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Review Article

Should the direct aspiration first pass technique be advocated over the stent-retriever technique for acute ischemic stroke? A systematic review and meta-analysis of 7692 patients

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ABSTRACT

Background: The present meta-analysis aimed to synthesize evidence from all published studies with head-to-head data on the outcomes of a direct aspiration first pass technique (ADAPT) and the stent-retriever (SR) in acute ischemic stroke (AIS) patients.

Methods: We searched PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials from inception to March 2021 for relevant clinical trials and observational studies. Eligible studies were identified, and all relevant outcomes were pooled in the meta-analysis random-effects model of DerSimonian-Laird.

Results: Thirty studies were included in the meta-analysis with a total of 7868 patients. Compared with the SR, the ADAPT provides slightly higher rates of successful recanalization (RR 1.06, 95% CI [1.02 to 1.10]) and complete recanalization (RR 1.20, 95% CI [1.01 to 1.43]) but with more need for rescue therapy (RR 1.81, 95% CI [1.29 to 2.54]). There were no significant differences between the two techniques in terms of mortality at discharge, mortality at 90 days, change in the National Institutes of Health Stroke Scale score, the favorable outcome (modified Rankin scale (mRS) of 0-2), time to the groin puncture, or frequency of complications as intracerebral hemorrhage (ICH), symptomatic intracranial hemorrhage (sICH), embolus in a new territory (ENT), hemorrhagic infarction, parenchymal hematoma, subarachnoid hemorrhage, or procedural complications (all $P > 0.05$).

Conclusion: Current evidence supports the use of the ADAPT technique to achieve successful and complete recanalization while considering the higher need for rescue therapy in some patients.

Keywords: A direct aspiration first pass technique, Direct aspiration first pass technique, Endovascular therapy, Ischemic stroke, Meta-analysis, Stent retriever, Thrombectomy

INTRODUCTION

Acute ischaemic stroke (AIS) is considered to be one of the leading causes of the mortality worldwide.[1] Moreover, stroke is associated with a high rate of disability among the survivors.[8]

There are two major methods to treat AIS; mechanical thrombectomy and standard medical therapy, which can be considered if patients present to a thrombectomy-capable facility in a timely manner. Over the last decade, several randomized controlled trials (RCTs) showed the superiority of mechanical thrombectomy techniques over medical management in thrombectomy-eligible patients.[6,11,34] These RCTs have drawn more attention to mechanical thrombectomy, which is now considered one of the main lines of treatment for AIS.[35]

The reference mechanical thrombectomy technique is the stent-retriever (SR) for selected patients, especially those with AIS due to vascular occlusion in the anterior circulation, according to the results of a recently published meta-analysis by Sivan-Hoffmann *et al.*,[35] which showed that the SR is a safe method with favorable clinical outcomes. The SR technique is the gold standard technique for mechanical thrombectomy in patients with AIS.

Recently, a direct aspiration first pass technique (ADAPT) was proposed by Turk *et al.*[39] and started to gain acceptance due to the lower costs of the procedure, increased rates of successful recanalization, and the better clinical outcomes reported by some studies when used either alone or as an adjunctive technique to the SR.[40] However, data from the literature are controversial regarding the comparative outcomes of the ADAPT technique compared with the conventional thrombectomy technique of the SR.

Therefore, the present meta-analysis aimed to synthesize evidence from all published studies with head-to-head data on the outcomes of ADAPT and SR in AIS patients.

MATERIALS AND METHODS

We followed the most recent version of the preferred reporting items for systematic reviews and meta-analysis (PRISMA statement 2020) guidelines during this systematic review and meta-analysis.[23]

Eligibility criteria

Studies satisfying the following criteria were included in this meta-analysis:

1. Population: studies on patients with AIS undergoing thrombectomy
2. Intervention: studies where the exposed group received ADAPT
3. Comparator: studies where the control group received SR
4. Outcome: studies reporting recanalization outcomes, National Institutes of Health Stroke Scale (NIHSS) score at baseline, 24 h and/or 7 days after the stroke event, mRS at 90 days, complications of the procedure and/or procedure time
5. Study design: studies with comparative designs, whether RCTs or observational studies comparing the outcomes of ADAPT and SR.

We excluded studies that were not in English language and studies on either ADAPT or SR without direct comparison between the two techniques.

Information sources

We performed a comprehensive search of four electronic databases (PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials) from inception to March 1, 2021.

Search strategy

We used the following search query ([aspiration OR ADAPT] AND [SR OR Solitaire OR Trevo OR Merci] AND [stroke OR Large vessel occlusion OR LVO]) in the four databases with no filters or limitations.

Selection process

Retrieved records from the literature search were screened in two steps. In the first step, the title and abstracts of all articles were screened for eligibility. Then, the full-text articles of the eligible abstracts were retrieved and further screened for eligibility.

Data collection process and data items

Data were extracted to a uniform data extraction sheet. The extracted data included (1) Characteristics of the included studies, (2) Characteristics of the population of included studies, (3) Risk of bias domains, and (4) Outcome measures.

Study risk of bias assessment

For RCTs, we used the Cochrane Risk of Bias assessment tool (ROB 2.0) while for observational studies; we used the Newcastle Ottawa Scale (NOS scale).

Effect measures

In this meta-analysis, we considered the following outcome measures:

- Successful recanalization (%): defined angiographically, according to the modified thrombolysis in cerebral infarction (mTICI) scale, as mTICI2b/3 at the end of the procedure
- Complete recanalization (%): defined angiographically, according to the mTICI scale, as mTICI-3 at the end of the procedure
- Favorable neurological outcome (%): defined as the number of patients with an mRS score of 0-2 at 90 days after the stroke event

- Complications (%): defined as any complication reported in the included studies with a frequency of more than 5%. This includes intracranial hemorrhage (ICH), symptomatic ICH (sICH), Subarachnoid haemorrhage (SAH), parenchymal hematoma, hemorrhagic infarction, and embolization to a new territory (ENT)
- Procedural time (%): defined as the time interval from groin puncture to reperfusion time.

