The Claw Sign: An angiographic Predictor of Recanalization After Mechanical Thrombectomy for Cerebral Large Vessel Occlusion

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Background: Mechanical thrombectomy undoubtedly improves functional outcomes for patients with acute ischemic stroke. Although we have observed occlusion sites that protrude proximally into the vessel on angiography, termed the "claw sign," we have been unable to state its clinical significance. In this study, we aimed to determine whether the presence of a claw sign was related to recanalization success after mechanical thrombectomy. *Materials and Methods:* We retrospectively included 73 consecutive patients treated for acute cerebral large vessel occlusion by mechanical thrombectomy between January 2014 and December 2017. The angiographic claw sign was defined as a thrombus that protruded proximally by more than half the diameter of the parent artery. Claw sign positivity, clinical and etiological features, and outcomes were compared between groups with and without recanalization. *Results:* The claw sign was observed in 29 of 73 (40%) patients and was positive significantly more frequently in those with recanalization (50.0%) than in those without recanalization (5.9%) ($P < .01$). By multivariate analysis, the claw sign was the only pretreatment parameter to predict successful recanalization (odds ratio, 12.50; 95% confidence interval, 1.50-103.00; $P = .019$). *Conclusions:* The presence of the claw sign might predict successful recanalization in patients undergoing mechanical thrombectomy for large vessel occlusion.

Key Words: Mechanical thrombectomy—angiography—recanalization—large vessel occlusion

Introduction

In 2015, five randomized clinical trials demonstrated a clear advantage for using mechanical thrombectomy to treat cerebral large vessel occlusion, establishing the procedure as the new standard of care.[1-5] Since then, the recanalization rate for occluded arteries has continued to improve, reaching over 80% with the use of stent retrievers or large-bore aspiration catheters.[6,7] A high recanalization rate is directly linked to better functional outcomes and is the key objective of mechanical thrombectomy.[8] In several studies, findings on computed tomography(CT) or magnetic resonance imaging (MRI) were reported to predict recanalization and favorable outcomes after thrombectomy. However, these failed to report the intraoperative angiographic findings related to recanalization. Consoli et al[9] showed that the angiographic phenotype of the occlusion site might be associated with differences in recanalization rates. To date, though, there is no clear relationship among the angiographic findings of the occlusion site and the total

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recanalization rate, demographic characteristics, and stroke subtypes. We have previously identified an angiographic finding of the occlusion site that presents as a convexity that protrudes to the proximal side in the vessel. We termed this the "claw sign" because its appearance is that of a crab's claw.

In this study, our aim was to investigate whether the presence of the claw sign was an independent prognostic factor for successful recanalization in patients undergoing mechanical thrombectomy for large vessel occlusion.

Materials and methods

Study Design

We retrospectively examined patients who underwent mechanical thrombectomy for acute occlusion of a proximal intracranial artery at our hospital between January 1, 2014, and December 31, 2017. Arteries considered suitable for inclusion were the internal carotid artery, the proximal middle cerebral artery, and the vertebral or basilar artery. The study was approved by the relevant local ethics committee and consent was obtained from participants.

All patients were evaluated by experienced neurologists and neurosurgeons and were diagnosed by MRI or MR angiography. The eligibility criteria for thrombectomy were an Alberta Stroke Program Early CT Score greater than equal to 6 on diffusion-weighted imaging and the presence of large vessel occlusion. We did not deny thrombectomy based on neurological deficit severity according to the National Institute of Health Stroke Scale score.

Data Collection and Outcomes

After mechanical thrombectomy, results were assessed according to the Thrombolysis in Cerebral Infarction grading scale[10] as follows: 0-2a for no recanalization and 2b-3 for recanalization. On this basis, the study population was divided into a recanalization group and a no recanalization group. We compared demographic, clinical, and radiological characteristics between the groups. Functional outcome was evaluated by the modified Rankin Scale (mRS) scores at 90 days (0-2 = a good outcome; >2 = a bad outcome). We determined stroke subtype and mechanism on the basis of National Institute of Neurological Disorders and Stroke classification of cerebrovascular diseases[11] using 12 channel electrocardiogram, echocardiography, 24-hour electrocardiogram monitoring, carotid ultrasonography, and MRI scans.

