

ONLINE SUPPLEMENT

Mechanical Thrombectomy for MCA Division Occlusions: A Systematic Review and Meta- analysis

PubMed Search Strategy:

- #1 (("Thrombectomy"[Mesh] OR "Embolectomy"[Mesh] OR thrombectom* OR embolectom*)) 11054
- #2 (("Intracranial Embolism and Thrombosis"[Mesh] OR occlusion* OR occlude*)) 194912
- #3 ((m2 OR secondary-division OR insular-segment OR secondary-segment)) 82680
- #4 #1 AND #2 AND #3 55
- #5 #5 NOT (("case reports"[Publication Type] OR "editorial"[Publication Type] OR "review"[Publication Type])) 47

Table I. Characteristics of included studies

Study	Country	Setting, Center	Recruitment Dates	Inclusion criteria	Exclusion criteria	Study Design	Outcomes Measured	Device / Technique Used	MT Time Cut-off	Imaging Criteria	NO S (16)
Protto 2016	Finland	Single Center	Jan 13 – Dec 14	ICA and/or M1 or M2 MT with stent retrievers	Posterior circulation, ACA, or M3 occlusions	Prospective, observational	TICI recanalization & 90 day MRS Secondary: Bleeding	TREVO (40%), CAPTURE (40%), ERIC (9%), REVIVE (1%), Multiple (10%)	NR	CTA	14
Dorn 2016	Germany	Stroke Registry, Multicenter (4)	Jan 10 – Oct 14	Ineligible for TPA	Posterior circulation, received TPA	Retrospective observational	TICI recanalization, MRS 90d, hemorrhage (ECASS III)	Solitaire FR (68%), TREVO (25%), pREset (5%), TREVO + Solitaire (2%)	NR	CT or MR ± CTA + CTP / MRA	11
Goyal 2016	International	Multicenter [MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, EXTEND-IA]	Dec 10 – Dec 14	RCT endovascular treatment with modern neurothrombectomy techniques (between Jan 2010 – Dec 2015)	ASPECTS < 5, large infarct on baseline brain imaging	Prospective randomized, pooled analysis	MRS at 90 days Secondary: NIHSS at 24h, early neurological recovery, baseline to 24h change in NIHSS, sICH, PH2, mortality	Second generation devices [EXTEND IA, SWIFT PRIME, REVASCAT – Solitaire	MR CLEAN 6h EXTEND IA 6h SWIFT PRIME 6h REVASCAT 8h ESCAPE 12h	CTA ± CTP ± MRI	14

								only]			
Shi 2010	US & Canada	Multicenter [MERCI (80), Multi MERCI (98)]	May 01 – Dec 03; Jan 04 – July 06	Ineligible for TPA or ineffective revascularization with TPA; isolated M1 or M2	ICA-T or tandem occlusions	Multicenter prospective single arm trial	MRS at 30 & 90 days, TIMI recanalization , procedure related complications , hemorrhage (ECASS), mortality at 90 days	Both trials: X5 Merci series (1 st gen) Multi MERCI: L5 Merci (2 nd gen)	8 h	CT or MRI, with confirmation on DSA ^a	14
Lemmens 2016	International	Multicenter [STAR (151), SWIFT (89), DEFUSE 2 (66), IMS III (214)]	IMS III: Aug 06 – April 12 DEFUSE 2: July 08 – Sept 11 SWIFT: Feb 10 – Feb 11 STAR: Oct 10 – May 12	IMS III: TPA + MT vs. TPA, NIHSS > 10, RCT DEFUSE 2: MRI prior to MT SWIFT: Angiographically confirmed & ineligible for TPA or ineffective revascularization, Solitaire vs. Merci STAR: Anterior circulation, NIHSS > 8, single arm	IMS III: Age > 83yr, pregnancy DEFUSE 2: MRS > 2, pregnancy SWIFT: Uncontrolled hypertension STAR: Posterior circulation , life expectancy < 90 d, AVM or aneurysm	IMS: RCT STAR & DEFUSE 2: Prospective single arm SWIFT: randomized parallel group	IMS III: 90 day MRS Secondary: TICI recanalization DEFUSE 2: Target mismatch profile, NIHSS improvement ≥ 8 or ≤ 1 at day 30 Secondary: MRS ≤ 2 at 90 days, infarct growth, sICH SWIFT: Successful recanalization (TIMI), procedure related AE	IMS III: Merci (77), Penumbra (39), Solitaire (4), or IA TPA (65) DEFUSE 2: Merci (45) & Penumbra (41) [Also Acculink (5), Solitaire (4), Trevo (2), Enterprise (2)]	IMS III – TPA within 3 h DEFUSE 2 12h SWIFT 8h STAR 8h	IMS III: None or CTA ^a DEFUSE 2: MRI + MRA SWIFT: Angiographically confirmed STAR: CTA or MRA; confirmed by DSA	14