Synthesis methods

For outcomes that constitute continuous data, the mean difference (MD) between the two groups from the baseline to the endpoint, with its confidence interval (CI), was pooled in the DerSimonian-Laird random-effect model. In the case of studies reporting data in multiple time points, we considered the last endpoint for the primary analysis. For outcomes that constitute dichotomous data, the frequency of events and the total number of patients in each group were pooled as relative risk between the two groups in the DerSimonian-Laird random-effect model.

Subgroup analysis

We conducted subgroup analysis according to the study design (RCTs only vs. observational studies) and according to the site of stroke (anterior circulation vs. posterior circulation).

Assessing the heterogeneity

Heterogeneity (non-combinability) of the included studies and subgroups was examined by visual inspection of the forest plot and assessed by the Cochrane Q and I-square tests using RevMan version 5.3 for windows. For heterogeneity testing, a $P < 0.1$ and I-square >50% were considered for significant heterogeneity.

Calculating the missing data

When the MD from baseline to endpoint was not provided, we calculated it from the pre- and post-treatment means (MD = Posttreatment-pretreatment). Then, we calculated the MD between the ADAPT and SR groups as follows: (MD = MD experiemental-MD placebo).

When the standard error (SE) of MD was not provided, we calculated it from the standard deviation [SE=SD/(√n)], 95% CI ([upper limit-lower limit]/3.92), or 90% CI ([upper limit-lower limit]/3.29).

For studies and groups with a sample size of <60 patients, the numbers (3.92 and 3.29) were substituted by a value from the table of t distributions with degrees of freedom equal to the group sample size minus 1.

Reporting bias assessment

To explore the publication bias across studies, we constructed funnel plots to present the relationship between effect size and SE. Two methods assessed evidence of publication bias; (1) Egger's regression test and (2) Begg and Mazumdar rank correlation test (Kendall's tau).

Certainty assessment

To test the robustness of the evidence, we conducted a certainty assessment through sensitivity analysis (also called, leave-one-out meta-analysis). For every outcome in the meta-analysis, we run sensitivity analysis in multiple scenarios excluding one study in each scenario to make sure the overall effect size was not dependent on any single studies.

RESULTS

Study selection

Our literature search process retrieved 2,832 records. Following titles and abstract screening, 351 articles were eligible for full-text screening. From these 351 studies, 30 studies were included in the meta-analysis.[2-5,7,9-10, 12,14-22,24-28,30,32,33,36-38,40,41] The references of the included studies were manually searched, and no further articles were included. The flow chart of the study selection process is shown in the PRISMA flow diagram in [Figure 1].

Study characteristics

The population of the studies was homogenous; all studies enrolled 7868 patients with AIS. Two studies were RCTs while 28 studies were observational studies. The characteristics of the included studies are summarized in [Table 1], while summary and baseline characteristics of populations of these studies are shown in [Table 2].

Risk of bias within studies

The quality of included studies ranged from moderate to high quality according to the Cochrane Risk of Bias assessment tool for RCTs and the NOS for the observational studies.

Improvement in NIHSS score

The overall standardized MD (SMD) of improvement in the NIHSS from baseline did not favor either of the two techniques (SMD 0.01, 95% CI [−0.11 to 0.13]). Subgroup analysis did not show any difference between the two techniques after 24 h (SMD 0.01, 95% CI [−0.14 to 0.15]), after 7 days (SMD −0.04, 95% CI [−0.26 to 0.18]) or at discharge (SMD 0.08, 95% CI [−0.25 to −0.41]), [Figure 2] and [Supplementary File 1]. Subgroup analysis of the

