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Title Page

Selection criteria for endovascular therapy for acute ischaemic stroke: Are patients missing out?

Running title:

Endovascular stroke selection criteria

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Abstract

Aims

Endovascular clot retrieval (ECR) following intravenous thrombolysis is superior to intravenous thrombolysis alone for acute stroke with large vessel occlusion. However, trial selection criteria may exclude potentially salvageable patients. We investigated the impact of published selection criteria on the different proportions of patients excluded and clinical outcome.

Methods

We included patients with anterior circulation stroke treated with ECR from a single centre. Selection criteria from five trials (REVASCAT, EXTEND IA, MR CLEAN, SWIFT PRIME, ESCAPE) and American Stroke Association (ASA) guidelines were applied. We calculated the proportion of patient's ineligible for ECR according to different selection criteria. Clinical benefit and harm were quantified as the number of patients benefiting per 1 patient harmed (NB1H) for each of the 6 applied selection criteria.

Results

One hundred and seventy-eight patients were included. Mean age was 74 (SD 14) years, 60.1% were male, median baseline NIHSS was 17 (IQR 13-21). Patients were hypothetically excluded from ECR: REVASCAT 35.4%, EXTENDA IA 86%, SWIFT PRIME 86%, MR CLEAN 2.3%, ESCAPE 93.3% and ASA 29.2%. The NB1H for included and excluded patients respectively in decreasing order of magnitude: EXTEND IA >100 vs 3, ESCAPE >100 vs 3.4, SWIFT PRIME 10 vs 3.3, REVASCAT 4.4 vs 2.9, MR CLEAN 3.7 vs >100, and ASA 3.7 vs 3.9.

Conclusion

We found that criteria from MR CLEAN, ASA and REVASCAT excluded the lowest proportion of patients with comparable NB1H. We believe that these criteria would be reasonable to be utilized for ECR selection.

Key Words
acute ischaemic stroke (AIS), selection criteria, endovascular, intra-arterial, modified ranking scale (mRS), stentriever, outcomes

1. Introduction

The recent publication of several randomised clinical trials demonstrated significant benefit of endovascular clot retrieval for acute ischaemic stroke with large vessel occlusion. [1-5]. In addition, the HERMES collaboration pooled patient data from the 5 published trials, demonstrating favourable outcomes in the endovascular intervention group across all pre-specified subgroups based on the modified Rankin Scale (mRS) distribution shift at 90 days [6].

However, while selection criteria used in the endovascular trials ensure patient population homogeneity, there remains uncertainly regarding the potential benefits to patients who have been excluded. For example, SWIFT PRIME excludes patients

greater than 80 years old and those with minor or more severe strokes (NIHSS 8-29) EXTEND IA excludes those with large ischaemic cores on mismatch imaging and those ineligible for intravenous tissue plasminogen activator (IV tPA), ESCAPE excludes M2 occlusions, tandem lesions and those unable to be enrolled in a timely manner and REVASCAT excludes patients who recanalise after IV tPA [1-5]. In addition, the American Stroke Association (ASA) guidelines expressly excludes the following patients: pre-morbid mRS greater than 1, NIHSS score less than 6, ASPECTS on non-contrast CT scan less than 6 [7]. The implication from these stringent selection criteria and guidelines is that patients aged greater than 80 years, too mild or too severe strokes based on NIHSS, distal occlusions and large infarcts on neuroimaging and those ineligible for IV tPA are excluded from treatment.

Despite these criteria and recommendations, the HERMES collaboration and two further meta-analyses including pooled data from earlier trials (IMS3, MR RESCUE and SYNTHESIS) demonstrated consistent benefit across many pre-specified subgroups. Of interest, the analyses suggested that patients previously thought to be inappropriate for ECR might potentially benefit from intervention. Patients aged greater than 80 years, a baseline NIHSS < 10 and > 20, those with M2 segment occlusion, pre-treatment CT ASPECTS 0-7, patients not receiving IV tPA, delayed randomisation more than 300 minutes after onset and presence of tandem lesions all demonstrated favourable odds ratios for favourable functional outcome at 90 days. Intervention was significantly favoured in those aged greater than 80 years, patients not receiving IV tPA and delayed randomisation [6, 8, 9].

We aimed to demonstrate the differing proportions of patients hypothetically excluded according to different selection criteria, utilizing a retrospective analysis of patients who were treated with ECR at a single centre. Furthermore, the potential favourable clinical outcomes in the hypothetically excluded patients were analysed and the magnitude of benefit for each of the 6 applied selection criteria were estimated.

2. Methods

2.1 Patients

This was a single centre retrospective analysis assessing patients with anterior circulation stroke treated with ECR between 2009 and 2016 (Figure 1). Our selection criteria for endovascular treatment are outlined in table 1.

Patients suitable for this study were retrospectively identified from a pre-existing neurointervention database. Relevant data was collected from this database and from the paper medical record. Data collection included basic demographic data, vascular risk factors, stroke severity and angiographic data including occlusion location and stentriever use.