							<p>Secondary: Time to recanalization , MRS \leq 2 at 90 days, NIHSS improvement \geq 10, mortality, sICH</p> <p>STAR: TICI revascularization</p> <p>Secondary: MRS at 90 days, procedure related AE, time to recanalization</p>	<p>SWIFT: Solitaire (58), Merci (55)</p> <p>STAR: Solitaire (202)</p>			
Dorn 2015	Germany	Single	Oct 11 – Apr 13	MCA occlusion	-	Retrospective Observational	90 day MRS	Solitaire or TREVO or BonNET	NR	NR	13

Abbreviations: ACA (anterior cerebral artery), AE (adverse effects), ASPECTS (Alberta Stroke Program Early CT Score), DSA (digital subtraction angiography), ECASS (European-Australasian acute Stroke Study), ICA (internal carotid artery), ICA-T (internal carotid artery terminus), M1 (middle cerebral artery main trunk), M2 (middle cerebral artery division), MRS (modified Rankin score), MT (mechanical thrombectomy), NIHSS (National Institutes of Health Stroke Scale), NOS (Newcastle-Ottawa Scale for Quality Assessment, total score=16), NR (not reported), PH2 (parenchymal hematoma type 2), RCT (randomized controlled trial), sICH (symptomatic intra-cranial hemorrhage), TPA (tissue plasminogen activator)

^aOnly patients with DSA proven occlusions were included in the analysis

Table II. Baseline demographic variables of the included studies

Study	Groups	N	Age (IQR)	Male (%)	DM (%)	HPL (%)	HTN (%)	A FIB (%)	Smoking (%)	Prior Stroke / TIA	IV-TPA (%)	ASPECTS (IQR)	Median NIHSS (IQR)	Left Side	Median Onset to Groin (min)
Proto 2016^a	M1	46	65.3 ± 12.8	35	20	-	46	54	-	-	65	9 ± 3	14 ± 6	-	-
	M2	22	69.8 ± 9.3	68	12	-	41	50	-	-	41	10 ± 1	14 ± 6	-	-
	Total ^a	105	66.1 ± 11.2	43	17	-	44	51	-	-	63	9 ± 3	14.5 (5)	-	-
Dorn 2016^a	M1	77	-	-	-	-	-	-	-	-	-	-	-	-	-
	M2	11	-	-	-	-	-	-	-	-	-	-	-	-	-
	Total ^a	130	68.8	51	-	-	-	-	-	16.2	0	-	16 ± 6	-	176 ± 45
Goyal 2016^a	M1	439	-	-	-	-	-	-	-	-	-	-	-	-	-
	M2	51	-	-	-	-	-	-	-	-	-	-	-	-	-
	Total ^a	634	68 (57-77)	52	13	-	56	33	31	-	83	9 (7-10)	17 (14-20)	-	-
Shi 2010	M1	150	73 (60-80)	44	25	34	77	42	20	-	14	-	18 (15-23)	47	252 (192-330)
	M2	28	71.5 (61.5-81)	32	25	39	79	57	12	-	21	-	17 (14-22)	68	282 (222-318)
	Total	178	73 (60-80)	42	25	35	78	44	18	-	15	-	18 (14-23)	51	258 (192-324)
Lemmens 2016^a	M1	389	-	-	-	-	-	-	-	-	-	-	-	-	-
	M2	131	-	-	-	-	-	-	-	-	-	-	-	-	-
	Total ^a	710	66.7 ± 12.9	46	18	-	-	-	-	12	74	-	-	-	260 (215-318)

Dorn 2015	M1	104	69.4 ± 14 (21- 91)	-	-	-	-	-	-	-	51	-	15	-	-
	M2	15	68.1 ± 14.8 (37-86)	-	-	-	-	-	-	-	47	-	12	-	-
	Total	119	-	-	-	-	-	-	-	-	50	-	-	-	-

Abbreviations: A FIB (atrial fibrillation), ASPECTS (Alberta Stroke Program Early CT Score), DM (diabetes mellitus), HPL (hyperlipidemia), HTN (hypertension), IQR (inter-quartile range), IV-TPA (intravenous tissue plasminogen activator), M1 (main middle cerebral artery trunk), M2 (first division of the middle cerebral artery), TIA (transient ischemic attack)

