The claw sign predicts first-pass effect in mechanical thrombectomy for cerebral large vessel occlusion in the anterior circulation

Yuki Yamamoto¹, Nobuaki Yamamoto¹, Yasuhisa Kanematsu², Izumi Yamaguchi³, Manabu Ishihara¹, Takeshi Miyamoto³, Shu Sogabe², Kenji Shimada², Yasushi Takagi², Yuishin Izumi¹

Departments of ¹Clinical Neuroscience, ²Neurosurgery, Tokushima University, Tokushima, Japan.

E-mail: *Yuki Yamamoto - yuki.yamamoto412@gmail.com; Nobuaki Yamamoto - nobyamamoto521129@gmail.com; Yasuhisa Kanematsu - yasuhisa_kanematsu@yahoo.co.jp; Izumi Yamaguchi - blond007@peice@hotmail.com; Manabu Ishihara - isihara.manabu.2@tokushima-u.ac.jp; Takeshi Miyamoto - takeshi_edit@yahoo.co.jp; Shu Sogabe - c200001043@yahoo.co.jp; Kenji Shimada - s_kenji1032@yahoo.co.jp; Yasushi Takagi - yetakagi@tokushima-u.ac.jp; Yuishin Izumi - yizumi@tokushima-u.ac.jp

*Corresponding author:
Yuki Yamamoto,
Department of Clinical Neuroscience, Tokushima University, Tokushima, Japan.
yuki.yamamoto412@gmail.com

ABSTRACT

Background: Mechanical thrombectomy (MT) is an effective treatment for acute cerebral large vessel occlusion (LVO). Complete recanalization of vessels in a single procedure is defined as the first-pass effect (FPE) and is associated with good prognosis. In this study, angiographic clot protruding sign termed the "claw sign," was examined as candidate preoperative imaging factor for predicting the FPE.

Methods: We retrospectively analyzed data from 91 consecutive patients treated for acute LVO in the anterior circulation by MT between January 2014 and December 2019. The claw sign was defined as a thrombus that protruded proximally by more than half of the diameter of the parent artery. Radiological findings such as claw sign, clinical and etiological features, and outcomes were compared between groups with and without successful FPE. Multivariate analysis was conducted to evaluate perioperative factors associated with FPE.

Results: FPE was achieved in 26 of 91 (28.6%) patients and the claw sign was observed in 34 of 91 (37.4%) patients. The claw sign was significantly more frequent in the successful FPE group than in the failed FPE group (53.8% vs. 30.8%; P = 0.040). After the multivariate analysis, the claw sign was the only pretreatment parameter that could predict FPE (odds ratio, 2.67; 95% confidence interval, 1.01–7.06; P = 0.047).

Conclusion: The claw sign is an angiographic imaging factor that might predict FPE after MT for anterior circulation acute ischemic stroke.

Keywords: Acute ischemic stroke, Angiography, Claw sign, First pass, Mechanical thrombectomy

INTRODUCTION

As a result of recent major clinical trials, mechanical thrombectomy (MT) has been established as the standard treatment in patients with acute intracranial large vessel occlusion (LVO).¹ In recent years, achieving complete recanalization with a single procedure that does not require additional treatment has been defined as the first-pass effect (FPE) and has been shown to be associated with good functional prognosis.² FPE is considered to lead to good prognosis by
Yamamoto, et al.: Claw sign predicts first-pass effect in MT

Reducing procedural time and periprocedural complications such as arterial endothelial injury. FPE is currently the best angiographic goal in MT, and several procedural techniques are being developed to achieve it.\textsuperscript{[10,11,16,21]}

Zaidat \textit{et al.} reported that FPE was more likely to be obtained in cases with balloon guide catheter use and noninternal carotid artery (ICA) occlusion.\textsuperscript{[22]} However, there have been few subsequent reports on preoperative factors that predict FPE. Intraprocedural angiographic morphological characteristics of the clot at the occlusion site have been the focus of attention in recent years.\textsuperscript{[7]} Proximal protrusions of the thrombus, called the claw sign\textsuperscript{[20]} or clot meniscus sign,\textsuperscript{[4]} have been known to be useful in predicting recanalization and stroke subtype. The aim of this study was, thus, to investigate whether perioperative imaging findings, including claw sign, are predictive of FPE in patients with anterior circulation LVO treated by MT.

