

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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7
8 **Abstract**

9 Aims

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

15
16 Methods

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

24
25 Results

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

33
34 Conclusion

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

38

39 *Key Words*

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

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58 **1. Introduction**

59 The recent publication of several randomised clinical trials demonstrated significant
60 benefit of endovascular clot retrieval for acute ischaemic stroke with large vessel
61 occlusion. [1-5]. In addition, the HERMES collaboration pooled patient data from the
62 5 published trials, demonstrating favourable outcomes in the endovascular
63 intervention group across all pre-specified subgroups based on the modified Rankin
64 Scale (mRS) distribution shift at 90 days [6].

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

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

79
80 Despite these criteria and recommendations, the HERMES collaboration and two
81 further meta-analyses including pooled data from earlier trials (IMS3, MR RESCUE
82 and SYNTHESIS) demonstrated consistent benefit across many pre-specified
83 subgroups. Of interest, the analyses suggested that patients previously thought to be
84 inappropriate for ECR might potentially benefit from intervention. Patients aged
85 greater than 80 years, a baseline NIHSS < 10 and > 20, those with M2 segment
86 occlusion, pre-treatment CT ASPECTS 0-7, patients not receiving IV tPA, delayed
87 randomisation more than 300 minutes after onset and presence of tandem lesions all
88 demonstrated favourable odds ratios for favourable functional outcome at 90 days.
89 Intervention was significantly favoured in those aged greater than 80 years, patients
90 not receiving IV tPA and delayed randomisation [6, 8, 9].

91
92 We aimed to demonstrate the differing proportions of patients hypothetically
93 excluded according to different selection criteria, utilizing a retrospective analysis of
94 patients who were treated with ECR at a single centre. Furthermore, the potential
95 favourable clinical outcomes in the hypothetically excluded patients were analysed
96 and the magnitude of benefit for each of the 6 applied selection criteria were
97 estimated.

98
99

100 **2. Methods**

101 2.1 Patients

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

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

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

115

116 2.2 Image analysis

117 All TICI scores were assigned at the conclusion of ECR by three trained
118 neurointerventionists. Subsequent follow up non-contrast CT brain was performed at
119 24hours to assess for haemorrhagic transformation. A significant haemorrhagic
120 transformation was classified as a symptomatic parenchymal haematoma type 2
121 (PH2) based on the Fiorelli classification [10]

122

123

124 2.3 Intervention

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

130

131

132 2.4 Application of trial criteria/algorithm

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

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

143

144 2.4 Statistical analysis

145 Statistical analysis was performed on STATA131C (StataCorp, College Station, TX,
146 USA). The value of $p = 0.05$ was selected as the threshold for statistical significance.
147 Fisher's exact test and the Wilcoxon-Mann-Whitney rank sum test were used to
148 investigate the differences in baseline characteristics and clinical outcomes between
149 included and excluded patient groups based on the 5 trial and ASA criteria.
150 A "number benefitted per 1 harmed" (NB1H) index for included and excluded groups
151 was calculated. Two versions of the index were considered using different notions of
152 harm: the ratio of the proportion of patients with mRS 0–2 to either the proportion of
153 patients with mRS 6 (mRS 0–2 / mRS 6) or with sICH (mRS 0-2 / sICH). The 2
154 versions of the index provided an estimation of the magnitude of benefit of each of
155 the 6 applied criteria. In the scenarios where no patients were harmed, thereby
156 resulting in the denominator of 0, the value of the index was given a notional value of
157 > 100 .

