CMIK Available **Number of Stent Retriever Passes Associated With Futile Recanalization in Acute Stroke**

Jang-Hyun Baek, MD; Byung Moon Kim, MD; Ji Hoe Heo, MD; Hyo Suk Nam, MD; Young Dae Kim, MD; Hyungjong Park, MD; Oh Young Bang, MD; Joonsang Yoo, MD; Dong Joon Kim, MD; Pyoung Jeon, MD; Seung Kug Baik, MD; Sang Hyun Suh, MD; Kyung-Yul Lee, MD; Hyo Sung Kwak, MD; Hong Gee Roh, MD; Young-Jun Lee, MD; Sang Heum Kim, MD; Chang Woo Ryu, MD; Yon-Kwon Ihn, MD; Byungjun Kim, MD; Hong-Jun Jeon, MD; Jin Woo Kim, MD; Jun Soo Byun, MD; Sangil Suh, MD; Jeong Jin Park, MD; Woong Jae Lee, MD; Jieun Roh, MD; Byoung-Soo Shin, MD

Background and Purpose—Stent retriever (SR) thrombectomy has become the mainstay of treatment of acute intracranial large artery occlusion. However, it is still not much known about the optimal limit of SR attempts for favorable outcome. We evaluated whether a specific number of SR passes for futile recanalization can be determined.

Methods—Patients who were treated with a SR as the first endovascular modality for their intracranial large artery occlusion in anterior circulation were retrospectively reviewed. The recanalization rate for each SR pass was calculated. The association between the number of SR passes and a patient's functional outcome was analyzed.

Results—A total of 467 patients were included. Successful recanalization by SR alone was achieved in 82.2% of patients. Recanalization rates got sequentially lower as the number of passes increased, and the recanalization rate achievable by ≥5 passes of the SR was 5.5%. In a multivariable analysis, functional outcomes were more favorable in patients with 1 to 4 passes of the SR than in patients without recanalization (odds ratio [OR] was 8.06 for 1 pass; OR 7.78 for 2 passes; OR 6.10 for 3 passes; OR 6.57 for 4 passes; all P < 0.001). However, the functional outcomes of patients with ≥ 5 passes were not significantly more favorable than found among patients without recanalization (OR 1.70 with 95% CI, 0.42-6.90 for 5 passes, P=0.455; OR 0.33 with 0.02–5.70, P=0.445 for ≥6 passes).

Conclusions—The likelihood of successful recanalization got sequentially lower as the number of SR passes increased. Five or more passes of the SR became futile in terms of the recanalization rate and functional outcomes. (Stroke. 2018;49:2088-2095. DOI: 10.1161/STROKEAHA.118.021320.)

Key Words: stents ■ stroke ■ thrombectomy

tent retriever (SR) thrombectomy has been recommended as an endovascular treatment (EVT) for acute intracranial large artery occlusion.1 However, SR is ineffective in 20% to 30% patients.^{2,3} According to a recent review based on in vitro experiments, the likelihood of successful recanalization decreases as the number of SR passes (SRP#) increases.⁴ At

a certain point, another mechanical thrombectomy technique (eg, contact aspiration thrombectomy) or rescue modality can be required for rapid and successful recanalization.⁵⁻⁷ Thus, even when SR is the principal endovascular modality, it is necessary to set an optimal endovascular strategy for the best EVT result.

Continuing medical education (CME) credit is available for this article. Go to http://cme.ahajournals.org to take the quiz.

Received February 27, 2018; final revision received June 7, 2018; accepted July 2, 2018.

From the Department of Neurology, National Medical Center, Seoul, Korea (J.-H.B.); Department of Radiology, Severance Hospital Stroke Center (B.M.K., D.J.K.), Department of Neurology, Severance Hospital Stroke Center (J.-H.B., J.H.H., H.S.N., Y.D.K., H.P.), Department of Radiology, Gangnam Severance Hospital (S.H.S.), and Department of Neurology, Gangnam Severance Hospital (K.-Y.L.), Yonsei University College of Medicine, Seoul, Korea; Departments of Neurology (O.Y.B.) and Radiology (P.J.), Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; Department of Neurology, Keimyung University Dongsan Medical Center, Daegu, Korea (J.Y.); Department of Radiology, Pusan National University Yangsan Hospital, Korea (S.K.B., J.R.); Departments of Radiology (H.S.K.) and Neurology (B.-S.S.), Chonbuk National University Medical School and Hospital, Jeonju, Korea; Departments of Radiology (H.G.R.) and Neurology (J.J.P.), Konkuk University Hospital, Seoul, Korea; Department of Radiology, Hanyang University Hospital, Seoul, Korea (Y.-J.L.); Department of Radiology, CHA Bundang Medical Center, CHA University School of Medicine, Seongnam, Korea (S.H.K.); Department of Radiology, Kyung Hee University Gangdong Hospital, Seoul, Korea (C.W.R.); Department of Radiology, St. Vincent's Hospital, Catholic University School of Medicine, Suwon, Korea (Y.K.I.); Department of Radiology, Korea University Anam Hospital, Seoul (B.K.); Department of Neurosurgery, Kangdong Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Korea (H.J.-J.); Department of Radiology, Inje University Ilsan Paik Hospital, Korea (J.W.K.); Department of Radiology, Chung-Ang University Hospital, Seoul, Korea (J.S.B., W.J.L.); and Department of Radiology, Korea University Guro Hospital, Seoul (S.S.).

