Aspiration Thrombectomy for Posterior Circulation Stroke: A Systematic Review and Meta-Analysis

Abstract

Purpose: This study aims to analyze the efficacy of aspiration thrombectomy for large vessel occlusion of the posterior circulation, with an emphasis on comparison with stent retriever thrombectomy. **Methods:** A systematic review and meta-analysis were performed to analyze the outcomes of aspiration thrombectomy for acute posterior circulation stroke. For those studies that included data for both aspiration and stent-retriever thrombectomy, we additionally performed a second meta-analysis comparing their outcomes against each other. **Results:** A total of 17 articles were included. For the primary outcomes, the weighted pooled rate of mortality was 26.71% (95% confidence interval [CI] 19.35%–34.71%), modified Ranking Score (mRS) 0–2 at 3 months was 36.71 (95% CI 32.02%–41.52%), and successful recanalization 89.26% (95% CI 83.12%–94.31%). Primary stent retriever thrombectomy was inferior to primary aspiration thrombectomy for the outcomes of successful recanalization (odds ratio [OR] 0.57, 95% CI 0.36–0.91, $P = 0.018$), complete recanalization (OR 0.65, 95% CI 0.42–0.1.00, $P = 0.048$), procedure time (mean difference 28.17, 95% CI 9.47–46.87), and rate of embolization to new territory (OR 5.01, 95% CI 1.20–20.87, $P = 0.027$). No significant difference was seen for other outcomes. Further subgroup analysis suggests that for the outcome of recanalization, this may be dependent on the availability of second-line stent retriever thrombectomy. **Limitations:** The included studies were observational in nature. There was unresolved heterogeneity in some of the outcomes. **Conclusions:** There was no statistically significant difference seen for the primary outcomes of mortality and favorable outcome (mRS score 0–2) at 3 months. While superior rates of successful recanalization, complete recanalization, faster procedural time, and improved safety profile for primary aspiration thrombectomy were seen compared to primary stent retriever thrombectomy, this did not translate into superior clinical outcomes.

Keywords: *Aspiration, posterior circulation, stent retriever, stroke, thrombectomy*

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Introduction

Endovascular thrombectomy has been established as the standard for care for patients with anterior circulation stroke caused by large vessel occlusion, with several randomized controlled trials and meta-analyses demonstrating superior clinical outcomes of stent-retriever-based thrombectomy over standard medical care.[1-6]

Previous observational studies have demonstrated higher rates of revascularization and shorter procedural times for primary contact aspiration thrombectomy compared with stent-retriever thrombectomy.[7-13] A single-center retrospective cost-effectiveness study also showed that contact aspiration represented the most technically successful and cost-effective approach.[7] However, there

have only been two prospective randomized trials to date, ASTER[14] and COMPASS (not yet published at the time of writing), that have compared contact aspiration against stent retriever thrombectomy in the anterior circulation. In the ASTER trial, contact aspiration showed no statistically significant difference in angiographic and clinical outcomes. Interestingly, however, the result was significant for the nonprespecified outcome of clot contact to recanalization in the contact aspiration group (13 vs. 22 min, $P = 0.03$).[14]

Within the literature, the terms a direct aspiration first pass technique (ADAPT) or contact aspiration generally describe a first-line approach to thrombectomy with a large bore catheter (generally with a distal inner lumen of ≥0.060 inches) being used to aspirate the thrombus.[8,14-16] If this fails, then the catheter can be used to facilitate

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further techniques such as stent retriever thrombectomy. As a more general term, aspiration thrombectomy also includes use of the traditional Penumbra aspiration system with separator and contact aspiration with smaller intermediate sized catheters.[7]

The situation, however, is much less clear for the posterior circulation. There are currently only observational data available on endovascular thrombectomy for posterior circulation stroke (Class III evidence), with no published randomized trial to date that has evaluated endovascular intervention versus standard medical treatment or different methods of endovascular intervention against each other. In particular, there is limited research on the effectiveness of aspiration thrombectomy. Hence, we decided to perform a systematic review and meta-analysis of the efficacy (angiographic and clinical) and safety outcomes of aspiration thrombectomy. For those studies, that included both aspiration and stent-retriever thrombectomy, we additionally performed a second meta-analysis comparing their outcomes against each other.

Methods

Independent ethics committee approval was not required given the study design, i.e., systematic review and meta-analysis of already published literature. This paper was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[17]

Search strategy

The databases Ovid MEDLINE, PubMed, and EMBASE were searched between December 2010 and November 1, 2018. The following terms and their combinations were used as either keywords or MeSH headings: "posterior circulation" "basilar" "stroke," "thrombectomy," "ADAPT," "aspiration," or "stent retriever." Reference lists of research articles were further analyzed to look for potentially appropriate additional studies. All studies were included which satisfied inclusion and exclusion criteria within search terms.

Studies were included if they reported aspiration thrombectomy for acute posterior circulation stroke. All studies regardless of design (including retrospective and prospective) were allowed. The sample size needed to be a minimum of five patients, with studies reporting less than this being excluded. Other inclusion criteria included English language articles or articles translated into English. Other exclusion criteria included duplicate studies, intervention other than aspiration thrombectomy, and lack of information regarding study outcomes. Gray literature such as conference abstracts was permissible given the limited amount of data in this particular area, with sensitivity analyses being conducted to account for study quality.

If studies included the technique of concurrent stent retriever thrombectomy with contact aspiration through an intermediate sized catheter, also known as the Solumbra technique, then this was included with the primary stent retriever thrombectomy group for the second meta-analysis.[9,18,19] If studies included aspiration thrombectomy with rescue stent retriever thrombectomy, then this was included with the primary aspiration thrombectomy group.

Data extraction and quality appraisal

Titles and abstracts were screened by two independent reviewers (K. S. and M. T.), with the full-text paper accessed if they were deemed potentially suitable. Research articles were read in their entirety if a decision on study inclusion could not be determined at title/abstract level. Contact with corresponding authors was attempted if further information was needed. Data on baseline characteristics and study outcomes were then independently extracted into an *a priori* standardized form by the two reviewers (K. S. and M. T.) and combined into a single table once this process was complete. Any disagreements were resolved through consensus of the two reviewers. We planned to settle discrepancies through discussion or adjudication by a third reviewer; however, this was deemed unnecessary given there were no major disagreements.

