Review

Safety and Efficacy of Mechanical Thrombectomy Using Stent Retrievers in the Endovascular Treatment of Acute Ischaemic Stroke: A Systematic Review

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Key Words

Endovascular procedures · Stent · Stroke · Thrombectomy

Abstract

Background: The treatment of choice for acute ischaemic stroke is the intravenous administration of recombinant tissue plasminogen activator within 3–4.5 h of symptom onset. However, the use of a thrombolytic would be limited by its narrow therapeutic window and contraindications. As a result, in recent years, techniques such as mechanical thrombectomy have emerged, which employ thrombus retrieval devices, such as stent retrievers (Solitaire™, Trevo® or Revive™), whose safety and efficacy in the endovascular treatment of acute ischaemic stroke is analysed in this article. **Methods:** A systematic literature search was undertaken until March 2015. The quality of evidence was assessed according to the GRADE methodology. A meta-analysis of the results of randomised controlled trials (RCTs) was performed, and the weighted average for the case series' sample size was calculated (Review Manager v5.2 and SPSS v19). **Results:** Seventeen primary studies (2 RCTs, Solitaire™ and Trevo® vs. Merci®, and 15 case series) were selected. The RCT results show that stent retrievers have a safety profile similar to the Merci® device. However, both Solitaire™ and Trevo® achieved a higher recanalisation success rate (OR, 4.56; 95% CI, 2.63–7.90; $p < 0.00001$) and appropriate clinical outcome at 90 days (OR, 2.54; 95% CI, 1.52–4.25; $p < 0.0004$), although the 90-day mortality rate was similar in both groups (OR, 0.75; 95% CI, 0.17–3.37; $p = 0.70$). **Conclusions:** Stent retrievers appear to be safe and effective devices, achieving high recanalisation rates and good clinical outcomes in the endovascular treatment of patients with acute ischaemic stroke due to the occlusion of intracranial arteries in comparison with the clot retriever Merci®.

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Background

Approximately 17 million cases of incident stroke occurred worldwide in 2010, with an estimated prevalence rate of about 502 cases per 100,000 people [1]. Stroke was the second most leading cause of death, accounting for 6.2 million deaths (~11% of the total) [2] and the third most frequent cause of burden of disease (loss of disability-adjusted life years) worldwide [3].

Currently, intravenous recombinant tissue plasminogen activator (rtPA), administered within 3–4.5 h of symptom onset, is recommended as the treatment of choice in acute ischaemic stroke [4, 5]. However, in some patients, the use of a thrombolytic would be limited by its narrow therapeutic window and contraindications [6, 7] or due to achieving a poor reperfusion rate [8], e.g. in a patient with a large thrombus [9].

Up to two thirds of ischaemic stroke cases arrive at the emergency department 3 h after the onset of symptoms [10]. Hence, extending the time window could be an important strategy to maximise thrombolytic therapy in stroke [11].

The therapeutic alternative both in patients who are not candidates for rtPA and in whom the optimal recanalisation rate is not achieved is endovascular therapy. This involves the use of intra-arterial thrombolytics (recombinant prourokinase or r-proUK) within 6 h of symptom onset or the use of mechanical thrombectomy, which allows the removal or mechanical fragmentation of the thrombus within 8 h of symptom onset [12–14].

Mechanical thrombectomy for acute ischaemic stroke has shown significant technical advances in the past 5 years. The Penumbra System[®] and Merci[®] Retrieval System, known as clot retrieval devices, were the first generation of mechanical thrombectomy devices that were based on extraction techniques. Currently, novel thrombectomy devices known as stent retrievers, i.e. the Solitaire[™] Flow Restoration Device and the Trevo[®] Pro Retrieval System, unlike their predecessors, apply a radial retrieval force in the centre of the thrombus and along its whole length. This technical evolution might increase their rate of recanalisation. These devices received FDA approval for the distribution in the US in 2012 [12, 13]. Recently, another stent retriever called Revive[™] SE Thrombectomy Device has emerged. The main disadvantage of clot retrieval is the inability to achieve recanalisation in as many as 20–40% of large-vessel occlusion strokes [15, 16]. This feature has not been established in stent retrievers yet. The proposed benefits of stent retrievers over other techniques are a higher rate of recanalisation and easier use leading to shorter procedural times and early flow restoration even before the clot is retrieved.

The aim of this paper was to analyse, through a systematic review, the safety and efficacy of stent retrievers in the endovascular treatment of acute ischaemic stroke.

Methods

Systematic Review and Study Selection

Literature searches were conducted in the major databases of the medical literature: Centre for Reviews and Dissemination (CRD) Database, Cochrane Library Plus, Medline (PubMed), Embase (OVID), Web of Science (Web of Knowledge) and Scopus. References from the included studies and review articles were scanned. The main terms used in the search were a combination of MeSH terms (e.g. 'Stroke', 'Thrombectomy' or 'Stent') and/or free-text terms ('stent retrievers', 'stent like-devices', 'Solitaire', 'Trevo' or 'Revive'). This strategy was implemented until March 2015. Two independent investigators reviewed and selected articles according to predefined selection criteria. Randomised controlled trials (RCTs), observational studies and case series that assessed the safety and efficacy of mechanical thrombectomy using stent retrievers were included. Studies that used mechanical thrombectomy simultaneously with other endovascular therapies or submitted pooled results were excluded.

Definition and Selection of Variables

According to the GRADE methodology [17], different outcomes of interest were identified in the literature and then classified by neurologists using a scale from 1 to 9 (1: lesser importance; 9: maximum importance), taking into account their clinical relevance. Only those outcomes that were critical for decision-making (final score between 7 and 9) were taken into account for the analysis. Those outcomes scoring >4 points were not considered further. Finally, 8 out of 14 variables were selected: 3 regarding safety [symptomatic intracranial haemorrhage (ICH; European Cooperative Acute Stroke Study definition), asymptomatic ICH and perioperative mortality from all causes] and 5 regarding efficacy [successful recanalisation defined as thrombolysis in cerebral infarction (TICI) flow ≥ 2 in the territory of the occlusion, procedure time, i.e. the median or mean time from the initial placement of the guide catheter to the achievement of recanalisation (TICI flow ≥ 2), level of neurological deficit, i.e. the median or mean National Institutes of Health Stroke Scale (NIHSS) score at 24 h, good clinical outcome defined as a modified Rankin Scale (mRS) score ≤ 2 at 90 days and all-cause mortality at 90 days].

Evaluation of Quality of Evidence

Data were extracted and summarised in evidence tables, and the GRADE system was used to judge the quality of evidence [18]. Design limitations of the selected RCTs were evaluated using the risk of bias assessment tool of the Cochrane Collaboration.