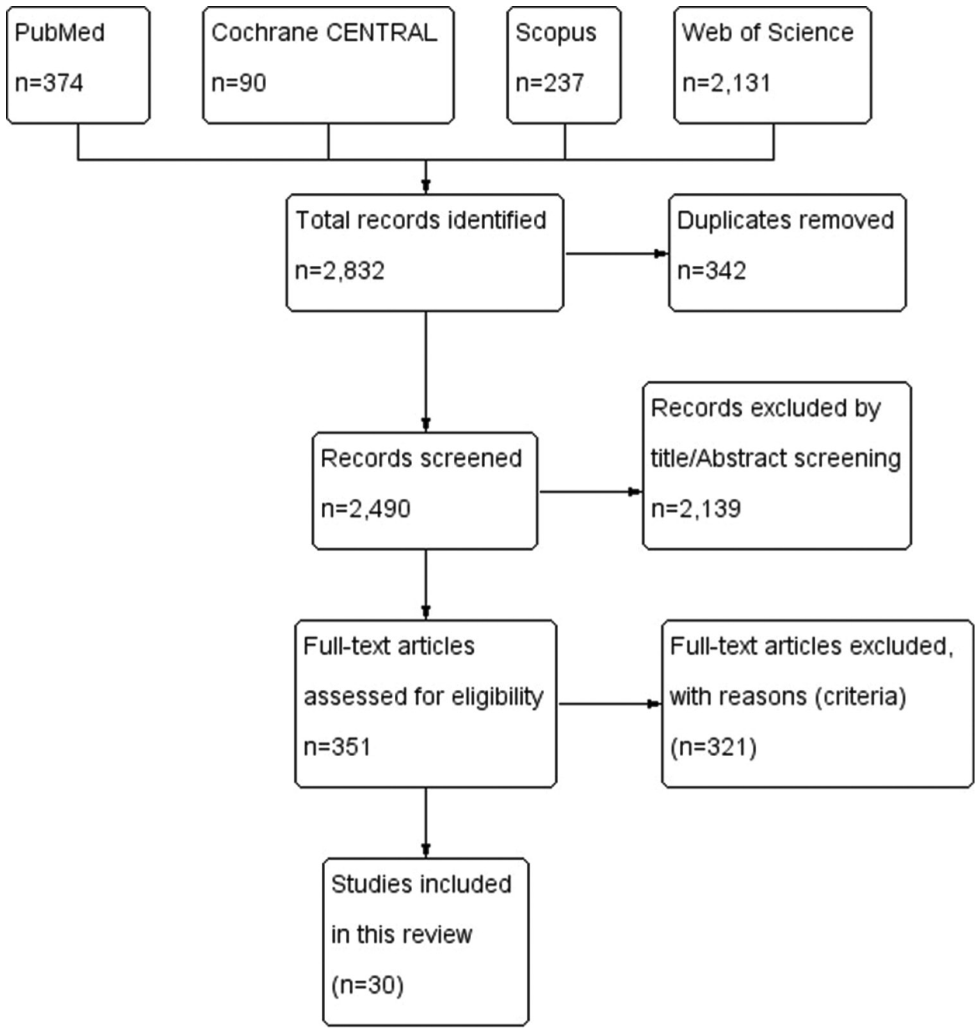

Figure 1: PRISMA flow diagram of the study selection process.

improvement in NIHSS according to the study design did not show the superiority of either of the two techniques in the subgroup of the RCTs (SMD −0.01, 95% CI [−0.16 to 0.15]) or in the subgroup of the observational studies (SMD 0.05, 95% CI [−0.16 to 0.25]) [Figure 2] and [Supplementary File 1].

Similarly, subgroup analysis of the improvement in the NIHSS according to the site of vascular occlusion did not show superiority of either of the two techniques for the 4 studies conducted on patients with AIS in the anterior circulation occlusion (SMD −0.03, 95% CI [−0.16 to 0.09]), the two studies conducted on patients with basilar artery occlusion (SMD −0.11, 95% CI [−0.45 to 0.24]) or the two studies with (unspecified) intracranial arterial occlusion (SMD 0.36, 95% CI [0.04 to 0.68]). The pooled effect estimates on all subgroups were homogenous (Chi-square $P > 0.1$) [Figure 2] and [Supplementary File 1].

Time to groin puncture

The pooled analysis of the time to groin puncture reported by 18 studies ($n = 5729$ patients) did not favor either of the two techniques (SMD 0.81, 95% CI [−11.78 to 13.40]). The difference was not statistically significant in the subgroups of the RCTs or the observational studies [Supplementary File 2].

Successful recanalization (TICI 2b-3)

Twenty-nine studies ($n = 7560$ patients) reported the frequency of achieving successful recanalization (TICI 2b-3) by both techniques. The pooled risk ratio (RR) of successful recanalization (TICI 2b-3) favored aspiration thrombectomy technique (RR 1.06, 95% CI [1.02 to 1.10]) [Figure 3] and [Supplementary File 3].

Subgroup analysis of the rates of successful recanalization (TICI 2b-3) according to the study design showed that

Table 1: Characteristics of the included studies.

Study ID	Design	Setting	From	To	N	Occluded Vessel	Time frame
Gerber *et al.* 2017[9]	Retrospective	Single center, Germany	January 2013	April 2016	33	Basilar Artery	NR
Gory *et al.* 2018[10]	Retrospective	3 stroke centers, France	March 2010	October 2016	100	Basilar Artery	NR
Kang *et al.* 2018[18]	Retrospective	3 stroke centers, Korea	January 2011	August 2017	212	Basilar Artery	NR
Lapergue *et al.* 2016[21]	Prospective clinical registry	2 stroke centers, France	November 2012	June 2014	243	Anterior circulation large vessel occlusion	Within 6 h
Lapergue *et al.* 2017[20]	RCT	8 stroke centers, France	October 2015	October 2016	381	Intracranial internal carotid artery M1 or M2 branches of the middle cerebral artery	Within 6 h
Maegerlein *et al.* 2017[24]	Retrospective	Germany	June 2014	March 2016	97	Distal internal carotid artery (ICA) Carotid-T, Middle cerebral artery (MCA), Anterior cerebral artery (ACA) Basilar artery (BA) occlusion	NR
Mokin *et al.* 2016[27]	Retrospective	Multiple centers, USA	March 2012	July 2015	102	Posterior circulation	NR
Mokin *et al.* 2017[26]	Retrospective	Multiple centers, USA	March 2012	March 2016	113	MCA M2	Within 24 h
Nishi *et al.* 2018[29]	Retrospective	Single center, Japan	December 2013	February 2016	89	Large intracranial arteries	Within 8 h
Son *et al.* 2016[36]	Retrospective	Single center, Korea	March 2011	December 2011	31	Basilar Artery	Within 8 h
Stapleton *et al.* 2018[37]	Retrospective	Single center, USA	June 2012	October 2015	117	Anterior circulation large vessel occlusion	Within 8 h
Turk *et al.* 2014[40]	Retrospective	Single center, USA	January 2009	December 2013	222	Middle cerebral artery (76.6%) Internal carotid artery (13.5%) Basilar artery (8.2%)	NR
Turk *et al.* 2019[38]	RCT	14 centers in the USA and one hospital in Canada	June 1, 2015	July 5, 2017	270	Anterior circulation large vessel occlusion	Within 6 h
Hesse *et al.* 2018[14]	Retrospective study	Five high-volume German centers	2013	2016	266	Anterior circulation large vessel occlusion	NR
Procházka *et al.* 2018[32]	Prospective study	Single center, Czech Republic	NR	NR	296	NR	Within 6 h
Martini *et al.* 2019[25]	Retrospective study	13 stroke centers, USA.	2015	2016	228	Internal carotid artery (28%) Middle cerebral artery (72%)	NR
O'Neill *et al.* 2019[30]	Retrospective study	Single center, Ireland	September 2017	September 2018	254	Anterior circulation large vessel occlusion	Within 24 h

(Contd...)