Primary outcomes were mortality, favorable outcome (modified Ranking Score [mRS] score 0–2) at 3 months, and successful recanalization. Secondary outcomes were symptomatic intracranial hemorrhage (SICH), any intracranial hemorrhage (ICH), complete recanalization, embolization to new territory, dissection and perforation, procedure time, and conversion to alternate therapy. For the analysis, comparing primary stent retriever thrombectomy against primary aspiration thrombectomy, the additional outcome of procedure time was also parsed.

Mortality was evaluated at 90 days; however, if this was not available, then the nearest value was used. Favorable outcome was defined as mRS 0–2 at 90 days or the nearest value. SICH was defined as any ICH associated with a worsening of the National Institutes Health Stroke Scale (NIHSS) score by $\geq$4 within 24 h, as per the European Cooperative Acute Stroke Study-II definition.[20] If these data were not available, then the rate of Type 2 Parenchymal Hematoma was used as a surrogate. Successful recanalization was defined as thrombolysis in cerebral infarction (TICI) 2b/3 (if not available, then modified TICI (mTICI) 2b/3 or thrombolysis in myocardial infarction 2/3 was used).

Each study was critically appraised by two independent reviewers (K. S. and M. T.) using the checklist published by the National Institute of Health for before-after studies with

no control group.[21] This is a 12-item quality assessment tool that enabled an overall quality rating to be assigned to the studies.

Data synthesis

For the first meta-analysis on outcomes of aspiration thrombectomy, the Freeman-Tukey double arcsine transformation was applied to the extracted data from individual studies, which were then back-transformed to form mean weighted probabilities with 95% confidence intervals (CIs). If heterogeneity was insignificant ($I^2 < 50\%$), then the fixed effect model was used to generate standard errors. For significant heterogeneity ($I^2 < 50\%$), the random effects model was used.

For the second meta-analysis on the comparison of outcomes of primary stent retriever thrombectomy versus primary aspiration thrombectomy, two by two tables for binary outcomes and continuous outcomes with standard deviations were extracted from individual studies. If heterogeneity was significant, then a random effect was used; otherwise, the fixed effects model was used. 95% CIs for odds ratios (ORs) and weighted mean differences (MDs) for continuous outcomes were subsequently calculated.

Assessment of heterogeneity and publication bias

Heterogeneity was assessed through the Cochran Q test and Higgin's I^2 statistic. $P < 0.05$ and $I^2 > 50\%$ was considered statistically significant. Publication bias was evaluated with the Begg and Mazumdar's rank correlation test, with $P < 0.05$ being deemed statistically significant and qualitatively through the assessment of funnel plots. Trim and fill plot analysis was performed to generate publication bias adjusted mean weighted probabilities and pooled ORs.

Sensitivity analysis

Sensitivity analyses and meta-regression were planned *a priori* and performed to determine potential sources of heterogeneity. Subgroup syntheses were performed based on publication year (≥2016 and <2016) and study quality (low quality and moderate-high quality). Meta-regression was done to compare outcomes against the rate of intravenous thrombolysis, time to groin puncture, age, sex, and baseline NIHSS.

Software

All analyses and calculations in this meta-analysis were performed using the Mix V2.0 Pro statistical package. (BiostatXL, Sunnyvale, California, USA).

Results

Study selection

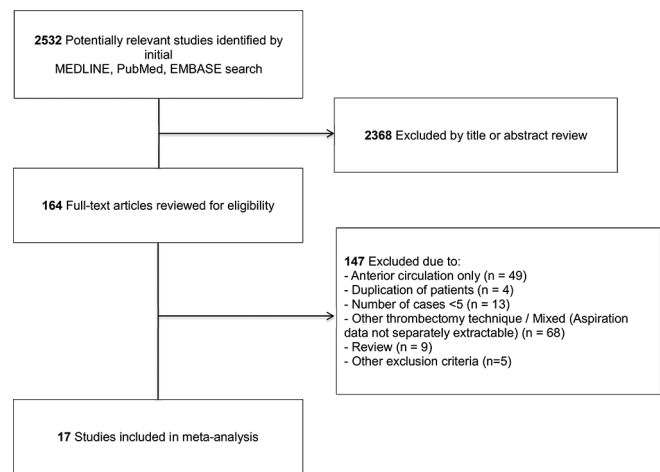A PRISMA flow diagram is presented in Figure 1.

Figure 1: Preferred reporting items for systematic reviews and meta-analyses flow diagram

A total of 2532 articles were identified from Ovid MEDLINE, PubMed, and EMBASE. After evaluating the titles and abstracts of these articles, 164 remained eligible for assessment. The full texts of these articles were assessed, and 17 articles fulfilled the inclusion criteria. There were no major disagreements between the authors of this review.

Baseline characteristics and study outcomes

Tables 1 and 2 show the weighted mean age of the combined aspiration thrombectomy group was 68.5 years and 57.9% were male. The weighted mean NIHSS was 18.7, time to groin puncture was 329.2 min, and time to recanalization was 47.3 min. Intravenous thrombolysis was used on average in 39.1% of cases. The weighted mean prevalence of hypertension was 52.4%, dyslipidemia was 35.4%, atrial fibrillation was 36.4%, diabetes mellitus was 27.9%, history of stroke was 33.9%, Supplementary Table 1 presents more detailed information on baseline characteristics.

For the second meta-analysis, the baseline characteristics of the aspiration thrombectomy and stent retriever thrombectomy groups are presented in Table 3. Pooled standard deviations were not calculated given many studies reported sample medians, ranges and/or interquartile ranges, which may lead to inaccurate and unreliable results.

Meta-analysis of outcomes for aspiration thrombectomy

Figures 2-4 show for the primary outcomes, pooled mortality for the combined aspiration thrombectomy group was 26.71% (95% CI 19.35%–34.71%), successful recanalization was 86.26% (95% CI 83.12%–94.31%), and favorable outcome at 3 months was 36.71% (95% CI 32.02%–41.52%).