Analysis and Presentation of the Results

An independent analysis of the clinical results obtained from RCTs or case series was performed [19]. For RCTs, a meta-analysis of outcomes (Review Manager v. 5.2) was performed using inverse variance weights and both the fixed-effects model and the random-effects model (DerSimonian and Laird) were used depending on the heterogeneity level. Statistical heterogeneity was assessed with Cochran's Q test (χ^2 test) and quantified with the I^2 test. An I^2 value represents the percentage of total variation across studies, which is caused by heterogeneity rather than by chance. We considered a low I^2 value as $\leq 25\%$ and a high I^2 value as $\geq 75\%$.

In the case series, the mean $\pm$ SD weighted by the sample size (SPSS v. 19) was calculated. For continuous variables, the estimation of the mean was established from the median [20]. The results were entered into evidence tables, using the GRADE profiler (GRADEpro) v. 3.2, along with the level of evidence and the importance of each variable.

In order to simplify the analysis and presentation of the results, the two retrieval systems Solitaire™ and Trevo® were jointly evaluated in the RCTs, as these devices are similar in structure and operation. In fact, the only difference is that the Trevo® system presents a closed distal end design with the aim of minimising the risk of vascular damage.

Results

Search Results

Overall, 830 references were obtained of which 29 were selected for full-text reading. According to the inclusion and exclusion criteria, 17 primary studies were finally selected: 2 RCTs, 3 comparative studies (stent retrievers vs. rtPA, Merci® or another stent) and 12 case series (table 1). The Solitaire™ device was assessed alone in 10 studies ($n = 1,267$) [21–30], Trevo® in 4 ($n = 221$) [30–33] and Revive™ in 1 ($n = 10$) [34]. One study evaluated both Solitaire™ and Trevo® stents ($n = 43$ and $n = 26$, respectively) [35], and another study assessed both the Solitaire™ and Revive™ devices ($n = 9$ and $n = 12$, respectively) [36]. Finally, 1 study included patients for whom the 3 latter devices were used ($n = 138$, $n = 2$ and $n = 4$, respectively) [37]. Two case series evaluating patients with exclusive basilar artery occlusion were not included in the pooled analysis [23, 36].

Table 1. Characteristics of the assessed population in the included studies

Study/year/countries	Design	Therapy evaluated: patients, n	Age ¹ , years	Main lesion location	Baseline NIHSS ¹
Nogueira et al. [31]/2012/ USA and Spain	RCT	Intervention (Trevo [®]): 88 Control (Merci [®]): 90	Trevo [®] : 67.4±13.9 Merci [®] : 67.0±14.7	Trevo [®] : CM: 76%; CI: 16%; AB: 8% Merci [®] : CM: 75%; CI: 18%; AB: 6%	Trevo [®] : 18±5.3 Merci [®] : 17.9±4.8
Saver et al. [21]/2012/ USA and France	RCT	Intervention (Solitaire TM): 58 Control (Merci [®]): 55	Solitaire TM : 67±12 Merci [®] : 67±11	Solitaire TM : CM: 76%; CI: 21%; Post/other: 4% Merci [®] : CM: 70%; CI: 25%; Post/other: 4%	Solitaire TM : 17±4.5 Merci [®] : 17±4.8
Ribo et al. [35]/2013/ USA and Spain	Comparative case series	Intervention: Solitaire TM : 43; Trevo [®] : 26 Control: IAT rtPA: 127; Merci [®] : 119	Stents: 72±13 rtPA: 71±12 Merci [®] : 69±13	Stents: CM: 8.9%; CI: 33% rtPA: CM: 6%; CI: 26% Merci [®] : CM: 6.7%; CI: 27%	Stents: 18 (17–20) rtPA: 19 (16–21) Merci [®] : 17 (12–21)
Leker et al. [22]/2012/Israel	Comparative case series	Intervention (Solitaire TM): 22 Control (rtPA): 66	Solitaire TM : 64.7±15 rtPA: 71±14.3	CM: 100% (inclusion criteria)	Solitaire TM : 20±3.9 rtPA: 15±3.8
Mendonça et al. [30]/2014/ Portugal and Spain	Comparative case series	Intervention (Trevo [®]): 13 Control (Solitaire TM): 20	Trevo [®] : 74±9 Solitaire TM : 70±14	Trevo [®] : CM: 61%; CI: 39% Solitaire TM : CM: 55%; CI: 45%	Trevo [®] : 19 (16–22) Solitaire TM : 17 (16–19)
Baek et al. [23]/2014/Korea	Case series	Solitaire TM : 25	68	AB: 100%	11 (3–25)
Möhlenbruch et al. [36]/2014/ Germany	Case series	23 (Solitaire TM : 9; Revive TM : 12; both: 2)	70 (33–83)	AB: 100%	24 (7–42)
Gratz et al. [24]/2014/Switzerland	Case series	Solitaire TM : 227	68.2±14.7	CM: 64.7%; CI: 19%; tandem/multiple: 15.8%	16 (2–36)
Gascon et al. [37]/2013/France	Case series	144 (Solitaire TM : 138; Revive TM : 4; Trevo [®] : 2)	70 (26–91)	CM: 41.7%; CI: 22.8%; tandem: 11%	16 (3–36)
Jansen et al. [32]/2013/ USA, Sweden, Germany, Spain and Austria	Case series	Trevo [®] : 60	64.7±13.4	CM: 70%; CI: 21.7%; AB: 8.3%	17.7±4.8
Zaidat et al. [25]/2013/USA	Case series	Solitaire TM : 354	67.3±15.2	CM: 56%; CI: 23%; AB: 10%	18.1±6.6
Pereira et al. [26]/2013/ Switzerland, Spain, France, Germany, Canada and USA	Case series	Solitaire TM : 202	68.4±12.5	CM: 81.6%; CI: 18%	16.5±4.7
Yoon et al. [27]/2013/Korea	Case series	Solitaire TM : 74	66.2	CM: 59.5%; CI: 25.7%; AB: 14.8%	12.9
Akins et al. [28]/2014/USA	Case series	Solitaire TM : 144	67.1±12.0	CM: 76%; CI: 21%; Post/others: 4%	17.3±4.5
Rohde et al. [34]/2011/Germany	Case series	Revive TM : 10	78.3±6	CM: 50%; tandem: 40%; AB: 10%	19.0±9.2
Dávalos et al. [29]/2012/Spain, Germany, Switzerland, France, and Sweden	Case series	Solitaire TM : 141	66.3±13.1	CM: 59%; CI: 27%; AB: 11%; other: 2%	18 (14–21)
San Román et al. [33]/2012/Spain	Case series	Trevo [®] : 60	71.2±12.4	CM: 70%; CI: 20%; AB: 10%	18 (12–22)

IAT = Intra-arterial; CM = middle cerebral artery; CI = internal cerebral artery; AB = basilar artery; Post = posterior circulation.

¹ Figures are median (range) or mean ± SD.