Table 1: *(Continued).*

Study ID	Design	Setting	From	To	N	Occluded Vessel	Time frame
Alawieh *et al.* 2019[2]	Retrospective study	Seven stroke centers in USA	June 2013	February 2018	1380	Internal carotid artery Middle cerebral artery, M1 Middle cerebral artery, M2/M3 Anterior cerebral artery A1/A2 Basilar artery Posterior cerebral artery, P1 Vertebral artery, V1/V2	NR
Jeon *et al.* 2020[15]	Retrospective study	Single center, Korea	January 2013	October 2019	62	Middle cerebral artery M1 (53.2%0 Middle cerebral artery M2 or more (22.6%) Internal carotid artery distal (14.5%0 Basilar (9.7)	Within 24 h
Nabil *et al.* 2020[28]	Retrospective study	Single Center, Switzerland	September 2014	March 2017	70	Middle cerebral artery, M1/M2 Basilar artery Posterior cerebral artery Carotid T	NR
Lee *et al.* 2020[22]	Retrospective study	Single center, USA	March 2010	December 2017	40	vertebrobasilar occlusion	Within 24 h
Atchaneeyasakul *et al.* 2020[3]	Retrospective study	Three centers, USA	October 1999	June 2016	197	Middle Cerebral Artery M2 Occlusion	NR
Bernsen *et al.* 2019[4]	Retrospective study	Multi centers, Netherlands	March 2014	June 2016	1175	Anterior circulation large-vessel occlusion	NR
Kang *et al.* 2019[19]	Retrospective study	17 stroke centers, South Korea	January 2011	December 2015	955	Anterior circulation large-vessel occlusion	NR
Haussen *et al.* 2020[12]	Retrospective study	Single center, USA	January 2014	July 2018	144	Distal arterial occlusions (DAO) involving the MCA (mid or distal M2 segment, M3 segment), ACA (A1, A2, A3), or PCA (P1, P2)	NR
Xing *et al.* 2020[41]	Retrospective study	Single center, China	September 2013	November 2018	109	Terminal internal carotid artery	Within 16 h
Brehm *et al.* 2019[5]	Retrospective study	Single center, Germany	January 2014	September 2017	171	Anterior circulation large-vessel occlusion	NR
Consoli *et al.* 2018[7]	Retrospective study	Two stroke centers, France	January 2016	April 2016	84	M1-middle cerebral artery occlusion	NR
Kaiser *et al.* 2020[16]	Retrospective study	Single centre, Germany	January 2016	December 2018	203	M1-middle cerebral artery	NR
Kaneko *et al.* 2019[17]	Retrospective study	12 stroke centers, Japan	January 2015	December 2017	48	Basilar artery	NR

NR: Not reported

the observational studies (1.06, 95% CI [1.02 to 1.11]) but not the RCTs (1.05, 95% CI [0.97 to 1.15]) had statistically significant pooled RR in favor of the ADAPT group.

Complete recanalization (TICI 3)

Seventeen studies (n=3824 patients) reported the frequency of achieving complete perfusion (mTICI 3) by

Table 2: The characteristics of the included studies' populations.