For the secondary outcomes, the mean weighted probability of SICH was 3.20% (95% CI 1.20%–5.82%), any ICH was

Table 1: Study outcomes

Study (main author)	Group (n)	Study Period (year)	Design	Recan	mRS ≤2 (score)	Mortality	Full	Recan time (min)	SICH/ PH 2	Any	HI	PH	SAH
Alawieh et al.[22]	Asp (56)	2013-2017	P, SC	96.4	42.9	28.6	-	26.3±20	5.4	26.8	-	-	-
De La Riva et al.[23]	Asp (21)	2015-2016	P, MC	90.5	52.4	19.0	-	55 (30-90)	-	14.3	-	-	-
	SR (40)	2105-2016		75.0	50.0	17.5	-	90 (30-118)	-	12.5	-	-	-
Eom et al.[24]	As P (32)	2006-2013	R, MC	88	34 (≤3)	25	-	75.5±42.2	0	18.8	12.5	0	6.25
Gerber et al.[25]	Asp (20)	2013-2016	R, SC	85	45 (≤3, discharge)	20	75	55±12	25	13.5	35	5	10
	SR (13)	2013-2016		69.2	7.7 (≤3, discharge)	31	46.2	97±28	23.1	50	15.4	7.7	7.7
Giorgianni et al.[26]	Asp (27)	2010-2015	R, MC	75	-	-	-	-	-	-	-	-	-
	SR (60)			70	-	-	-	-	-	-	-	-	-
Gory et al.[27]	Asp (46)	2010-2016	P, MC	87.0	40	46.7	54.3	45 (34-62)	0	12.8	-	5.1	0
	SR (54)			72.2	34	42.0	31.5	56 (40-90)	4	18	-	4.0	2
Haussen et al.[28]	Asp (20)	2010-2017	P, SC	-	41	41	-	-	0	-	-	-	-
	SR (48)			-	31	53	-	-	2	-	-	-	-
Kang et al.[29]	Asp (67)	2011-2017	P, MC	94.0	46.9	16.4	61.2	44	2.9	16.5	13.4	2.9	0
	SR (145)			90.3	40.3	15.9	64.1	38	4.8	30.3	20.7	4.8	4.8
	All (212)							40 (25-70)					
Lee et al.[30]	Asp (8)	2012-2016	R, SC	62.5	25	37.5	50	51.3±32.6	0	50	-	-	-
	SR (7)			57.1	42.9	37.5	42.9	82.7±48.2	0	57.1	-	-	-
Li et al.[31]	All (68)	2014-2016	P, SC	89.7	45.6[SR (40), Asp (71)]	-	-	90 (65-118)	3.2	11.76	-	-	-
Mokin et al.[32]	Asp (42)	2012-2015	R, MC	83.3	33	-	-	46±28	-	-	-	-	-
	SR (58)			77.6	36	-	-	56±44	-	-	-	-	-
Park et al.[33]	Asp (16)	2012-2013	R, SC	81.3	56.3	6.3	43.75	97±45.2	0	6	6	0	0
Psychogios et al.[34]	Asp (16)	2007-2010	R, SC	68	7	-	-	-	0	-	-	-	-
Rentzos et al.[35]	Asp (18)	1991-2015	R, SC	94.4	-	-	-	-	-	-	-	-	-
	SR (11)			45.5	-	-	-	-	-	-	-	-	-
Roth et al.[36]	Asp (12)	2009-2010	R, SC	83.3	33.3	33.3	83.3	-	0	0	0	0	0
Son et al.[37]	Asp (18)	2011	R, SC	100	44.5	38.9	72.2	62.3±34.8	-	-	-	-	-
	SR (13)	2012-2013		84.6	38.5	46.2	23.1	101.9±41.4	-	-	-	-	-
Uno et al.[38]	Asp (34)	2011-2016	R, SC	100	56	12	74	25 (12-66)	0	-	-	-	-

Unless otherwise specified, all values are percentages. Mean and standard deviation is given in the form x±y, whereas median and interquartile range is given in the form x (y - z). Asp – Aspiration thrombectomy; SR – Stent retriever thrombectomy; P – Prospectively collected data; R – Retrospectively collected data; SC – single center; MC – Multi-center; Recan – Successful recanalization; mRS – Modified Ranking Score; Full – Complete recanalization; Recan time – Time to recanalization; SICH; – Symptomatic intracranial hemorrhage; PH – Parenchymal hematoma; Any – Any ICH; SAH – Subarachnoid hemorrhage
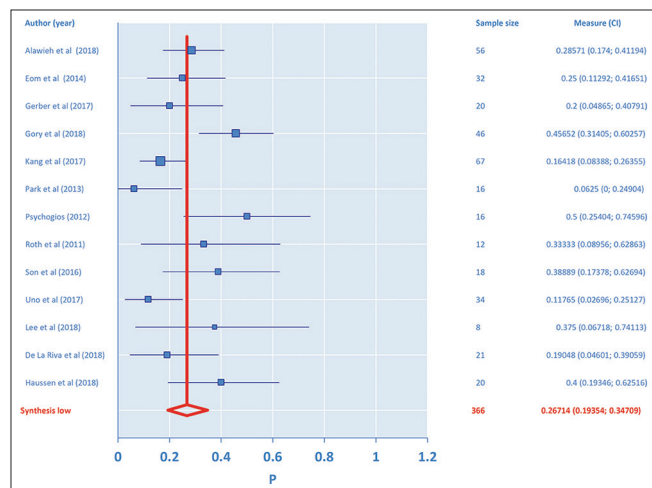

Figure 2: Forest plot for aspiration thrombectomy based on mortality

22.96% (95% CI 15.06%–31.82%), complete recanalization was 64.95% (95% CI 57.89%–71.64%), conversion to alternate therapy was 19.84% (95% CI 14.04%–26.27%), dissection and perforation was 2.39% (95% CI 0.13%–6.32%), Supplementary Table 2 presents more detailed statistics on heterogeneity and publication bias.

Meta-analysis of outcomes for stent retriever thrombectomy versus aspiration thrombectomy

As shown in Figures 5-7 for the primary outcomes, stent retriever thrombectomy was inferior for the outcome of successful recanalization (OR 0.57, 95% CI 0.36–0.91, $P = 0.018$), but this did not reach statistical significance for mortality (OR 1.06, 95% CI 0.70–1.62, $P = 0.78$) or favorable outcome at 3 months (OR 0.99, 95% CI 0.70–1.39, $P = 0.94$).