Table 2. GRADE evidence profile: safety results of stent retrievers in acute ischaemic stroke

Quality assessment		Summary of findings					Importance of outcome				
studies/design (patients)	limitations	consistency	indirect-ness	precision	publication bias	quality of the evidence		event rate (%)	control retrievers (Merci)	relative effect (95% CI)	absolute effect
Symptomatic ICH 24 h (ECASS definition; assessed by brain MRI or CT)											
2 RCT's (288 patients)	not significant	no important inconsistency	direct	imprecision ^b	none detected	⊕⊕⊕0 MODERATE	7/144 (4.9)	14/144 (9.7)	OR 0.43 (0.09–2.06) p = 0.29	5 fewer per 100 (from 8 less to 2 more)	CRITICAL
13 case series (1,538 patients)	very serious ^c	no important inconsistency	direct	imprecision not significant	none detected	⊕000 VERY LOW	110/1,538 (7.3±3.7) ^d	–	–	–	CRITICAL
Asymptomatic ICH 24 h (assessed by brain MRI or CT)											
2 RCT's (291 patients)	not significant ^a	no important inconsistency	direct	imprecision not significant	none detected	⊕⊕⊕⊕ HIGH	45/146 (30.8)	62/145 (42.8)	OR 0.59 (0.35–0.97) p = 0.04	12 fewer per 100 (from 1 less to 22 less)	CRITICAL
4 case series (451 patients)	very serious ^c	no important inconsistency	direct	imprecision not significant	none detected	⊕000 VERY LOW	83/451 (18.3±8.9)	–	–	–	CRITICAL
All-cause perioperative mortality rate (24 h)											
1 RCT (178 patients)	not significant ^a	no important inconsistency	direct	imprecision not significant	none detected	⊕⊕⊕⊕ HIGH	2/88 (2.3)	0/90 (0)	not applicable	not applicable	CRITICAL
^a The study of Saver et al. [21] used an independent imaging laboratory and a clinical committee blinded to the group assigned to each patient. The interventional neurologist knows the type and size of device. They do not indicate whether losses occurred during the study, nor were analyses performed with intention to treat. The study by Nogueira et al. [31] is an open study, but does not specify whether the patients knew the device they were treated with. It is also indicated that a committee analysed the data and drafted the article independently. These limitations were not considered relevant enough to lower the quality of the evidence.											
^b The confidence interval includes an OR: 1.											
^c They do not have a control group.											
^d Weighted mean ± SD.											

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^bThe confidence interval includes an OR: 1.

^cThey do not have a control group.

^dWeighted mean ± SD.

Fig. 1. Forest plot for safety outcomes. **a** Symptomatic haemorrhage. **b** Asymptomatic haemorrhage.

Safety of Stent Retrievers

Symptomatic ICH

In the 2 RCTs included, symptomatic ICH at 24 h occurred in 4.9% of patients [21, 31] (table 2). In total, 288 patients were included in the combined analysis, and no significant differences were observed between groups (OR, 0.43; 95% CI, 0.09–2.06; $p = 0.29$; fig. 1).

In the 13 included case series ($n = 1,538$), the rate of symptomatic haemorrhage was $7.3 \pm 3.7\%$ [22, 24–30, 32–35, 37]. Additionally, no significant differences between stent retrievers and intravenous rtPA were found [30], nor were they found in patients treated with Trevo[®] or Solitaire[™] devices. In the 2 case series with basilar artery occlusion [23, 36], only 1 case of symptomatic ICH was observed [36].

According to the GRADE system, the quality of evidence for this outcome ranged from moderate in RCTs (due to the presence of imprecision) to very low in case series (table 2).

Asymptomatic ICH

The rate of asymptomatic ICH in patients treated with stent retrievers was 31% in RCTs [21, 31] (table 2). Meta-analyses ($n = 291$) achieved a significant difference ($p = 0.04$) favourable to the stent retriever group (OR, 0.59; 95% CI, 0.35–0.97; fig. 1).

The 4 case series included ($n = 451$) had a weighted mean of asymptomatic haemorrhage rate of $18 \pm 8.9\%$ [22, 24, 28, 32]. In patients with basilar artery occlusion, only Möhlenbruch et al. [36] reported a single case of asymptomatic haemorrhage.

The quality of evidence from RCTs was high because they did not present methodological limitations, whereas case series had a very low evidence quality (table 2).

Perioperative All-Cause Mortality (at 24 h)

In only 1 RCT in which Trevo[®] was compared with Merci[®], 2 deaths at 24 h were recorded in the first group (2%) and none in the comparison group [31] (table 2).

Available evidence to assess this finding was limited, with only 1 high-quality RCT (table 2).

Efficacy of Stent Retrievers

Recanalisation Success

The rate of successful recanalisation (defined as TICI flow ≥ 2) in the 2 RCTs ($n = 285$) was 79.6% (table 3) [21, 31], resulting in a significant difference ($p < 0.00001$) in favour of the stent retriever group (OR, 4.56; 95% CI, 2.63–7.90; fig. 2). In the 12 case series ($n = 1,397$), the weighted mean of successful recanalisation was $80.8 \pm 7.7\%$.

Ribo et al. [35] compared the success of recanalisation in patients treated with stent retrievers (Solitaire[™] and Trevo[®]), Merci[®] and intra-arterial rtPA, finding a higher success rate in the first group (67.2, 57.3 and 50.8%, respectively; $p = 0.05$). Comparing the Solitaire[™] device with Trevo[®], no significant differences were found [30]. In patients with exclusive basilar artery occlusion, recanalisation success ranged between 75 [36] and 84% [23].

Procedure Time

In RCTs, the time to recanalisation in patients treated with stent retrievers ranged from 36 ± 11.75 to 47.8 ± 44.2 min, while in the control group (Merci[®]), it ranged from 47.3 ± 28.8 to 52 ± 10.5 min [21, 31] (table 3). The pooled analysis showed a similar procedure time in both groups (mean difference: -8.8 , 95% CI, -24.8 to 7.2 ; $p = 0.28$).

In case series (9 studies, $n = 1,156$), the weighted mean value of this outcome ranged from 29 ± 27 to 97 ± 46.7 min [24–26, 29, 30, 32–35]. In a comparative case series, a shorter procedure time was observed in patients treated with stent retrievers (Solitaire[™] and Trevo[®]) versus intra-arterial rtPA or the Merci[®] clot retriever (88 ± 46 , 103 ± 70 and 128 ± 62 min, respectively; $p < 0.01$) [35]. Mendonça et al. [30] found no differences between Solitaire[™] and Trevo[®] stent retrievers. Finally, the procedure time (from the first angiogram to recanalisation) in patients with basilar artery occlusion was variable, ranging between 30 (13–100) [23] and 77 (30–324) min [36].

Neurological Deterioration (24 h)

In RCTs, the level of neurological deficit after the intervention as measured by the NIHSS varied between 4.5 ± 2.9 and 12 ± 2.3 points in patients treated with stent retrievers, and between 18 ± 1.6 and 30 ± 10 points in those in whom recanalisation was performed with the Merci[®] device [21, 31] (table 3). The pooled analysis of the RCTs showed no statistically significant differences (mean difference: -15.7 ; 95% CI, -34.8 to -3.4 ; $p = 0.11$; fig. 2).