Basic angiographic and clinical outcomes were thrombolysis in cerebral infarction (TICI) scores, complication rate (groin complication, any intracranial haemorrhage and symptomatic type 2 parenchymal haematoma (PH2)), modified rankin scale (mRS) at 90 days, 30- and 90-day mortality. An mRS of ≤ 2 was considered a favourable clinical outcome.

2.2 Image analysis

All TICI scores were assigned at the conclusion of ECR by three trained neurointerventionists. Subsequent follow up non-contrast CT brain was performed at 24hours to assess for haemorrhagic transformation. A significant haemorrhagic transformation was classified as a symptomatic parenchymal haematoma type 2 (PH2) based on the Fiorelli classification [10]

2.3 Intervention

All endovascular procedures were performed by trained Endovascular Neurointerventionists (BY, PM, RD). A selection of approaches and treatment devices were employed including intra-arterial thrombolysis, Merci Retriever (Concentric Medical), Penumbra system (Penumbra Inc), Solitaire FR (ev3), Trevo XP (Stryker Neurovascular) and ReVive SE (Codman Neurovascular) stentrievers.

2.4 Application of trial criteria/algorithm

Published clinical trial criteria from 5 recent endovascular trials (REVASCAT, EXTEND IA, MR CLEAN, SWIFT PRIME, ESCAPE) and recent American Stroke Association (ASA) were reviewed and selectively applied retrospectively to the

database of patients. Major trial and ASA criteria and the relative proportion of patients excluded are outlined in Figure 2. The number of patients who would have been included (eligible) and excluded (ineligible) based on these criteria was calculated. Clinical and angiographic outcome data between included and excluded groups were compared. Favourable clinical outcomes between groups were compared (mRS 0 – 2) as well as the complication rate as defined as symptomatic PH2 intracranial haemorrhage (sICH) with symptomatic decline.

2.4 Statistical analysis

Statistical analysis was performed on STATA131C (StataCorp, College Station, TX, USA). The value of $p = 0.05$ was selected as the threshold for statistical significance. Fisher's exact test and the Wilcoxon-Mann-Whitney rank sum test were used to investigate the differences in baseline characteristics and clinical outcomes between included and excluded patient groups based on the 5 trial and ASA criteria.

A "number benefitted per 1 harmed" (NB1H) index for included and excluded groups was calculated. Two versions of the index were considered using different notions of harm: the ratio of the proportion of patients with mRS 0 – 2 to either the proportion of patients with mRS 6 (mRS 0 – 2 / mRS 6) or with sICH (mRS 0-2 / sICH). The 2 versions of the index provided an estimation of the magnitude of benefit of each of the 6 applied criteria. In the scenarios where no patients were harmed, thereby resulting in the denominator of 0, the value of the index was given a notional value of > 100.

3. Results

A total of 399 patients were treated with ECR since 1999. Between 2009 (after the widespread introduction of stentrievers) and 2016, 265 patients with an anterior circulation stroke were treated. Of these patients, 178 were identified who had appropriate imaging and clinical outcome data available at the time of the analysis (Figure 1). Table 2 describes the overall baseline characteristics of all patients included in the analysis including basic demographic, vascular risk factors, stroke location and basic clinical outcome data. These features were comparable to those included in recent interventional endovascular trials including baseline median NIHSS.

Figure 2 outlines the proportion of patients excluded (deemed ineligible) for ECR based on respective trial selection criteria. Very few patients were excluded using MR CLEAN criteria (2.3%) given their similarity to our centres patient selection criteria outlined in table 1. Between 86% and 93.3% of patients were excluded (deemed ineligible) for ECR using EXTEND IA, SWIFT PRIME and ESCAPE criteria.

Comparison of baseline characteristics between patients included and excluded for endovascular therapy based on each of the 6 criteria analysed are outlined in table 3. REVASCAT, SWIFT PRIME, MR CLEAN and ASA excluded distal (M2, M3), tandem and anterior cerebral artery occlusions from ECR and this was reflected in baseline imaging characteristics. Time to randomisation was also a significant discriminator in excluding patients for ECR using EXTEND IA, SWIFT PRIME and ESCAPE criteria. This was reflected in differences in CT-to-groin time (also presumed to then prolong onset-to-groin and onset-to-recanalisation times) between included and excluded groups. The requirement for IV tPA using EXTEND IA, SWIFT PRIME and ASA criteria resulted in significant differences between included and excluded patients.

Table 4 outlines angiographic and clinical outcome data between included and excluded patients based on the relative criteria. The effect of each of the criteria was quantified using "number benefitted per 1 harmed" (NB1H) index in table 4. As expected the differences between NB1H for included and excluded patients using EXTEND IA and ESCAPE criteria were large (>100 vs 3 and >100 and 3.4 respectively) with demonstration of significant improvement in outcomes in patients deemed eligible for ECR (84% vs 54.9%, p-value 0.008 and 80% vs 55.6%, p-value 0.03 respectively). A large difference was also observed using SWIFT PRIME criteria (10 vs 3.3) although this was not reflected in a significant difference in clinical outcomes. Using REVASCAT and ASA criteria did not produce appreciable differences in NB1H (4.4 vs 2.9 and 3.7 vs 3.9 respectively). The NB1H for included and excluded patients using MR CLEAN criteria demonstrated an apparent large difference of 3.7 and >100 respectively however this reflects the low proportion of patients excluded with 50% demonstrating a good outcome with no death at 90days within this group. Between 50% and 59.6% of those excluded demonstrated a favourable clinical outcome at 90 days (summarised in table 5). Figures 3 and 4

further emphasises the proportion of patients who could potentially benefit from ECR who are deemed ineligible by trial criteria.