Table 2: Technical aspects

Study	Group (n)	Devices	Location (n)	IVT	D/P	Delay (min)	Rescue	ENT	Quality
Alawieh et al.	Asp (56)	Penumbra 064/068/3 MAX/4 MAX/5 MAX/5 MAXACE	BA (42)/PCA (21)/VA (1)	33.9	-	480±846	-	-	Mod
De La Riva et al.	Asp (21)	-	BA (18)/PCA (3)	76.2	-	5.4 (3.2-9.3)	-	-	Low
	SR (40)	-	BA (31)/PCA (6)/VA (3)	75	-	4.8 (3.5-6.8)	-	-	
Eom et al.	Asp (32)	Penumbra 032 (3)/041 (29)	-	36	-	281±138.3	-	-	Mod
Gerber et al.	Asp (20)	041 (10)/5 MAXACE (9)/both (1)	VA (1)/Prox (3)/Mid (11)/Dist (5)	60	0	253±68	10	10	Mod
	SR (13)	Penumbra 3D (6)/Preset (6)/Solitaire (1)	VA (1)/Prox (2)/Mid (9)/Dist (1)	85	23.1	353±114	0	23.1	
Giorgianni et al.	Asp (27)	-	-	-	-	295 (247-370)	-	-	Mod
	SR (60)	-	-	-	-	-	-	-	
Gory et al.	Asp (46)	Penumbra 5 MAXACE (3)/5 MAX (8)/other (8)	-	50	2.7	342 (241-440)	26.1	2.2	High
	SR (54)	Solitaire (42)/Trevo (7)/other (5)	-	40.7	7.41	276 (198-355)	3.7	18.5	
Haussen et al.	All (68)	Penumbra 5 MAX/064/068 Solitaire/Trevo	-	-	-	-	-	-	Low
			-	-	-	-	-	-	
Kang et al.	All (212)	N/A	Prox (52)/Mid (48)/Dist (112)	30.7	1.42	295 (224-424)	22.4	6	High
							22.1	-	
Lee et al.	Asp (8)	Penumbra 5Fr Aspiration Catheter	Trunk (5)/Tip (2)/BA+PCA (1)	50	-	-	3	-	Mod
	SR (7)	Solitaire/Trevo	Trunk (5)/Tip (1)/BA+PCA (1)	28.6	-	-	-	-	
Li et al.	All (68)	5 MAXACE, Navien Intracranial Support Catheter, Solitaire AB/FR	-	2.9	1.47	395 (312-517)	-	-	Mod
Mokin et al.	Asp (42)	Penumbra reperf catheter (large bore)	VA (21)/Tip (46)/Other BA (48) PCA (31)	32	-	562±466	14.3	-	High
	SR (58)	Solitaire FR/Trevo			-		22.4	-	
Park et al.	Asp (16)	Penumbra reperf catheter (1st gen)	BA (16)	25	0	5.8	-	-	Mod
Psychogios et al.	Asp (16)	Penumbra reperf catheter (1st gen)	BA (15)/VA+BA (3)/PCA (1)	-	0	-	-	-	Mod
Rentzos et al.	Asp (18)	Penumbra 5 MAXACE	Prox (5)/Mid (8)/Dist (49)/ All (12) Mid + Dist (18)/ Prox + Mid (12)/VA (6)	14	0	300 (175-463)	-	5.6	Mod
	SR (11)	Solitaire FR			0		-	18.2	
Roth et al.	Asp (12)	Penumbra 041	-	91.6	0	-	-	66.7	Mod
Son et al.	Asp (18)	Penumbra 054 (18)	-	50	0	236.4	-	0	Mod
	SR (13)	Solitaire AB (13)	-	38.5	15.4	348.6	-	0	
Uno et al.	Asp (34)	054/041/, 3/4/5 MAX/5 MAXACE	-	53	-	197 (160-256)	-	12	Mod

Unless otherwise specified, all values are percentages. Mean and SD is given in the form x±y, whereas median and interquartile range is given in the form x (y - z). Asp – Aspiration thrombectomy; SR – Stent retriever thrombectomy; BA – Basilar artery; PCA – Posterior cerebral artery; VA – Vertebral artery; Prox – Proximal BA; Mid – Mid BA; Distal – Distal BA; IVT – Intravenous thrombolysis; D/P – Dissection or perforation; Delay – Time to groin puncture; Rescue – Conversion to alternate strategy; ENT – Embolization to new territory; Mod – Moderate; N/A – Not available; SD – Standard deviation

For the secondary outcomes, stent retriever thrombectomy was inferior for the outcome of complete recanalization (OR 0.65, 95% CI 0.42–0.1.00, $P = 0.048$), procedure time (MD 28.17, 95% CI 9.47–46.87, $P = 0.0032$), and rate of embolization to new territory (OR 5.01, 95% CI 1.20–20.87, $P = 0.027$), but this did not reach statistical significance for the outcomes of SICH, any ICH, Supplementary Table 3 presents more detailed statistics on heterogeneity and publication bias.

Subgroup analysis

As shown in Tables 4 and 5, pooled outcomes remained robust to subgroup analyses based on the study quality.

Meta-regression

Meta-regression failed to identify a statistically significant correlation with the primary outcomes of mortality, mRS 0–2 and successful recanalization across time to groin puncture, intravenous thrombolysis, age, sex, and baseline NIHSS for aspiration thrombectomy.

Table 3: Comparison of baseline characteristics between groups

Baseline characteristics (mean weighted averages)	Aspiration thrombectomy	Stent retriever thrombectomy
Age (years)	65.5	68.3
NIHSS (score)	15.8	19.5
IVT (%)	56.6	56.1
Time to groin puncture (min)	303.3	296.2
Male (%)	60.7	59.1

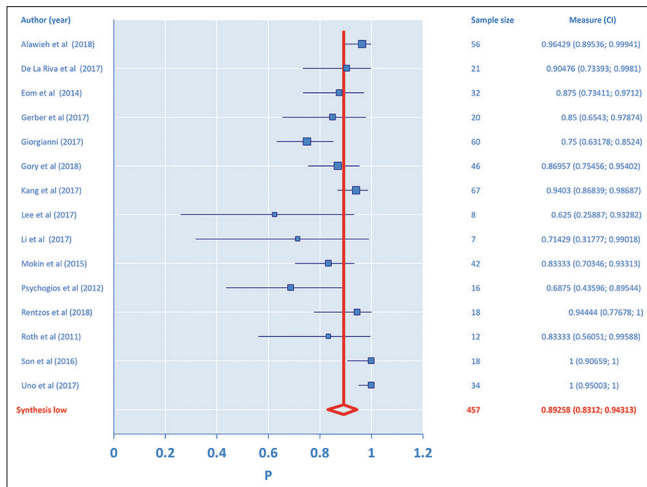NIH – National Institutes of Health; NIHSS – NIH stroke scale; IVT – Intravenous thrombolysis

Meta-regression was not performed for the meta-analysis on outcomes comparing aspiration thrombectomy versus stent retriever thrombectomy due to the inadequate number of studies.

