ) after backward selection are presented. In addition, we conducted a sensitivity analysis to assess the difference in recanalization rates between different operators (operators with or without more than 5 years of experience in neuroendovascular therapy) and thrombectomy techniques (techniques using a stent retriever only or other techniques). All analyses were conducted using EZR [15] (version 1.33; Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, EZR is a modified version of R Commander designed to add statistical functions frequently used in biostatistics.

## Results

The mean age of the patients was 79 years, and 55 (46.2%) were female and 64 (53.8%) were male. Table 1 shows the demographic and clinical characteristics of patients with successful and unsuccessful recanalization. Successful recanalization was achieved in 88 patients (73.9%). In the univariate analysis, female sex (38.6 vs. 67.7%,  $p = 0.007$ ), a history of hypertension (53.4 vs. 83.9%,  $p = 0.003$ ), and a longer time from groin puncture to recanalization (median 75 vs. 124 min,  $p < 0.001$ ) were significantly associated with unsuccessful recanalization. Although the difference was not significant, patients with unsuccessful recanalization tended to be younger (median 81 vs. 75 years,  $p = 0.17$ ) and had occlusion of more distal vessels (M2–3 segment of the MCA, 23.9 vs. 38.7%,  $p = 0.16$ ), a longer time from stroke onset to admission (median 124 vs. 153 min,  $p = 0.12$ ), and a lower frequency of cardioembolism (72.7 vs. 54.8%,  $p = 0.076$ ). The multivariate analysis showed that female sex (OR 3.18; 95% CI 1.12–9.02,  $p = 0.030$ ), a history of hypertension (OR 4.84; 95% CI 1.32–17.8,  $p = 0.018$ ), M2–3 occlusion (OR 4.26; 95% CI 1.36–13.3,  $p = 0.013$ ), and the time from groin puncture to recanalization (per 10-min increase, OR 1.22; 95% CI 1.09–1.37,  $p < 0.001$ ) were independently associated with unsuccessful recanalization (Table 2). All sensitivity analyses showed a similar association between these 4 factors and unsuccessful recanalization in each patient group (online suppl. Tables 1–4; for all online suppl. material, see [www.karger.com/doi/10.1159/000503001](http://www.karger.com/doi/10.1159/000503001)).

## Discussion

This study's findings suggested that female sex, a history of hypertension, occlusion of distal vessels, and a longer procedure time are significant predictors of unsuccessful recanalization. Previous reports have shown that occlusion at more proximal sites in anterior circulation is associated with successful recanalization [5, 6], which is consistent with our results. Longer procedure times seem to be the result of technical difficulties during MT and not a cause of unsuccessful recanalization. To the best of our knowledge, this is the first study to

**Table 1.** Demographic and clinical characteristics of the patients

	All (n = 119)	Successful recanalization (n = 88)	Unsuccessful recanalization (n = 31)	p value
Age, years	79 (70–84.5)	81 (71–85)	75 (69–84)	0.17
Females	55 (46.2)	34 (38.6)	21 (67.7)	0.007
Medical history				
Ischemic stroke or TIA	27 (22.7)	21 (23.9)	6 (19.4)	0.80
Coronary artery disease	12 (10.1)	9 (10.2)	3 (9.7)	>0.99
Hypertension	73 (61.3)	47 (53.4)	26 (83.9)	0.003
Diabetes mellitus	24 (20.2)	17 (19.3)	7 (22.6)	0.80
Dyslipidemia	28 (23.5)	22 (25.0)	6 (19.4)	0.63
Atrial fibrillation	54 (45.4)	41 (46.6)	13 (41.9)	0.68
Smoking	46 (38.7)	35 (39.8)	11 (35.5)	0.67
Antiplatelet agents	25 (21.0)	20 (22.7)	5 (16.1)	0.61
Anticoagulants	29 (24.4)	20 (22.7)	9 (29.0)	0.48
BMI	22.4 (20.0–24.7)	22.5 (20.1–24.7)	21.5 (19.6–24.5)	0.54
Prestroke mRS	0 (0–3)	0 (0–3)	0 (0–2)	0.93
Systolic blood pressure, mm Hg	159 (141–171)	159 (140–171)	160 (143–168)	0.97
Initial NIHSS	19 (14–23.5)	19 (14–24)	19 (15.5–22)	0.76
DWI-ASPECTS	7 (5–8)	7 (5–9)	6 (5.3–7.8)	0.48
Occluded vessel				
CCA, ICA, or M1	86 (72.3)	67 (76.1)	19 (61.3)	0.16
M2–3	33 (27.7)	21 (23.9)	12 (38.7)	0.16
Treatment with intravenous alteplase	46 (38.7)	34 (38.6)	12 (38.7)	>0.99
Thrombectomy procedure				
Stent retriever only	61 (51.3)	43 (48.9)	18 (58.1)	0.41
Aspiration only	35 (29.4)	28 (31.8)	7 (22.6)	0.37
Both	21 (17.6)	15 (17.0)	6 (19.4)	0.79
Time from onset to admission, min	130 (72–239)	124 (66–222)	153 (86–271)	0.12
Time from admission to puncture, min	73 (60–97)	73 (60–94)	68 (61–110)	0.84
Time from puncture to recanalization, min	88 (57–133)	75 (50–108)	124 (103–159)	<0.001
Stroke subtype				
Cardioembolism	81 (68.1)	64 (72.7)	17 (54.8)	0.076
Large-artery atherosclerosis	13 (10.9)	9 (10.2)	4 (12.9)	0.74
Other determined etiology	5 (4.2)	3 (3.4)	2 (6.4)	0.60
Undetermined etiology	20 (16.8)	12 (13.6)	8 (25.8)	0.16

Data are presented as medians (IQR) or numbers (%). Differences between the groups were tested using Fisher's exact tests for categorical variables and the Mann-Whitney U test for continuous variables. Successful recanalization indicates mTICI 2b or 3. Unsuccessful recanalization indicates mTICI 0–2a. TIA, transient ischemic attack; mRS, modified Rankin scale; NIHSS, National Institute of Health Stroke Scale; DWI-ASPECTS, Alberta Stroke Program Early Computed Tomography Score for Diffusion-Weighted Imaging; CCA, common carotid artery; M1, M1 segment of the MCA; M2–3, M2 or M3 segment of the MCA.

