

# Research Progress on the Effect of Number of Stent Retriever Passes on the Outcome of Endovascular Treatment of Acute Ischemic Stroke

Shijie Yang<sup>1</sup>, Huan Xi<sup>1</sup>, Erqing Chai<sup>2\*</sup>

<sup>1</sup>The First Clinical Medical College of Gansu University of Chinese Medicine (Gansu Provincial Hospital), Gansu University of Chinese Medicine, Lanzhou, China

<sup>2</sup>Key Laboratory of Cerebrovascular Disease of Gansu Province, Gansu Provincial Hospital, Lanzhou China

Email: \*happybirds998@126.com

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## Abstract

**Introduction:** Endovascular treatment is an effective treatment for large vessel occlusive ischemic stroke. The number of Stent Retriever passes is an important link in the strategy of endovascular treatment, and is closely related to the clinical outcome and prognosis of patients with acute ischemic stroke, but there is still a lack of unified understanding. In order to provide reference for clinical practice and related research, this paper reviewed the recent important literatures. **Methods:** We searched PubMed, Embase, and Cochrane databases, using the terms “stents”, “stroke” and “thrombectomy”. Priority was given to human studies. Only English language papers were accepted. Analyze the articles by title and abstract. **Results:** The number of Stent Retriever passes is closely related to the rate of recanalization, hemorrhagic transformation, recanalization time, surgical procedures and clinical prognosis. Along with the increase of the number of Stent Retriever passes, the vascular recanalization rate decreased successively, in turn, reduced the rate of blood vessels, 3 times may be the target vascular occlusion which should try the best of times,  $\geq 4$  times may not improve the opportunity of recanalization and not conducive to the prognosis, at the same time, increase the risk of HT and related complications occurred. **Conclusion:** It is necessary to avoid unplanned, additional attempts at EVT. The number of Stent Retriever passes has significant effects on the outcome of EVT of AIS in many aspects. How to better personalized EVT strategy is the focus of future research.

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## Keywords

Stents, Ischemic Stroke, Thrombectomy, Endovascular Procedures

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### 1. Introduction

The burden of stroke in low- and middle-income countries is higher than in high-income countries and is rising [1]. Endovascular treatment (EVT) is an effective treatment for acute ischemic stroke (AIS) caused by large vessel occlusion (LVO). Relevant studies have confirmed that EVT can bring significant clinical benefits for patients with anterior circulation LVO stroke [2] [3] [4]. With the further promotion and popularization of EVT in clinical application, it has been found that EVT has considerable benefits on the functional prognosis of AIS, but about 50% of the patients died or were still dependent after 3 months [5]. These adverse results may not be solely attributable to unsuccessful recanalization, as approximately one third of patients who achieve early complete recanalization even after EVT does not have ideal results [6]. The occurrence of this situation may be a problem of patient screening, or may be related to the EVT procedures [7].

Related studies have reported that the number of Stent Retriever passes is closely related to the clinical outcome and prognosis of patients with AIS [2] [3] [4]. However, due to the large individual differences of patients, many influencing factors, and the differences in therapeutic concepts and practices among clinicians, there is still a lack of unified understanding at present. This paper reviews and summarizes the relevant guidelines and studies, in order to provide reference for clinical practice and later related research.