The online-only Data Supplement is available with this article at https://www.ahajournals.org/doi/suppl/10.1161/STROKEAHA.118.021320. Correspondence to Byung Moon Kim, MD, PhD, Department of Radiology, Severance Hospital Stroke Center, Yonsei University College of Medicine,

50-1 Yonsei-ro, Seodaemoon-gu, Seoul 03722, Republic of Korea. Email bmoon21@hanmail.net © 2018 American Heart Association, Inc.

An optimal endovascular strategy involving the SR thrombectomy procedure requires a breaking point—a specific time (1) to give up further SR attempts and switch to other rescue modalities for recanalization, or (2) that further treatment will not benefit the patient's outcome anymore. In terms of clinical outcome, the breaking point is fundamentally based on time; however, the SRP# can act as a surrogate breaking point marker for procedural time.⁸

In this study, we set out to determine the specific breaking point associated with futile recanalization in SR thrombectomy. We primarily evaluated the following hypotheses: (1) at a specific SRP#, the additional recanalization rate from further SR attempts is extremely low, and (2) at a specific SRP#, the patient's functional outcome is no longer more favorable than that of a patient without recanalization, even if recanalization is achieved.

Methods

The data that support the findings of this study are available from the corresponding author on reasonable request.

We retrospectively reviewed consecutive patients with acute stroke who underwent EVT in 16 comprehensive stroke centers between September 2010 and December 2015. All patients were originally identified based on the criteria as follows: (1) intracranial large artery occlusion in anterior circulation (intracranial internal carotid artery, M1, or proximal M2), (2) endovascular procedure with modern mechanical thrombectomy technique (SR and contact aspiration thrombectomy), (3) computed tomographic (CT) angiography performed to assess occlusion and collateral status, (3) age ≥18 years, (4) initial National Institutes of Health Stroke Scale score ≥ 4 , (5) time from onset to puncture ≤ 600 minutes, and (6) modified Rankin Scale score before qualifying stroke ≤1. All clinical and procedural data were obtained from the prospectively maintained registries of the participating hospitals. For this particular study, we included only patients with internal carotid artery and M1 occlusion who received SR as the first endovascular modality. The institutional review boards of all participating hospitals approved this study and waived the requirement of informed consent for study inclusion based on the retrospective study design.

SR Thrombectomy Procedure

For patients eligible for intravenous tPA (tissue-type plasminogen activator) treatment, the full dose of tPA (0.9 mg/kg) was administered. The SR thrombectomy procedures were performed under local anesthesia and according to common recommendations.⁵ An 8- to 9-F regular or balloon guiding catheter (BGC) was used. The use of a BGC depended on the protocol of each participating site. Two types of SR—Solitaire (AB or FR, Medtronic, Dublin, Ireland) and Trevo (XP or ProView, Stryker, Kalamazoo, MI)—were used for SR thrombectomy. No distal access catheter was used in the study population because it had not yet been introduced during the study period.

SR was delivered and then deployed over the thrombus with a 0.021 or 0.027-inch microcatheter. The SR was left deployed for a few minutes before retrieval. For retrieval, the balloon of the BGC was inflated, and then the SR and microcatheter were cautiously retrieved under constant aspiration with a 20- or 50-mL syringe through the BGC. Even in cases without a BGC, constant aspiration was mostly performed though the guiding catheter under the manual compression of the relevant common carotid artery. This process was repeated until a modified Thrombolysis In Cerebral Infarction (mTICI) grade of 2b or 3 was achieved. The timing to stop the SR attempts or switch to another endovascular modality was determined by the operator's judgment, considering the occlusion pathogenesis, clinical or patient condition, and so on.