MATERIALS AND METHODS

Study design and data collection

We retrospectively examined 130 consecutive patients who underwent MT at our hospital from January 2014 to December 2019. During this period, 121 cases were treated for acute intracranial LVO in the ICA or proximal portion of the middle cerebral artery (MCA M1-2). After excluding patients with tandem occlusion and extensive infarction defined as Alberta Stroke Program Early Computed Tomography (CT) Score <6 on diffusion-weighted imaging, 91 patients were finally analyzed [Figure 1]. Vascular risk factors were recorded for each patient and defined as follows: (1) hypertension: a history of antihypertensive drug use, a systolic blood pressure of ≥140 mmHg, or a diastolic blood pressure of ≥90 mmHg at hospital discharge; (2) diabetes mellitus: current hypoglycemic drug use, a random glucose level of ≥200 mg/dL, or a glycosylated hemoglobin level of ≥6.5% at the time of admission.

Diagnosis of acute cerebral LVO was performed using magnetic resonance imaging (MRI). MT was performed either alone or with intravenous recombinant tissue plasminogen activator (IV-TPA), depending on the adaption. According to our institutional protocol, patients with eligibility for IV-TPA were administered this at a dose of 0.6 mg/kg within 4.5 h of onset.\textsuperscript{[24]} Either a stent retriever or aspiration catheter, or both, was used for MT by the choice of the operator. Balloon guiding catheters were used in all cases. After the procedure, recanalization results were assessed according to the modified Thrombolysis in Cerebral Infarction (mTICI) grading scale. In this study, FPE was defined as the achievement of mTICI 2c or 3\textsuperscript{[9]} with a single procedure pass regardless of device type, such as stent retriever, direct aspiration, or combination of them. Functional outcome was evaluated using the modified Rankin scale (mRS) scores at 90 days after onset. Additional clinical outcomes included National Institute of Health Stroke Scale (NIHSS) at discharge, hospitalization days. Symptomatic intracranial hemorrhage (ICH) was classified according to the second European-Australasian Acute Stroke Study classification,\textsuperscript{[13]} as any ICH with an increase of NIHSS ≥4 within 24 h.

Susceptibility vessel sign (SVS), two-layered SVS (TL-SVS), and claw sign were selected as candidates for perioperative imaging factors that predict FPE. SVS was defined as a hypointense signal exceeding the size of the contralateral arterial diameter on MRI T2*-weighted image in a vessel cistern. TL-SVS was defined as SVS with a low-intensity core and higher intensity signal around the core.\textsuperscript{[10,21]} The claw sign was defined as a contrast morphology of the occlusion site in which a convexity protruded to the proximal side with a protrusion length that was more than half of the arterial vessel diameter\textsuperscript{[24]} [Figures 2 and 3]. The claw sign was considered positive if it was observed in either the anterior-posterior or lateral views on digital subtraction angiography (DSA), using a biplane Philips AlluraClarity machine (Philips Healthcare, Best, the Netherlands). All imaging findings were retrospectively evaluated by a neurologist who was not informed of other patient information.

Statistical analyses

Results are expressed as means ± standard deviations or as medians (minimum-maximum) for quantitative variables and as count and percentages for categorical variables. Univariate analyses were performed with the Mann–Whitney U-test for continuous or ordinal variables and the χ\textsuperscript{2} test for categorical variables. A one-way analysis of variance was used to compare the difference of variables...
among the three groups (the Bonferroni correction was used as post hoc analysis). All statistical tests were two sided, and the significance ($P$) level was set at 0.05. Multivariate analysis was performed including non-ICA terminus occlusion as a known FPE predictor and preoperative factors with $P < 0.05$ obtained by univariate analysis. All statistical analyses were performed with SPSS 26.0 (IBM, Armonk, New York).