### 2. Materials and Methods

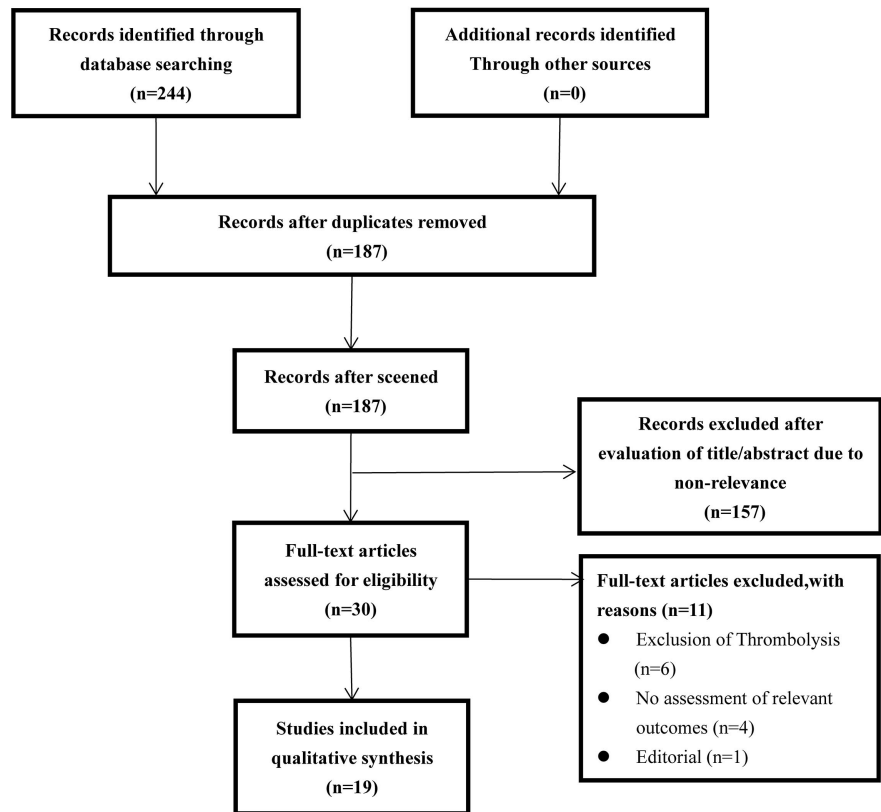
We searched PubMed, Embase, and Cochrane databases for the terms “stents”, “stroke” and “thrombectomy”. A total of 244 records were found, and 30 records remained after removing duplicate and unrelated documents. After careful review of the title, abstract, and full text, 11 articles were deleted as follows: 1) thrombolytic exclusion, (n = 6), 2) unevaluated related results (n = 4), and 3) edited (n = 1). Nineteen articles were included (Figure 1, Table 1).

### 3. Results

#### 3.1. The Relationship between the Number of Stent Retriever Passes and the Rate of Vascular Successful Recanalization

In recent years, it has been found in clinical practice that unplanned continuous EVT attempts have not significantly increased the rate of vascular successful recanalization or degree of recanalization.

Garcia-Tornel A *et al.* found in a single-center retrospective study that the vascular recanalization rates of the first to fourth Stent Retriever passes were 39%



**Figure 1.** Flow chart of literature search and selection.

**Table 1.** Characteristics of included studies.

Author	Year	Population	Number of cases	research characteristic
García-Tornel Á	2019	Spain	704	Retrospective single-center
Filioglo A	2020	Israel	271	Retrospective single-center
Kharouba R	2019	Israel	96	Retrospective single-center
Baek J	2018	Korea	467	Retrospective multicenter
Flottmann F	2018	Germany	330	Retrospective single-center
LOH Y	2010	America	97	prospective cohort study
Angermaier A	2016	Germany	63	Retrospective single-center
Li W	2020	China	88	Retrospective single-center
Renú A	2017	Spain	146	Retrospective single-center
Kalinin MN	2017	Russia	783	Retrospective single-center
Hao Y	2017	China	632	Retrospective multicenter
Bourcier R	2019	France	281	prospective cohort study
Hassan AE	2019	America	329	Retrospective single-center
Khatri P	2014	America	656	Retrospective multicenter
Kleine JF	2017	Germany	352	Retrospective single-center
Seker F	2017	Germany	104	Retrospective single-center
Tan IYL	2009	Canada	85	Retrospective single-center
Goyal N	2019	America	287	Retrospective single-center
Tonetti DA	2020	America	250	Retrospective single-center

(213/542), 35% (113/310), 33% (63/190) and 24% (26/154), respectively. The vascular recanalization rate was 28% (45/158) in patients with more than 4 Stent Retriever passes ( $P < 0.001$ ) [7]. A multi-center retrospective study by Jang-Hyun Baek *et al.* found that as the number of Stent Retriever passes increased, the rate of vascular recanalization in each successive thrombectomy group decreased sequentially, from 45.3% in the first attempts to 0.3% in the seventh attempts, and was expected to increase by only 5.5% after the fifth attempts [8]. Moreover, modified thrombolysis in cerebral infarction score (mTICI) 3 patients were more likely to experience fewer the number of Stent Retriever passes. Two-thirds of the patients achieved successful recanalization during the first 3 Stent Retriever passes [9].