Vascular risk factors were recorded for each patient and defined as follows: (1) hypertension, as a history of antihypertensive drug use, a systolic blood pressure of ≥140 mmHg, or a diastolic blood pressure of greater than equal to 90 mmHg at hospital discharge; (2) diabetes mellitus, as current hypoglycemic drug use, a random glucose level of greater than equal to 200 mg/dL, or a glycosylated hemoglobin level of greater than equal to 6.5% on admission were observed; (3) hyperlipidemia, as a history of antihyperlipidemic drug use, a serum total cholesterol level of greater than equal to 220 mg/dL, or a low-density lipoprotein cholesterol level of greater than equal to 140 mg/dL.

Claw Sign Definition

The occlusion site was evaluated angiographically before passage of the treatment device. At this point, we defined the claw sign as contrast morphology of the occlusion site in which a convexity protruded to the proximal side with a protrusion length that was more than half the arterial vessel diameter (Fig 1). The claw sign was considered positive if it was observed in either anterior–posterior or lateral views on digital subtraction angiography, using a biplane Philips Allura Clarity machine (Philips Healthcare, Best, the Netherlands).

Procedure for Mechanical Thrombectomy

Mechanical thrombectomy was performed either alone or with intravenous recombinant tissue plasminogen activator, depending on the site and time since occlusion. According to our institutional protocol, patients eligible for intravenous recombinant tissue plasminogen activator were given 0.6 mg/kg within 4.5 hours of onset.[12] A stent retriever, an aspiration catheter, or both were used for mechanical thrombectomy. The retrievers used during the study period in our institution were the Trevo (Stryker, Kalamazoo, MI), the Solitaire FR (Covidien, Irvine, CA), the Revive (Codman

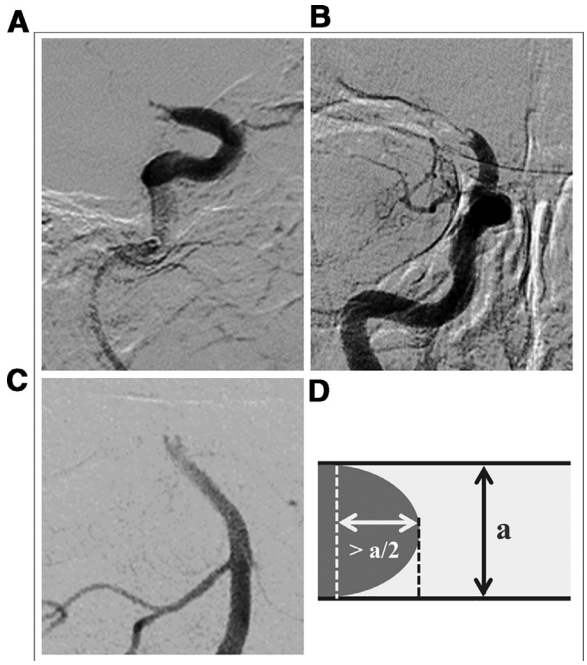

Figure 1. *Case examples of positive claw signs. The claw sign observed in internal carotid artery by lateral view (A) and anterior-posterior view (B) on digital subtraction angiography. The claw sign observed in the basilar artery (C). Claw sign positivity is defined as thrombus that protrudes by more than half of the diameter,* a, *of the parent artery (D).*

endovascular, Raynham, MA), or the Merci (Stryker). Only the Penumbra (Penumbra, Alameda, CA) aspiration catheter was used during this period; it was used either in a direct aspiration first-pass technique or in combination with the use of a stent retriever.