**RESULTS**

**Basic characteristics and clinical outcomes**

We included and analyzed data from 91 consecutive patients (50 females; mean age: $75.6 \pm 11.0$ years). The baseline characteristics of patients are summarized in Table 1. Overall, 28.1% (26/91) achieved FPE. Comparing the groups with and without FPE, female sex (73.1% vs. 47.7%; $P = 0.028$), not smoking (80.8% vs. 58.5%; $P = 0.044$), and the presence of claw sign (53.8% vs. 30.8%; $P = 0.040$) were significantly observed more often in the successful FPE group. The claw sign was positive in 37.4% (34/91) of all patients. Of these positive cases, 41.2% (14/34) of successful FPE cases and 88.2% (30/34) of final recanalization (mTICI >2b) were observed. There were no differences between the two groups in the presence of SVS and TL-SVS.

Procedural outcomes significantly demonstrated a smaller number of passes (median, 1 vs. 2; $P < 0.01$) and shorter puncture to reperfusion time (33 min vs. 76 min; $P < 0.01$) in the FPE group. Clinical outcomes showed a lower NIHSS at discharge (median, 0 vs. 8; $P < 0.01$) and a better mRS score at 90 days after onset (mRS 0–1, 57.7% vs. 29.2%; $P = 0.11$) in the FPE group [Table 2].

**Predictors of FPE**

The multivariate analysis included non-ICA terminus occlusion as a known FPE predictor and the preoperative factors (presence of claw sign, female sex, and not smoking) for which there were significant differences identified in the univariate analysis [Table 3]. Only the presence of claw sign was significantly associated with successful FPE, with an odds ratio of 2.67 (95% CI = 1.01–7.06; $P = 0.047$).
In this study, we selected SVS, TL-SVS, and claw sign as imaging candidates to predict FPE after MT for anterior circulation acute ischemic stroke. Univariate analysis showed that female sex, not smoking, and the presence of claw sign were significantly more frequently seen in the successful FPE group. From multivariate analysis in which non-ICA occlusion was added to these three factors, claw sign emerged as an independent predictor of FPE with an odds ratio of 2.67.

In recent years, several studies have described the morphological characteristics of clots observed on angiography during MT\textsuperscript{[3,4,11,19,24]} [Table 4]. Baik et al. examined 89 patients who underwent MT for acute basilar artery occlusion and reported a clot meniscus sign in 62.9%, with a higher successful recanalization rate (89.3%) and successful FPE rate (32.1%) in the clot meniscus sign-positive group than in the negative group.\textsuperscript{[4]} The judgment of the clot meniscus sign is based on the macroscopic subjectivity, the definition of claw sign uses a proximal protrusion of more than half of the diameter of the mother vessel as an objective index. There are small differences, however, both can be considered equivalent in essence. In our study, successful recanalization rate (88.1%) and successful FPE rate (41.2%) in the claw sign-positive group were similarly high, and the positive claw sign may be used as a predictor of procedural success. By contrast, the positive rate of claw sign in this study was 41.2%, which is lower than that in the previous report. One reason may be the difference in target occlusion vessels, including the ICA and MCA M1-2. When evaluating the clot morphology, it is necessary to observe the longitudinal axis of the target vessel from the lateral direction. This may cause false negatives when detecting the claw sign in tortuous vessels like the terminal ICA. The basilar artery, which runs along the craniocaudal axis of the body, can be observed in both anterior-posterior and lateral images of DSA, while the MCA M1 is usually observed only in anterior-posterior images. Although claw sign is a useful predictor of FPE, its detection requires evaluation of the occluded vessel from an appropriate angle.

Consoli et al. classified the morphological phenotype of the occlusion site in the M1 segment of the MCA into regular and irregular.\textsuperscript{[7]} Baik et al. reported that contact aspiration showed higher complete recanalization rates compared with a stent retriever in patients with the clot meniscus sign.\textsuperscript{[3]} These suggest that selecting treatment devices depending on the morphological features of the clot may improve recanalization rate and patients’ clinical outcomes. In our study, there was no difference in FPE