The study of Loh *et al.* showed that the number of Stent Retriever passes in patients with AIS was not consistently correlated with successful recanalization of vessels. After 3 Stent Retriever passes, each subsequent attempt only produced a very small recanalization of vessels and increased the incidence of complications. At the same time, in the Loh team's experience, 3 Stent Retriever passes may be the optimal number for occlusion of the target vessel, and  $\geq 4$  attempts not improve the chance of recanalization and increase the risk of complications [10]. However, according to the study of Angermaier A, 2.5 Stent Retriever passes was the best indicator for the discrimination of successful recanalization (area under the curve [AUC], 0.69; 95% confidence interval [CI], 0.54 - 0.84;  $P = 0.02$ ), and, in univariate regression analysis, 2 Stent Retriever passes or less was significantly associated with a 4.28-fold increase in the chance of revascularization [11]. Through the above studies, it is not difficult to find that the more times of Stent Retriever passes, the lower the rate of vascular recanalization, and the increase of vascular recanalization rate is extremely limited when the number of Stent Retriever passes exceeds a certain number.

### 3.2. The Relationship between the Number of Stent Retriever Passes and Hemorrhagic Transformation

Hemorrhagic transformation (HT) is a common and frequent complication for patients undergoing EVT. Several risk factors for HT in AIS have been reported in relevant studies, including atrial fibrillation, diabetes mellitus, congestive heart failure, platelet count, blood glucose level, total cholesterol level, NIHSS score at admission, baseline ASPECTS and surgical related factors [3] [12] [13] [14].

The effect of surgical factors on HT, such as the number of Stent Retriever passes, has not been well established. A study that analyzed 632 patients found that among the patients with HT after EVT, more patients underwent more than 3 Stent Retriever passes [15]. In univariate analysis, compared with patients who underwent  $\leq 3$  Stent Retriever passes, patients with  $>3$  Stent Retriever passes had significantly more intracranial hemorrhage or parenchymal hematomas [16].

Other studies have found that Stent Retriever causes greater vascular injury than contact aspiration (CA), and has a higher probability of hemorrhagic transformation after multiple aspiration [17] [18]. Romain Bourcier *et al.* performed

grouping analysis based on CA vs. Stent Retriever, and found only in the Stent Retriever treatment group, patients with 3 Stent Retriever passes had an increased risk of parenchymal hematoma (PH) (adjusted odds ratio [OR], 9.24; 95% CI, 2.65 - 32.13) and not found in the CA treatment group (adjusted relative risk [RR], 1.73; 95% CI, 0.57 - 5.19) [16].

However, Hassan AE *et al.* found that there was no correlation between the number of Stent Retriever passes and the incidence of HT [19]. Based on the current study, whether there is a correlation between the number of Stent Retriever passes and HT needs to be further verified by higher quality evidence.

### 3.3. The Relationship between the Number of Stent Retriever Passes and Procedure Time

Recanalization is very important, but it is not the only factor affecting the functional outcome. The time from symptom onset to recanalization (SORT) is also an important factor [20]. In patients with successful recanalization, 1 Stent Retriever pass was associated with a shorter (SORT) (238 minutes vs. 280 minutes,  $p < 0.001$ ) [21]. Jeffrey L. Saver *et al.* analyzed 390 patients with substantial recanalization after endovascular thrombectomy and found that each hour of delay in recanalization was associated with poorer disability (common odds ratio [cOR], 0.84 [95% CI, 0.76 - 0.93]; absolute risk difference [ARD], -6.7%) and related functional independence (OR, 0.81 (95% CI, 0.71 to 0.92); ARD, -5.2% [95% CI, -8.3% - -2.1%]). For every 9 minute delay in SORT, 1 in 100 treated patients had a more severe disability outcome (a higher modified Rankin Scale [mRS] score of 1 point or higher). The probability of 3-month functional independence (mRS 0 - 2) decreased from 64.1% for 180 minutes by SORT to 46.1% for 480 minutes by SORT [22]. In addition, Mazighi M *et al.* found that every 30 min reduction in SORT resulted in a 20% reduction in intracranial bleeding [23].

Equally, the time from onset to groin puncture (OTP) is also an important factor. The longer the OTP, the lower the chance of a better disability outcome at 90 days: 3 hours, cOR 2.79 (95% CI, 1.96 to 3.98), ARD 39.2%; 6 h, cOR 1.98 (95% CI 1.30 to 3.00), ARD 30.2%; 8 h, cOR 1.57 (95% CI 0.86 to 2.88), ARD 15.7%. It remained significant for 7 hours and 18 minutes, and the benefit was not significant after 7.3 hours [22]. Hao Y *et al.* found that the OTP delay was 270 minutes (OR, 1.70; 95% CI, 1.03, 2.80) was associated with symptomatic intracranial hemorrhage (SICH) after endovascular treatment. The OTP of patients with SICH was longer than that of patients without SICH (median, 307 minutes vs. 269 minutes;  $P = 0.035$ ) [15].