Study ID	Group	N	Age	Males	NIHSS (Pre)	Prior thrombolysis	General Anesthesia
Xing *et al*. 2020	ADAPT	40	68.3 (14.0)	21	21 (15–23)	12	NR
	SR	69	69.5 (9.2)	28	19 (16–22)	33	
Brehm *et al*. 2019	ADAPT	72	72.6 (14.1)	30	16 (9–20)	50	NR
	SR	99	74.5 (11.45)	41	16 (12–20)	68	
Kaiser *et al*. 2020	ADAPT	155	75.3 (65.5–81.2)	73	16 (11–20)	118	NR
	SR	48	78.8 (65.8–85.0)	23	17 (13–21)	31	
Bernsen *et al*. 2019	ADAPT	207	68.50 (54–77)	112	16 (12–21)	156	110
	SR	968	69 (57–78)	516	16 (12–19)	741	219
Kang *et al*. 2019	ADAPT	429	68.4 (11.4)	215	15 (8) (median)*	210	NR
	SR	526	67. 2 (12.5)	292	15 (7) (median)*	271	
Haussen *et al*. 2020	ADAPT	52	65 (49–75)	NR	18 (12–21)	24	NR
	SR	92	66 (55–74)		16 (11–23)	36	
O'Neill *et al*. 2019	ADAPT	127	70.4 (14.8)	NR	15.6 (6.7)	64	NR
	SR	127	67.9 (16.4)		15.7 (5.9)	68	
Alawieh *et al*. 2019	ADAPT	868	67.5 (15.0)	420	16.2 (7)	372	NR
	SR	512	68.9 (16.0)	236	16.6 (7)	253	
Jeon *et al*. 2020	ADAPT	28	67 (61–75)	12	16 (10–19)	4	NR
	SR	34	71 (60–77)	17	14 (9–19)	5	
Nabil *et al*. 2020	ADAPT	35	63.6	14	14.3	NR	NR
	SR	35	67.2	18	12.2		
Lee *et al*. 2020	ADAPT	11	63.0 (12.2)	10	13.2 (8.60)	3	NR
	SR	29	68.5 (12.3)	21	13.9 (5.8)	12	
Atchaneeyasakul *et al*. 2020	ADAPT	77	67.7 (13.4)	44	17 (12–20)	28	NR
	SR	120	68.6 (13.1)	72	15 (11–20)	66	
Hesse *et al*. 2018	ADAPT	164	72 (60–79)	75	15.3 (6.1)	NR	NR
	SR	102	74 (67–80)	57	15.5 (5.5)		
Procházka *et al*. 2018	ADAPT	100	69 (61–75)	53	NR	52	53
	SR	196		90		85	93
Martini *et al*. 2019	ADAPT	107	69.8 (15.1)	49	16.4 (6.9)	59	NR
	SR	121	68.9 (15.8)	56	15.7 (6.7)	65	
Kang *et al*. 2018	ADAPT	67	71 (64–78)	120	20 (median)	65	NR
	SR	145			16 (median)		
Turk 2019 (COMPASS trial)	ADAPT	134	71.8 (13.1)	58	7.5 (9)	92	39
	SR	136	71.1 (12.9)	68	7.3 (8.5)	96	41
Stapleton *et al*. 2018	ADAPT	47	63.5	26	16.5	34	7
	SR	70	69.4	34	16.5	40	21
Gory *et al*. 2018	ADAPT	46	61 (53–71) *	27	14 (9–25) *	23	38
	SR	54	67 (53–78) *	34	20 (11–30) *	22	46
Lapergue *et al*. 2017 (ASTER trial)	ADAPT	192	71.7	103	16.3 (5.9)	126	21
	SR	189	68.1	104	16.1 (6.5)	124	25
Nishi *et al*. 2018	ADAPT	44	73.1	24	17 (12–23)	23	NR
	SR	45	77.8	26	19 (15–26)	21	
Mokin *et al*. 2017	ADAPT	51	67.0 (14.5)	67	15 (median)	52	31
	SR	62					
Mokin *et al*. 2016	ADAPT	42	63.5 (14.2)	67	19.2 (8.2)	32	60
	SR	58					
Maegerlein *et al*. 2017	ADAPT	36	72.4 (15.7)	22	NR	21	NR
	SR	61	75.8 (11.9)	30		37	
Lapergue *et al*. 2016	ADAPT	124	64.3 (15.7)	61	15.9 (6.5)	82	NR
	SR	119	65.5 (14.7)	55	15.9 (6.1)	54	

(Contd...)

Table 2: *(Continued).*

Study ID	Design	Setting	From	To	N	Occluded Vessel	Time frame
Gerber *et al.* 2017	ADAPT	20	62.8	14	18 (28) *	12	NR
	SR	13	63.2	8	25 (19) *	11	
Son *et al.* 2016	ADAPT	18	66.4 (11.4)	14	21.3 (9.7)	9	NR
	SR	13	68.9 (10.4)	7	27.3 (11)	5	
	SR	55	69.6	23	16.8	33	

NR: Not reported, ADAPT: A direct aspiration first pass technique, SR: Stent-retriever

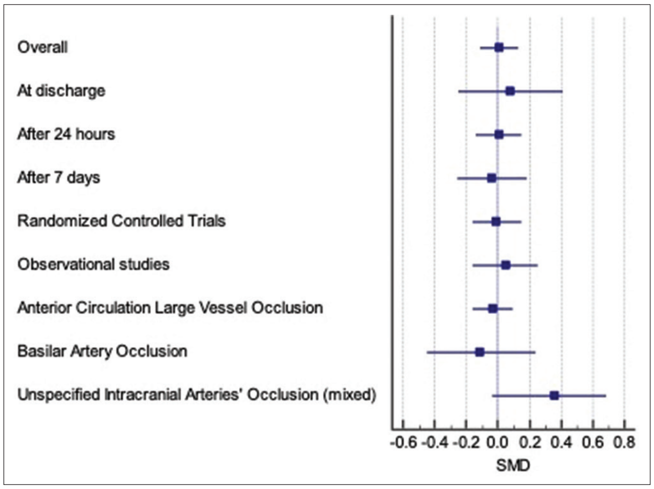

Figure 2: Forest plot of the pooled SMD of change in National Institutes of Health Stroke Scale score overall and subgroup by different time points, study designs, and location of vascular occlusion; SMD = standardized mean difference of the change from baseline to endpoint between the A direct aspiration first pass technique and Stent-retriever groups.

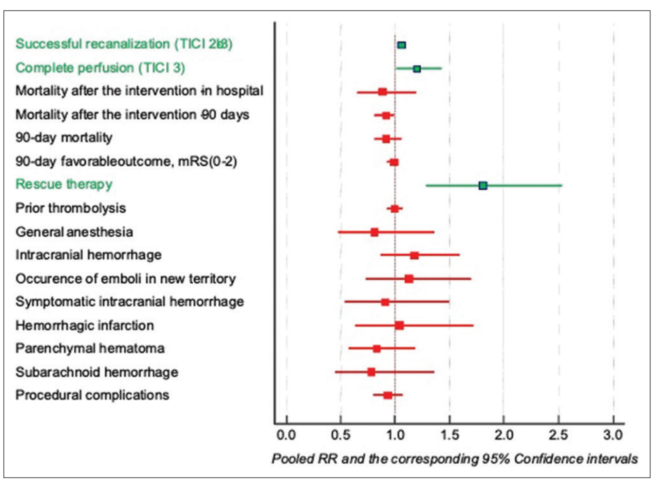

Figure 3: Forest plot summarizing the pooled RR of the dichotomous study outcomes between the A direct aspiration first pass technique and stent-retriever groups; outcomes in green are statistically significant. The green colour means a significant difference exists while the red colour means no significant difference exists.

both techniques, the pooled RR of complete perfusion (mTICI 3) favored the ADAPT technique (RR 1.20, 95% CI [1.01 to 1.43]) [Figure 3] and [Supplementary File 4].