Imaging Analysis

For imaging analyses, anonymized digital imaging and communication in medicine files depicting EVTs and noncontrast CT and CT angiography images performed before the endovascular procedure were sent to a core laboratory. Two neuroradiologists independently assessed the Alberta Stroke Program Early CT Score (ASPECTS) and collateral status. The ASPECTS was evaluated on 5-mm thickness noncontrast CT images. Each patient's collateral status was evaluated on 20-mm thickness maximum intensity projection images of single phase CT angiography. The collateral status was dichotomized as good and poor. For cases in which vessel markings were not seen in more than half of the affected middle cerebral artery territory, the collateral status was rated as poor.9 If vessel markings on the contralateral side were not well documented, the case was excluded for obscurity. Because the ASPECTS and collateral status were anonymized in different ways and evaluated separately, reviewers were blind to collateral status when evaluating ASPECTS and vice versa. Furthermore, reviewers who assessed ASPECTS and collateral status were blinded to clinical information of patients. The κ values for interrater reliability of the dichotomized ASPECTS (≤7 and >7) and collateral status (good and poor) were 0.657 and 0.875, respectively. 10,11 mTICI grades were evaluated by 2 independent neurointerventionalists in the core laboratory. 12 Those reviewers were blind to ASPECTS, collateral status, and clinical outcome. The k value of the dichotomized mTICI grades (0-2a and 2b-3) was 0.813. Successful recanalization was defined as achieving an mTICI grade 2b or 3 using only the SR. All discrepant cases for ASPECTS, collateral status, and mTICI grade were resolved by consensus.

Breaking Points

We chose the SRP# (the number of SR passes) to get successful recanalization as the primary breaking point. We used the SRP# as a surrogate marker of procedural time; it is easier to analyze than time because it is naturally segmented into fewer values than time, which needs to be arbitrarily divided for analysis. Also, the SRP# is an intuitive way to express procedural endurance. The times from puncture to recanalization (PTR) and from onset to recanalization (OTR) were defined as the secondary breaking point.

Statistical Analysis

First, to observe individual and accumulative yields by SR attempt, we calculated the recanalization rate for each SR pass. The SRP# was not regulated under a specific protocol; therefore, this calculation was performed only for patients with successful recanalization.

Second, to evaluate the specific SRP# that led to futile recanalization, we divided the patients into 2 groups: favorable and unfavorable outcome groups. Patient with an modified Rankin Scale ≤2 at 3 months after EVT were assigned to the favorable outcome group. The endovascular result was defined and grouped by considering both recanalization itself and the SRP#: no recanalization, successful recanalization by 1 SR pass, 2 passes, 3 passes, 4 passes, 5 passes, and ≥6 passes. We compared the endovascular results between the favorable and unfavorable outcome groups. Basic demographics, stroke risk factors, ASPECTS, collateral status, and symptomatic intracerebral hemorrhage were also compared (in the online-only Data Supplement). The Mann-Whitney U test, χ^2 test, and Fisher exact test were used for those comparisons. To determine the independent variables for a favorable outcome, variables with a P < 0.10 in the univariable analyses were entered into a multivariable analysis using binary logistic regression. In this process, we specifically considered whether a specific SRP# could be an independent cutoff point for an unfavorable outcome compared with cases without recanalization (the cutoff SRP# for futile recanalization).

Third, using that SRP# for futile recanalization, we also tried to find a specific time limit for futile recanalization. (1) Because the concept was based on the significant relationship between the SRP# and the time to recanalization (PTR and OTR), we first checked PTR

2090

times against the SRP# and calculated a correlation coefficient. We also performed the Jonckheere trend test and a linear regression analysis. (2) In a logistic regression analysis, we calculated the probability (with a 95% CI) of a favorable outcome at the cutoff SRP# for futile recanalization. A patient whose probability of a favorable outcome is below the calculated level might have a futile recanalization. So, we then compared the calculated probability with the probabilities derived from a regression analysis of PTR times. With this, we could inversely estimate a possible range of PTR times for futile recanalization. (3) Finally, we checked all PTR values in the range using 5-minute intervals to see whether they indicated futile recanalization. For the relevant value, a multivariable analysis was performed to verify that it is independently significant for futile recanalization. The same statistical analyses were also performed for OTR values using 10-minute intervals.

A P<0.05 was considered statistically significant for the 95% CIs. All statistical analyses were performed using R software (version 3.2.2, r-project.org).

Results

A total of 710 patients who met the identification criteria were reviewed. Among them, 467 patients (mean age, 67.3±12.4 years; male patients, 55.5%) were included in the study (Figure I in the online-only Data Supplement). Patients whose occlusion was far distal (M2, n=99) and those whose collateral status could not be determined because of inadequately visualized contralateral vessel markings (n=20) were excluded. We also excluded patients who were not first treated with SR (n=112) and those whose recanalization was achieved by a non-SR rescue modality (n=12). Median values of the initial National Institutes of Health Stroke Scale scores and ASPECTS were 15.0 (interquartile range, 12.0–19.0) and 8.0 (7.3–9.0), respectively. Eighty-two percent of patients had good collateral status. Median OTR time was 215.0 minutes (150.0–290.0 minutes).