In case series (6 studies, $n = 327$), the weighted mean deficit after the intervention ranged from 7 ± 6.25 to 17.5 ± 12.3 points (mean calculated from median if required) [22, 27, 29, 30, 34, 35]. In a comparative case series, a minor neurological deficit was observed in patients treated with stent retrievers compared with those for whom a Merci[®] retriever or rtPA was used [median (range): 7 (1–26), 12 (5–30) and 14 (2–30), respectively, $p = 0.05$] [35].

In another comparative case series, no significant differences were found between the Solitaire[™] stent and rtPA [22], nor between the Trevo[®] and Solitaire[™] devices [30]. In patients with basilar artery occlusion treated with a Solitaire[™] device, a lower post-intervention neurological deficit was observed than in the aforementioned studies [median (range): 5 (0–28) [36], 4 (0–24) [23]].

Table 3. GRADE evidence profile: efficacy/effectiveness results of stent retrievers in acute ischaemic stroke

Quality assessment			Summary of findings						Importance of outcome		
studies (patients)	study limitations	consistency	indirectness	precision	publication bias	quality of the evidence	event rate (%) or mean ±SD		relative effect (95% CI)	absolute effect or mean difference stents vs. Merci®	
							stent retrievers	control (Merci®)			
Recanalisation success (TICI flow ≥2) ¹ (evaluated by angiography)											
2 RCTs (285 patients)	not significant ²	no important inconsistency ³	direct	imprecision not significant	not detected	⊕⊕⊕⊕ HIGH	113/142 (79.6)	70/143 (49)	OR 4.56 (2.63–7.90) p < 0.00001	32 fewer per 100 (from 23 to 39 less)	CRITICAL
12 case series (1,397 patients)	very serious ⁴	no important inconsistency	direct	imprecision not significant	not detected	⊕⊕⊕⊕ VERY LOW	1,128/1,397 (80.8±7.7) ⁷	–	–	–	CRITICAL
Procedure time (min)											
2 RCTs (291 patients)	not significant ²	no important inconsistency	direct	imprecision not significant	not detected	⊕⊕⊕⊕ HIGH	36±11.7 to 47.8±44.2 ⁸ (n = 146)	47.3±28.8 to 52±10.5 ⁸ (n = 145)	–	MD: 8.8 min fewer in stents ⁹ (95% CI: –24.8; 7.2)	CRITICAL
9 case series (1,156 patients)	very serious ⁴	no important inconsistency	direct	imprecision not significant	not detected	⊕⊕⊕⊕ VERY LOW	29±27 to 97±46.7 ⁸	–	–	–	CRITICAL
Neurological deficit at 24 h (evaluated by the NIHSS scale, points)											
2 RCTs (291 patients)	not significant ²	no important inconsistency	direct	imprecision not significant	not detected	⊕⊕⊕⊕ HIGH	4.5±2.9 to 12±2.3 ⁸ (n = 146)	18±1.6 to 30±10 ⁸ (n = 145)	–	MD: 15.7 points fewer in stents ⁹ (95% CI: –34.8; 3.4)	CRITICAL
6 case series (327 patients)	very serious ⁴	no important inconsistency	direct	imprecision not significant	not detected	⊕⊕⊕⊕ VERY LOW	7±6.25 to 17.5±12.3 ⁸	–	–	–	CRITICAL
Good neurological outcome at 90 days (mRS score ≤2)											
2 RCTs (275 patients)	not significant ²	no important inconsistency	direct	imprecision not significant	not detected	⊕⊕⊕⊕ HIGH	66/140 (47.1)	35/135 (25.9)	OR 2.54 (1.52–4.25) p < 0.0004	21 more per 100 (from 9 to 34 more)	CRITICAL
10 case series (1,236 patients)	very serious ⁴	no important inconsistency	direct	imprecision not significant	not detected	⊕⊕⊕⊕ VERY LOW	561/1,236 (47.2±7.3) ⁷	–	–	–	CRITICAL
Mortality from all causes at 90 days											
2 RCTs (289 patients)	not significant ²	serious inconsistency ⁵	direct	imprecision ⁶	not detected	⊕⊕⊕⊕ LOW	39/146 (26.7)	42/143 (29.4)	OR 0.75 (0.17–3.37) p = 0.70	3 fewer per 100 (11 less to 8 more)	CRITICAL
8 case series (1,168 patients)	very serious ⁴	no important inconsistency	direct	imprecision not significant	not detected	⊕⊕⊕⊕ VERY LOW	242/1,168 (21.4±9.4) ⁷	–	–	–	CRITICAL

¹ In the study by Saver et al. [21], they used the thrombolysis in myocardial infarction flow. ² See limitations of RCTs in safety. ³ No heterogeneity tests. ⁴ No control group. ⁵ The measure of effect is different and the CIs do not overlap (I²: 87%). ⁶ The confidence interval includes an OR: 1 in the study by Nogueira et al. [31]. ⁷ Weighted mean ± SD. ⁸ Range of mean values shown in RCTs and case series. ⁹ Standardised difference time of recanalisation: –0.70, 95% CI –2.11 to 0.71; standardised difference of neurological deficit: –3.19, 95% CI –3.67 to –2.71.

Good Clinical Outcome (90 Days)

According to the 2 RCTs included (table 3), around 47% of patients with acute ischaemic stroke treated with stent retrievers had a good clinical outcome at 90 days compared with 26% of patients treated with the Merci® device. The combined analysis of the 2 RCTs (n = 275) [21, 31] observed a significant difference in favour of the stent retriever group (OR, 2.54; 95% CI, 1.52–4.25; p = 0.0004).

The result was similar in the 10 case series included (n = 1,236), with a good clinical outcome of $47.2 \pm 7.3\%$ [22, 24–27, 29, 30, 32, 33, 35]. Two case series found a higher percentage of appropriate clinical outcomes in those patients who received stent retrievers than in those in whom rtPA (60 vs. 37.5%, p = 0.001 [22]; 50.9 vs. 10%, p = 0.03 [35]) or Merci® (50.9 vs. 37.1%, p = 0.03) [35] was used. No differences between the Solitaire™ and Trevo® stents were found (40 vs. 38%, p = 0.435) [30]. In patients with basilar artery occlusion, the rates of good clinical outcome were similar to other studies (33 [36] and 48% [23]).

All-Cause Mortality (90 Days)

Mortality at 90 days was assessed in 2 RCTs and 8 case series (table 3). Of the 2 RCTs, 1 found a lower risk of death using the Solitaire™ device compared with the Merci® clot retriever (OR, 0.34; 95% CI, 0.14–0.81; p = 0.02) [21], with no significant differences seen with the Trevo® stent in the other RCT (OR, 1.61; 95% CI, 0.83–3.13; p = 0.18) [31]. The pooled analysis of 2 RCTs (n = 289) [21, 31] found no significant differences (OR, 0.75; 95% CI, 0.17–3.37; p = 0.62; fig. 2). These results should be interpreted with caution due to the low quality of the available scientific evidence.