\begin{table}[ht]
\centering
\begin{tabular}{|l|c|c|c|}
\hline
 & \textbf{Successful FPE (n=26) (%)} & \textbf{No FPE (n=65) (%)} & \textbf{P} \\
\hline
Age, years & 77.9±9.1 & 74.6±11.7 & 0.21 \\
Sex, female & 19 (73.1) & 31 (47.7) & 0.028* \\
Past ischemic stroke & 6 (23.1) & 16 (24.6) & 0.88 \\
Coronary artery disease & 5 (19.2) & 11 (16.9) & 0.77 \\
Hypertension & 18 (69.2) & 33 (50.8) & 0.11 \\
Diabetes mellitus & 5 (19.2) & 15 (23.1) & 0.69 \\
Not smoking & 21 (80.8) & 38 (58.5) & 0.044* \\
Atrial fibrillation on the ECG & 12 (46.2) & 25 (38.5) & 0.50 \\
Baseline mRS score & 0 (0-5) & 0 (0-5) & 0.40 \\
Systolic blood pressure, mmHg & 153±27 & 153±32 & 0.98 \\
Diastolic blood pressure, mmHg & 89±16 & 84±19 & 0.32 \\
Heart rate/min & 88±22 & 80±20 & 0.10 \\
NIHSS on admission & 13.5 (2–31) & 17 (2–35) & 0.48 \\
IV-TPA & 12 (46.2) & 32 (49.2) & 0.79 \\
ASPECTS-DWI & 8.5 (6–11) & 9 (6–11) & 0.69 \\
TL-SVS & 12 (46.2) & 21 (32.3) & 0.22 \\
SVS & 15 (57.7) & 29 (44.6) & 0.26 \\
Claw sign & 14 (53.8) & 20 (30.8) & 0.040* \\
Occlusion vessel & & & \\
ICA & 9 (34.6) & 26 (40.0) & 0.88 \\
MCA M1 & 13 (50.0) & 29 (44.6) & \\
MCA M2 & 4 (15.4) & 10 (15.4) & \\
\hline
\end{tabular}
\caption{Baseline characteristics.}
\end{table}
Yamamoto, et al.: Claw sign predicts first-pass effect in MT

Table 2: Clinical outcomes.

|                      | Successful FPE (n=26) (%) | No FPE (n=65) (%) | P       |
|----------------------|---------------------------|-------------------|---------|
| Number of passes     | 1 (1–1)                   | 2 (2–6)           | <0.01*  |
| mTICI grade          |                           |                   |         |
| 0                    | 0 (0.0)                   | 4 (6.2)           | <0.01*  |
| 1                    | 0 (0.0)                   | 3 (4.6)           |         |
| 2a                   | 0 (0.0)                   | 10 (15.4)         |         |
| 2b                   | 0 (0.0)                   | 23 (35.4)         |         |
| 2c                   | 3 (11.5)                  | 5 (7.7)           |         |
| 3                    | 23 (88.5)                 | 20 (30.8)         |         |
| Onset to puncture    | 228 (60–945)              | 235 (85–1135)     | 0.30    |
| time, min            |                           |                   |         |
| Puncture to          | 33 (13–105)               | 76 (22–160)       | <0.01*  |
| reperfusion time, min|                           |                   |         |
| Device for the first pass |                     |                   |         |
| Combination          | 6 (23.1)                  | 11 (16.9)         | 0.34    |
| Direct aspiration    | 8 (30.8)                  | 31 (47.7)         |         |
| Stent retriever      | 12 (46.2)                 | 23 (35.4)         |         |
| Etiology             |                           |                   |         |
| Cerebral embolism    | 20 (76.9)                 | 43 (66.2)         | 0.22    |
| Large artery         |                           |                   |         |
| atherosclerosis      | 2 (7.7)                   | 15 (23.1)         |         |
| Others               | 4 (15.4)                  | 7 (10.8)          |         |
| ICAD                 | 0 (0.0)                   | 16 (24.6)         | 0.004*  |
| sICH                 | 0 (0.0)                   | 3 (4.6)           | 0.56    |
| Hospital days        | 14.5 (4–30)               | 15 (2–36)         | 0.83    |
| NIHSS at discharge   | 0 (0–13)                  | 8 (0–42)          | <0.01*  |
| mRS score of 0–2 at 90 days |           | 15 (57.7)        | 0.011*  |