158

159 3. Results

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

169 Figure 2 outlines the proportion of patients excluded (deemed ineligible) for ECR
170 based on respective trial selection criteria. Very few patients were excluded using
171 MR CLEAN criteria (2.3%) given their similarity to our centres patient selection
172 criteria outlined in table 1. Between 86% and 93.3% of patients were excluded
173 (deemed ineligible) for ECR using EXTEND IA, SWIFT PRIME and ESCAPE
174 criteria.
175 Comparison of baseline characteristics between patients included and excluded for
176 endovascular therapy based on each of the 6 criteria analysed are outlined in table 3.
177 REVASCAT, SWIFT PRIME, MR CLEAN and ASA excluded distal (M2, M3),
178 tandem and anterior cerebral artery occlusions from ECR and this was reflected in
179 baseline imaging characteristics. Time to randomisation was also a significant
180 discriminator in excluding patients for ECR using EXTEND IA, SWIFT PRIME and
181 ESCAPE criteria. This was reflected in differences in CT-to-groin time (also
182 presumed to then prolong onset-to-groin and onset-to-recanalisation times) between
183 included and excluded groups. The requirement for IV tPA using EXTEND IA,
184 SWIFT PRIME and ASA criteria resulted in significant differences between included
185 and excluded patients.
186
187 Table 4 outlines angiographic and clinical outcome data between included and
188 excluded patients based on the relative criteria. The effect of each of the criteria was
189 quantified using “number benefitted per 1 harmed” (NB1H) index in table 4. As
190 expected the differences between NB1H for included and excluded patients using
191 EXTEND IA and ESCAPE criteria were large (>100 vs 3 and >100 and 3.4
192 respectively) with demonstration of significant improvement in outcomes in patients
193 deemed eligible for ECR (84% vs 54.9%, p-value 0.008 and 80% vs 55.6%, p-value
194 0.03 respectively). A large difference was also observed using SWIFT PRIME criteria
195 (10 vs 3.3) although this was not reflected in a significant difference in clinical
196 outcomes. Using REVASCAT and ASA criteria did not produce appreciable
197 differences in NB1H (4.4 vs 2.9 and 3.7 vs 3.9 respectively). The NB1H for included
198 and excluded patients using MR CLEAN criteria demonstrated an apparent large
199 difference of 3.7 and >100 respectively however this reflects the low proportion of
200 patients excluded with 50% demonstrating a good outcome with no death at 90days
201 within this group. Between 50% and 59.6% of those excluded demonstrated a
202 favourable clinical outcome at 90 days (summarised in table 5). Figures 3 and 4

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

205

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

211

212

213 **Discussion**

214 Acute ischaemic stroke (AIS) is the fifth leading cause of death within the United
215 States with an estimated 6.5 million stroke related deaths worldwide in 2013.

216 Approximately 610 000 people experience new stroke symptoms each year in the
217 United States at an estimated cost between 2011 and 2012 of \$33 billion. In 2009,
218 between 3.4% and 5.2% of patients with AIS were treated with IV tPA [11].

219

220 Published endovascular trials have demonstrated safety and efficacy in improving
221 patient outcomes post AIS [1-6, 8, 9]. To maintain homogeneity in the patient
222 population, keep sample sizes as low as reasonably possible and still demonstrating
223 treatment effect without excess harm, trial design must be efficacious.

224 Correspondingly many of the published trials maintained strict clinical and
225 neuroimaging patient selection criteria.

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

233 Despite these trial specific restrictions, the HERMES collaboration and two further
234 meta-analyses including pooled data from earlier trials (IMS3, MR RESCUE and
235 SYNTHESIS) demonstrated consistent benefit across many prespecified subgroups.

236 Intervention with ECR was favoured in patients aged greater than 80 years, a baseline

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

247
248 Overall, we observed patient outcomes to be favourable with low rates of intracranial
249 haemorrhage. Furthermore, we demonstrated that in those hypothetically excluded
250 from ECR, a large proportion (up to 59.6%) will demonstrate favourable clinical
251 outcomes. Furthermore, less than 20% of our patients were deemed eligible for ECR
252 using the strict criteria of EXTEND IA, SWIFT PRIME and ESCAPE with up to
253 57.8% of these patients having favourable outcomes at 90days.

254
255 This compares to Tawil et al who demonstrated that in a large cohort of patients 3%
256 to 53% would be eligible for ECR with less than 20% eligible for four trials and under
257 and 1% eligible for all recently published trials [12]. Their study, however, did not
258 report on clinical outcomes on patients hypothetically excluded from ECR. Given a
259 similar proportion of patients were deemed ineligible with comparable clinical
260 features to our patient cohort we assume that the proportion of ineligible patients with
261 favourable outcomes may be similar.

262
263 We calculated a “number benefitted per 1 harmed” (NB1H) index to quantify
264 treatment effect and potential harm in the 86% - 93.3% of patients treated at our
265 institution that would have been excluded using differing trial criteria or published
266 guidelines. Our results indicate that treatment with ECR produced a higher proportion
267 of favourable outcomes in included groups when strict selection criteria of EXTEND
268 IA, SWIFT PRIME and ESCAPE were used, as highlighted by significant differences
269 in NB1H (table 4) between included and excluded groups. REVASCAT, MR CLEAN
270 and ASA criteria excluded a lower proportion of patients (2.3% to 35.4%) with

271 comparable benefit indices between included and excluded groups with fewer patients
272 in the mRS 0-2 category for a given number of patients with mRS 6, results reflected
273 in figure 3. Accordingly, strict criteria resulted in a shift towards poor outcomes (mRS
274 3 – 5 and mRS 6) in the excluded groups. However, despite NB1H favouring strict
275 selection criteria between 50 to 59.6% of patients who would be excluded using any
276 of the 6 criteria had favourable outcomes at 90 days (tables 3 and 6 and figure 3).
277 Additionally, the calculated NB1H index using sICH did not indicate increased rates
278 of sICH in treating patients who were hypothetically excluded (table b) with overall
279 lower rates of sICH per patient with mRS 0 – 2 in excluded patient cohorts.