Recanalization Rates According to the SRP#

Of the 467 patients, 384 (82.2%) had successful recanalization. Among patients with successful recanalization, the median SRP# was 2 (1-3), with a range from 1 to 7. The individual recanalization rate for each successive SR pass got sequentially lower as the SRP# increased—from 45.3% on the first pass to 0.3% on the seventh pass (Table 1). Only 5.5% more recanalization was further expected from the fifth SR attempt.

Table 1. Individual and Accumulative Recanalization Rates for Each Pass of a Stent Retriever in Patients With Successful Recanalization

No. of Stent Retriever Passes	No. of Patients With Recanalization by Each Pass (Individual Rate, %)	Total Number of Patients With Recanalization up to Each Pass (Accumulative Rate, %)
First	174 (45.3)	174 (45.3)
Second	106 (27.6)	280 (72.9)
Third	53 (13.8)	333 (86.7)
Fourth	30 (7.8)	363 (94.5)
Fifth	15 (3.9)	378 (98.4)
Sixth	5 (1.3)	383 (99.7)
Seventh	1 (0.3)	384 (100.0)

SRP# for Futile Recanalization

Among the 467 patients, 235 (50.3%) patients had a favorable outcome. Based on the univariable analyses, younger age, male sex, absence of hypertension and diabetes mellitus, hypercholesterolemia, smoking, absence of previous stroke, low initial National Institutes of Health Stroke Scale score, ASPECTS ≥7, good collateral status, absence of symptomatic intracerebral hemorrhage, and endovascular results were associated with a favorable outcome (Table 2). In the multivariable analysis, younger age, lower initial National Institutes of Health Stroke Scale score, ASPECTS ≥7, good collateral status, absence of symptomatic intracerebral hemorrhage, and successful recanalization in ≤4 SR passes (for 1 pass, odds ratio [OR] 8.06, 95% CI, 3.69–17.6; for 2 passes, OR 7.78, 95% CI, 3.37–18.0; for 3 passes, OR 6.10, 95% CI, 2.31–16.1; and for 4 passes, OR 6.57, 95% CI, 2.11–20.4) were independent predictors for a favorable outcome. Patients with a successful recanalization after ≥5 passes of SR had functional outcomes that were not significantly more favorable than those of patients without recanalization (for 5 passes, OR 1.70, 95% CI, 0.42–6.90, P=0.455; for \geq 6 passes, OR 0.33, 95% CI, 0.02-5.70, P=0.445).

Relationship Between the SRP# and Time to Recanalization

For patients with successful recanalization, the median PTR and OTR times were 54.0 (40.0-80.0) and 281.0 (210.0-351.2), respectively. Median PTR values at each SRP# became significantly higher as the SRP# increased (P for trend <0.001; r=0.542, P<0.001; Figure 1A). We noted a significant linear relationship between the PTR value and the SRP#: each SR pass increased the PTR time by 15.9 minutes (P<0.001). OTR values also increased significantly the SRP# increased (*P* for trend <0.001; Figure 1B). However, that correlation was much weaker (r=0.170) than with the PTR times.

Estimation of Time to Recanalization Associated With Futile Recanalization

The probability of a favorable outcome was 0.357 (95% CI, 0.297-0.419) with successful recanalization at the fifth SR pass (Figure 2A; Table I in the online-only Data Supplement). For the PTR time, successful recanalization in a range of 110 to 155 minutes showed a similar probability of a favorable outcome (Figure 2B; Table II in the online-only Data Supplement). Within that range, 125 minutes of PTR was a significant cutoff associated with futile recanalization. With successful recanalization after 125 minutes of PTR, the patient's functional outcome was not significantly more favorable than that of a patient without recanalization. This cutoff time was also an independent predictor of futile recanalization in the multivariable analysis (OR, 1.87; 95% CI, 0.55–6.31; *P*=0.313; Table 3). In the same way, we determined a significant OTR cutoff for futile recanalization to be 580 minutes (Figure 2C; Table III in the online-only Data Supplement; OR, 2.23; 95% CI, 0.42–11.9; *P*=0.349; Table 3).