FPE: First-pass effect, ICAD: Intracranial atherosclerotic disease, NIHSS: National Institutes of Health Stroke Scale, mRS: Modified Rankin scale, mTICI: Modified thrombolysis in cerebral infarction, sICH: Symptomatic intracerebral hemorrhage

Table 3: Multivariate analysis of predictors for FPE.

|                        | Odds ratio | 95% CI   | P       |
|------------------------|------------|----------|---------|
| Positive claw sign     | 2.67       | 1.01–7.06| 0.047*  |
| Sex, female            | 2.39       | 0.62–9.20| 0.21    |
| Not smoking            | 1.56       | 0.37–6.63| 0.55    |
| Not ICAO               | 0.97       | 0.35–2.71| 0.95    |

CI: Confidence interval, ICAO: Internal carotid artery occlusion

There are some potential limitations of this study. First, this study was performed in a single center and followed a retrospective design. Further investigations are needed with a larger sample size to validate our results. The procedure technique and the devices were not unified in advance and were left to the operator. Finally, in some cases, the proximal end of the thrombus might not be accurately evaluated due to tortuous nature of the vessels or inadequate contrast injection.
CONCLUSION

The claw sign is an angiographic imaging factor that predicts FPE after MT for anterior circulation acute ischemic stroke. Angiographical clot protruding features at the occlusion site can predict treatment outcomes and stroke subtypes and may be useful in the future for procedure and device selection.