280

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

295

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

299

300

301 **Conclusion**

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

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

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Selection criteria
Age \geq 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%)
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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

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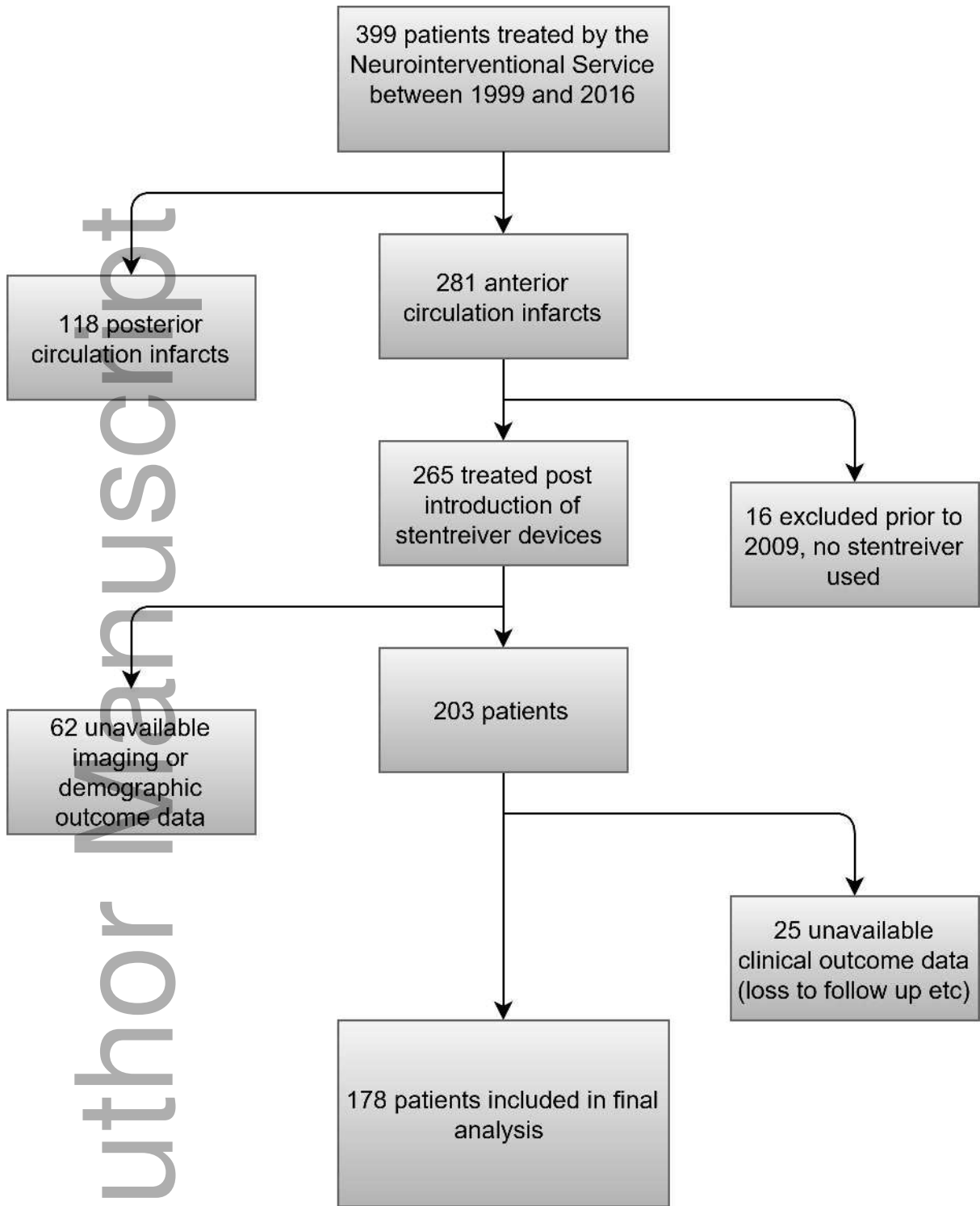
Onset-to-CT – mins (SD)	101.6 (48.2)	94.2 (40)	0.38	95.5 (40.3)	99.6 (46.4)	0.89	103.6 (50.3)	98.2 (44.8)	0.83	99.4 (45.6)	73.3 (38.7)	0.21	119.2 (52.4)	97.6 (44.9)	0.14	101.1 (47.2)	93.6 (40.9)	0.36
CT-to-groin – mins (SD)	134.7 (53.2)	130.2 (58.1)	0.43	97.6 (42.2)	138.9 (54.6)	<0.001	91.8 (53.6)	139.9 (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