Table 2. Comparison of Variables and Endovascular Results Between Patients With and Without a Favorable Outcome

	U	Inivariable Analysis		Multivariable Analysis	
	With Favorable Outcome (n=235)	Without Favorable Outcome (n=232)	<i>P</i> Value	Odds Ratio* (95% CI)	<i>P</i> Value
Age	64.5 (±12.7)	70.0 (±11.5)	<0.001	0.96 (0.94-0.98)	≤0.001
Sex, male	145 (61.7)	114 (49.1)	0.006	1.62 (0.90–2.94)	0.110
Hypertension	123 (52.3)	150 (64.7)	0.007	1.03 (0.61–1.74)	0.917
Diabetes mellitus	45 (19.1)	69 (29.7)	0.008	0.62 (0.35–1.11)	0.107
Hypercholesterolemia	49 (20.9)	31 (13.4)	0.032	1.67 (0.88–3.16)	0.118
Smoking	101 (43.0)	62 (26.7)	<0.001	1.27 (0.68–2.37)	0.451
Coronary artery disease	50 (21.3)	38 (16.4)	0.176		
Atrial fibrillation	118 (50.2)	130 (56.0)	0.207		
History of previous stroke	25 (10.6)	53 (22.8)	<0.001	0.50 (0.25–1.01)	0.054
Occlusion sites			0.615		
Internal carotid artery	109 (46.4)	113 (48.7)			
Middle cerebral artery	126 (53.6)	119 (51.3)			
Initial NIHSS score	13.0 (10.0; 17.0)	17.0 (14.0; 20.0)	<0.001	0.89 (0.84-0.94)	≤0.001
ASPECTS >7	209 (88.9)	168 (72.4)	<0.001	2.37 (1.21–4.63)	0.012
Good collateral status	230 (97.9)	154 (66.4)	<0.001	19.8 (7.03–55.6)	≤0.001
Use of IV tPA	128 (54.5)	113 (48.7)	0.213		
Onset to puncture, min	216.0 (150.0; 295.5)	215.0 (150.0; 286.5)	0.885		
Use of BGC	146 (62.1)	150 (64.7)	0.571		
Symptomatic ICH	2 (0.9)	37 (15.9)	≤0.001	0.05 (0.01-0.24)	≤0.001
Endovascular result			<0.001		
No recanalization	16 (6.8)	67 (28.9)		Reference	
Successful recanalization by					
1 pass of stent retriever	103 (43.8)	71 (30.6)		8.06 (3.69–17.6)	≤0.001
2 passes	60 (25.5)	46 (19.8)		7.78 (3.37–18.0)	≤0.001
3 passes	32 (13.6)	21 (9.1)		6.10 (2.31–16.1)	≤0.001
4 passes	17 (7.2)	13 (5.6)		6.57 (2.11–20.4)	≤0.001
5 passes	6 (2.6)	9 (3.9)		1.70 (0.42–6.90)	0.455
≥6 passes	1 (0.4)	5 (2.2)		0.33 (0.02-5.70)	0.445

Univariate results are expressed as the number of patients (%) or median (interquartile range). ASPECTS indicates Alberta Stroke Program Early CT Score; BGC, balloon guiding catheter; ICH, intracerebral hemorrhage; IV tPA, intravenous tissue-type plasminogen activator; and NIHSS, National Institutes of Health Stroke Scale.

*Odds ratio for a favorable outcome.

Subgroup Analysis According to ASPECTS and Collateral Status

For patients with ASPECTS >7 (n=377), the cutoff values for futile recanalization in the SRP#, PTR time, and OTR time did not shift (Table 4). However, patients with ASPECTS ≤7 (n=90) had lower values of SRP# (3 passes), PTR time (60 minutes), and OTR time (310 minutes) than those with ASPECTS >7. For patients with good collateral status (n=384), the cutoff values did not shift much from their original values. However, for patients with ASPECTS ≤7 and good collateral status (n=59), the SRP# (5 passes) and PTR time (90 minutes) increased. We could not run a regression analysis for poor collateral status because none of the patients without recanalization had a favorable outcome.

Discussion

In this study, we found that additional recanalization rates got sequentially lower as more SR passes were attempted. The expected recanalization rate was remarkably low from SRP# 5. More important, if recanalization was achieved by ≥5 SR passes, patient outcomes were not significantly more favorable than among patients without recanalization.

