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AJNR Am J Neuroradiol published online 11 February 2021
<http://www.ajnr.org/content/early/2021/02/11/ajnr.A6989>

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ABSTRACT

BACKGROUND AND PURPOSE: In acute ischemic stroke, the negative susceptibility vessel sign on T2*-weighted images traditionally highlights fibrin-rich clots, which are particularly challenging to remove. In vitro, fast stent retrieval improves fibrin-rich clot extraction. We aimed to evaluate whether the speed of stent retrieval influences the recanalization and clinical outcome of patients presenting with the negative susceptibility vessel sign.

MATERIALS AND METHODS: Patients were identified from a registry of patients with ischemic stroke receiving mechanical thrombectomy between January 2016 and January 2020. Inclusion criteria were the following: 1) acute ischemic stroke caused by an isolated occlusion of the anterior circulation involving the MCA (Internal Carotid Artery-L, M1, M2) within 8 hours of symptom onset; 2) a negative susceptibility vessel sign on prethrombectomy T2*-weighted images; and 3) treatment with a combined technique (stent retriever + contact aspiration). Patients were dichotomized according to retrieval speed (fast versus slow). The primary outcome was the first-pass recanalization rate.

RESULTS: Of 68 patients who met inclusion criteria, 31 (45.6%) were treated with fast retrieval. Patients receiving a fast retrieval had greater odds of first-pass complete (relative risk and 95% confidence interval [RR 95% CI], 4.30 [1.80–10.24]), near-complete (RR 95% CI, 3.24 [1.57–6.68]), and successful (RR 95% CI, 2.60 [1.53–4.43]) recanalization as well as greater odds of final complete (RR 95% CI, 4.18 [1.93–9.04]), near-complete (RR 95% CI, 2.75 [1.55–4.85]), and successful (RR 95% CI, 1.52 [1.14–2.03]) recanalization. No significant statistical differences in procedure-related serious adverse events, distal embolization, or symptomatic intracranial hemorrhage were reported. No differences were noted in terms of functional independence (RR 95% CI, 1.01 [0.53–1.93]) and all-cause mortality (RR 95% CI, 0.90 [0.35–2.30]) at 90 days.

CONCLUSIONS: A fast stent retrieval during mechanical thrombectomy is safe and improves the retrieval of clots with the negative susceptibility vessel sign.

ABBREVIATIONS: eTICI = extended TICI; ICA-L occlusion = internal carotid artery distal L-type occlusion; RR = relative risk; SVS = susceptibility vessel sign

In acute ischemic stroke, the susceptibility vessel sign (SVS) on T2*-weighted sequences is thought to highlight the red blood cells in the clot.^{1–3} Histopathologic correlations of retrieved

thrombi with MR imaging features showed that clots not visible on T2*-weighted images (negative SVS) contained a high proportion of fibrin,^{1,2} which makes them particularly firm and sticky,^{4,5} and thus very challenging to remove mechanically.^{5–7} Approximately 20% of patients receiving bridging therapy cannot achieve recanalization,^{7,8} possibly due, in part, to how difficult it is to tailor the retrieval technique to clot properties.⁹ Recent in vitro experiments have shown that fast retrieval of the clot using a combined technique (contact aspiration + stent retriever) can improve recanalization, especially with fibrin-rich clots.¹⁰ Currently, device manufacturers' instructions advise operators to withdraw stent retrievers slowly to avoid potential artery dissection or rupture. Yet, the effect of retrieval speed on mechanical thrombectomy success in vivo has yet to be explored. A fast retrieval may mobilize the clot suddenly, enhance clot wedging, and minimize loss of apposition during retrieval.¹⁰ The present

Received September 23, 2020; accepted after revision November 2.

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 Indicates article with online supplemental data.

 Indicates article with supplemental on-line videos.

<http://dx.doi.org/10.3174/ajnr.A6989>

study aimed to evaluate whether stent-retrieval speed influences recanalization rates and clinical outcome in patients presenting with negative SVS clots.