Discussion

This systematic review and meta-analysis show a high degree of effectiveness of aspiration thrombectomy as a primary approach for therapy of large vessel posterior circulation occlusion stroke, with mean weighted probabilities of successful recanalization 89.26% (95% CI, 83.12–94.31), mortality 26.71% (95% CI, 19.35–34.71), and favorable outcome at 3 months 36.71 (95% CI, 32.02–41.52).

The above results are comparatively similar to those seen in the meta-analysis by Gory *et al*. of stent retriever thrombectomy for acute basilar artery occlusion.[39] In their study, rates of successful recanalization were 81% (95% CI 73%–87%), mortality 30% (95% CI, 25%–36%), and

Figure 3: Forest plot for aspiration thrombectomy based on successful recanalization
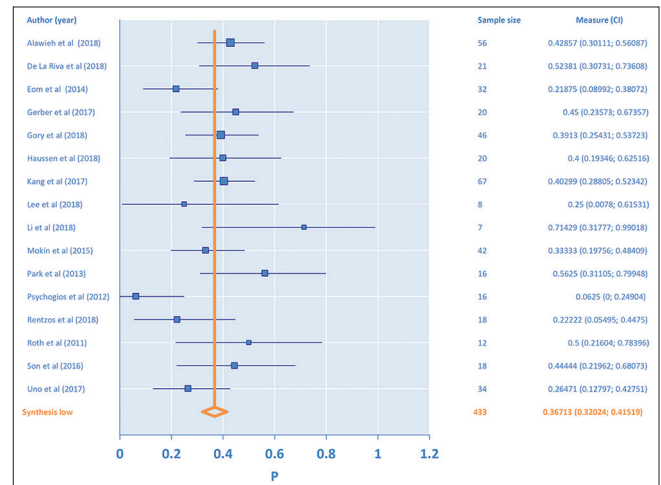

Figure 4: Forest plot for aspiration thrombectomy based on modified Ranking Score 0–2 at 3 months
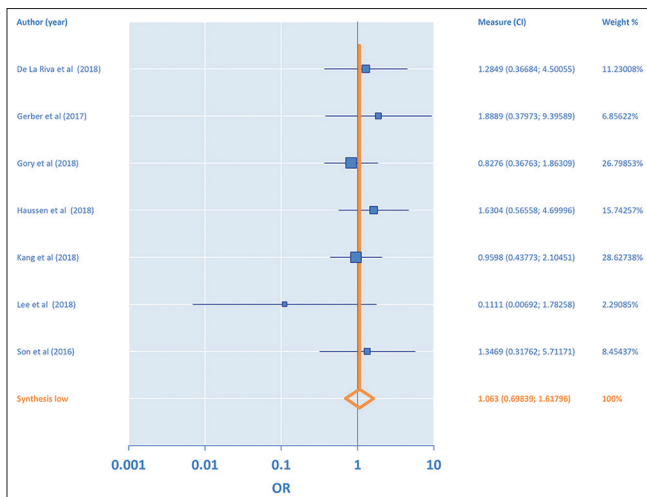

Figure 5: Forest plot for primary stent retriever thrombectomy versus primary aspiration thrombectomy based on mortality
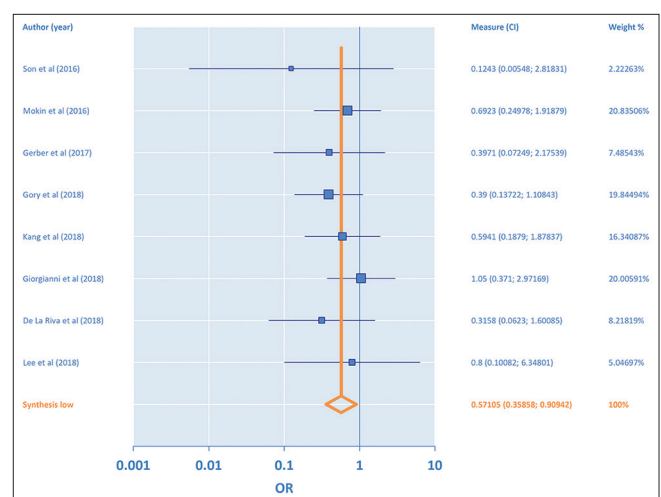

Figure 6: Forest plot for primary stent retriever thrombectomy versus primary aspiration thrombectomy based on successful recanalization
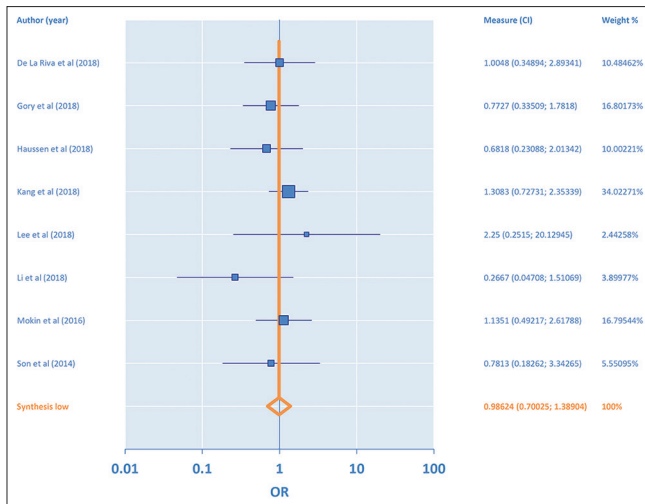
Figure 7: Forest plot for primary stent retriever thrombectomy versus primary aspiration thrombectomy based on modified Ranking Score 0–2 at 3 months

favorable outcome at 3 months 42% (95% CI 36%–48%).[39] While there is no randomized data available, the results of recent systematic reviews comparing intravenous or intra-arterial thrombolysis with mechanical thrombectomy suggest that the introduction of mechanical thrombectomy techniques, including aspiration and stent retriever thrombectomy, have resulted in better clinical and angiographic outcomes and safety profile.[40-42] A systematic review of mechanical thrombectomy in the anterior circulation supports higher rates of favorable outcome at 3 months (range 33%–71%, average 41%). However, there are very limited data directly comparing the efficacy of mechanical thrombectomy in the anterior versus posterior circulation. Observational studies by Alawieh *et al.* and Weber *et al.* show that comparable outcomes with similar safety profile are seen; however, in both studies, the sample size of the posterior circulation group was relatively small compared to the anterior circulation group.[22,43] Further follow-up research is required in this area.