Although current guidelines recommend SR as the first-line endovascular device, operators should contemplate the best modality for their endovascular procedures. 1,4,5 Even if SR is preferred, an optimal endovascular strategy should be designed for it. The strategy should essentially indicate when SR should be abandoned in favor of another endovascular modality for large artery occlusion refractory to SR, which

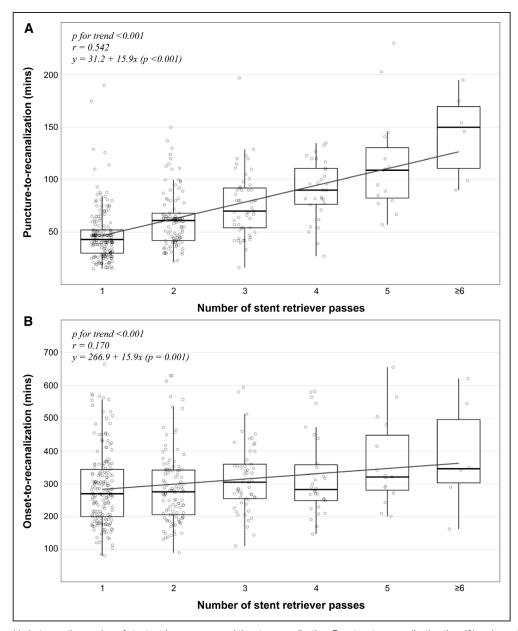


Figure 1. Relationship between the number of stent retriever passes and time to recanalization. Puncture to recanalization time (A) and onset to recanalization time (B) have a significant linear relationship with the number of stent retriever passes.

might be caused by a hard clot. A high coefficient of friction between the hard clot and vessel wall makes SR less engaged and inefficient. In addition, each SR thrombectomy failure can increase the coefficient of friction by shortening the thrombus length (thrombus compression) and increasing its hardness (Figure II in the online-only Data Supplement).⁴ Thus, each SR failure can further decrease the likelihood of recanalization, as documented in this study. The recanalization rate after ≥4 SR attempts was <10%. However, that finding alone is not enough to decide to give up further SR attempts. If successful recanalization after ≥5 SR attempts made patient outcomes more favorable, further SR attempts could be justifiable irrespective of probability. Rather, our findings demonstrate that most successful SR recanalization (≈95%) occurs within SRP# 4 if a recanalization is destined. Practically, it might be necessary to consider switching to non-SR modalities for

recanalization when the SRP# is approaching 5. In a previous case series, switching to contact aspiration thrombectomy after the failure of 5 SR passes achieved successful recanalization 83.3% and also showed a favorable outcome in $\approx\!40\%$ of patients. 13 Therefore, setting a significant breaking point in SR thrombectomy seems meaningful.

As explained above, setting a significant breaking point during SR thrombectomy might require more than the recanalization rate alone. Patient outcomes should also be considered. If patients do not benefit from a successful recanalization, their SR thrombectomy procedures were futile. To prevent futile procedures, the outcomes of patients with successful recanalization should be more favorable than those of patients without recanalization. Therefore, we tried to find a specific breaking point at which the outcomes of patients with successful recanalization are not significantly more favorable than those

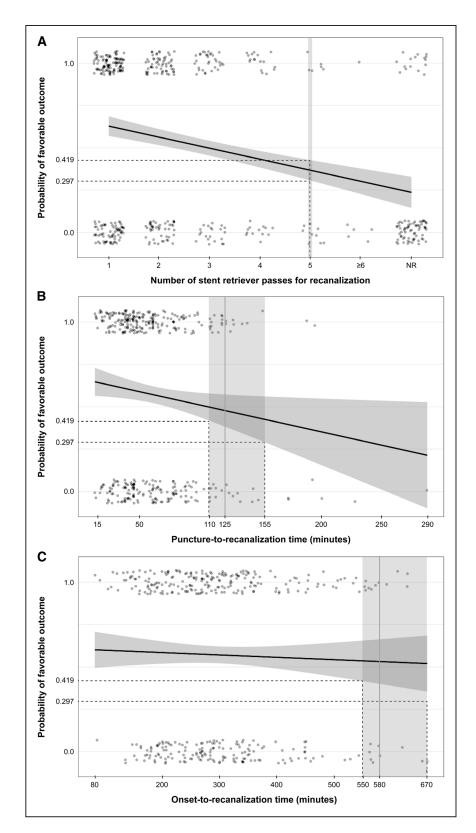


Figure 2. The probability of a favorable outcome according to the number of stent retriever passes and time to recanalization. Based on the probability range at the fifth pass of the stent retriever (0.297–0.419, A), corresponding ranges of probability were estimated at 110 to 155 minutes of puncture to recanalization time (B) and 550 to 670 minutes of onset to recanalization time (C).

of patients without recanalization. Based on our results, we modestly recommend that successful recanalization should be achieved within SRP# 4 or a PTR of 125 minutes.

Importantly, such a breaking point should be understood under the concept of time. When comparing study variables that might affect outcomes between patients with SRP# 1 to 4 and ≥5, all but time to recanalization (eg, use of IV tPA, symptomatic intracerebral hemorrhage, and the location of occlusion) were not different to each other (Table IV in the online-only Data Supplement).