MATERIALS AND METHODS

Study Setting

Patients were identified from a registry of patients with ischemic stroke treated by mechanical thrombectomy between January 2016 and January 2020. Inclusion criteria for this retrospective review included the following:

1. A patient with an acute ischemic stroke caused by an isolated occlusion of the anterior circulation involving the MCA (Internal Carotid Artery-L, M1, M2) confirmed by MRA within 8 hours of symptom onset
2. A negative SVS on prethrombectomy MRI T2*-weighted images
3. Treatment with an aspiration + stent retriever technique (see “Thrombectomy Techniques”).¹¹⁻¹³

During the study period, mechanical thrombectomy was provided regardless of age, baseline NIHSS severity, or infarct size. Patients experienced either fast or slow stent retrieval (and a distal aspiration catheter), depending on the operator's discretion. Catheters and stent retrievers were standardized to reduce bias risk. The present report follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement guidelines.¹⁴

Collected Data

We collected demographic data, vascular risk factors, the NIHSS score at several time points (admission, 24 hours, discharge), admission blood glucose levels, stroke side, symptom onset to imaging and to groin puncture times, intravenous thrombolysis administration (bridging therapy), baseline imaging and angiographic variables, 24-hour imaging assessment, and 90-day mRS score. Functional independence was defined as mRS ≤ 2 . Hemorrhagic transformation was graded in line with the European Cooperative Acute Stroke Study (ECASS III).¹⁵ Symptomatic intracranial hemorrhage corresponded to any hemorrhagic transformation or subarachnoid hemorrhage responsible for an increase of ≥ 4 points on the NIHSS. Stroke etiology was determined in line with the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification.¹⁶

Imaging Protocol and Analysis

All prethrombectomy examinations were performed on a 3T unit (Magnetom Skyra; Siemens), with a protocol including at least DWI, FLAIR, T2*, and TOF-MRA sequences. The T2* sequence parameters were the following: TR = 658 ms, TE = 10 ms, flip angle = 20°, FOV = 220 × 220 mm, matrix size (reconstructed) = 282 × 352, and section thickness = 3 mm without a gap.

Images were anonymized and reviewed by 2 neuroradiologists (with 5 and 8 years of experience) blinded to clinical data in a consensus fashion. The SVS was defined as a hypointense signal on T2*-weighted images within a vascular cistern exceeding the size of the homologous contralateral arterial diameter.^{1-3,17-20} The SVS was classified as present or absent.

Thrombectomy Techniques

All patients were treated with a combined technique,¹¹⁻¹³ aiming to wedge the thrombus between a stent retriever (Solitaire 2/Platinum; Medtronic) and an aspiration distal catheter (ACE 64/68, Penumbra; Sofia Plus, MicroVention) connected to a pump or a syringe. The use of a balloon-guide catheter was optional. Depending on the operator's discretion, retrieval speed of the stent retriever + the distal aspiration catheter unit was fast or slow. Fast retrieval involved a strong and very quick movement to remove the stent retriever + the distal aspiration catheter unit in < 5 seconds (Supplemental Online Video 1); in contrast, slow retrieval was a smoother, uniform movement, lasting approximately 15 seconds (Supplemental Online Video 2). Stent retriever sizes were standardized at 4 × 20 mm or 4 × 40 mm for M1 or M2 occlusions and 6 × 20 mm for ICA-L occlusions. When possible, procedures were performed with the patient under conscious sedation rather than general anesthesia. The procedures were performed by 4 operators with 15 and 8 years' experience (slow retrieval) and 8 and 5 years' experience (fast retrieval).

Angiographic Evaluation

Two researchers reviewed blinded, anonymized angiographic records: no patient/procedural data, imaging data, or stent retrieval speed was included. Researchers assessed occlusion site and anterior cerebral artery collaterals using the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology classification. Researchers then rated the first-pass and final angiographic result using the extended TICI (eTICI) score.²¹ Complete recanalization was defined as eTICI 3; near-complete recanalization, as eTICI $\geq 2c$; and successful recanalization, as eTICI $\geq 2b$. Procedure-related serious adverse events were also collected (artery perforation or dissection).