Tandem occlusion referred to simultaneous proximal extracranial occlusion in conjunction with a downstream intracranial occlusion (eg, terminal internal carotid or middle cerebral artery). In case of tandem occlusion, the claw sign was evaluated only in the intracranial distal occlusion site. Either an anterograde approach (ie, balloon angioplasty, stenting, and mechanical thrombectomy) or a retrograde approach (ie, balloon angioplasty, mechanical thrombectomy, with no stenting) was used. The endovascular approach applied in these cases was selected by the operator.

Statistical Analysis

Results are expressed as means ± standard deviations or as medians (minimum−maximum) for quantitative variables and as counts and percentages for categorical variables. Bivariate parametric tests (χ^2 or Mann-Whitney *U*) were used for group comparisons. All statistical tests were two-sided, and the significance (*P*) level was set at 0.05, unless stated otherwise. All statistical analyses were performed with SPSS Statistics version 20.0 software package (IBM Corporation, Tokyo, Japan). We input pretreatment variables with *P* values of less than .20 from the univariate analyses in a multivariate analysis, removing factors with higher *P* values that might affect each other. The results of multivariate analysis are expressed as adjusted odds ratios and 95% confidence intervals.

Results

We retrospectively examined 73 patients (41 men and 32 women, age: 75.0 ± 10.9 years) who met our inclusion criteria. The Trevo, Solitaire FR, Revive, and Merci retrieval devices were used in 24, 13, 2, and 1 case, respectively. The Penumbra aspiration catheter was used in 51 cases. Recanalization was achieved in 56 (77%) patients. The baseline characteristics of the participants are summarized in Table 1.

Table 1. *Comparison of demographic, clinical, and radiological characteristics between patients with and without recanalization*

	Recanalization n = 56	No recanalization n = 17	*P* values
Age, years (mean)	74.3 ± 10.4	77.6 ± 12.7	.28
Sex, male, n (%)	33 (58.9)	8 (47.1)	.39
Medical history			
Past ischemic stroke, n (%)	12 (21.4)	4 (23.5)	1.00
Atrial fibrillation, n (%)	22 (39.3)	3 (17.6)	.10
Hypertension, n (%)	30 (53.6)	11 (64.7)	.42
Diabetes mellitus, n (%)	15 (26.8)	3 (17.6)	.54
Dyslipidemia, n (%)	7 (12.5)	4 (23.5)	.27
Smoking, n (%)	19 (33.9)	9 (52.9)	.16
Clinical findings			
Systolic BP, mmHg (mean)	150.9 ± 33.5	151.4 ± 25.7	.96
NIHSS score (median)	18 (1-40)	18 (3-25)	.66
IV rt-PA, n (%)	26 (46.4)	10 (58.8)	.42
O2P time, min (median)	247.2 (81-630)	251.6 (105-715)	.89
P2R time, min (median)	62.0 (15-240)	110.5 (52-158)	.021
Presence of claw sign, n (%)	28 (50.0)	1 (5.9)	<.01
Site of occlusion			
ICA, n (%)	23 (41.1)	10 (58.8)	.27
MCA M1, n (%)	22 (39.3)	7 (41.2)	1.00
MCA M2, n (%)	6 (10.7)	0 (0.0)	.36
VA/BA, n (%)	5 (8.9)	0 (0.0)	.58
Tandem occlusion, n (%)	8 (14.3)	0 (0.0)	.19
Stroke subtype			
LAA, n (%)	17 (30.4)	6 (35.3)	.77
CE, n (%)	36 (64.3)	9 (52.9)	.41
Other or unknown, n (%)	3 (5.4)	2 (11.8)	.33
Stroke mechanism			
Embolic stroke, n (%)	47 (83.9)	12 (70.6)	.29
mRS score of 0-2 at 90 days, n (%)	20 (35.7)	0 (0.0)	<.01

Abbreviations: BA, basilar artery; BP, blood pressure; CE, cardiogenic embolism; ICA, internal carotid artery; IV, intravenous; LAA, large artery atherosclerosis; NIHSS, National Institutes of Health Stroke Scale; MCA middle cerebral artery; mRS, modified Rankin Scale; O2P, onset-to-puncture; P2R, puncture-to-recanalization; rt-PA, recombinant tissue plasminogen activator; VA, vertebral artery.