Jang-hyun Baek *et al.* also found that there is a significant linear relationship between the time from groin puncture to recanalization (PTR) value and the times of EVT, each additional Stent Retriever passes increased PTR by 15.9 minutes ( $P < 0.001$ ). In addition, the sort value increased significantly with the increase of the number of Stent Retriever passes ( $P < 0.001$ ), however, was much

weaker than the correlation with the number of PTR ( $r = 0.170$ ). PTR = 125 minutes is a cutoff point, associated with invalid reconnects. After 125 minutes of PTR treatment, even if the vessels were recanalized successfully, the patient's functional prognosis was not significantly better than that of patients without recanalization. In multivariate analysis, this cutoff time was also an independent predictor of ineffective recanalization (OR, 1.87; 95% CI, 0.55-6.31;  $P = 0.313$ ); Similarly, Baek *et al.* determined a valid OTR cutoff time of 580 minutes for invalid recalculations [8].

In terms of clinical outcomes, the time to successful recanalization of the vessels is an important reference. In addition, the number of Stent Retriever passes can be used as a surrogate marker for surgical time, and successful recanalization of the vessel within 125 minutes of PTR may benefit the patient's ultimate prognosis.

### 3.4. The Relationship between the Number of Stent Retriever Passes and Prognosis

As approximately one third of patients who achieve early complete recanalization even after EVT do not have ideal results [24]. This can be explained by the so-called "ineffective recanalization", *i.e.*, in patients who achieved mTICI 2B/3 scores after EVT, after 3 months failure to achieve functional independence (mRS > 2) [25]. Rawan Kharouba *et al.* found a very significant correlation between the number of Stent Retriever passes and favorable outcomes (mRS  $\leq 2$ ) ( $P = 0.008$ ) [4].

The first pass recanalization (FPR) and degree of recanalization are associated with better clinical outcomes [4] [26]. A number of studies have found that the rate of good outcome in FPR group is higher than that in patients with multiple Stent Retriever passes or with mTICI 2C/3 achieved by rescue therapy, and successful recanalization of vessels after FPR is still independently associated with good outcome. In addition, in a multivariate analysis, less than 4 Stent Retriever passes were an independent predictor of better outcomes (1 time, OR: 8.06, 95% CI, 3.69 - 17.6; OR: 7.78, 95% CI, 3.37 - 18.0; OR 6.10, 95% CI, 2.31 - 16.1; OR 6.57, 95% CI, 2.11 - 20.4;  $P < 0.001$ ) [2] [4] [7] [26]. Another study found that patients with recanalization of vessels after more than 4 Stent Retriever passes had a better prognosis than those without recanalization. However, the functional prognosis of patients with  $\geq 5$  Stent Retriever passes and recanalization was not significantly better than that of patients with incomplete recanalization (5 times, OR: 1.70, 95% CI, 0.42 - 6.90,  $P = 0.455$ ; 6 OR higher, OR 0.33, 95% CI, 0.02-5.70,  $P = 0.445$ ) [4] [11] [26].

Patients with fewer than 4 Stent Retriever passes had significantly better outcomes (52% vs. 30%;  $P = 0.009$ ) [3]. Seker F *et al.* found that each additional Stent Retriever passes resulted in worse outcomes ( $P < 0.01$ ), and patients who require only one thrombectomy procedure to obtain mTICI 2B or 3 are more likely to have a good outcome than patients who require two or more attempts

to obtain the same degree of recanalization. In addition, the rate of good outcomes in final mTICI 2B patients began to decline after the 2 Stent Retriever passes, but for final mTICI 3 patients, this progressive decline only occurred after the 3 Stent Retriever passes [27]. This observation may suggest that the benefit of mTICI 3 recanalization is offset by the adverse effect of 3 Stent Retriever passes, beyond which the ultimate outcome is adversely affected. A single-center retrospective study showed that 3 Stent Retriever passes were an important predictor of prognosis [14]. Patients with 1 to 3 Stent Retriever passes had a higher rate of clinical good outcome (28.9% vs. 7.4%;  $P = 0.018$ ) [13]. There is a significant correlation between the number of Stent Retriever passes and the good prognosis of acuteAIS. In patients with the same degree of recanalization, the fewer times of Stent Retriever passes experienced, the greater the possibility of good prognosis, and 3 times may be the best number of Stent Retriever passes for target vessel occlusion. These results need to be further verified by high quality randomized controlled trial (RCT) tests.

### 3.5. Factors Influencing the Number of Stent Retriever Passes

At present, the number of Stent Retriever passes is closely related to the clinical outcomes and prognosis of patients with AIS, and there are still many problems that have not reached a unified understanding of the related factors that affect the number of Stent Retriever passes.