Subgroup analysis of the complete perfusion (mTICI 3) according to the study design showed that the pooled RR did not favor any of both techniques either in the RCTs (RR 1.10, 95% CI [0.83 to 1.46]) or in the observational studies (RR 1.22, 95% CI [1.0 to 1.49]).

Mortality

Five studies (n = 729 patients) reported the in-hospital mortality while ten studies (n = 2901 patients) reported the 90-day mortality. Neither the pooled RR of the in-hospital mortality nor the 90-day mortality favored either of the two groups (RR 0.89 and RR 0.92; both $P > 0.05$) [Figure 3] and [Supplementary Files 5 and 6].

Favorable outcome (mRS of 0-2)

The frequency of patients with favorable outcome according to the mRS score (ranging from 0 to 2) was reported by 22 studies (n = 6244 patients), the pooled RR of favorable outcome (mRS 0-2) did not favor either of the two techniques (RR 0.99, 95% CI [0.93 to 1.05]) [Figure 3] and [Supplementary File 7].

Rescue therapy

The frequency of the patients who required rescue therapy was reported by 15 studies (n = 3079 patients), the pooled RR of rescue therapy showed that more patients in the ADAPT group required rescue therapy compared with the SR group (RR 1.81, 95% CI [1.29 to 2.54]) [Figure 3] and [Supplementary File 8].

Prior thrombolysis

The frequency of patients with prior thrombolysis was reported by 23 studies (n = 6763 patients), the pooled RR of prior thrombolysis did not favor either of the two techniques (RR 1.00, 95% CI [0.93 to 1.07]) [Figure 3] and [Supplementary File 9].

General anesthesia

The frequency of patients who underwent general anesthesia was reported by 7 studies (*n* = 3561 patients), the pooled RR of the frequency of general anesthesia did not favor either of the two techniques (RR 0.81, 95% CI [0.48 to 1.36]) [Figure 3] and [Supplementary File 10].

Intracerebral haemorrhage

The frequency of patients with ICH was reported by 8 studies (*n* = 2063 patients), the pooled RR of intracranial haemorrhage did not favor either of the two techniques (RR 1.22, 95% CI [0.90 to 1.66]) [Figure 3] and [Supplementary File 11].

Occurrence of embolus in a new territory

The frequency of patients with ENT was reported by 11 studies (*n* = 1876 patients), the pooled RR of occurrence of an embolus in a new territory did not favor either of the two techniques (RR 1.13, 95% CI [0.73 to 1.73]) [Figure 3] and [Supplementary File 12].

Symptomatic intracerebral haemorrhage

The frequency of patients with sICH was reported by 14 studies (*n* = 4504 patients), the pooled RR of symptomatic intracranial haemorrhage did not favor either of the two techniques (RR 0.91, 95% CI [0.54 to 1.54]) [Figure 3] and [Supplementary File 13].

Haemorrhagic infarction

The frequency of the patients with haemorrhagic infarction was reported by 3 studies (*n* = 626 patients), the pooled RR of haemorrhagic infarction did not favor either of the two techniques (RR 1.04, 95% CI [0.63 to 1.72]) [Figure 3] and [Supplementary File 14].

Parenchymal hematoma

The frequency of patients with parenchymal hematoma was reported by 9 studies (*n* = 1389 patients), the pooled RR of parenchymal hematoma did not favor either of the two techniques (RR 0.83, 95% CI [0.58 to 1.19]) [Figure 3] and [Supplementary File 15].

SAH

The frequency of SAH in the two groups was reported by 9 studies (*n* = 1289 patients), the pooled RR of SAH did not favor either of the two techniques (RR 0.78, 95% CI [0.45 to 1.37]) [Figure 3] and [Supplementary File 16].

Procedural complications

The frequency of patients with procedural complications was reported by 9 studies (*n* = 3916 patients), the pooled RR of procedural complications did not favor either of the two techniques (RR 0.93, 95% CI [0.80 to 1.08]) [Figure 3] and [Supplementary File 17].

Subgroup analysis

We conducted subgroup analysis for the main outcomes according to the study design (RCTs only vs. observational studies vs. all studies). Data showed consistent results in both RCTs and observational studies except for the outcome of successful recanalization (TICI 2b-3) where RCTs showed no difference between the ADAPT, and the SR while observational studies reported significantly higher

Table 3: Summary of the subgroup analysis results, data are stratified according to the study design into RCTs only, observational studies only, and all studies.