On comparison of primary stent retriever thrombectomy with primary aspiration thrombectomy, stent retriever thrombectomy was found to be inferior for the outcomes of successful recanalization (OR 0.57, 95% CI 0.36–0.91, $P = 0.018$), complete recanalization (OR 0.65, 95% CI 0.42–0.1.00, $P = 0.048$), procedure time (MD 28.17, 95% CI 9.47–46.87), and rate of embolization to new territory (OR 5.01, 95% CI 1.20–20.87, $P = 0.027$). The pooled outcomes do not reach statistical significance for the outcomes of mortality, favorable outcome at 3 months, SICH, any ICH, conversion to alternative therapy, and dissection and perforation.

The difference between these two groups may be explained by the advantages inherent to the aspiration thrombectomy. Aspiration thrombectomy is technically easier and faster to perform, with the procedure being achieved by advancing the catheter to the face of the thrombus, without the need for the occluding thrombus to be traversed with a microguidewire and microcatheter.[7,44,45] Either the clot is ingested by aspiration alone, or it is affixed to the catheter, which is slowly withdrawn under continuous aspiration. Because there is no need to navigate distal to the occlusive thrombus, the theoretical risk of dissection and thrombus disruption and fragmentation is reduced.[7,45] There is also reduced traction exerted on the vasculature with thrombus withdrawal by aspiration catheters compared to stent retriever thrombectomy, reducing the risk of endothelial damage and hemorrhagic complications.[46] In terms of safety profile, there was only a statistically significant difference seen with the outcome of embolization to new territory; however, this may be due to the limited sample size.

The increased recanalization rates seen are important because early successful revascularization is the chief determinant of good outcome. A meta-analysis by Kumar *et al.* showed that successful recanalization is associated with a two-fold decrease in mortality (number needed to treat [NNT] = 2.5) and a 1.5-fold decrease in futile outcome (NNT = 3).[47] In addition, full recanalization (mTICI3) after thrombectomy has been shown to have better functional outcomes than those with mTICI2b (71.7% vs. 50%, $P = 0.001$) in a series of 222 consecutive patients with acute large intracranial artery occlusion of the anterior circulation.[48] However, no statistically significant difference was seen for the primary clinical outcomes of mortality and favorable outcome at 3 months.

Subgroup analysis showed that there was a difference for the outcome of successful recanalization with aspiration thrombectomy depending on whether second-line stent retriever thrombectomy was available. There was a statistically significant difference seen when second-line stent retriever thrombectomy was available (pooled OR 0.54 [95% CI 0.31–0.94]), compared to when it was not available (pooled OR 0.65 [95% CI 0.28–1.51]). This suggests that primary aspiration plus second-line stent retriever thrombectomy may represent the most optimal strategy for achieving successful recanalization. This may be because having an aspiration catheter proximal to the clot helps to facilitate the utilization of second-line devices, as it provides a direct channel to the clot, and unlike with other first-line strategies, does not prevent the utilization of other techniques should aspiration fail.[45]

Further techniques such as Cosmic Axion Spin Precession Experiment,[49] Solumbra,[9,18] or ARTS[50] that combine aspiration with stent retriever thrombectomy are being increasingly used over time. Currently, there are limited data relating to their efficacy in posterior circulation stroke. A new outcome has also recently been introduced called the first-pass effect, which refers to the rate of

Table 4: Subgroup analysis for aspiration thrombectomy

Outcome of interest	MWP (%)	CI (%), P	Begg's test	Trim and fill	Q/p	I^2	T^2	n
Mortality ≥2016	26.77	18.31-36.10, <0.0001	0.30	19.51, 15.42-23.91	20.21, 0.010	60.42	0.012	290
Mortality <2016	26.71	10.85-45.94, <0.0001	1.00	-	8.21, 0.042	63.47	0.023	76
Mortality (mod-high quality studies)	26.40	18.22-35.40, <0.0001	0.39	-	26.21, 0.0035	61.85	0.014	325
Mortality (mod-high quality studies) ≥2016	26.35	16.52-37.41, <0.0001	0.37	19.58, 15.12-24.41	17.96, 0.0063	66.60	0.015	249
mRS 0-2 ≥2016	39.31	33.74-45.01, <0.0001	1.00	38.58, 33.09-44.20	10.03, 0.44	0.28	0.000020	315
mRS 0-2 <2016	31.06	15.92-48.37, <0.0001	1.00	-	13.11, 0.011	69.48	0.025	118
mRS 0-2 (mod-high quality)	35.72	30.82-40.75%, P<0.0001	0.83	-	23.98, 0.031	45.76	0.0077	392
mRS 0-2 (mod-high quality studies) ≥2016	38.25	32.31-44.36, <0.0001	0.92	-	8.57, 0.38	6.64	0.00061	274
Successful recanalization ≥2016	91.40	84.22-96.82, <0.0001	0.59	92.57, 89.26-95.41	33.02, 0.00027	69.71	0.018	355
Successful recanalization <2016	83.05	74.68-90.17%, <0.0001	0.73	-	2.31, 0.51	0	0	102
Successful recanalization (mod-high quality studies)	89.12	82.52-94.49, <0.0001	0.25	90.65, 87.45-93.49	40.29, 0.00012	67.74	0.017	436
Successful recanalization (mod-high quality studies) ≥2016	91.42	83.52-97.23, <0.0001	0.59	92.70, 89.31-95.60	32.97, 0.00013	72.71	0.021	249
SICH ≥2016	2.86	0.81-5.70, <0.0001	0.32	2.26, 0.52-4.76	2.99, 0.89	0	0	269
SICH <2016	6.91	0-21.44, <0.0001	0.17	-	7.80, 0.050	61.52	0.023	72
SICH (mod-high quality studies)	3.24	1.18-5.96%, <0.0001	0.073	2.06, 0.50-4.29	11.64, 0.31	14.06	0.0014	321
SICH (mod-high quality studies) ≥2016	2.90	0.78-5.87, <0.0001	0.55	2.24, 0.47-4.84	2.99, 0.81	0	0	249
Any ICH ≥2016	24.68	14.85-35.91,<0.0001	0.45	15.52, 11.47-20.00	14.74, 0.012	66.07	0.013	231
Any ICH <2016	19.14	5.21-37.92,<0.0001	1	24.10, 14.39-35.16	4.51, 0.10	55.64	0.017	60
Complete Recanalization ≥2016	63.66	56.47-70.59,<0.0001	0.71	-	6.83, 0.23	26.84	0.0030	193
Dissection ≥2016	2.18	0-6.79, <0.0001	0.17	-	0.20, 0.98	0	0	102
Dissection pre <2016	3.35	0-12.29, <0.0001	0.60	-	0.044, 0.98	0	0	44
ENT ≥2016	5.44	1.77-10.43, <0.0001	1	2.66, 0.45-6.02	3.58, 0.47	0	0	136