The NB1H calculated using sICH as the harm metric (table 4) was used to estimate potential procedure related harm caused by treating patients who would otherwise be excluded. No significant increase in harm was observed where excluded groups tended to have a higher index consistent with lower rates of sICH per patient with a good outcome.

Discussion

Acute ischaemic stroke (AIS) is the fifth leading cause of death within the United States with an estimated 6.5 million stroke related deaths worldwide in 2013. Approximately 610 000 people experience new stroke symptoms each year in the United States at an estimated cost between 2011 and 2012 of $33 billion. In 2009, between 3.4% and 5.2% of patients with AIS were treated with IV tPA [11].

Published endovascular trials have demonstrated safety and efficacy in improving patient outcomes post AIS [1-6, 8, 9]. To maintain homogeneity in the patient population, keep sample sizes as low as reasonably possible and still demonstrating treatment effect without excess harm, trial design must be efficacious. Correspondingly many of the published trials maintained strict clinical and neuroimaging patient selection criteria.

However, identifying realistic selection criteria for ECR in AIS is complex and overly strict criteria excludes potentially salvageable patients who may benefit from intervention. Distal occlusion of M2 and M3 segments, particularly if involving eloquent brain, lower ASPECT scores (as a surrogate for infarct volume), NIHSS restrictions, older age (>80 to 85 years old), and poor premorbid status as well as delays to CT and or groin puncture were typically used to exclude patients from treatment.

Despite these trial specific restrictions, the HERMES collaboration and two further meta-analyses including pooled data from earlier trials (IMS3, MR RESCUE and SYNTHESIS) demonstrated consistent benefit across many prespecified subgroups. Intervention with ECR was favoured in patients aged greater than 80 years, a baseline

NIHSS < 10 and > 20, those with M2 segment occlusion, pre-treatment CT ASPECTS 0-7, patients not receiving intravenous (IV) tPA, delayed randomisation more than 300 minutes after onset and presence of tandem lesions. Intervention was significantly favoured in those aged greater than 80 years, patients not receiving IV tPA and delayed randomisation [6, 8, 9]. Treating patients with low NIHSS is controversial. While very mild strokes may have an excellent prognosis, acute large vessel occlusion (LVO) can still present with mild symptoms due to adequate collateral blood flow. In these patients presenting with lower NIHSS, intervention is still favoured (as demonstrated in the HERMES collaboration) as collateral vessels invariably fail leading to established infarction across large vascular territories.

Overall, we observed patient outcomes to be favourable with low rates of intracranial haemorrhage. Furthermore, we demonstrated that in those hypothetically excluded from ECR, a large proportion (up to 59.6%) will demonstrate favourable clinical outcomes. Furthermore, less than 20% of our patients were deemed eligible for ECR using the strict criteria of EXTEND IA, SWIFT PRIME and ESCAPE with up to 57.8% of these patients having favourable outcomes at 90days.

This compares to Tawil et al who demonstrated than in a large cohort of patients 3% to 53% would be eligible for ECR with less than 20% eligible for four trials and under and 1% eligible for all recently published trials [12]. Their study, however, did not report on clinical outcomes on patients hypothetically excluded from ECR. Given a similar proportion of patients were deemed ineligible with comparable clinical features to our patient cohort we assume that the proportion of ineligible patients with favourable outcomes may be similar.

We calculated a “number benefitted per 1 harmed” (NB1H) index to quantify treatment effect and potential harm in the 86% - 93.3% of patients treated at our institution that would have been excluded using differing trial criteria or published guidelines. Our results indicate that treatment with ECR produced a higher proportion of favourable outcomes in included groups when strict selection criteria of EXTEND IA, SWIFT PRIME and ESCAPE were used, as highlighted by significant differences in NB1H (table 4) between included and excluded groups. REVASCAT, MR CLEAN and ASA criteria excluded a lower proportion of patients (2.3% to 35.4%) with

comparable benefit indices between included and excluded groups with fewer patients in the mRS 0-2 category for a given number of patients with mRS 6, results reflected in figure 3. Accordingly, strict criteria resulted in a shift towards poor outcomes (mRS 3 – 5 and mRS 6) in the excluded groups. However, despite NB1H favouring strict selection criteria between 50 to 59.6% of patients who would be excluded using any of the 6 criteria had favourable outcomes at 90 days (tables 3 and 6 and figure 3). Additionally, the calculated NB1H index using sICH did not indicate increased rates of sICH in treating patients who were hypothetically excluded (table b) with overall lower rates of sICH per patient with mRS 0 – 2 in excluded patient cohorts.