Outcome Measures

The primary outcome was the proportion of patients with first-pass complete, near-complete, and successful recanalization. Secondary outcomes included the occurrence of distal emboli, emboli in a new territory, procedure-related serious adverse events, the number of device passes, time from puncture to the end of thrombectomy, the degree of disability at 90 days (mRS), and all-cause mortality at 90 days.

We also evaluated the rate of hemorrhagic transformation, subarachnoid hemorrhage, symptomatic intracranial hemorrhage (defined by any hemorrhage responsible for an increase of ≥ 4 points on the NIHSS), and perforating artery lesions (defined as a subarachnoid hemorrhage restricted to the vicinity of the M1 segment) on 24-hour CT follow-up.

Statistical Analyses

Interreader agreement for eTICI grading was assessed using the Cohen κ coefficient. Discrepancies were resolved by consensus.

Distribution normality was assessed using the Shapiro-Wilk test. Continuous variables were described as mean [SD] or median and interquartile range and were compared using the Student *t* test or Mann-Whitney *U* test. Categorical variables were presented as counts and compared using the χ^2 or Fisher exact

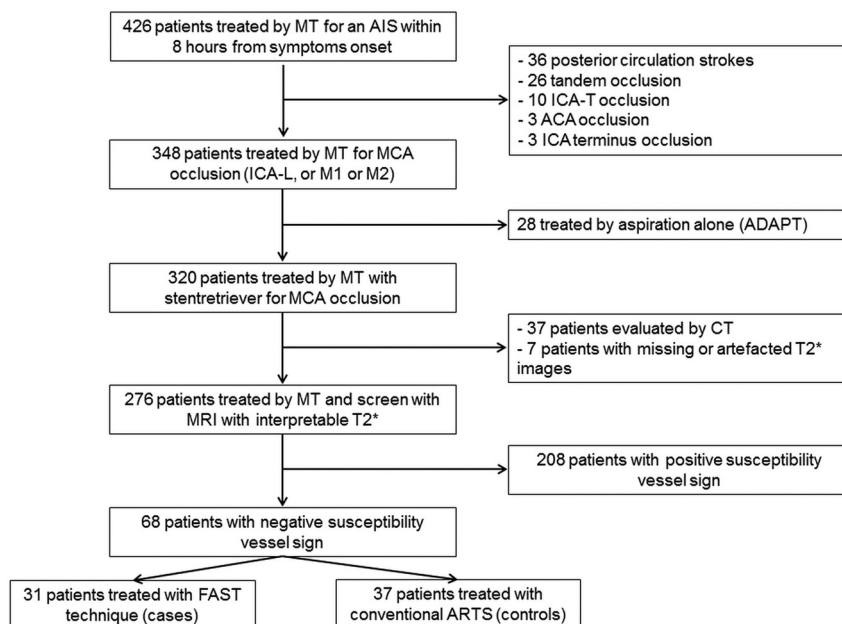


FIG 1. Study flow chart. AIS indicates acute ischemic stroke; MT, mechanical thrombectomy; ACA, anterior cerebral artery; ADAPT, a direct aspiration first pass technique.

test. The relative risk and 95% confidence intervals (RR 95% CIs) were calculated. A P value $< .05$ was considered statistically