**Table 2.** Backward stepwise multivariate logistic regression analysis for predictors of unsuccessful recanalization

	OR (95% CI)	p value
Female	3.18 (1.12–9.02)	0.030
Hypertension	4.84 (1.32–17.8)	0.018
M2–3 occlusion	4.26 (1.36–13.3)	0.013
Puncture to recanalization per 10-min increase	1.22 (1.09–1.37)	<0.001

M2–3, M2 or M3 segment of the MCA.

demonstrate the significance of sex differences and hypertension as predictors of unsuccessful recanalization.

Hypertension has been reported to be associated with a high prevalence of elongated and tortuous vessels [10, 16], which often make navigating the catheter to the target vessel difficult. We speculate that this is how hypertension is related to unsuccessful recanalization. Another possible explanation is that hypertension is strongly associated with arterial stiffness [17]. A previous study reported that increased arterial stiffness was associated with a poor collateral flow in large vessel occlusion [18], and pretreatment poor collateral flow was a predictor of unsuccessful recanalization during endovascular therapy for acute ischemic stroke [19]. There are few previous reports showing the relationship between hypertension and unsuccessful recanalization. Ribo et al. [10] reported that hypertension was significantly associated with difficult carotid access. Baek et al. [12] reported that hypertension was significantly associated with MT failure. Why hypertension was found to be related to unsuccessful recanalization in these 2 studies and not in other studies is not known. We speculate that it might be attributable to the age of the patient populations; the mean age in the 2 studies was relatively high at over 70 years, and our cohort was significantly older at a mean age of 79 years. Hypertension might be more strongly associated with elongated/tortuous vessels and arterial stiffness in older patients because they would have had hypertension for a longer period of time, and thus vessel wall damage caused by hypertension would be more critical.

As for differences according to patients' sex, previous studies had revealed that women with ischemic stroke have worse functional outcomes than men [20], although no compelling explanations have yet been published. The Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke study, i.e., a meta-analysis of the first 5 positive randomized controlled trials of MT, showed no differences in treatment effect between women and men [1]. However, whether the treatment effect would differ in nonclinical trial populations remains unknown. One study showed that, among patients undergoing MT for acute ischemic stroke, women had worse functional outcomes at 90 days, but there was no difference in recanalization rate [21]. Another study showed that female sex was independently associated with unsuccessful recanalization, but the underlying reason was not discussed [9].

Why the recanalization rates were low among the women in our study is unknown. One possible explanation is the smaller vessel diameter. The mean diameters of the ICA and the MCA are significantly larger in men than in women [22]. The relationship between arterial diameter and procedural success or failure has been previously studied in extracranial vascular disease. Hong et al. [23] reported that smaller diameters of the external iliac artery and the target lesion artery were independent predictors of procedural failure or vessel-specific complications in endovascular treatment of iliac artery disease. It is possible that a smaller vessel diameter is also related to procedural failure during intracranial endovascular therapy. Another explanation is that there may be sex-based differences in coagulation and fibrinolysis. A previous study reported significantly higher levels of plasminogen activator inhibitor-1 in women with acute stroke compared to men [24]. High plasminogen activator inhibitor-1 levels increase coagulation activities and reduce tPA-mediated plasmin production [25], which may lead to a reduced recanalization rate in women during MT, particularly when intravenous thrombolysis is performed.

This study has several limitations. First, this was a retrospective, single-center study with a small number of patients. Further prospective multicenter studies are needed to confirm our preliminary results. Second, pathological findings in the thrombus were not examined. Pathological characteristics might be associated with the recanalization rate. For example, an erythrocyte-rich thrombus was reported to be soft and deformable, which might make thrombectomy easier [9]. To further investigate predictors of recanalization, future studies should include a pathological examination.

In conclusion, this study showed that female sex and a history of hypertension might be associated with unsuccessful recanalization in MT for anterior circulation acute ischemic stroke. Further prospective studies are needed to fully evaluate predictors of recanalization, which may help to develop improved thrombectomy strategies.

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None.

### Statement of Ethics

The study protocol complied with the Declaration of Helsinki and was approved by the Ethics Committee of the Kawasaki Medical School Hospital. The procedures complied with institutional guidelines. Given the retrospective enrollment, patient consent for participation was waived.

### Disclosure Statement

The authors have no conflict of interests to declare.

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None.

### Author Contributions

Toshiaki Goda designed this study and wrote the initial draft of this paper. Takaya Kitano, Shunji Matsubara, and Yoshiki Yagita contributed to the analysis and interpretation of data and assisted in the preparation of this paper. All other authors contributed to data collection and interpretation and critically reviewed this paper. All of the authors approved the final version of this paper and agree to be accountable for all aspects of this work in ensuring that questions related to the accuracy and integrity of any part of this work are appropriately investigated and resolved.

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