^a Included patients with internal carotid artery occlusions as well

Table III. Treatment outcomes

Study	Groups	N	MRS % (n)	Excellent MRS % (n)	Mortality % (n)	Onset to Recanalization (min)	Recanalization Rate % (n)	Procedure Time (min)	Sx ICH % (n)	Procedural Complications
Protto 2016^a	M1	46	63 (29)	41 (19)	13 (6)	246 ± 110	94 (43)	25 (24)	7 (3) ^b	-
	M2	22	50 (11)	23 (5)	14 (3)	211 ± 99	77 (17)	32 (21)	9 (2) ^b	-
	Total ^a	105	57	40	14 (15)	238 ± 103	88 (92)	28 (IQR 27)	6 (6) ^b	-
Dorn 2016^a	M1	76	40.5 (30)	-	-	-	-	-	-	-
	M2	11	45.5 (5)	-	-	-	-	-	-	-
	Total ^a	124	37.9 (47)	23.4 (29)	24.2	246 ± 72	78	-	13.1 (17) ^c	8.5% ^d
Goyal 2016^a	M1	438	48.9 (214)	27.4 (120)	14.6 (64)	-	-	-	-	-
	M2	51	49 (25)	33.3 (17)	15.7 (8)	-	-	-	-	-
	Total ^a	634	46 (291)	26.9 (170)	15.3 (97/633)	285 (210-362)	71	-	4.4 (28) ^e	-
Shi 2010	M1	150	33.3 (46/138)	-	32.9 (48/146)	-	60 (90/150) ^f	102 (18-282)	6.7 (10) ^g	5.3%
	M2	28	40.7 (11/27)	-	25.9 (7/27)	-	82.1 (23/28) ^f	90 (48-168)	3.6 (1) ^g	3.6%
	Total	178	34.5	-	31.8	-	63.5 ^f	96 (18-282)	6.2 (11) ^g	5.1%
Lemmens 2016^a	M1	389	43.7 (170)	32.1 (125)	17.0 (66)	-	64.5 (251)	-	5.1 (20) ^h	-
	M2	131	45.8 (60)	30.5 (40)	15.3 (20)	-	51.1 (67)	-	6.9 (9) ^h	-
	Total ^a	710	41.7 (296)	29.9 (212)	19.0 (135)	-	58.1 (413)	-	6.2 (44) ^h	-

Dorn 2015	M1	104	43.3 (45)	37.5 (39)	21.2 (22)	257 ± 75.9	76.0 (79)	55.6 ± 37.1	5.8 (6) ⁱ	2.9% ^j
	M2	15	60 (9)	60 (9)	6.7 (1)	247.3 ± 132.3	93.3 (14)	49.3 ± 28.6	6.7 (1) ⁱ	0 (0)
	Total	119	45.3 (54)	40.3 (48)	19.3 (23)	-	78.2 (93)	54.8	5.9 (7) ⁱ	2.5% (3) ^j

Abbreviations: MRS (modified Rankin score), ECASS (European-Australasian acute Stroke Study), IVH (intra-ventricular hemorrhage), NIHSS (National Institutes of Health Stroke Scale), PH (parenchymal hematoma), M1 (main middle cerebral artery trunk), M2 (first division of the middle cerebral artery), NR (not reported), pH2 (parenchymal hematoma type 2), SAH (subarachnoid hemorrhage), Sx ICH (symptomatic intracranial hemorrhage), TIMI (Thrombolysis in Myocardial Infarction)

^a Included patients with internal carotid artery occlusions as well

^b Parenchymal Hematoma type 2; No definition of symptomatic hemorrhage provided

^c ECASS III criteria used

^d Subarachnoid hemorrhage (n=6), dissection (n=2), thrombus loss (n=1), loss of device (n=2) (total includes patients with internal carotid artery occlusions)

^e Includes patients with internal carotid artery occlusions. Symptomatic ICH defined in each study: MR CLEAN: ICH + ≥ 4-point increase in NIHSS, ESCAPE: ICH + ≥ 2-point increase in NIHSS, EXTEND-IA: Parenchymal hematoma type 2 or subarachnoid hemorrhage + ≥ 4-point increase in NIHSS, SWIFT PRIME: Parenchymal hematoma or subarachnoid hemorrhage or intra-ventricular hemorrhage + ≥ 4-point increase in NIHSS, REVASCAT: Parenchymal hematoma type 2 + ≥ 4-point increase in NIHSS; total rate of parenchymal hematoma type 2 5.1% (32 / 629)

^f TIMI Recanalization

^g ECASS criteria used

^h Symptomatic ICH defined in each study: DEFUSE 2: SITS MOST criteria, SWIFT: ICH + ≥ 4-point increase in NIHSS, STAR: ECASS criteria, IMS III: ICH with decline in neurological status and new or worsening neurological symptoms (≥4-point increase in NIHSS score from baseline was used as a guide)

ⁱ Parenchymal Hematoma type 2; No definition of symptomatic hemorrhage provided

^j n=3; dissection (n=1), loss of device (n=1), thrombus loss (n=1)