Table 1: Baseline patient characteristics^a

Variables	Fast Retrieval (n = 31)	Slow Retrieval (n = 37)	P Value
Demographics			
Age (yr)	77 (57.5–83.7)	65 (49–75.7)	.10
Women	20 (64.5%)	19 (51.4%)	.28
Medical history			
Smoking	7 (22.6%)	13 (35.1%)	.26
Hypertension	19 (61.3%)	22 (59.5%)	.88
Diabetes mellitus	7 (22.6%)	8 (21.6%)	.92
Dyslipidemia	12 (38.7%)	12 (32.4%)	.59
Cardiovascular events	9 (29.0%)	11 (29.7%)	.95
Clinical data at presentation			
NIHSS	17 (13.25–19.75)	17 (14–20)	.94
Serum glucose level (mmol/L) ^b	7.5 (5.9–8.7)	6.8 (5.7–9.5)	.92
Intravenous thrombolysis	16 (51.6%)	26 (70.3%)	.12
Imaging data			
DWI-ASPECTS	6 (6–8)	7 (5–8.25)	.47
Left cerebral territory	10 (32.3%)	19 (51.4%)	.12
Occlusion site			.50
ICA-L	4 (12.9%)	5 (13.5%)	
M1	24 (77.4%)	25 (67.6%)	
M2	3 (9.7%)	7 (18.9%)	
Stroke etiology			.76
Large-artery atherosclerosis	4 (12.9%)	7 (18.9%)	
Cardioembolism	10 (32.3%)	11 (29.7%)	
Other known etiology	3 (9.7%)	2 (5.4%)	
Unknown	14 (45.2%)	17 (45.9%)	
Angiographic data			
Symptom onset to thrombectomy (min)	254.5 (184–295)	230.5 (189.5–310.5)	.90
Good collaterals (ASITN/SIR 3–4)	10 (32.3%)	18 (48.6%)	.37
Balloon-guided catheter	2 (6.5%)	3 (8.1%)	1

Note:—ASITN/SIR indicates American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology.

^a Continuous variables are described as median and interquartile range, and categoric variables, as number and percentage.

^b Missing data for 13 and 10 patients, respectively.

significant. Analyses were performed using MedCalc (Version 18.2, MedCalc Software).

RESULTS

Patients

Of 426 patients receiving mechanical thrombectomy during the study period, 68 patients met the inclusion criteria. Of the 68 patients, 31 (45.6%) were treated with fast retrieval, and 37 (54.4%), with slow retrieval (Fig 1). No significant differences in baseline demographic, clinical, and imaging data between the 2 groups were reported (Table 1). Interreader agreements ranged from moderate to excellent for first-pass and final angiographic assessments (Online Supplemental Data).

Primary Outcome

Patients receiving fast retrieval had greater odds of first-pass complete (RR 95% CI, 4.30 [1.80–10.24]), near-complete (RR 95% CI, 3.24 [1.57–6.68]), and successful (RR 95% CI, 2.60 [1.53–4.43]) recanalization than those receiving slow retrieval (Fig 2A). Patients receiving fast retrieval also had greater odds of final complete (RR 95% CI, 4.18 [1.93–9.04]), near-complete (RR 95% CI, 2.75 [1.55–4.85]), and successful (RR 95% CI, 1.52 [1.14–2.03]) recanalization than those receiving slow retrieval (Fig 2B).

Secondary Outcomes

No significant differences were found between fast and slow retrieval with regard to distal embolization, embolization in a new territory, procedure-related serious adverse events, thrombectomy duration, and the number of device passes (Table 2).

At 24 hours, follow-up CT was available for 31 (100%) patients receiving fast retrieval and 35 patients (94.6%) receiving slow retrieval. There were no differences in terms of hemorrhagic transformation, subarachnoid hemorrhage, and symptomatic intracranial hemorrhage between the 2 groups (Table 2).

At 90 days, there were no differences in terms of functional independence (RR 95% CI, 1.01 [0.53–1.93])