Comparing the groups with and without recanalization, the puncture-to-recanalization times (62.0 minutes and 110.5 minutes, respectively; $P = .02$) and the mRS of 0-2 at 90 days (35.7% and 0%, respectively; $P < .01$) were more favorable. The claw sign was also present more frequently in the recanalization group than in the no recanalization group (50.0% and 5.9%, respectively; $P < .01$) (Table 1). When comparing the groups with and without the claw sign, the puncture-to-recanalization time was shorter in the group with the claw sign than in the group without the claw sign (53 minutes and 90 minutes, respectively; $P = .02$). The prevalence of atrial fibrillation (48.3% and 25.0%, respectively; $P = .04$), M2 occlusion of the middle cerebral artery (17.2% and 2.3%, respectively; $P = .03$) and embolic stroke (93.1% and 72.7%, respectively; $P = .04$) were significantly higher in the group with positive claw signs compared with the group without the claw sign (Table 2). By multivariate analysis, the presence of the claw sign was significantly associated with recanalization, with an odds ratio of 12.50 (95% confidence interval, 1.50-103.00; $P = .019$) (Table 3).

Discussion

This study provides the first analysis of the predictive value of the claw sign as an angiographic marker of recanalization in mechanical thrombectomy. Of note, there were significantly more cases with the claw sign in the recanalization group when compared with the no recanalization group. Also, when comparing the groups with and without the claw sign, the puncture-to-recanalization time was shorter in the group with a positive claw sign. Ensuring recanalization and early reperfusion are associated with improved functional outcomes after mechanical thrombectomy.[8,13] We have therefore demonstrated that the claw sign is an auspicious imaging marker of likely recanalization.

To predict recanalization and good functional outcomes based on preoperative image examination, the morphological features of thrombi and the expressive features of each imaging modality have been investigated. The presence of an association between thrombi with a high Hounsfield unit value on CT and successful recanalization has been reported, but is

Table 2. *Comparison of demographic, clinical, and radiological characteristics between patients with and without a positive claw sign*

	Claw sign positive n = 29	Claw sign negative n = 44	*P* values
Age, years	76.2 ± 10.4	74.3 ± 11.3	.48
Sex, male (%)	15 (51.7)	26 (59.1)	.54
Medical history (%)			
Past ischemic stroke	4 (13.8)	12 (27.3)	.17
Atrial fibrillation	14 (48.3)	11 (25.0)	.040
Hypertension	14 (48.3)	27 (61.4)	.27
Diabetes mellitus	7 (24.1)	11 (25.0)	.93
Dyslipidemia	4 (13.8)	7 (15.9)	1.00
Smoking	9 (31.0)	19 (43.2)	.30
Clinical findings			
Systolic BP, mmHg	150.6 ± 27.1	151.3 ± 34.6	.92
Presence of SVS, n (%)	16 (55.2)	18 (40.1)	.23
Pre-anticoagulants use, n (%)	8 (27.6)	4 (9.1)	.05
Pre-antiplatelets use, n (%)	2 (6.9)	7 (15.9)	.30
IV rt-PA, n (%)	16 (55.2)	20 (45.5)	.48
O2P time, min (median)	242.7 (81-575)	251.8 (105-715)	.74
P2R time, min (median)	53 (15-160)	90 (19-240)	.015
Site of occlusion			
ICA, n (%)	10 (34.5)	23 (52.3)	.16
MCA M1, n (%)	11 (37.9)	18 (40.9)	1.00
MCA M2, n (%)	5 (17.2)	1 (2.3)	.034
VA/BA, n (%)	3 (10.3)	2 (2.4)	.38
Tandem occlusion, n (%)	5 (17.2)	4 (9.1)	.47
Stroke subtype			
LAA, n (%)	7 (24.1)	16 (36.4)	.31
CE, n (%)	20 (69.0)	25 (56.8)	.33
Other or unknown, n (%)	2 (6.9)	3 (6.8)	1.00
Stroke mechanism			
Embolic stroke, n (%)	27 (93.1)	32 (72.7)	.036

Abbreviations: BA, basilar artery; BP, blood pressure; CE, cardiogenic embolism; ICA, internal carotid artery; IV, intravenous; LAA, large artery atherosclerosis; MCA middle cerebral artery; O2P, onset-to-puncture; P2R, puncture-to-recanalization; rt-PA, recombinant tissue plasminogen activator; SVS, susceptibility vessel sign; VA, vertebral artery.