Intravenous thrombolysis was the previous standard of care in treating AIS. In fact, most endovascular trials excluded those who were contraindicated or unable to receive IV tPA. Pooled data from trials of IV tPA for AIS demonstrated improved outcomes (mRS 0-1) in 31% (2110 of 6756 patients) at 3-6 months [13], a proportion significantly lower than that in our hypothetically excluded or ineligible for ECR patients. While the use of alteplase was favoured across all treatment time groups and ages for improved outcomes, fatal intracranial haemorrhage and 90 day mortality were significantly affected by the use of alteplase. [13]. Our results show that even in patients hypothetically excluded from ECR based on published patient selection criteria, the proportion with favourable clinical outcomes are far superior to published data using IV tPA alone with no significant procedure related harm between included and excluded groups reflected in the NB1H indices (table 4). These results are not surprising given that only 12.7% of patients demonstrate large vessel recanalization post IV tPA on digitial subtraction angiography [14].

Overall, using the more permissive criteria of MR CLEAN resulted in few numbers of excluded patients. The produced NB1H indices in MR CLEAN did not differ significantly from those using ASA guidelines.

Conclusion

Strict trial criteria potentially exclude a large proportion of patients from ECR, many of who are likely to demonstrate favourable clinical outcomes without any detectable increase in procedure related harm. We found that criteria from MR CLEAN, ASA

and REVASCAT excluded the lowest proportion of patients with comparable NB1H indices between included and excluded groups. We believe that these criteria would be reasonable to be utilized for ECR selection.

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Selection criteria
Age ≥ 18 years
Large artery occlusion (distal ICA, M1, M2, A1 segments)
If presenting within 4.5 hours then patients with >1/3 MCA territory infarcted on NCCT are excluded from endovascular treatment
If presenting between 4.5 to 6 hours then CT and CT Perfusion are not used to exclude patients. Eligibility is at the discretion of the physician.
Pre-morbid mRS 0-2 eligible Pre-morbid mRS 3 considered on a case-by-case basis

Variable	Total (n=178)
Baseline Demographic data	
Male sex	60.1% (107)
Mean Age	67+-14 (SD)
Median baseline NIHSS	17 (IQR 13-21, range 2-42)
Vascular Risk factors	
Diabetes mellitus	17.4% (31)
Hypertension	49.4% (88)
Hypercholesterolaemia	27% (48)
Atrial Fibrillation	34.8% (62)
Ischaemic Heart Disease	14% (25)
Previous stroke/TIA	13.5% (24)
Neuroimaging data	
Median CT ASPECTS	9 (IQR 8-10)
Angiographic data	
Occlusion location	
M1	107 (60.1%)
M2	20 (11.2%)
M3	2 (1.1%)
ICA	47 (26.4%)
Other (ACA)	2 (1.1%)
Treatment approaches	
IV tPA	104 (58.4%)
Stentriever use (Solitaire, TREVO, Revive)	135 (76.3%)
Mean onset-to-CT time (mins)	99 (SD 45.5)
Mean CT-to-groin (mins)	133 (SD 54.9)
Mean onset-to-DSA (mins)	232 (SD 65.5)
Outcome data	
Thrombolysis in Cerebral Infarction (TICI) 2b-3	135 (75.8%)
Complications	
Groin complications	3 (1.7%)
Vessel perforation	0 (0)
Haemorrhage	39 (21.9%)
Symptomatic PH2 haemorrhage	7 (3.9%)
Overall mRS ≤ 2	105 (59%)
30 day mortality	25 (14%)

90 day mortality	15 (15.7%)