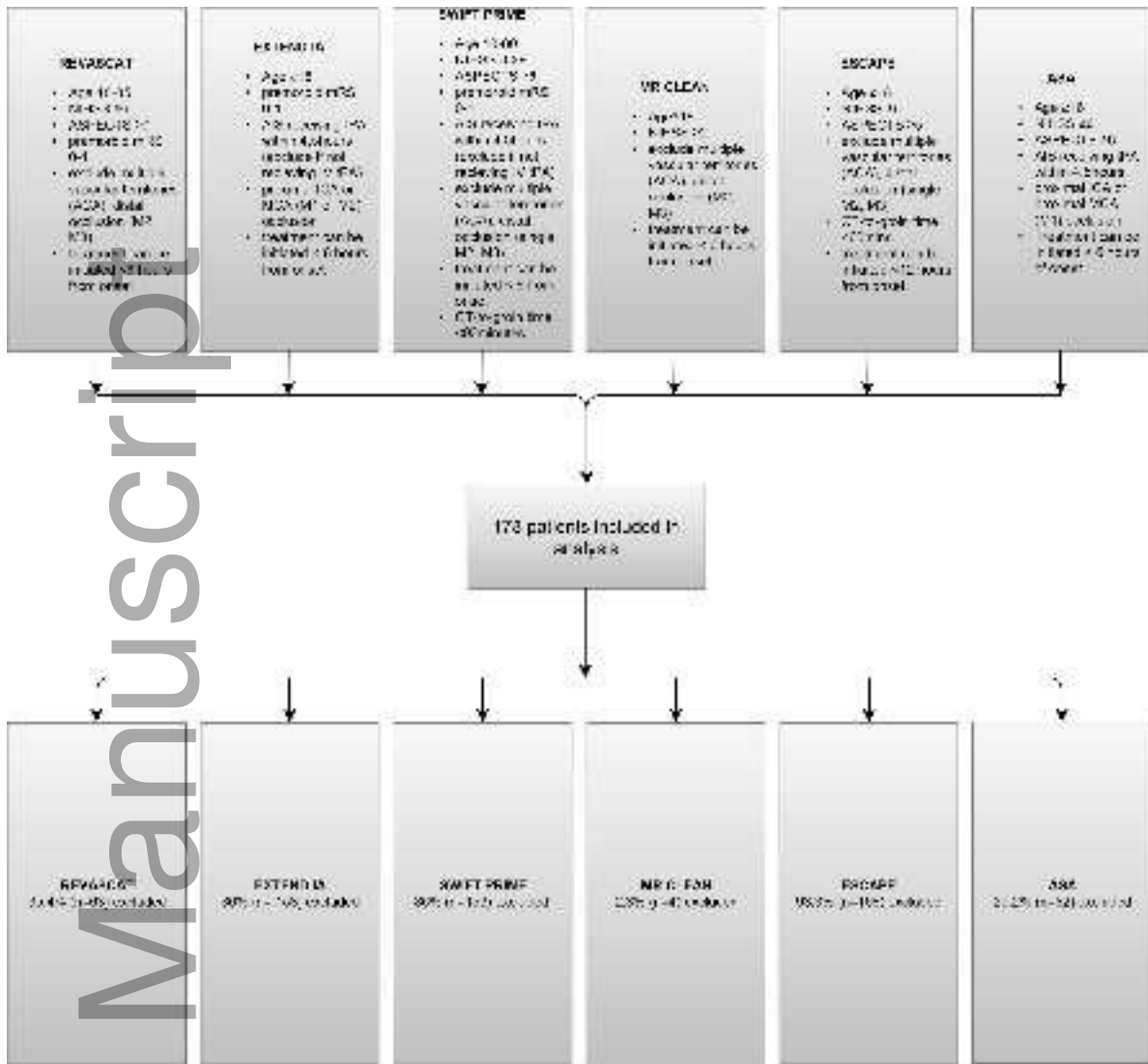
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Number benefitted per 1 harmed (NB1H) index using mRS	0.609 / 0.139 = 4.4	0.556 / 0.19 = 2.9	NA	0.84 / 0 = ">100"	0.549 / 0.183 = 3	NA	0.80 / 0.08 = 10	0.556 / 0.17 = 3.3	NA	0.592 / 0.161 = 3.7	0.50 / 0 = ">100"	NA	0.75 / 0 = ">100"	0.578 / 0.169 = 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