Table 3. *Results of the multivariate analysis for the predictors of recanalization*

	OR	95% CI	*P* values
Presence of claw sign	12.50	1.50-103.00	.019
Tandem occlusion	2.81	0.27-28.80	.39
Atrial fibrillation	2.23	0.51-9.87	.29
No smoking	1.89	0.56-6.38	.30

Abbreviations: CI, confidence interval; OR, odds ratio.

controversial.[14-17] In other research, Bourcier et al[18] have reported that the recanalization rate after mechanical thrombectomy was higher in cases positive for the susceptibility vessel sign (SVS); but, Soize et al[19] reported that there was no association for recanalization, and that the recanalization rate actually decreased when the SVS was longer. More recent data indicate that the recanalization rates and functional outcomes after 3 months are better after using the stent retriever than after using contact aspiration in SVS-positive cases.[20]

A few studies have focused on the morphological features of thrombi on digital subtraction angiography. Consoli et al[9] classified the morphological phenotype of the occlusion site into regular and irregular. They showed that the stent retriever and contact aspiration methods produced different treatment outcomes depending on the thrombotic form. However, there was no mention of what caused the difference in thrombotic form, or indeed, what relationship the forms had with the stroke subtype. In our study, there were significantly more cases with a history of atrial fibrillation in the group with a positive claw sign. We also examined the relationship between the claw sign and stroke mechanisms. The embolic stroke, which included cardiogenic embolism, artery-to-artery embolism of large artery atherosclerosis, and embolism of another source, was significantly higher in the group with a positive claw sign. If spherical thrombus formed by embolic source moves to the occlusion site with keeping its shape, its protruding appearance resembles that of a crab's claw as an angiographic phenotype. It is also possible that the local blood pressure and fibrinolysis status at the occlusion site contribute to forming the conditions necessary for the claw sign to develop, but further investigation is necessary to investigate this possibility.

The claw sign tended to appear at the M2 segment of the middle cerebral artery in this study. When evaluating the claw sign, it is necessary that it is observed from the lateral direction with respect to the occluded artery path. The claw sign in the M2 segment can be observed in both anterior-posterior and lateral views on digital subtraction angiography, while the M1 segment is observed mainly on the anterior-posterior view. This may cause false negatives when detecting the claw sign in M1 segments. Although the claw sign in the internal carotid artery can be observed in both views, its detection may be difficult when the artery takes a particularly tortuous course (eg, in the carotid siphon). When the injection of the contrast medium was insufficient, there was also a possibility that the evaluation of occlusion site was insufficient.

The limitations of this study are that we included a small number of cases, that it was performed in a single center, and that we used a retrospective design. Further investigations are needed with more cases to validate our results. It was also problematic that the devices we used for mechanical thrombectomy were not unified. There were also cases where stent retrievers or aspiration catheters were used alone, or where an aspiration catheter was used to assist when using a stent retriever. Because we did not evaluate recanalization success by device type, further research is needed to determine whether the outcomes in cases with a positive claw sign are different with each device.

Conclusions

We have shown that a positive claw sign is related to successful recanalization after mechanical thrombectomy for patients with large vessel occlusion. The claw sign may be a novel angiographic predictor of recanalization.

Authors' Contributions

Y.Y. designed the project, analyzed the data, drafted the manuscript, and oversaw the project. N.Y., Y.K., M.K., and K.S. performed treatment procedure, interpreted the data and drafted the manuscript. Y.I. and Y.T. supervised this study.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jstrokecerebrovasdis.2019.03.007.

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