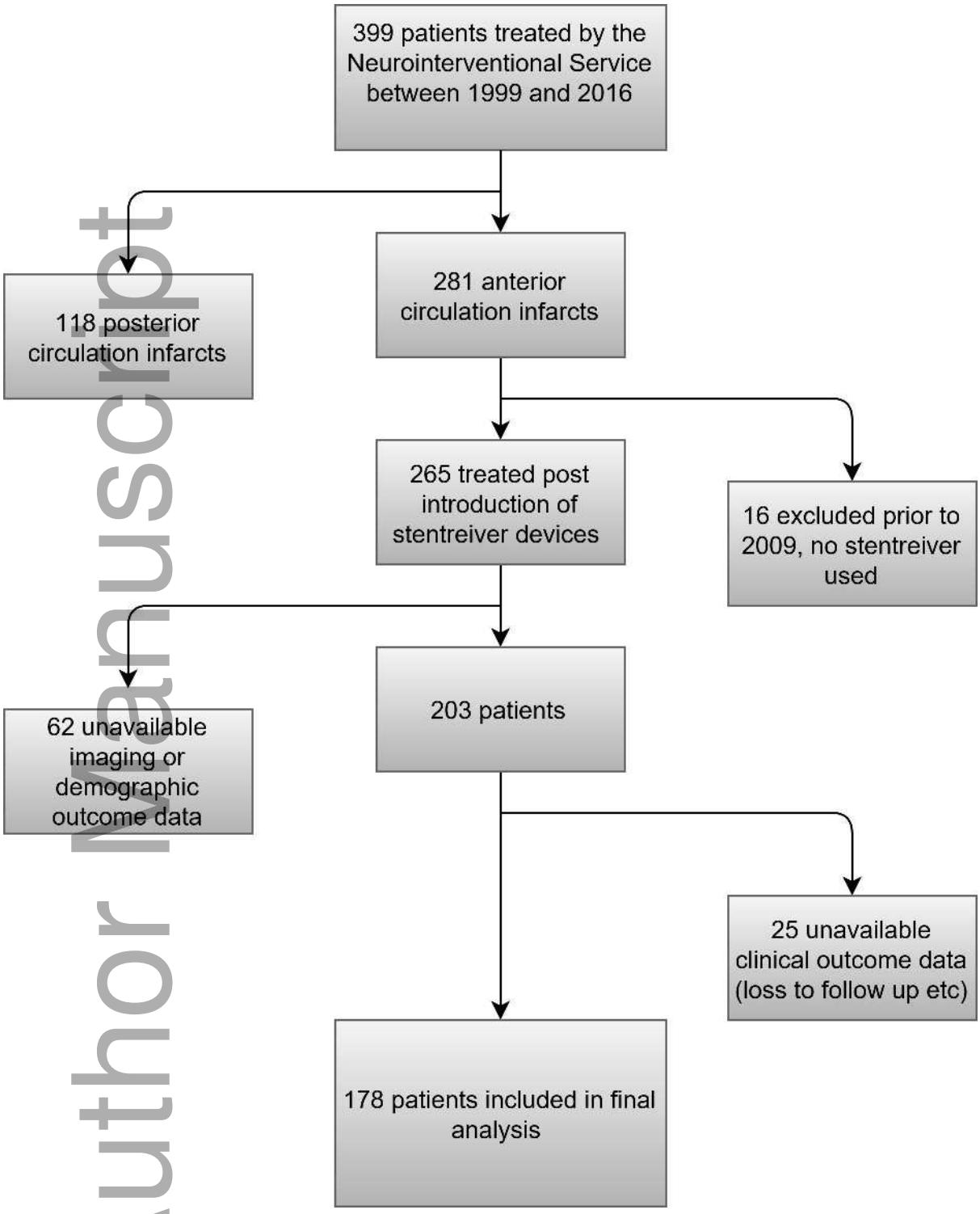
Baseline characteristics	REVASCAT			EXTEND IA			SWIFT PRIME			MR CLEAN			ESCAPE			ASA		
	Included	Excluded	p-value	Included	Excluded	p-value	Included	Excluded	p-value	Included	Excluded	p-value	Included	Excluded	p-value	Included	Excluded	p-value
Total (n)	**115**	**63**		**25**	**153**		**25**	**153**		**174**	**4**		**12**	**166**		**126**	**52**	
Age - mean (SD)	65.8 (14.2)	69.4 (14.4)	0.09	70 (11.5)	66.6 (14.7)	0.76	67.8 (12.6)	67 (14.6)	0.96	67.1 (14.3)	66.5 (17.9)	>0.999	60.7 (17)	67.7 (14.1)	0.13	67.2 (14.7)	66.9 (13.5)	0.71
Male Sex – no. (%)	67 (58.3)	40 (63.5)	0.53	13 (52.0)	94 (61.4)	0.39	8 (32)	99 (64.7)	0.003	104 (59.8)	3 (75)	>0.999	7 (58.3)	100 (60.2)	>0.999	71 (56.4)	36 (69.2)	0.13
Baseline NIHSS – median (IQR)	17 (15-20)	16.5 (9-22)	0.12	18 (16-22)	17 (13-21)	0.31	17 (13.5-19.5)	17 (13-21)	0.71	17 (13-21)	13 (6-22)	0.44	16 (14-19)	17 (13-21)	0.65	17 (15-21)	14 (8 – 21)	0.02
CT ASPECTS (?mean)	8.8 (1.1)	8.3 (2.1)	0.56	8.8 (1)	8.6 (1.6)	0.84	8.7 (1.0)	8.6 (1.6)	0.67	8.6 (1.6)	10 (0)	0.03	8.8 (1.0)	8.6 (1.6)	>0.999	8.7 (1.3)	8.3 (2.1)	0.94
Occlusion location – no. (%)																		
M1	83 (72.2)	24 (38.1)	<0.001	16 (64.0)	91 (59.5)	0.64	22 (88)	85 (55.6)	0.08	107 (61.5)	0 (0)	<0.001	8 (66.7)	99 (59.6)	0.82	100 (79.4)	7 (13.5)	<0.001
M2	2 (1.7)	18 (28.6)	<0.001	5 (20.0)	15 (9.8)	0.64	0 (0)	20 (13.1)	0.08	20 (11.5)	0 (0)	<0.001	2 (16.7)	18 (10.8)	0.82	0 (0)	20 (38.5)	<0.001
M3	0 (0)	2 (3.2)	<0.001	0 (0)	2 (1.3)	0.64	0 (0)	2 (1.3)	0.08	0 (0)	2 (50)	<0.001	0 (0)	2 (1.2)	0.82	0 (0)	2 (3.9)	<0.001
ICA	30 (26.1)	17 (27)	<0.001	4 (16)	43 (28.1)	0.64	3 (12)	44 (28.8)	0.08	47 (27)	0 (0)	<0.001	2 (16.7)	45 (27.1)	0.82	26 (20.6)	21 (40.4)	<0.001
ACA	0 (0)	2 (3.2)	<0.001	0 (0)	2 (1.3)	0.64	0 (0)	2 (1.3)	0.08	0 (0)	2 (50)	<0.001	0 (0)	2 (1.2)	0.82	0 (0)	2 (3.9)	<0.001
IV tPA – no. (%)	68 (59.1)	36 (57.1)	0.87	23 (92.0)	81 (52.9)	<0.001	25 (100)	79 (51.6)	<0.001	102 (58.6)	2 (5)	>0.999	9 (75)	95 (57.2)	0.36	77 (61.1)	27 (51.9)	0.32
Stentriever use	89 (77.4)	46 (74.2)	0.87	20 (80)	115 (75.7)	0.87	23 (92)	112 (73.7)	0.14	134 (77)	1 (33.3)	0.19	11 (91.2)	124 (75.2)	0.43	99 (78.6)	36 (70.6)	0.51