Outcome	RCTs only	Observational studies only	All studies
Improvement in NIHSS score	No difference −0.01 (−0.16, 0.15)	No difference 0.05 (−0.16, 0.25)	No difference 0.01 (−0.11, 0.13)
Onset to groin time	No difference −6.67 (−23.17, 9.83)	No difference 3.19 (−12.77, 19.15)	No difference 0.81 (−11.78, 13.40)
Successful recanalization (TICI 2b-3)	No difference 1.05 (0.97, 1.15)	Favours ADAPT technique 1.06 (1.02, 1.11)	Favours ADAPT technique 1.06 (1.02, 1.10)
Complete perfusion (TICI 3)	No difference 1.10 (0.83, 1.46)	No difference 1.22 (1.00, 1.49)	No difference 1.20 (1.01, 1.43)
Prior thrombolysis	No difference 0.99 (0.89, 1.10)	No difference 1.00 (0.92, 1.09)	No difference 1.00 (0.93, 1.07)
General anesthesia	No difference 0.92 (0.68, 1.25)	No difference 0.77 (0.40, 1.49)	No difference 0.81 (0.48, 1.36)
Parenchymal hematoma	No difference 0.74 (0.47, 1.18)	No difference 0.99 (0.55, 1.79)	No difference 0.83 (0.58, 1.19)
90-day mortality	No difference 1.00 (0.73, 1.36)	No difference 0.91 (0.78, 1.05)	No difference 0.92 (0.81, 1.06)
90-day favorable outcome (mRS 0-2)	No difference 0.97 (0.82, 1.13)	No difference 0.99 (0.93, 1.06)	No difference 0.99 (0.93, 1.05)
Occurrence of ENT	No difference 1.55 (0.61, 3.97)	No difference 1.06 (0.64, 1.75)	No difference 1.13 (0.73, 1.73)
Procedural complications	No difference 0.98 (0.68, 1.41)	No difference 0.88 (0.67, 1.15)	No difference0.93 (0.80, 1.08)

RCT: Randomized controlled trials, NIHSS: National Institutes of Health Stroke Scale, ADAPT: A direct aspiration first pass technique successful recanalization rates in ADAPT compared with the SR [Table 3].

Further, we conducted subgroup analysis for the main outcomes according to the site of stroke (anterior circulation vs. posterior circulation). Data were consistent in the subgroups of anterior circulation and posterior circulation except that the risks of emboli in a new terrorist was significantly lower in the ADAPT compared with the SR in the subgroup of posterior circulation [Table 4].

DISCUSSION

The development of mechanical thrombectomy technology has revolutionized the treatment of patients with AIS. The SR technique is the current gold-standard mechanical thrombectomy technique used in patients with AIS. However, despite the results of RCTs showing favorable outcomes of this technique, the rate of successful revascularization is still considered suboptimal. Therefore, using large-bore aspiration catheters during routine clinical practice has been widely debated in medical literature.

The ADAPT method was developed by Turk *et al.*[13] to achieve a higher recanalization rate in a shorter period of time. The method was initially described as fast, safe, simple, and effective.[39] However, the major limitation of the ADAPT method was the unavailability of the catheter technology needed to perform such a procedure. This technique started to gain acceptance recently after solving the catheter availability problem by developing the latest generation of tractable large-bore aspiration catheter, which provides sufficient aspiration force and easy manoeuvrability to navigate through the cerebral vasculature. However, it is still debatable whether the ADAPT technique should be preferred over the conventional SR technique for AIS owing to the inconsistent data reported in the literature. Therefore, we conducted this meta-analysis to synthesize evidence from published studies on ADAPT outcomes compared with SR using data from head-to-head comparative studies.

Our meta-analysis provides evidence that the ADAPT technique achieves slightly higher rates of successful recanalization and complete recanalization than the conventional SR technique. However, the subgroup analysis showed that this significant effect size in successful recanalization was mainly driven by observational studies but not RCTs. On the contrary, the ADAPT method was associated with higher need for rescue therapy (defined as the use of another endovascular strategy after failure of the initially used technique [mTICI 0-2a]) as compared with the SR. There were no significant differences between the two techniques in terms of mortality at discharge, mortality after 90 days, change in NIHSS score, the favorable outcome (mRS of 0-2), time to the groin puncture, or frequency of complications as ICH, sICH, the occurrence of an embolus in a new territory, hemorrhagic infarction, parenchymal hematoma, SAH, and procedural complications.

The main finding of our meta-analysis that ADAPT provides higher successful recanalization rates compared with the conventional SR is concordant with the findings of Phan *et al.*[31] and Ye *et al.*[42] The meta-analysis of Phan *et al.*[31] provided an indirect comparison between the two techniques, pooling single-arm data into two subgroups. Our findings are consistent with Phan *et al.*[31] that ADAPT provides a higher successful recanalization rate, but we found a superiority of ADAPT in the rate of complete perfusion, which was not significant in their meta-analysis. A limitation of their meta-analysis methods was the indirect comparison between the two arms, limiting the generalizability of their findings. Our meta-analysis provides more robust evidence by including comparative data from a head-to-head comparison between the two techniques.

Our finding that the ADAPT provides a higher successful recanalization rate and a higher complete recanalization rate (mTICI 3) is reasonable and is supported by the previous

Table 4: Summary of the subgroup analysis results, data are stratified according to the site of stroke into anterior circulation, posterior circulation, and all studies.

Outcome	Anterior circulation	Posterior circulation	All studies
Improvement in NIHSS score	No difference –0.03 (–0.16, 0.09)	No difference –0.11 (–0.45, 0.24)	No difference –0.04 (–0.16, 0.08)
Onset to groin time	No difference 0.04 (–0.18, 0.11)	No difference 0.06 (–0.08, 0.20)	No difference –0.01 (–0.11, 0.11)
Successful recanalization (TICI 2b-3)	No difference 1.05 (0.99, 1.12)	No difference 1.10 (0.98, 1.25)	No difference 1.06 (1.00, 1.12)
Complete perfusion (TICI 3)	No difference 1.09 (0.89, 1.33)	No difference 1.22 (0.92, 1.62)	No difference 1.13 (0.97, 1.32)
Prior thrombolysis	No difference 1.01 (0.93, 1.10)	No difference 0.89 (0.58, 1.37)	No difference 1.00 (0.93, 1.09)
Parenchymal hematoma	No difference 0.82 (0.54, 1.24)	No difference 1.06 (0.37, 2.99)	No difference 0.85 (0.57, 1.25)
90-day mortality	No difference 1.06 (0.77, 1.46)	No difference 1.03 (0.63, 1.67)	No difference 1.05 (0.81, 1.37)
Occurrence of emboli in new territory	No difference 1.18 (0.82, 1.71)	Favors ADAPT 0.25 (0.07, 0.96)	No difference 1.06 (0.66, 1.70)
90-day favorable outcome (mRS 0-2)	No difference 0.97 (0.90, 1.04)	No difference 0.93 (0.74, 1.18)	No difference 0.96 (0.90, 1.03)

NIHSS: National Institutes of Health Stroke Scale, ADAPT: A direct aspiration first pass technique

Table 5: A summary of the findings of previous meta-analyses.