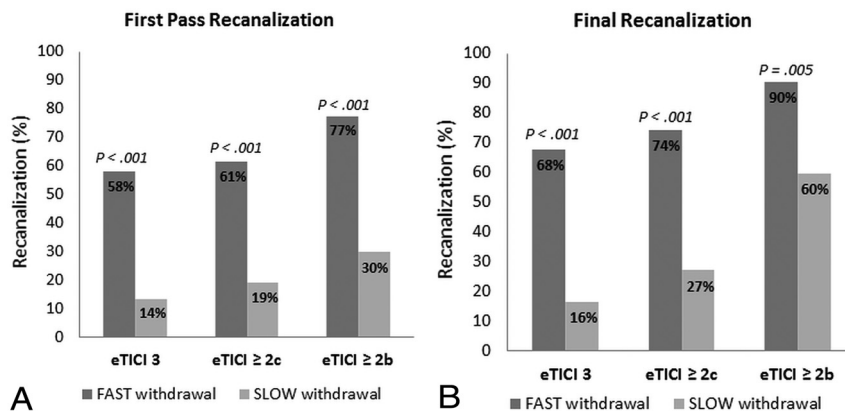


FIG 2. A, First-pass recanalization rates according to fast and slow retrieval. B, Recanalization rates according to fast and slow retrieval.

Table 2: Secondary outcomes^a

	Fast Retrieval (n = 31)	Slow Retrieval (n = 37)	P Value
Angiographic outcomes			
Distal embolization	4 (12.9%)	9 (24.3%)	.35
Embolization in a new territory	0 (0%)	3 (8.1%)	.24
Procedure-related SAE	2 (6.5%)	1 (2.7%)	.59
Thrombectomy duration (min)	29 (19–75.5)	44 (26.5–71.25)	.16
No. of passes	1 (1–2)	1 (1–3)	.16
One-pass thrombectomy	21 (67.7%)	19 (51.4%)	.22
Imaging outcomes at 24 h^b			
Hemorrhagic transformation			.48
None	18 (58.1%)	24 (68.6%)	
HI 1	3 (9.7%)	4 (11.4%)	
HI 2	6 (19.4%)	3 (8.6%)	
PH 1	2 (6.4%)	1 (2.8%)	
PH 2	2 (6.4%)	3 (8.6%)	
Subarachnoid hemorrhage	2 (6.4%)	3 (8.6%)	1
Symptomatic ICH	2 (6.4%)	2 (5.7%)	1
Perforating artery lesions	1 (3.2%)	1 (2.8%)	.60
Clinical outcome at 90 days			
Functional independence	11 (35.5%)	13 (35.1%)	.98
All-cause mortality	6 (19.4%)	8 (21.6%)	.82

Note:—SAE indicates serious adverse event; HI, hemorrhage infarction; PH, parenchymal hematoma; ICH, intracranial hemorrhage.

^a Continuous variables are described as median and interquartile range, and categorical variables, as counts. Functional independence is defined by an mRS ≤ 2 .

^b Missing data for 2 patients in the slow retrieval group.

and all-cause mortality (RR 95% CI, 0.90 [0.35–2.30]) (Table 2). Even after adjusting for common confounding variables (age, baseline NIHSS, DWI-ASPECTS, occlusion site, collateral status, left-sided infarction, and bridging therapy), a fast retrieval did not lead to better functional outcomes (OR 95% CI, 2.08 [0.47–9.15]; $P = .33$).

DISCUSSION

In patients with an acute occlusion involving the MCA and a negative SVS, a fast stent retrieval during thrombectomy led to a higher chance of first and final recanalization. The safety of a fast retrieval did not differ from that of conventional slow retrieval. However, this result did not translate into better functional

outcome in this small series of patients, a result likely due to the small sample of patients with wide selection criteria for mechanical thrombectomy.

The primary challenge for neuro-interventionists is the 20%–30% of thrombi resistant to current retrieval approaches.^{7,8} Among causes for recanalization failure, 1 reason may be the discrepancy between the thrombus mechanical properties and the device/technique used to remove it.^{7,9} Thrombus composition determines friction forces and adhesion to the vessel wall.⁷ A negative SVS corresponds to the presence of a fibrin-rich clot, which is particularly difficult to remove with mechanical approaches.^{6,17,18} Indeed, in vitro experiments demonstrated that such clots were firm and sticky, with higher friction coefficients and more difficulty in fitting into stent-retriever mesh.^{4,5} Moreover, the negative SVS is more frequently observed in patients with underlying intracranial atherosclerotic stenosis¹⁹ or atypical thrombi (such as infective endocarditis).²⁰