Onset-to-CT – mins (SD)	101.6 (48.2)	94.2 (40)	0.38	95.5 (40.3)	99.6 (46.4)	0.89	103.6 (50.3)	98.2 (44.8)	0.83	99.4 (45.6)	73.3 (38.7)	0.21	119.2 (52.4)	97.6 (44.9)	0.14	101.1 (47.2)	93.6 (40.9)	0.36
CT-to-groin – mins (SD)	134.7 (53.2)	130.2 (58.1)	0.43	97.6 (42.2)	138.9 (54.6)	<0.001	91.8 (53.6)	139.9 (52.2)	<0.001	133.5 (54.6)	116 (74.4)	0.52	49.7 (7.5)	138.6 (52.1)	<0.001	133.8 (51.9)	131.2 (62.1)	0.55
Onset-to-DSA – mins (SD)	236.7 (64.4)	223.3 (67.1)	0.19	193 (60.3)	238.5 (64.2)	0.001	195.4 (63.6)	238.1 (64)	0.002	233.2 (64.5)	162.7 (101.9)	0.14	181.3 (65.5)	235.8 (64.1)	0.006	235.5 (63.1)	223.2 (71)	0.28
Onset-to-recanalisation – mins (SD)	304.2 (84.8)	296.3 (84.9)	0.50	234.8 (62.7)	312.5 (82.9)	<0.001	246.8 (71.8)	310.5 (83.4)	<0.001	302.2 (84)	257.3 (130.5)	0.44	241.8 (72.6)	305.8 (84)	0.01	304 (87.5)	294.9 (77.5)	0.62

Clinical outcomes	REVASCAT			EXTEND IA			SWIFT PRIME			MR CLEAN			ESCAPE			ASA		
	Included	Excluded	p-value	Included	Excluded	p-value	Included	Excluded	p-value	included	excluded	p-value	Included	Excluded	p-value	Included	Excluded	p-value
TICI 2b, 3 – no. (%)	88 (76.5)	47 (74.6)	0.86	22 (88)	113 (73.9)	0.21	23 (92)	112 (73.2)	0.04	132 (75.9)	3 (75)	>0.999	12 (100)	123 (74.1)	0.07	92 (73)	43 (82.7)	0.18
Groin complication – no. (%)	1 (0.87)	2 (3.2)	0.29	1 (4)	2 (1.3)	0.37	0 (0)	3 (2.0)	>0.999	3 (1.7)	0 (0)	>0.999	1 (8.3)	2 (1.2)	0.19	2 (1.6)	1 (1.9)	>0.999
Any ICH – no. (%)	26 (22.6)	13 (20.6)	0.85	10 (40)	29 (19)	0.03	7 (28)	32 (20.9)	0.44	38 (21.8)	1 (25)	>0.999	4 (33.3)	35 (21.1)	0.3	30 (23.8)	9 (17.3)	0.43
Symptomatic ICH – no. (%)	5 (4.4)	2 (3.2)	>0.999	2 (8)	5 (3.3)	0.26	2 (8)	5 (3.3)	0.26	7 (4)	0 (0)	>0.999	1 (8.3)	6 (3.6)	0.39	6 (4.8)	1 (1.9)	0.68
30day mortality – no. (%)	16 (13.9)	9 (14.3)	>0.999	0 (0)	25 (16.3)	0.03	3 (12)	22 (14.4)	>0.999	25 (14.4)	0 (0)	>0.999	1 (8.3)	24 (14.5)	>0.999	17 (13.5)	8 (15.4)	0.81
90day mortality – no. (%)	16 (13.9)	12 (19.1)	0.22	0 (0)	28 (18.3)	0.02	2 (8)	26 (17.0)	0.17	28 (16.1)	0 (0)	0.36	0 (0)	28 (16.9)	0.12	20 (15.9)	8 (15.4)	0.83
Good clinical outcome (mRS 0-2) – no. (%)	70 (60.9)	35 (55.6)	0.53	21 (84)	84 (54.9)	0.008	20 (80)	85 (55.6)	0.03	103 (59.2)	2 (50)	>0.999	9 (75)	96 (57.8)	0.36	74 (58.7)	31 (59.6)	>0.999