In case series (n = 1,168), the average percentage of death in patients treated with stent retrievers was $21.4 \pm 9.4\%$ [22, 24–27, 30, 32, 33].

All-cause mortality at 90 days was similar in patients treated with Solitaire™ stents to that of those who received rtPA (29 vs. 27%, p = 0.75) [22]. No differences between the Solitaire™ and Trevo® devices were found (25 vs. 30%, p = 1.00) [30]. Regarding studies about patients with exclusive occlusion of the basilar artery, the 90-day mortality rate reached 12 and 29%, respectively [23, 36].

For this efficacy endpoint, the quality of the evidence level according to the GRADE approach was low for RCTs and very low for case series because of the serious inconsistency and imprecision observed in the RCTs (table 3).

Discussion

This systematic review analyses all studies in which patients were treated with mechanical thrombectomy using the Solitaire™, Trevo® or Revive™ device for acute ischaemic stroke, after being ineligible to receive intravenous rtPA therapy or for whom intravenous rtPA therapy had failed or was bridged. The available evidence suggests that stent retrievers are safe and effective devices that enable high recanalisation rates and good neurological outcomes in patients with acute ischaemic stroke due to intracranial artery occlusion. Furthermore, Solitaire™ and Trevo® have shown higher recanalisation rates and improved long-term clinical outcomes compared to early mechanical thrombectomy devices such as Merci®. In the following sections, we discuss the main safety and effectiveness outcomes reported in published studies about stent retrievers.

Regarding the safety of mechanical thrombectomy with stent retrievers, several factors may be associated with the ICH rate, i.e. previous atrial fibrillation (AF). Thus, in a retrospective case series, a larger and more significant risk of symptomatic ICH at 24 h was found in patients with AF or haemodynamic instability during the procedure, even though there

a **b** **c**

(For legend see next page.)

were no predicting factors in the multivariate analysis. The baseline ASPECT score independently predicted symptomatic ICH at 24 h [38]. This possible relationship is not clear in the reviewed evidence. In the RCT comparing the Solitaire™ stent with Merci® [21], the rates of AF were 45 and 67%, respectively, with higher but no significant differences in the haemorrhage rates in the Merci® group (2 vs. 11%). In addition, 2 case series with AF rates of 30–40% among the patients reported a haemorrhage rate of 10–12% [25, 33], while Yoon et al. [27] only observed 1.4% of symptomatic ICH among 54% of patients with AF. Therefore, it is likely that in the assessment of ICH, there is an influence of factors other than AF, such as procedural complications (embolisation of a region that was not previously affected, vascular perforation, etc.) or characteristics of patients associated with an increased haemorrhage risk.

Fig. 2. Forest plot for efficacy outcomes. **a** Recanalisation success. **b** Procedure time. **c** Neurological deficit (24 h). **d** 90-day good neurological outcome. **e** 90-day all-cause mortality rate.

Regarding stent retriever effectiveness, it could depend on factors related to the procedure, such as the successful recanalisation rate, time to achieve recanalisation or patient characteristics, such as prior neurologic deficit or location of the occlusion.

Successful Recanalisation

According to Soize et al. [38], the recanalisation success is a predicting factor of good clinical outcome at 3 months (mRS score ≤ 2). In our review, the combined results of the RCTs showed a successful recanalisation rate of 79.6% in stent retriever-treated patients, but only in 49% of patients treated with Merci[®], with 47 and 26% having an mRS score of 0–2 at the 3 months' follow-up, respectively [21, 31]. However, considering the studies separately, we can see that in the SWIFT trial [21], successful recanalisation was achieved in 61% of the Solitaire[™]-treated patients, and 58% of the patients reached an mRS score of 0–2 at the 3-months follow-up. On the other hand, in the RCT that compared the Trevo[®] device with Merci[®] [31], the results were slightly different than those of the SWIFT trial: recanalisation was seen in 86% of stent retriever-treated patients, but only 40% of them reached independence (mRS score 0–2) after 90 days. It is important to point out that this study had a delay of 4.7 h (onset to groin puncture).

Two of the most successful case series of recanalisation (90–95%) achieved good clinical outcome rates of 55–60% [22, 32]. Pereira et al. [26] also obtained good clinical results in 58% of patients with a smaller percentage of recanalisation (79%), although in this case series, the procedure time was reduced (29 ± 27 min; this factor is evaluated below). Series

with a lower successful revascularisation rate (73–75%) obtained adequate clinical outcomes of 42–45% [27, 33], or even lower (33%) [36]; however, this series included patients with a high baseline neurological deficit (24 on the NIHSS scale).

Procedure Time

Some studies suggest that better clinical outcomes may not be associated with the rate of successful recanalisation, but rather that it is achieved at an early stage [39, 40].

Thus, 2 retrospective series in patients treated with the Solitaire™ stent retriever found an inverse relationship between good clinical outcomes at 3 months and the duration of the procedure [38] or the time from symptom onset to recanalisation [41].

In this review, only a few studies showed similar results [26, 35]. However, one of the RCTs observed a higher percentage of good clinical outcomes in the stent retriever group (Trepo®) than in the Merci® group despite showing no differences in terms of time of recanalisation [31]. In addition, 1 case series showed a similar percentage of appropriate clinical outcomes that other series reviewed despite having a shorter procedure time (median: 30 min) [23].

Baseline Neurological Deficit

A high NIHSS score on admission appears to be an adequate predictor of bad outcome at 90 days (1-point increase on the NIHSS; OR, 1.23; 95% CI, 1.07–1.40) [42]. In addition, patients with bad clinical outcomes at 90 days had a high baseline neurological deficit (median NIHSS score: 24 points) [36]. However, a comparative case series observed the highest percentage of good outcome (60%) in patients with a high baseline neurological deficit (NIHSS score: 20) [22].

In the RCTs with a comparable previous neurological deficit, patients treated with stent retrievers had a higher percentage of good outcomes than patients treated with the Merci® device [21, 31].

Location of the Occlusion

Some studies have suggested that the location of the lesion may influence the rate of recanalisation [8, 43], neurological improvement [43] and good outcome [38]. The case series evaluated in this review have observed low appropriate outcomes when a high percentage of patients had occlusions localised in the basilar artery, distal internal carotid or tandem occlusions [23, 24, 27, 30, 36].

However, as indicated above, there appears to be a direct relationship between the incidence of recanalisation and a good clinical outcome, with the location of the occlusion being the less influencing factor. In the series of Baek et al. [23], a good outcome of 48% was achieved in patients with basilar artery occlusion, which may be due to the fact that the success of recanalisation was 85%. This could suggest that the affected vessel and recanalisation success are additional factors that would ultimately condition, to a greater or lesser extent, the clinical outcome.