According to relevant studies, the closer the initial location of vascular occlusion was, the incidence of first pass recanalization (FPR) decreased gradually and became an independent predictor of FPR (internal carotid artery [ICA] terminal vs. middle cerebral artery [MCA]-M1 vs. MCA-M2, OR, 0.68; 95% CI, 0.49 to 0.94;  $P = 0.02$ ) [7]. Zaidat Oo *et al.* found that the independent predictors of FPR were the use of a balloon guided catheter and non-carotid terminal occlusion. In addition, the FPR group had a significantly higher proportion of women and over 80 years of age, and a lower incidence of ICA occlusion [26]. A. Filioglo *et al.* also found that the incidence of internal carotid artery occlusion was higher in patients with  $\geq 5$  Stent Retriever passes, and the incidence of middle cerebral artery occlusion was higher in patients with  $\leq 4$  Stent Retriever passes ( $P = 0.005$ ) [12].

Other studies have found that patients with lower clot burden score (CBS) need more times of Stent Retriever passes to achieve revascularization, and the number of operations in the process of thrombectomy depends on the efficiency of the equipment for revascularization and the thrombosis burden [15] [28]. Goyal N *et al.* found that the number of Stent Retriever passes required may be affected by intravenous thrombolysis (IVT) [29].

## 4. Discussion

EVT is the first-line treatment for AIS [30], and it is necessary to develop the best intravascular treatment strategy for the best EVT outcome. Current chal-

Challenges in this field focus on reducing recanalization time, optimizing patient selection, and evaluating the best technical approach. The number of Stent Retriever passes is closely related to the clinical outcome of EVT.

The number of Stent Retriever passes less than 3 times can improve the chance of vascular recanalization and is beneficial to the prognosis, while increasing the number of additional attempts on this basis is not beneficial and increases the incidence of related complications. In addition, each additional pass increased PTR by 15.9 minutes ( $P < 0.001$ ), while related studies have found that successful recanalization of the vessel within 125 minutes of PTR may benefit the patient's ultimate prognosis [8]. The benefits of recanalization are offset by the adverse effects of thrombectomy procedures, and the final outcome may be affected by the number of Stent Retriever passes.

However, in some cases, it is impossible to recanalization even after multiple Stent Retriever passes [8] [16] [31]. Another study found that, despite the need for more Stent Retriever passes and time, patients with multiple Stent Retriever passes who obtained recanalization had better clinical outcomes than patients without successful recanalization, and the most significant predictor of good prognosis was good recanalization of target vessels [3] [32]. A considerable number of patients can still achieve functional independence after 5 Stent Retriever passes [3]. Therefore, the strategy of EVT needs to be customized according to different patients. For some patients, it may not be necessary to limit the number of Stent Retriever passes, but the final good recanalization of the vessels should be the main goal. Therefore, the optimal number of Stent Retriever passes in patients who fail to achieve substantial recanalization is worthy of further study. Similarly, the effective indicators that can be screened out in relevant patients also need further verification.

There are many factors affecting the number of Stent Retriever passes, including the location of vascular occlusion, the origin and texture of the thrombus, vascular anatomy, bridging treatment, and even gender and age. In addition, Neurologists' different treatment concepts and experience preferences also make it more scientific and reasonable to make individualized treatment plans according to specific patients, imaging, characteristics of thrombosis and other relevant characteristic indicators. At present, studies on the reduction of thrombectomy times are devoted to the updating of thrombectomy materials, but little progress has been made recently, and further strengthening is needed in the future [33]. Each patient has a single optimal EVT strategy, so to what extent can patients finally achieve recanalization? If complete recanalization cannot be achieved, what is the maximum number of Stent Retriever passes required? What is the maximum number of Stent Retriever passes can withstand? Is there a more objective and effective indicator to screen and evaluate patients more accurately? These issues still need to be further studied and demonstrated by high-quality randomized controlled trials in order to further improve the effectiveness and safety of EVT for AIS and reduce repeated ineffective or even harmful endovascular procedures.



## 5. Conclusion

It is necessary to avoid unplanned, additional attempts at EVT. The number of Stent Retriever passes has significant effects on the outcome of EVT of AIS in many aspects. How to better personalized EVT strategy is the focus of future research.

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## Declarations

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## Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all the following areas: drafting, revising, or critically reviewing the article; giving final approval of the version to be published; agreeing on the journal to which the article will be submitted; and agreeing to be accountable for all aspects of the work.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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