After clot is wedged, fast retrieval may mobilize the clot more suddenly and minimize apposition loss during retrieval by reducing time for device compression during its passage in tight curves. Indeed, other in vitro experiments demonstrated that removal efficacy was related to the ability of a device to maintain constant expansion and apposition in the retrieval path, especially in sharp vessel angles.⁵ Moreover, in an in vitro model, when one used a fast retrieval, the extraction of fibrin-rich clots was 4 times greater.¹⁰

This result was confirmed by our in vivo study in which reaching a complete first-pass recanalization (first-pass effect) was 4 times greater with a fast retrieval. Although a first-pass effect is infrequently obtained (20%–35% of patients), it is associated with improved clinical outcome, reduced adverse effects, and decreased mortality.²² Even so, achieving complete first-pass recanalization did not translate into better functional outcome in our study. This result may be due to a significant number of futile recanalizations that resulted from the wide range of patients selected to receive mechanical thrombectomy. Indeed, during the study period, mechanical thrombectomy was provided without regard for age, baseline NIHSS severity, or infarct size. Additionally, more than one-quarter of our population was older than 80 years of age, had baseline a NIHSS score of >20 , and DWI-ASPECTS of <5 .

On the other hand, a negative SVS is only seen in approximately 25% of patients (in our study as well as in the literature),¹⁷⁻²⁰ resulting in fewer patients in each group and, therefore, reducing the likelihood that we could detect any potential differences. Larger studies in carefully selected patients are necessary to confirm whether fast retrieval translates into better patient outcomes.

The major concern when removing a device from the intracranial arteries is the risk of vessel damage.²³ In a negative SVS, this is all the more important because a significant number of patients have underlying atherosclerosis.¹⁹ When one performs a fast retrieval, the effect of stretching forces on perforating arteries and intracranial plaques is unknown. However, in this study, we did not observe differences in terms of artery perforation or dissection and symptomatic intracranial hemorrhage. We observed 1 case in each group of subtle subarachnoid hemorrhage on the perforating artery side of the M1 segment, likely due to perforator rupture after being sheared off. Although reassuring, these results need to be confirmed in a larger patient sample.

Our study has potential limitations. First, a primary limitation is its retrospective character and monocentric design, which may have contributed to selection bias. The mechanical thrombectomy technique and devices were standardized to limit bias among operators. Also, the small sample size limits the interpretability of the results. Second, the clot burden, which can impact recanalization rates, was not evaluable in this study. This evaluation would have necessitated systematic contrast-enhanced MRA or a double-injection technique during DSA. Third, only 1 thrombectomy setup was evaluated (the combined technique);¹¹⁻¹³ thus, our results cannot translate to other techniques such as direct aspiration. Also, balloon-guided catheter use was left to the operator's discretion and was rarely used in this study (7.4% of the patients). Although proximal aspiration was always provided, the use of a balloon-guided catheter may reduce distal embolization and enhance recanalization.^{24,25}

Another limitation comes from the lack of a precise measure of the retrieval speed; however, we think an overlap in withdrawal times between the two groups was very unlikely to occur. Indeed, the differences between retrieval speeds were obviously conspicuous, and the operators of the slow group were concerned about the uncertainty of the risk of vascular damage with fast retrieval. Finally, during the study period, patient selection criteria were broad, leading to potential futile recanalization. This feature means that our study cannot draw clear conclusions with regard to functional outcome. Ideally, our results need confirmation with a larger sample of selected patients. In addition, having additional information about the per-pass histologic composition of the retrieved thrombus would improve our understanding of negative SVS clot behavior during mechanical thrombectomy.^{26,27}

CONCLUSIONS

A fast stent retrieval during mechanical thrombectomy is safe and enhances the retrieval of negative SVS clots. Larger studies are needed to confirm this result and evaluate the potential impact on functional independence.

Disclosures: Laurent Pierot—UNRELATED: Consultancy: Balt, MicroVention, Perflow Medical, phenox, Vesalio.

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