90-Day All-Cause Mortality

One of the included RCTs found a lower mortality rate at 90 days with Solitaire™, despite having a symptomatic ICH percentage similar to those treated with Merci®. The reason could be that the first group obtained a lower procedure time and post-intervention neurologic deficit [21]. Finally, the retrospective series by Soize et al. [38] only found a higher mortality rate in those patients with large occlusions or symptomatic ICH.

The reviewed evidence shows an optimal recanalisation rate and clinical outcomes in patients treated with stent retrievers within 8 h after stroke onset. Two case series (49 patients) that included patients with basilar artery occlusion reported similar clinical

outcomes to other case series that included <10% patients with thrombosis in this location. However, some methodological limitations and the possibility of conflicts of interest should be considered. According to the GRADE method, the quality of the evidence derived from RCTs was moderate to low due to the existence of imprecision and inconsistency, and case series also provide a poor evidence level because of the absence of a control group. For this reason, the confidence in estimation of effects could be limited.

The outcome analysis of other published RCTs which compared intravenous rtPA with intra-arterial treatment may be useful to clarify existing uncertainties.

Recently, two randomised trials comparing endovascular procedures with medical treatment in acute ischaemic stroke have been published [44, 45]. In the IMS-III trial [44], patients were randomly assigned within 3 h after the onset of stroke symptoms to either intravenous alteplase alone or intravenous alteplase plus interventional techniques (intra-arterial alteplase alone, intra-arterial alteplase combined with low-intensity therapeutic ultrasound and use of the Merci® retriever or Penumbra® and Solitaire™ devices during the later phase of the study). The trial was stopped prematurely because it was clear that there was no significant difference between the two approaches.

In the SYNTHESIS trial [45], patients with acute ischaemic stroke were randomly allocated within 4.5 h after symptom onset to either intravenous alteplase alone or endovascular treatment (intra-arterial alteplase, mechanical clot disruption or retrieval, or a combination of these approaches). Again, endovascular treatment was no better than intravenous alteplase, possibly because of a delay in the start of treatment in the endovascular group.

These results have led to scepticism about the use of endovascular therapy in acute ischaemic stroke. However, in the opinion of Nogueira et al. [46], research results are only generalisable to a similar cohort as the target study population; however, the IMS-III and SYNTHESIS trials did not target the optimal population for endovascular therapy and used a small percentage of stent retrievers.

In contrast, the results of the MR CLEAN trial [47] presented a higher benefit, i.e. functional independence, of intra-arterial treatment (82% stent retrievers, 2% other devices and 0.4% intra-arterial thrombolytic agents) plus intravenous rtPA than intravenous rtPA alone, administered within 6 h after stroke onset, in the treatment of a proximal occlusion of the anterior circulation. On the same line, the ESCAPE trial showed evidence of the benefit of endovascular treatment in patients with moderate-to-severe ischaemic stroke. The trial authors reported a higher rate of functional independence (90-day mRS score ≤2) and a lower mortality rate with standard care plus endovascular treatment (preferably stent retrievers) than with standard care alone (intravenous alteplase alone) [48]. Another recently published RCT named EXTEND-IA trial showed that the Solitaire™ FR stent retriever used without delay alters alteplase as compared with alteplase alone and improved early neurological recovery and functional outcomes in patients with ischaemic stroke due to proximal occlusion [49].

Thus, an editorial paper reported that MR CLEAN data are ‘a step in the right direction’, although more well-designed trials are necessary to confirm these hopeful clinical results [50].

One of the possible limitations of this systematic review, as previously discussed, is that in order to simplify the analysis and the presentation of the RCT results, the two retrievable stents, Solitaire™ and Trevo®, were jointly evaluated, as they are devices with a similar structure and operation. This is based on a comparative study of these two devices carried out by Mendonça et al. [30] that found no significant differences in safety and effectiveness variables. Another potential limitation which could limit the analysis is the variability in the definitions of the study endpoints. However, only one outcome, successful recanalisation, was defined differently in both included RCTs, i.e. the thrombolysis in myocardial infarction or TICI flow. Another fact is that most of the included studies administered intravenous rtPA prior to the treatment with stent retrievers or other endovascular treatments (intra-arterial

thrombolysis, angioplasty/intracranial stent or other mechanical thrombectomy devices) used in those patients in whom recanalisation was not achieved. These adjuvant treatments may be confounding factors that could have more or less of an impact on the clinical findings shown by the stent retrievers in the reviewed evidence.

Conclusions

Considering the reviewed literature, it could be concluded that, for the endovascular treatment of acute ischaemic stroke, stent retrievers used within 8 h of stroke symptom onset lead to higher recanalisation rates and improved long-term clinical outcomes compared with early mechanical thrombectomy approaches. However, various factors such as the occlusion site or stroke severity should be analysed when establishing more precise indications for using this technique.

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On behalf of all authors, the corresponding author states that there is no conflict of interest.

References

- 1 Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, Moran AE, Sacco RL, Anderson L, Truelsen T, O'Donnell M, Venketasubramanian N, Barker-Collo S, Lawes CM, Wang W, Shinohara Y, Witt E, Ezzati M, Naghavi M, Murray C; Global Burden of Diseases I, and Risk Factors Study 2010 (GBD 2010) and the GBD Stroke Experts Group: Global and regional burden of stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. *Lancet* 2014;383:245–254.
- 2 WHO Department of Health Statistics and Information Systems: Cause-Specific Mortality: Regional Estimates for 2000–2011. Geneva, World Health Organization, 2013. http://www.who.int/healthinfo/global_burden_disease/estimates_regional/en/ (accessed November 7, 2013).
- 3 Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, Ezzati M: Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;380:2197–2223.
- 4 Jauch EC, Saver JL, Adams HPJ, Bruno A, Connors JJ, Demaerschalk BM, Khatri P, McMullan PWJ, Qureshi AI, Rosenfield K, Scott PA, Summers DR, Wang DZ, Wintermark M, Yonas H; American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Peripheral Vascular Disease, Council on Clinical Cardiology: Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2013;44:870–947.
- 5 Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D, Larrue V, Lees KR, Medeghri Z, Machnig T, Schneider D, von Kummer R, Wahlgren N, Toni D; ECASS Investigators: Thrombolysis with alteplase 3 to 4.5 h after acute ischemic stroke. *N Engl J Med* 2008;359:1317–1329.
- 6 Committee for Proprietary Medicinal Products (CPMP): Actilyse. Annex I. Amended Summary of Product Characteristics of the Reference Member State. The European Agency for the Evaluation of Medical Products (EMA). 2002. http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Actilyse_29/WC500010327.pdf (accessed September 15, 2014).
- 7 Center for Biologics Evaluation and Research. US License 1048: Activase®. Rockville, Food and Drug Administration, 2003. <http://www.fda.gov/downloads/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/therapeuticbiologicapplications/ucm080871.pdf> (accessed September 15, 2014).