It should be also noted that those breaking points were derived from a specific population in which ≈80% of patients

Table 3. Significance of Endovascular Results Defined by Time to Recanalization (Puncture to Recanalization [PTR] and Onset to Recanalization [OTR]) Instead of the Number of Stent Retriever Passes

	Univariable Analysis			Multivariable Analysis*	
	Favorable Outcome (n=235)	Unfavorable Outcome (n=232)	<i>P</i> Value	Odds Ratio† (95% CI)	<i>P</i> Value
Endovascular result defined by PTR			<0.001		
No recanalization	16 (6.8)	67 (28.9)		Reference	
Successful recanalization					
PTR ≤125 min	211 (89.8)	151 (65.5)		7.32 (3.63–14.7)	<0.001
PTR >125 min	8 (3.4)	13 (5.6)		1.87 (0.55–6.31)	0.313
Endovascular result defined by OTR			<0.001		
No recanalization	16 (6.8)	67 (28.9)		Reference	
Successful recanalization					
0TR ≤580 min	215 (91.5)	161 (69.4)		6.88 (3.43–13.8)	<0.001
OTR >580 min	4 (1.7)	4 (1.7)		2.23 (0.42–11.9)	0.349

Univariate results are expressed as the number of patients (%).

had ASPECTS >7 and good collateral status. In other words, changes in those conditions might also shift the breaking points. For example, when the conditions are unfavorable, breaking points could be smaller. Actually, for the subgroup of patients with ASPECTS ≤7, the SRP# decreased to achieve an outcome more favorable than for patients without recanalization.

This study had a few limitations associated with its retrospective design. First, the timing to stop SR attempts was at the operator's discretion without a specific protocol. In fact, limiting the SRP# is practically infeasible. Even in randomized controlled trials, limiting the SRP# is not evidence based. To eliminate possible errors from that bias, we analyzed only patients with successful recanalization when calculating the recanalization rates for each SR attempt. Patients without recanalization had from 1 to 12 SR passes in this study. For those patients, no one can be certain that successful recanalization could be achieved beyond their last SR pass. For example, a patient whose recanalization was not achieved by SRP# 3 might have had a successful recanalization at SRP# 4 or 5; however, we cannot be certain about that because we did not continue with SR attempts. In other words, it is unlikely that the SRP# reflects the real efficacy of SR attempts. For the same reason, we did not compare the median or mean values of the SRP# between patients with and without favorable outcomes because each group obviously included cases without recanalization.

Considering the retrospective nature of this study, we tried to minimize a bias associated with the presence of intracranial atherosclerosis-related occlusion. Although we excluded patients whose recanalization was achieved by non-SR modalities such as intracranial stenting, balloon angioplasty, or glycoprotein IIb/IIIa inhibitors, intracranial atherosclerosisrelated occlusions could be still in the study population.

Second, this retrospective study of the SRP# is limited because several clinical and procedural factors could affect the

SRP#. Clot pathology, arterial tortuosity, clot burden, use of BGC, use of intravenous tPA, concomitant use of intra-arterial thrombolytics, types of SR, and thrombectomy technique are all assumptive factors affecting the SRP# or recanalization result although evidence for any of them is scarce. Within a retrospective design, it is impossible to control all those factors, but a large number of patients from multiple experienced neurointerventionalists might mitigate some of those factors. This study had a large number of patients from 16 comprehensive stroke centers. Furthermore, in this study, the SR thrombectomy technique was mostly based on common recommendations and was performed with only 2 types of SR. In this study, ≈5% of patients had the intra-arterial infusion of urokinase. However, all of the infusion was just for distal artery occlusion of M3 or more distal after SR thrombectomy. So, the SRP# was not affected by the use of intra-arterial urokinase.

This study pointed a specific breaking point where SR thrombectomy would be futile. However, unfortunately, it could not explain why some of patients needed more SR retrievals to get a recanalization (eg, 5 or more times). To

Table 4. Cutoff Values for the Number of Stent Retriever Passes (SRP#), Puncture to Recanalization (PTR) Time, and Onset to Recanalization (OTR) Time for Futile Recanalization According to ASPECTS and Collateral Status

	ASPECTS	No. of Patients	SRP#	PTR, min	OTR, min
Any collateral status	Any	n=467	5	125	580
	>7	n=377	5	125	580
	≤7	n=90	3	60	310
Good collateral status	Any	n=384	5	120	560
	>7	n=325	5	120	570
	≤7	n=59	5	90	290

ASPECTS indicates Alberta Stroke Program Early CT Score.

^{*}Each multivariable logistic regression was performed with the variables of age, sex, hypertension, diabetes mellitus, hypercholesterolemia, smoking, history of previous stroke, initial NIHSS (National Institutes of Health Stroke Scale) score, ASPECTS (Alberta Stroke Program Early CT Score) >7, and good collateral status, which each had P<0.1 in the univariable analyses.