MWP – Mean weighted probability; CI – Confidence interval; Begg's test – Begg and Mazumdar rank correlation test; Q – Cochran's Q; mRS – Modified Ranking Score, SICH – Symptomatic intracranial hemorrhage; ENT – Embolization to new territory

Table 5: Subgroup analysis for stent retriever thrombectomy versus aspiration thrombectomy

Outcome of interest	OR	CI	P	Begg's test	Trim and fill	Q/p	I^2	T^2
Mortality (w/rescue SR)	0.89	0.53-1.52	0.69	0.73	0.97, 0.58-1.62	3.58, 0.47	2.27	0.0080
Mortality (mod-high quality studies)	0.94	0.58-1.54	0.81	0.81	-	3.34, 0.50	0	0
Mortality (w/o rescue SR)	1.44	0.71-2.93	0.31	1	-	0.093, 0.95	0	0
mRS 0-2 (w/rescue SR)	1.14	0.75-1.71	0.54	0.73	0.97, 0.58-1.62	1.41, 0.70	0	0
mRS 0-2 (mod-high quality studies)	1.03	0.70-1.51	0.88	0.71	-	4.10, 0.54	0	0
mRS 0-2 (w/o rescue SR)	0.77	0.42-1.41	0.40	0.81	0.71, 0.40-1.27	2.65, 0.61	0	0
Successful recanalization (w/rescue SR)	0.54	0.31-0.94	0.030	0.81	-	0.89, 0.06	0	0
Successful recanalization (w/o rescue SR)	0.65	0.28-1.51	0.32	0.30	1.05, 0.51-2.17	2.66, 0.27	24.68	0.25
Successful Recanalization (mod-high quality studies)	0.60	0.37-0.98	0.041	0.23	-	3.12, 0.79	57.04	226.75
Procedural time (w/rescue SR)	24.89	2.18-47.56	0.032	1	-	4.65, 0.70	57.04	226.75

OR – Odds ratio; CI – Confidence interval; Begg's test – Begg and Mazumdar rank correlation test; Q – Cochran's Q; mRS – Modified Ranking Score; SR – Stent retriever thrombectomy

complete recanalization with a single pass.[51] The analysis of a retrospective multi-center registry of 354 consecutive patients treated with stent retriever thrombectomy shows a statistically significant association with rates of good clinical outcome.[51] These areas represent potential future areas of research.

Limitations

There are numerous limitations to this study. The main limitation was the quality of studies included, with conference abstracts being included in the meta-analysis and data coming solely from retrospective observational studies of prospectively and retrospectively collected data. However, pooled outcomes remained robust to exclusion sensitivity analyses based on the study quality.

There was significant unresolved heterogeneity ($I^2 \geq 50\%$) in the analyses for the outcomes of mortality, successful recanalization, any ICH, and embolization to new territory in the first meta-analysis and in the analyses for procedure time and conversion to alternate therapy in the second meta-analysis. Meta-regression and subgroup analyses did not identify a statistically significant source of heterogeneity, suggesting unexplained di-erences in study populations and procedures as a causative factor. Factors such as inclusion and exclusion criteria, protocols used, country of origin, and patient population differed across studies, thereby introducing heterogeneity into the pooled outcomes.

There was information missing in many studies about baseline and technical characteristics, including thrombus volume, baseline ASPECTS, presence of collateral circulation, rescue therapy used, number of passes, aspiration technique, and stroke etiology, which may represent potential confounding factors.[52] A meta-analysis by Brinjikji *et al.*, of nonrandomized trials has shown that the concurrent use of a balloon guide catheter with mechanical thrombectomy had a statistically significant association with superior clinical and angiographic outcomes.[53] Other studies highlight the potential for confounding with catheter

size and brand,[54] choice of anesthesia,[55] and whether angiographic data were adjudicated by a central core laboratory.[56] This lack of data precluded further meta-regression or subgroup analysis that may have explained heterogeneity in some of the syntheses. In addition, the small amount of studies that compared ADAPT and stent retriever thrombectomy made meta-regression unfeasible for the second meta-analysis performed. The above limitations should be considered when evaluating the pooled outcomes.

Further limitations included incomplete reporting of certain outcomes including embolization to new territory, dissection and perforation, and complete recanalization, which reduces the reliability and power of the pooled results.

Conclusions

There was no statistically significant difference for the primary clinical outcomes of mortality and favorable outcome (mRS score 0–2) at 3 months. While there were superior rates of successful recanalization, complete recanalization, faster procedural time, and improved safety profile seen for primary aspiration thrombectomy compared with primary stent retriever thrombectomy, this did not translate into superior clinical outcomes. Further subgroup analysis suggests that for the outcome of recanalization, this may be dependent on the availability of second-line stent retriever thrombectomy. No statistically significant difference was seen for the other secondary outcomes of SICH, any ICH, dissection, and perforation or conversion to alternate therapy. More systematic and high-quality data are needed to determine its clinical efficacy and safety profile.

Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Baseline characteristics

Study/year	Group (n)	Age (years)	Male	HTN	CAD	DM	ETOH	HLD	AF	Prior stroke	CE	LVD	ASPECTS (score)	NIHSS (score)
Alawieh et al., 2018	Asp (56)	-	33.3	26.8	-	19.6	-	26.8	71.4	-	-	-	-	17.4±11
De La Riva et al., 2018	Asp (21)	74 (67-79)	31.1	61.9	-	19	-	47.6	19	-	52.4	19	-	12 (8-24)
	SR (40)	71 (60-78)	57.5	67.5	-	24	-	52.5	22.5	-	32.5	25	-	15 (6-22.5)
Eom et al., 2014	As P (32)	68.3±10.7	69	66	-	28	-	-	34	-	37	47	-	19.8±8.7
Gerber et al., 2017	Asp (20)	62.8±5.4	70	65	-	50	-	15	6	0	90	10	7.5 (2.5-12.5)	18 (4-32
	SR (13)	63.2±9.1	62	38.5	-	7.7	-	23.1	14.4	0	84.6	15.4	6.5 (1.5-11.5)	25 (16-33)
Giorgianni et al., 2018	All (102)	68 (57-76)	63.7	-	-	-	-	?	?	-	-	-	-	17 (10-24)
Gory et al., 2018	Asp (46)	61 (53-71)	58.7	25/46	-	19.6	-	31.1	?	-	37.2	32.6	7 (6-9)	14 (9-25)
	SR (54)	67 (53-78)	63	41.5	-	5.7	-	24.5	?	-	27.1	33.3	8 (6-8)	20 (11-30)
Haussen et al., 2018	All (68)	-	-	-	-	-	-	-	-	-	-	-	-	-
Kang et al., 2018	All (212)	71 (64-78)	56.6	62.7	10.4	28.8	-	25	44.8	19.8	47.6	38.7	-	17 (10-24)
Lee et al., 2018	Asp (8)	73.3±11.5	87.5	-	-	-	-	-	-	-	-	-	-	18.8±6.2
	SR (7)	70.4±9.0	42.9	-	-	-	-	-	-	-	-	-	-	17.4±6.8
Li et al., 2018	All (68)	57.9±11.8	86.8	82.4	13.2	30.9	45.6	19.1	14.7	33.8	13.2	64.7	8 (6-8)	24.5 (15-30)
Mokin et al., 2016	All (100)	63.5±14.2	67	75	34	37	-	59	28	-	-	-	-	19.2±8.2
Park et al., 2013	Asp (16)	68.7±11	75	75	-	43.8	-	-	18.8	25	18.8	81.2	-	12.3±8.2
Psychogios et al., 2012	Asp (16)	-	-	-	-	-	-	-	-	-	-	-	-	-
Rentzos et al., 2018	All (110)	62±13	74	52		9	-	23	20	-	20	38	-	31 (13-31)
Roth et al., 2011	Asp (12)	71±7.7	66.67	88.3	33.3	33.33	-	16.7	25	-	-	-	-	27.3±8.4
Son et al., 2016	Asp (18)	66.4±11.4	77.8	44.4	-	55.6	66.7	100	44.4	83.3	-	-	-	21.3±9.7
	SR (13)	68.9±10.4	53.8	53.8	-	15.4	23.1	7.7	46.2	23.1	-	-	-	27.3±11.0
Uno et al., 2017	Asp (34)	72 (66-77)	68	47	6	21	-	32	18	32	79	18	10 (9-10)	29 (14-33)

Unless otherwise specified, all values are percentages (%). Mean and standard deviation is given in the form x±y, whereas median and interquartile range is given in the form x (y - z). Asp – Aspiration thrombectomy; SR – Stent retriever thrombectomy; HTN – Hypertension; CAD – coronary artery disease; DM – Diabetes mellitus; ETOH – Alcohol usage; HLD – Hyperlipidemia; AF – Atrial fibrillation; CE – Cardio-embolic; LVD – Large vessel disease; ASPECTS – Alberta stroke programme early CT score; NIH – National Institutes of Health; NIHSS – NIH Stroke Scale

Supplementary Table 2: Heterogeneity and mean weighted probabilities for aspiration thrombectomy

Outcome	MWP (%)	CI (%), P	Begg's test	Trim and fill	Q/p	I^2	T^2	n
Mortality	26.71	19.35-34.71, <0.0001	0.30	N/A	28.44, 0.0048	57.81	0.012	366
mRS 0-2 at 3 months	36.71	32.02-41.52, <0.0001	0.65	-	26.16, 0.036	42.66	0.0069	433
Successful recanalization	89.26	83.12-94.31, <0.0001	0.26	N/A	40.29, 0.00023	65.26	0.016	457
SICH	3.198	1.20-5.82, <0.0001	0.034	2.09, 0.55-4.26	11.66, 0.39	5.70	0.00054	341
Any ICH	22.96	15.06-31.82, <0.0001	0.35	18.84, 14.47-23.59	19.38, 0.13	58.73	0.011	291
Complete recanalization	64.95	57.89-71.64, <0.0001	0.76	-	8.74, 0.19	31.36	0.0041	205
Conversion	19.84	14.04-26.27, <0.0001	0.81	-	4.54, 0.34	11.84	0.00098	183
Dissection and perforation	2.39	0.13-6.32, <0.0001	0.0069	2.18, 0.10-5.85	0.51, 1.0	0	0	146
Embolization to new territory	11.62	1.74-26.76, <0.0001	0.57	-	24.31, 0.00019	79.43	0.04	148

MWP – Mean weighted probability; CI – Confidence interval; Begg's test – Begg and Mazumdar rank correlation test; Q – Cochran's Q; mRS – Modified Ranking Score, SICH – Symptomatic intracranial hemorrhage; N/A – Not available; ICH – Intracranial hemorrhage

Outcome of interest	Pooled OR	CI	P	Begg's test	Trim and fill	Q/p	I^2	T^2
Mortality	1.06	0.70-1.62	0.78	1.0	-	4.29, 0.64	0	0
mRS 0-2	0.99	0.70-1.39	0.94	0.39	-	4.60, 0.71	0	0
Successful recanalization	0.57	0.36-0.91	0.018	0.27	0.63, 0.40-0.98	3.68, 0.82	0	0
Complete recanalization	0.65	0.42-1.00	0.048	0.81	0.81, 0.55-1.21	1.21, 0.0023	48.28	0.28
SICH	1.26	0.30-5.35	0.75	N/A	N/A	0.72, 0.39	0	0
Procedure time	28.17	9.47-46.87	0.0032	0.73	-	6.47, 0.091	53.63	188.85
Conversion	0.61	0.20-1.92	0.40	0.73	-	9.07, 0.028	66.91	0.81
Dissection and perforation	5.72	0.96-34.61	0.058	-	-	0.48, 0.49	0	0
ENT	5.01	1.20-20.87	0.027	-	-	0.83, 0.36	0	0
Any ICH	1.56	0.90-2.71	0.12	0.31	1.99, 1.20-3.28	3.71, 0.29	19.23	0.094

OR – Odds ratio; CI – Confidence interval; Begg's test – Begg and Mazumdar rank correlation test; Q – Cochran's Q; mRS – Modified Ranking Score; SICH – Symptomatic intracranial hemorrhage; ENT – Embolization to new territory; N/A – Not available