- 8 Bhatia R, Hill MD, Shobha N, Menon B, Bal S, Kochar P, Watson T, Goyal M, Demchuk AM: Low rates of acute recanalization with intravenous recombinant tissue plasminogen activator in ischemic stroke: real-world experience and a call for action. *Stroke* 2010;41:2254–2258.
- 9 Riedel CH, Zimmermann P, Jensen-Kondering U, Stingele R, Deuschl G, Jansen O: The importance of size: successful recanalization by intravenous thrombolysis in acute anterior stroke depends on thrombus length. *Stroke* 2011;42:1775–1777.
- 10 van den Berg JS, de Jong G: Why ischemic stroke patients do not receive thrombolytic treatment: results from a general hospital. *Acta Neurol Scand* 2009;120:157–160.
- 11 Shobha N, Buchan AM, Hill MD; Canadian Alteplase for Stroke Effectiveness Study (CASES): Thrombolysis at 3–4.5 h after acute ischemic stroke onset – evidence from the Canadian Alteplase for Stroke Effectiveness Study (CASES) registry. *Cerebrovasc Dis* 2011;31:223–228.
- 12 Center for Devices and Radiological Health: Solitaire™ FR Revascularization Device 510(K) Application. Rockville, US Food and Drug Administration, 2012. http://www.accessdata.fda.gov/cdrh_docs/pdf11/K113455.pdf (accessed November 5, 2013).
- 13 Center for Devices and Radiological Health: Modified Trevo Retriever 510(K) Application. Silver Spring, US Food and Drug Administration, 2012. http://www.accessdata.fda.gov/cdrh_docs/pdf12/K122478.pdf (accessed November 15, 2013).
- 14 Center for Devices and Radiological Health: Trevo Retriever 510(K) Application. Silver Spring, US Food and Drug Administration, 2012. http://www.accessdata.fda.gov/cdrh_docs/pdf12/K120961.pdf (accessed November 5, 2013).
- 15 Penumbra Pivotal Stroke Trial Investigators: The penumbra pivotal stroke trial: safety and effectiveness of a new generation of mechanical devices for clot removal in intracranial large vessel occlusive disease. *Stroke* 2009;40:2761–2768.
- 16 Smith WS, Sung G, Saver J, Budzik R, Duckwiler G, Liebeskind DS, Lutsep HL, Rymer MM, Higashida RT, Starkman S, Gobin YP; Multi MERCI Investigators; Frei D, Grobelny T, Hellinger F, Huddle D, Kidwell C, Koroshetz W, Marks M, Nesbit G, Silverman IE: Mechanical thrombectomy for acute ischemic stroke: final results of the Multi MERCI trial. *Stroke* 2008;39:1205–1212.
- 17 Guyatt GH, Oxman AD, Kunz R, Atkins D, Brozek J, Vist G, Alderson P, Glasziou P, Falck-Ytter Y, Schünemann HJ: GRADE guidelines: 2. Framing the question and deciding on important outcomes. *J Clin Epidemiol* 2011;64:395–400.
- 18 Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, Vist GE, Falck-Ytter Y, Meerpohl J, Norris S, Guyatt GH: GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol* 2011;64:401–406.
- 19 Guyatt GH, Oxman AD, Santesso N, Helfand M, Vist G, Kunz R, Brozek J, Norris S, Meerpohl J, Djulbegovic B, Alonso-Coello P, Post PN, Busse JW, Glasziou P, Christensen R, Schünemann HJ: GRADE guidelines: 12. Preparing summary of findings tables-binary outcomes. *J Clin Epidemiol* 2013;66:158–172.
- 20 Hozo SP, Djulbegovic B, Hozo I: Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol* 2005;20:13.
- 21 Saver JL, Jahan R, Levy EI, Jovin TG, Baxter B, Nogueira RG, Clark W, Budzik R, Zaidat OO, Trialists S: Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. *Lancet* 2012;380:1241–1249.
- 22 Leker RR, Eichel R, Gomori JM, Ramirez de Noriega F, Ben-Hur T, Cohen JE: Stent-based thrombectomy versus intravenous tissue plasminogen activator in patients with acute middle cerebral artery occlusion. *Stroke* 2012;43:3389–3391.
- 23 Baek JM, Yoon W, Kim SK, Jung MY, Park MS, Kim JT, Kang HK: Acute basilar artery occlusion: outcome of mechanical thrombectomy with solitaire stent within 8 hours of stroke onset. *AJNR Am J Neuroradiol* 2014;35:989–993.
- 24 Gratz PP, Jung S, Schroth G, Gralla J, Mordasini P, Hsieh K, Heldner MR, Mattle HP, Mono ML, Fischer U, Arnold M, Zubler C: Outcome of standard and high-risk patients with acute anterior circulation stroke after stent retriever thrombectomy. *Stroke* 2014;45:152–158.
- 25 Zaidat OO, Castonguay AC, Gupta R, Sun CH, Martin C, Holloway WE, Mueller-Kronast N, English JD, Linfante I, Dabus G, Malisch TW, Marden FA, Bozorgchami H, Xavier A, Rai AT, Froehler MT, Badruddin A, Nguyen TN, Taqi MA, Abraham MG, Janardhan V, Shaltoni H, Novakovic R, Yoo AJ, Abou-Chebl A, Chen PR, Britz GW, Kaushal R, Nanda A, Issa MA, Nogueira RG; North American Solitaire Stent Retriever Acute Stroke registry: post-marketing revascularization and clinical outcome results. *J Neurointerv Surg* 2014;6:584–588.
- 26 Pereira VM, Gralla J, Davalos A, Bonafe A, Castano C, Chapot R, Liebeskind DS, Nogueira RG, Arnold M, Sztajzel R, Liebig T, Goyal M, Bessermann M, Moreno A, Schroth G: Prospective, multicenter, single-arm study of mechanical thrombectomy using Solitaire Flow Restoration in acute ischemic stroke. *Stroke* 2013;44:2802–2807.
- 27 Yoon W, Jung MY, Jung SH, Park MS, Kim JT, Kang HK: Subarachnoid hemorrhage in a multimodal approach heavily weighted toward mechanical thrombectomy with Solitaire stent in acute stroke. *Stroke* 2013;44:414–419.
- 28 Akins PT, Amar AP, Pakbaz RS, Fields JD; on behalf of the SWIFT Investigators: Complications of endovascular treatment for acute stroke in the SWIFT trial with Solitaire and Merci devices. *AJNR Am J Neuroradiol* 2014;35:524–528.