[†]Odds ratio for a favorable outcome.

evaluate relevant factors increasing SRP#, all kinds of clinical, etiologic, and procedural conditions should be considered, which were not in the design of this study. It is absolutely necessary to evaluate possible causes of increasing the SRP# or its refractoriness and find effective ways to overcome it. Nevertheless, we think that the findings of this study could give an evident clue for when the first-line SR modality should be abandoned and switched to other rescue modalities, which is also essential for the optimal endovascular strategy.

Third, in terms of functional outcome, the SRP# might be merely a surrogate maker for procedural time. In certain conditions, the SRP# might not fairly represent procedural time—for example, in the time 1 operator can do 4 SR attempts, another might do 3 or fewer attempts with the same PTR. To address such differences, therefore, the SRP# should be figured out in the context of time. Although the SRP# was chosen primarily for its ease of analysis, we also set PTR and OTR times as secondary breaking points to support the SRP#.

Summary

Recanalization rates got sequentially lower as the number of passes increased and were remarkably low from SRP# 5 in this study population. Furthermore, recanalization was futile when it was achieved by ≥5 SR passes, which was well correlated with the time to recanalization. For better and more rapid recanalization, it might be better to switch from SR to another endovascular modality as the SRP# approaches 5.

Sources of Funding

This research was supported by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute, funded by the Ministry of Health & Welfare, Republic of Korea (HC15C1056).

Disclosures

None.

References

 Powers WJ, Derdeyn CP, Biller J, Coffey CS, Hoh BL, Jauch EC, et al; American Heart Association Stroke Council. 2015 American Heart Association/American Stroke Association focused update of the 2013

- guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2015;46:3020–3035. doi: 10.1161/STR.0000000000000074
- Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, et al; HERMES Collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387:1723–1731. doi: 10.1016/S0140-6736(16)00163-X
- Song D, Cho AH. Previous and recent evidence of endovascular therapy in acute ischemic stroke. *Neurointervention*. 2015;10:51–59. doi: 10.5469/neuroint.2015.10.2.51
- Yoo AJ, Andersson T. Thrombectomy in acute ischemic stroke: challenges to procedural success. *J Stroke*. 2017;19:121–130. doi: 10.5853/jos.2017.00752
- Kim BM. Causes and solutions of endovascular treatment failure. J Stroke. 2017;19:131–142. doi: 10.5853/jos.2017.00283
- Lapergue B, Blanc R, Guedin P, Decroix JP, Labreuche J, Preda C, et al. A direct aspiration, first pass technique (ADAPT) versus stent retrievers for acute stroke therapy: an observational comparative study. AJNR Am J Neuroradiol. 2016;37:1860–1865.
- Lee JS, Hong JM, Kim JS. Diagnostic and therapeutic strategies for acute intracranial atherosclerosis-related occlusions. *J Stroke*. 2017;19:143– 151. doi: 10.5853/jos.2017.00626
- Baek JH, Yoo J, Song D, Kim YD, Nam HS, Kim BM, et al. Predictive value of thrombus volume for recanalization in stent retriever thrombectomy. Sci Rep. 2017;7:15938. doi: 10.1038/s41598-017-16274-9
- Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, et al; ESCAPE Trial Investigators. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med. 2015;372:1019– 1030. doi: 10.1056/NEJMoa1414905
- Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study Group. Alberta Stroke Programme Early CT Score. *Lancet*. 2000;355:1670–1674.
- Hwang YH, Kim YW, Kang DH, Kim YS, Liebeskind DS. Impact of baseline ischemia on outcome in older patients undergoing endovascular therapy for acute ischemic stroke. *J Clin Neurol*. 2017;13:162–169. doi: 10.3988/jcn.2017.13.2.162
- Zaidat OO, Yoo AJ, Khatri P, Tomsick TA, von Kummer R, Saver JL, et al; Cerebral Angiographic Revascularization Grading (CARG) Collaborators; STIR Revascularization working group; STIR Thrombolysis in Cerebral Infarction (TICI) Task Force. Recommendations on angiographic revascularization grading standards for acute ischemic stroke: a consensus statement. Stroke. 2013;44:2650–2663. doi: 10.1161/STROKEAHA.113.001972
- Kim SK, Yoon W, Moon SM, Park MS, Jeong GW, Kang HK. Outcomes of manual aspiration thrombectomy for acute ischemic stroke refractory to stent-based thrombectomy. *J Neurointerv Surg.* 2015;7:473–477. doi: 10.1136/neurintsurg-2014-011203