Number benefitted per 1 harmed (NB1H) index using mRS	0.609 / 0.139 = 4.4	0.556 / 0.19 = 2.9	NA	0.84 / 0 = “>100”	0.549 / 0.183 = 3	NA	0.80 / 0.08 = 10	0.556 / 0.17 = 3.3	NA	0.592 /0.161 = 3.7	0.50 / 0 = “>100”	NA	0.75 / 0 = “>100”	0.578 / 0.169 = 3.4	NA	0.587 / 0.159 = 3.7	0.596 / 0.154 = 3.9	NA
Number benefitted per 1 harmed (NB1H) index using sICH	0.609 / 0.044 = 13.8	0.556 / 0.032 = 17.4	NA	0.84 / 0.08 = 10.5	0.549 / 0.033 = 16.6	NA	0.80 / 0.08 = 10	0.556 / 0.033 = 17.2	NA	0.592 / 0.04 = 14.8	0.50 /0 = “>100”	NA	0.75 / 0.083 = 9.0	0.578 / 0.036 = 12.2	NA	0.587 / 0.048 = 12.2	0.596 / 0.019 = 31.4	NA

Trial Criteria	Total excluded – n (%)	Proportion with a good clinical outcome at 90days – n (%)
REVASCAT	63 (35.4%)	35 (55.6%)
EXTEND IA	153 (86%)	84 (54.9%)
SWIFT PRIME	153 (86%)	85 (55.6%)
MR CLEAN	4 (2.3%)	2 (50%)
ESCAPE	166 (93.3%)	96 (57.8%)
ASA	52 (29.2%)	31 (59.6%)



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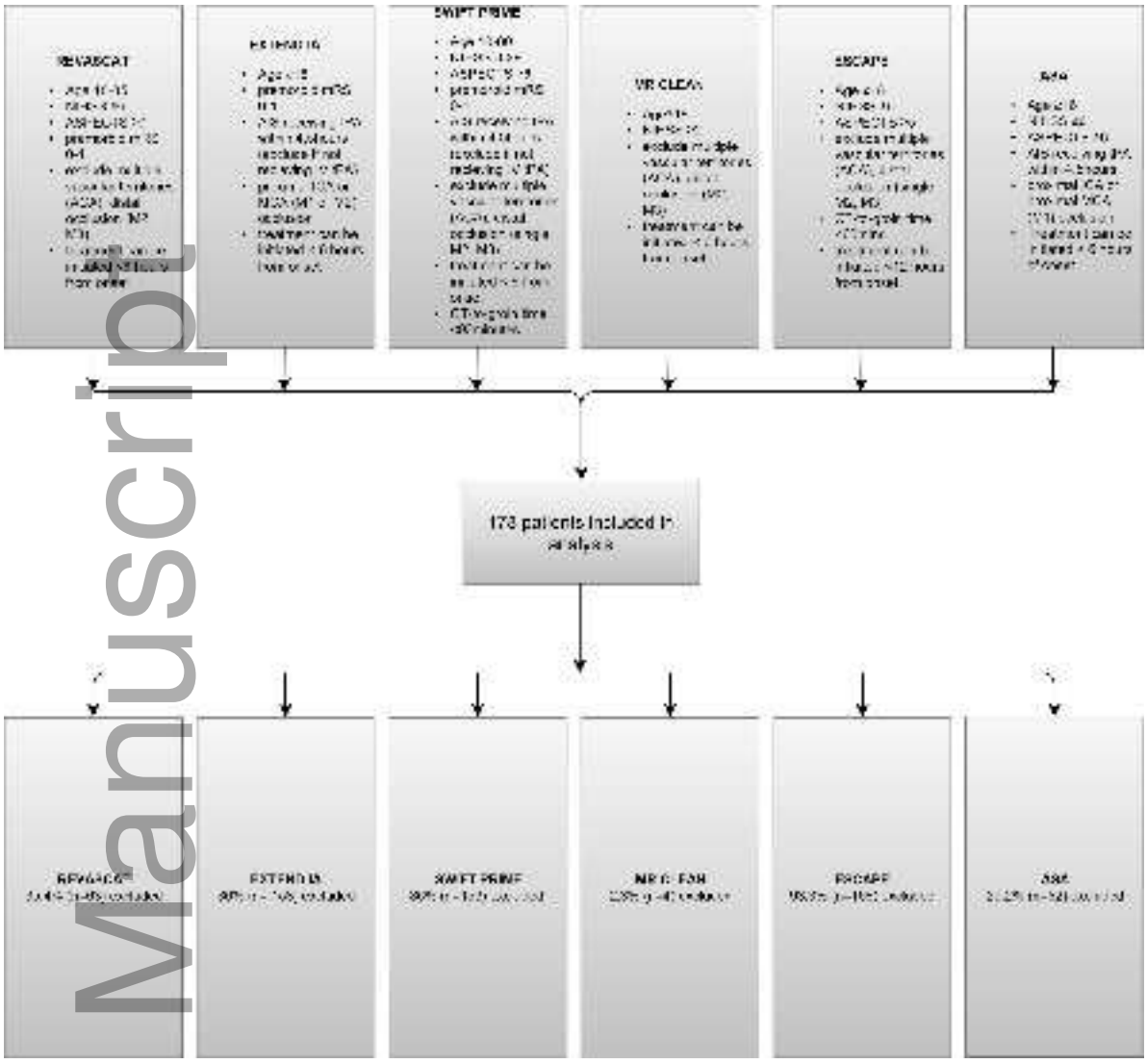