Ethics approval and consent to participate

The study protocol was approved by the local research ethics committee and consent for publication was obtained from all participants.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Al Kasab S, Almadidy Z, Spiotta AM, Turk AS, Chaudry MI, Hungerford JP, et al. Endovascular treatment for AIS with underlying ICAD. J Neurointerv Surg 2017;9:948-51.
2. Bai X, Zhang X, Yang W, Zhang Y, Wang T, Xu R, et al. Influence of first-pass effect on recanalization outcomes in the era of mechanical thrombectomy: A systematic review and meta-analysis. Neuroradiology 2021;63:795-807.
3. Baik SH, Jung C, Kim BM, Han K, Kim DJ. Clot meniscus sign: An angiographic clue for choosing between stent retriever and
contact aspiration in acute basilar artery occlusion. AJNR Am J Neuroradiol 2021;42:732-7.
4. Baik SH, Kim JW, Kim BM, Kim DJ. Significance of angiographic clot meniscus sign in mechanical thrombectomy of basilar artery stroke. J Neurointerv Surg 2020;12:477-82.
5. Bourcier R, Derraz I, Bracard S, Oppenheim C, Naggar O. Two-layered susceptibility vessel sign and high overestimation ratio on MRI are predictive of cardioembolic stroke. AJNR Am J Neuroradiol 2019;40:65-7.
6. Bourcier R, Hassen WB, Soize S, Roux P, Labreuche J, Kyheng M, et al. Susceptibility vessel sign on MRI predicts better clinical outcome in patients with anterior circulation acute stroke treated with stent retriever as first-line strategy. J Neurointerv Surg 2019;11:328-33.
7. Consoli A, Rosi A, Coskun O, Nappini S, di Maria F, Renieri L, et al. Thrombectomy for M1-middle cerebral artery occlusion: Angiographic aspect of the arterial occlusion and recanalization: A preliminary observation. Stroke 2018;49:1286-9.
8. Darcourt J, Withayasuk P, Vukasinovic I, Michelozzi C, Bellanger G, Guenego A, et al. Predictive value of susceptibility vessel sign for arterial recanalization and clinical improvement in ischaemic stroke. Stroke 2019;50:512-5.
9. Dargazanli C, Fahed R, Blanc R, Gory B, Labreuche J, Duhamel A, et al. Modified thrombolysis in cerebral infarction 2C/thrombolysis in cerebral infarction 3 reperfusion should be the aim of mechanical thrombectomy: Insights from the ASTER trial (contact aspiration versus stent retriever for successful revascularization). Stroke 2018;49:1189-96.
10. Di Maria F, Kyheng M, Consoli A, Desilles JP, Gory B, Richard S, et al. Identifying the predictors of first-pass effect and its influence on clinical outcome in the setting of endovascular thrombectomy for acute ischemic stroke: Results from a multicentric prospective registry. Int J Stroke 2021;16:20-8.
11. García-Bermejo P, Patro SN, Ahmed AZ, Al Rumaihi G, Akhtar N, Kamran S, et al. Baseline occlusion angiographic appearance on mechanical thrombectomy suggests underlying etiology and outcome. Front Neurol 2019;10:499.
12. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: A meta-analysis of individual patient data from five randomised trials. Lancet 2016;387:1723-31.
13. Hacke W, Kaste M, Fieschi C, von Kummer R, Davalos A, Meier D, et al. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). Second European-Australasian acute stroke study investigators. Lancet 1998;352:1245-51.
14. Kang DH, Kim YW, Hwang YH, Park SP, Kim YS, Baik SK. Instant recoclusion following mechanical thrombectomy of in situ thromboocclusion and the role of low-dose intra-arterial tirofiban. Cerebrovasc Dis 2014;37:350-5.
15. Kang DW, Jeong HG, Kim DY, Yang W, Lee SH. Prediction of stroke subtype and recanalization using susceptibility vessel sign on susceptibility-weighted magnetic resonance imaging. Stroke 2017;48:1554-9.
16. Liang W, Wang Y, Du Z, Mang J, Wang J. Intraprocedural angiographic signs observed during endovascular thrombectomy in patients with acute ischemic stroke: A systematic review. Neurology 2021;96:1080-90.
17. Liebeskind DS, Sanossian N, Yong WH, Starkman S, Tsang MP, Moya AL, et al. CT and MRI early vessel signs reflect clot composition in acute stroke. Stroke 2011;42:1237-43.
18. Maus V, Behme D, Kabbasch C, Borggreve J, Tsogkas I, Nikoubashman O, et al. Maximizing first-pass complete reperfusion with SAVE. Clin Neuroradiol 2018;28:327-38.
19. Mönch S, Boechk-Behrens T, Berndt M, Maegerlein C, Wunderlich S, Zimmer C, et al. Angiographic baseline proximal thrombus appearance of M1/M2 occlusions in mechanical thrombectomy. Clin Neuroradiol 2021;31:189-96.
20. Soize S, Batista AL, Regent CR, Trystram D, Tisserand M, Turc G, et al. Susceptibility vessel sign on T2* magnetic resonance imaging and recanalization results of mechanical thrombectomy with stent retrievers: A multicentre cohort study. Eur J Neurol 2015;22:967-72.
21. Tomasello A, Ribó M, Gramegna LL, Melendez F, Rosati S, Moreu M, et al. Procedural approaches and angiographic signs predicting first-pass recanalization in patients treated with mechanical thrombectomy for acute ischaemic stroke. Int Neuroradiol 2019;25:491-6.
22. Yamaguchi T, Mori E, Minematsu K, Nakagawara J, Hashi K, Saito I, et al. Alteplase at 0.6 mg/kg for acute ischemic stroke within 3 hours of onset: Japan alteplase clinical trial (J-ACT). Stroke 2006;37:1810-5.
23. Yamamoto N, Satomi J, Tada Y, Harada M, Izumi Y, Nagahiro S, et al. Two-layered susceptibility vessel sign on 3-tesla T2*-weighted imaging is a predictive biomarker of stroke subtype. Stroke 2015;46:269-71.
24. Yamamoto Y, Yamamoto N, Kanematsu Y, Korai M, Shimada K, Izumi Y, et al. The claw sign: An angiographic predictor of recanalization after mechanical thrombectomy for cerebral large vessel occlusion. J Stroke Cerebrovasc Dis 2019;28:1555-60.
25. Zaidat OO, Castonguay AC, Linfante I, Gupta R, Martin CO, Holloway WE, et al. First pass effect: A new measure for stroke thrombectomy devices. Stroke 2018;49:660-6.

How to cite this article: Yamamoto Y, Yamamoto N, Kanematsu Y, Yamaguchi I, Ishihara M, Miyamoto T, et al. The claw sign predicts first-pass effect in mechanical thrombectomy for cerebral large vessel occlusion in the anterior circulation. Surg Neurol Int 2022;13:72.