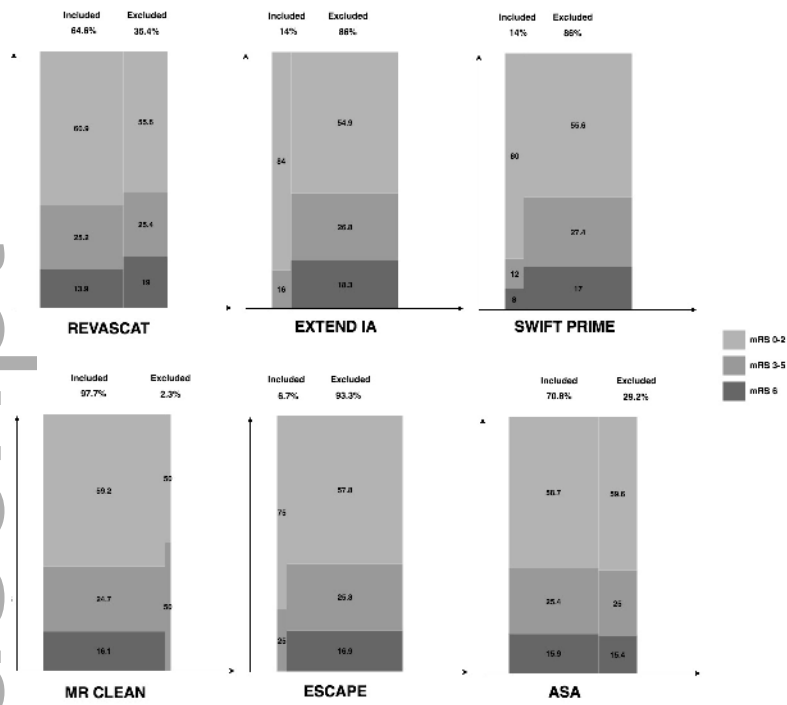
Trial Criteria	Total excluded – n (%)	Proportion with a good clinical outcome at 90days – n (%)
REVASCAT	63 (35.4%)	35 (55.6%)
EXTEND IA	153 (86%)	84 (54.9%)
SWIFT PRIME	153 (86%)	85 (55.6%)
MR CLEAN	4 (2.3%)	2 (50%)
ESCAPE	166 (93.3%)	96 (57.8%)
ASA	52 (29.2%)	31 (59.6%)



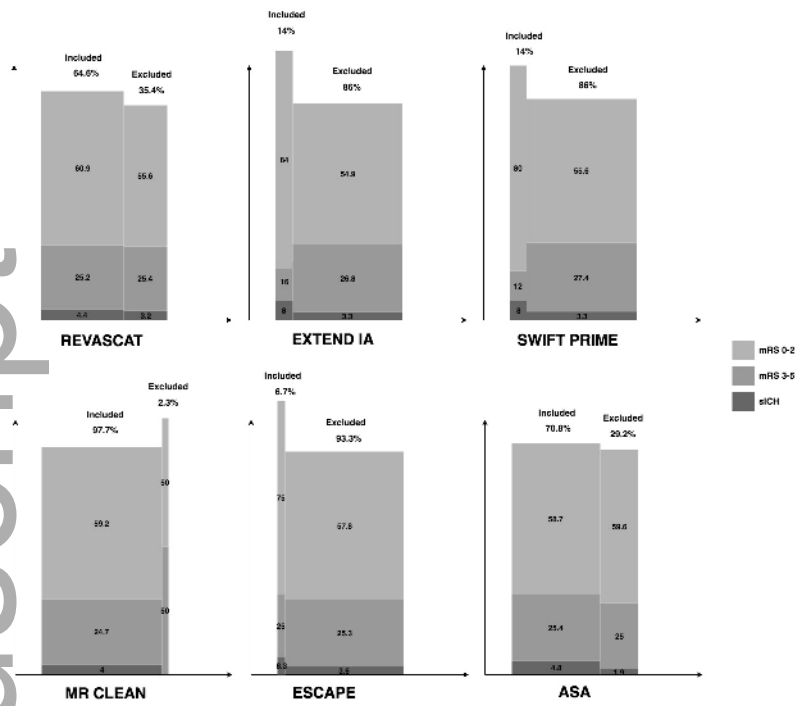
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