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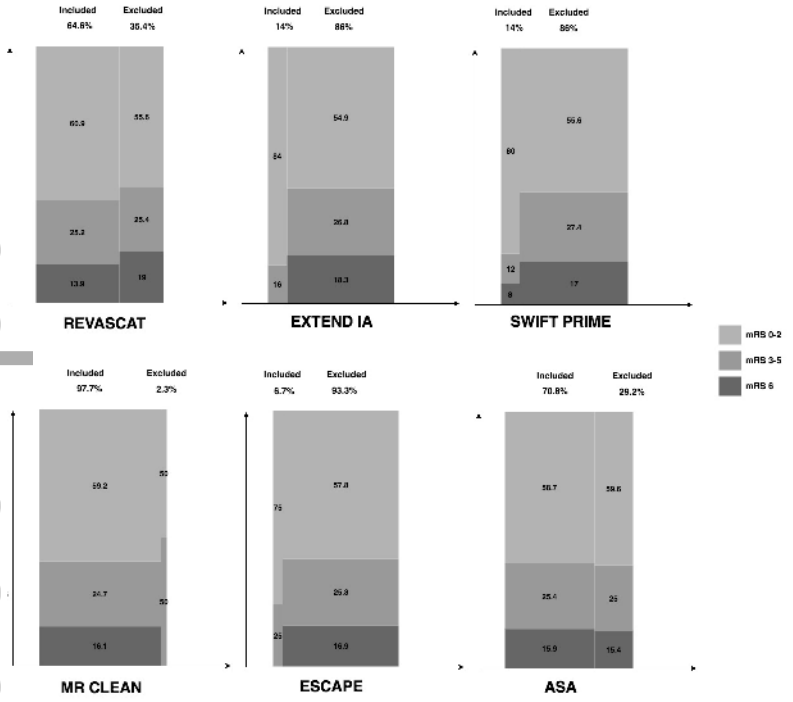

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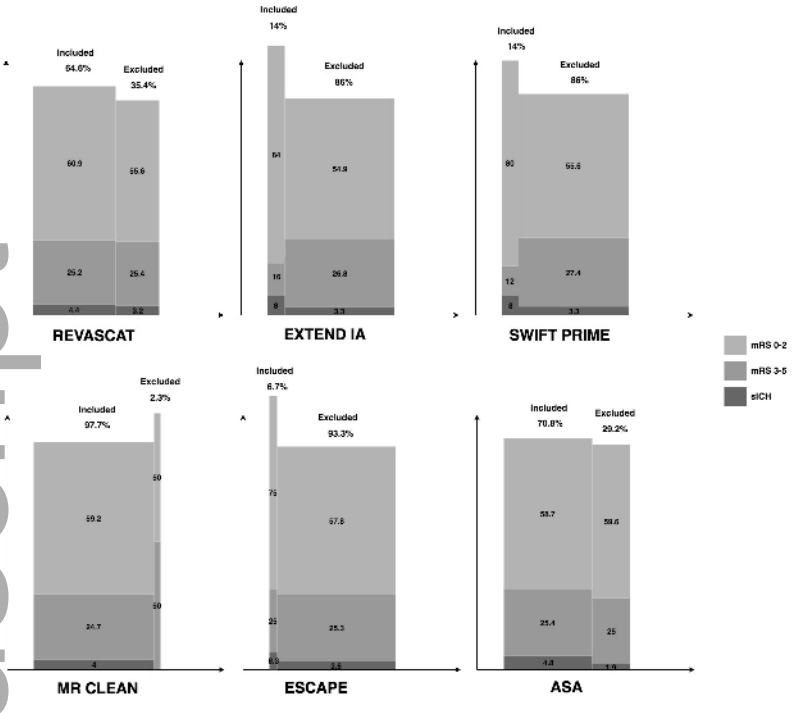

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