- 29 Dávalos A, Pereira VM, Chapot R, Bonafé A, Andersson T, Gralla J: Retrospective multicenter study of Solitaire FR for revascularization in the treatment of acute ischemic stroke. *Stroke* 2012;43:2699–2705.
- 30 Mendonça N, Flores A, Pagola J, Rubiera M, Rodríguez-Luna D, Miquel MA, Cardona P, Quesada H, Mora P, Alvarez-Sabin J, Molina C, Ribo M: Trevo versus Solitaire a head-to-head comparison between two heavy weights of clot retrieval. *J Neuroimaging* 2014;24:167–170.
- 31 Nogueira RG, Lutsep HL, Gupta R, Jovin TG, Albers GW, Walker GA, Liebeskind DS, Smith WS: Trevo versus Merci retrievers for thrombectomy revascularisation of large vessel occlusions in acute ischaemic stroke (TREVO 2): a randomised trial. *Lancet* 2012;380:1231–1240.
- 32 Jansen O, Macho JM, Killer-Oberpfalzer M, Liebeskind D, Wahlgren N: Neurothrombectomy for the treatment of acute ischemic stroke: results from the TREVO study. *Cerebrovasc Dis* 2013;36:218–225.
- 33 San Román L, Obach V, Blasco J, Macho J, Lopez A, Urrea X, Tomasello A, Cervera A, Amaro S, Perandreu J, Branera J, Capurro S, Oleaga L, Chamorro A: Single-center experience of cerebral artery thrombectomy using the TREVO device in 60 patients with acute ischemic stroke. *Stroke* 2012;43:1657–1659.
- 34 Rohde S, Haehnel S, Herweh C, Pham M, Stampfl S, Ringleb PA, Bendszus M: Mechanical thrombectomy in acute embolic stroke preliminary results with the Revive device. *Stroke* 2011;42:2954–2956.
- 35 Ribo M, Molina CA, Jankowitz B, Tomasello A, Zaidi S, Jumaa M, Coscojuela P, Oakley J, Alvarez-Sabin J, Jovin T: Stentriever versus other endovascular treatment methods for acute stroke: comparison of procedural results and their relationship to outcomes. *J Neurointerv Surg* 2014;6:265–269.
- 36 Möhlenbruch M, Stampfl S, Behrens L, Herweh C, Rohde S, Bendszus M, Hametner C, Nagel S, Ringleb PA, Pham M: Mechanical thrombectomy with stent retrievers in acute basilar artery occlusion. *AJNR Am J Neuroradiol* 2014;35:959–964.
- 37 Gascou G, Lobotesis K, Machi P, Maldonado I, Vendrell JF, Riquelme C, Eker O, Mercier G, Mourand I, Arquizán C, Bonafé A, Costalat V: Stent retrievers in acute ischemic stroke: complications and failures during the perioperative period. *AJNR Am J Neuroradiol* 2014;4:62–66.
- 38 Soize S, Barbe C, Kadziolka K, Estrade L, Serre I, Pierot L: Predictive factors of outcome and hemorrhage after acute ischemic stroke treated by mechanical thrombectomy with a stent-retriever. *Neuroradiology* 2013;55:977–987.
- 39 Khatri P, Abruzzo T, Yeatts SD, Nichols C, Broderick JP, Tomsick TA; IMS I and II Investigators: Good clinical outcome after ischemic stroke with successful revascularization is time-dependent. *Neurology* 2009;73:1066–1072.
- 40 Molina CA, Alexandrov AV, Demchuk AM, Saqqur M, Uchino K, Alvarez-Sabín J; CLOTBUST Investigators: Improving the predictive accuracy of recanalization on stroke outcome in patients treated with tissue plasminogen activator. *Stroke* 2004;35:151–156.
- 41 Raoult H, Eugene F, Ferre JC, Gentric JC, Ronziere T, Stamm A, Gauvrit JY: Prognostic factors for outcomes after mechanical thrombectomy with Solitaire stent. *J Neuroradiol* 2013;40:252–259.
- 42 Costalat V, Lobotesis K, Machi P, Mourand I, Maldonado I, Heroum C, Vendrell JF, Milhaud D, Riquelme C, Bonafé A, Arquizán C: Prognostic factors related to clinical outcome following thrombectomy in ischemic stroke (RECOSt study). 50 patients prospective study. *Eur J Neurol* 2012;81:4075–4082.
- 43 Kim YS, Garami Z, Mikulik R, Molina CA, Alexandrov AV; CLOTBUST Collaborators: Early recanalization rates and clinical outcomes in patients with tandem internal carotid artery/middle cerebral artery occlusion and isolated middle cerebral artery occlusion. *Stroke* 2005;36:869–871.
- 44 Broderick JP, Palesch YY, Demchuk AM, Yeatts SD, Khatri P, Hill MD, Jauch EC, Jovin TG, Yan B, Silver FL, von Kummer R, Molina CA, Demaerschalk BM, Budzik R, Clark WM, Zaidat OO, Malisch TW, Goyal M, Schonewille WJ, Mazighi M, Engelter ST, Anderson C, Spilker J, Carrozzella J, Ryckborst KJ, Janis LS, Martin RH, Foster LD, Tomsick TA: Endovascular therapy after intravenous t-PA versus t-PA alone for stroke. *N Engl J Med* 2013;368:893–903.
- 45 Ciccone A, Valvassori L, Nichelatti M, Sgoifo A, Ponzio M, Sterzi R, Boccardi E: Endovascular treatment for acute ischemic stroke. *N Engl J Med* 2013;368:904–913.
- 46 Nogueira RG, Gupta R, Dávalos A: IMS-III and SYNTHESIS expansion trials of endovascular therapy in acute ischemic stroke: how can we improve? *Stroke* 2013;44:3272–3274.
- 47 Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, Schonewille WJ, Vos JA, Nederkoorn PJ, Wermer MJ, van Walderveen MA, Staals J, Hofmeijer J, van Oostayen JA, Lycklama à Nijeholt GJ, Boiten J, Brouwer PA, Emmer BJ, de Bruijn SF, van Dijk LC, Kappelle LJ, Lo RH, van Dijk EJ, de Vries J, de Kort PL, van Rooij WJ, van den Berg JS, van Hasselt BA, Aerden LA, Dallinga RJ, Visser MC, Bot JC, Vroomen PC, Eshghi O, Schreuder TH, Heijboer RJ, Keizer K, Tielbeek AV, den Hertog HM, Gerrits DG, van den Berg-Vos RM, Karas GB, Steyerberg EW, Flach HZ, Marquering HA, Sprengers ME, Jenniskens SF, Beenen LF, van den Berg R, Koudstaal PJ, van Zwam WH, Roos YB, van der Lugt A, van Oostenbrugge RJ, Majoie CB, Dippel DW; MR CLEAN Investigators: A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med* 2014;372:11–20.
- 48 Goyal M, Demchuk AM, Menon BK, et al; ESCAPE Trial Investigators: Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med* 2015;372:1019–1030.
- 49 Campbell BC, Mitchell PJ, Kleinig TJ, et al; EXTEND-IA Investigators: Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med* 2015;372:1009–1018.
- 50 Hacke W: Interventional thrombectomy for major stroke – a step in the right direction. *N Engl J Med* 2014;372:76–77.