	Phan *et al.*[31]	Qin *et al.*[33]	Ye *et al.*[42]	Our study
Number of studies	23 studies	9 studies	5 studies (basilar artery stroke only)	30 studies
Number of patients	1915 patients	1273 patients	476 patients	7868 patients
Complete reperfusion	NR	No difference	No difference	ADAPT (higher)
Successful recanalization (partial perfusion)	ADAPT (higher)	No difference	ADAPT (higher)	ADAPT (higher)
Favorable outcome	No difference	ADAPT (higher)	No difference	No difference
Mortality	No difference	NR	No difference	No difference
sICH	No difference	ADAPT (less)	NR	No difference
ICH	NR	No difference	NR	No difference
ENT	NR	ADAPT (less)	ADAPT (less)	No difference
Rescue therapy	NR	NR	No difference	SR (less)
General anesthesia	NR	NR	NR	No difference
Time to groin	No difference	NR	NR	No difference
Procedure time	No difference	ADAPT (less)	ADAPT (less)	No difference

NR: Not reported; ICH: Intracranial hemorrhage, ADAPT: A direct aspiration first pass technique

literature. Phan *et al.*[31] reported from an indirect meta-analysis that ADAPT patients tended to have more excellent neurologic outcomes ($P = 0.11$), although the difference was not statistically significant. There is now a general understanding that patients with mTICI 3 are more likely to have the excellent neurologic outcome (mRS 0-1) after a stroke event. Therefore, our findings that ADAPT provides a higher complete recanalization rate corroborates the trend analysis of excellent neurologic outcome (mRS 0-1) reported by Phan *et al.*[31] previously. While this difference in complete recanalization rate was not statistically significant in previous individual studies, our meta-analysis provides a larger sample size and higher statistical power to allow small effect estimates to be detectable. However, the clinical significance of this slight difference remains questionable.

In terms of the need for rescue therapy, Gory *et al.*,[10] Lapergue *et al.*,[21] and Nishi *et al.*[29] reported that more patients in the ADAPT group required rescue therapy which is in line with our findings. Ye *et al.*[42] did not find any differences between the ADAPT and the SR groups in terms of the need for rescue therapy. However, our meta-analysis showed that patients who underwent the ADAPT required more rescue therapy than those who underwent the SR technique. This discrepancy could be justified by our meta-analysis pooling data from a larger set of studies (30 studies) and a larger sample size (7868 patients), which provides the high statistical power to detect small differences between the thrombectomy techniques.

In [Table 5], we provide a summary of findings from 3 previous meta-analyses that directly and indirectly provided partial evidence on the comparison between ADAPT and SR for AIS. However, it is noteworthy that these studies have major limitations, including (1) dropping significant portions of the literature at the screening process, or (2) the authors selected a particular type of stroke patients to study; Ye *et al.*[42] compared the ADAPT and SR for acute basilar artery occlusion, or (3) providing indirect rather than a direct head-to-head comparison between the two arms, which is unreliable method to establish the superiority of a technique as long as direct evidence exists in the literature.

We conducted subgroup analysis according to the study design and site of stroke. These results were consistent across the strata except that the difference in the successful recanalization was significant in observational studies but not in the RCTs suggesting that this difference was mainly driven by observational studies which have less internal validity and higher risk of confounders compared with well-designed RCTs. Besides, in the subgroup of posterior circulation occlusion, the occurrence of ENT was significantly lower in the ADAPT group compared with the SR. These results are consistent with the findings of Ye *et al.*[42] who meta-analyzed data from 5 studies to compare both ADAPT and SR in basilar artery occlusion. The authors explained this difference by the fact that ADAPT does not require passing through the thrombus and therefore carries a lower risk of thrombus fragmentation, in addition to the lower risks of endothelial injury with ADAPT as reported in studies on experimental animal models. However, this difference in emboli occurrence was not observed in the case of anterior circulation. This variation in the risk of ENT in anterior and posterior circulations remains open for discussion.

The strengths of our meta-analysis are the following: (1) we ran an extensive search on multiple medical electronic databases; (2) we included all observational studies and clinical trials comparing the two techniques; (3) we followed the guidelines of the Cochrane Handbook for Systematic Reviews of Interventions when conducting this systematic review and we reported this manuscript according to the PRISMA statement. The major limitation of our meta-analysis is that most of the included studies are observational; it is known that observational studies might suffer from confounding bias and are not reliable in establishing a causal relationship between the intervention and the clinical outcome. Only two studies were described as well-designed RCTs, and 28 studies were observational studies, which invites future research to compare both techniques in RCT design to confirm and update our findings.

CONCLUSION

Current evidence supports the use of the ADAPT technique to achieve successful and complete recanalization while considering the higher need for rescue therapy in some patients.

Availability of data, code, and other materials

Data of this study and the Review Manager file (.rm5 file) are available upon request.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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