Table IV: Modified Newcastle-Ottawa Quality Assessment Scale for Cohort Studies included in the Meta-analysis

Included Studies	Selection*				Comparability†	Outcome‡		
	Representativeness of the Exposed Cohort	Selection of the Non-exposed Cohort	Ascertainment of Exposure	Incident Disease		Assessment of outcome	Length of follow-up	Adequacy of follow-up
Protto 2016	A	A	A	A	B	B	A	A
Dorn 2016	A	A	A	A	B	C	A	C
Goyal 2016	A	A	A	A	B	A	A	B
Shi 2010	A	A	A	A	B	B	A	A
Lemmens 2016	A	A	A	A	B	A	A	B
Dorn 2015	A	A	A	A	B	C	A	A

***Selection:**

- (1) Representativeness of the exposed cohort: A, truly representative of the average patient with vessel-occlusion stroke; B, somewhat representative of the average patient with vessel-occlusion stroke; C, selected group; D, no description of the derivation of the cohort
- (2) Selection of the non-exposed cohort: A, drawn from the same community as the exposed cohort; B, drawn from a different source; C, no description of the derivation of the non-exposed cohort
- (3) Ascertainment of exposure: A, DSA, CTA, MRA, \pm CTP confirmation; B, physical examination only; C, no description
- (4) For demonstration that the outcome of interest was not present at start of study: A, yes; B, no

†Comparability: For comparability of cohorts on the basis of the design or analysis:

A, study controls for rate of TPA administration, time to groin puncture, ASPECT score, and / or device used; B, study controls for one of the previously mentioned or additional factors; C, not done.

‡Outcome:

- (1) Assessment of outcome: A, independent blind assessment; B, follow up visit or telephone-interview; C, no description
- (2) Was follow-up long enough for outcomes to occur (90 days)? A, yes; B, no
- (3) Adequacy of follow-up of cohorts: A, complete follow-up and all subjects accounted for; B, subjects lost to follow-up was unlikely to introduce bias, because a small number were lost (i.e., > 90% were available for follow-up) or a description was provided of those lost; C, follow-up rate 90% or lower and no description of those lost; D, no statement;

Table V. Results of Subgroup Analysis			
Analysis	Odds Ratio	95% Confidence Interval	No of included studies
Good Clinical Outcome	1.10	0.83 – 1.44	6
Second generation neurothrombectomy devices only*	1.04	0.68 – 1.60	4
Cohorts eligible for TPA	1.09	0.82 – 1.44	5
Excellent Clinical Outcome	1.07	0.65 – 1.79	4
Second generation neurothrombectomy devices only*	1.16	0.49 – 2.73	3
Cohorts eligible for TPA	1.07	0.65 – 1.79	4
Mortality	0.85	0.58 – 1.24	5
Second generation neurothrombectomy devices only*	0.87	0.45 – 1.67	3
Cohorts eligible for TPA	0.85	0.58 – 1.24	5
Successful Recanalization	1.06	0.32 – 3.48	4
Second generation neurothrombectomy devices only*	0.95	0.05 – 18.26	2
Cohorts eligible for TPA	1.06	0.32 – 3.48	4
Significant Intracranial Hemorrhage*	1.19	0.61 – 2.30	4
Second generation neurothrombectomy devices only*	1.31	0.32 - 5.40	2
Cohorts eligible for TPA	1.19	0.61 – 2.30	4
Procedural Complications	0.51	0.09 – 2.79	2

*All MERCI stents excluded

PRISMA 2009 Checklist

Section/topic	#	Checklist item 1	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5-6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5-6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5-6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5-6

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5-7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6-8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7-8

Page 1 of 2

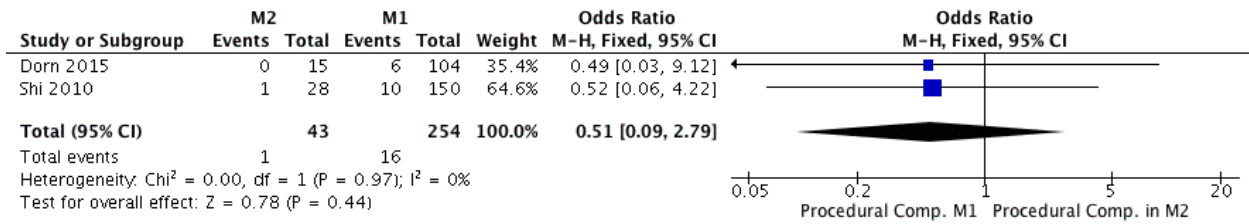
Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figure 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Figure 2
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10-11, Figure 3,

			Appendix Figure 1
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9-12
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	13-14
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	14-15
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org. Page 2 of 2

Forest Plots for pre-specified sub-group analysis Procedural Complications



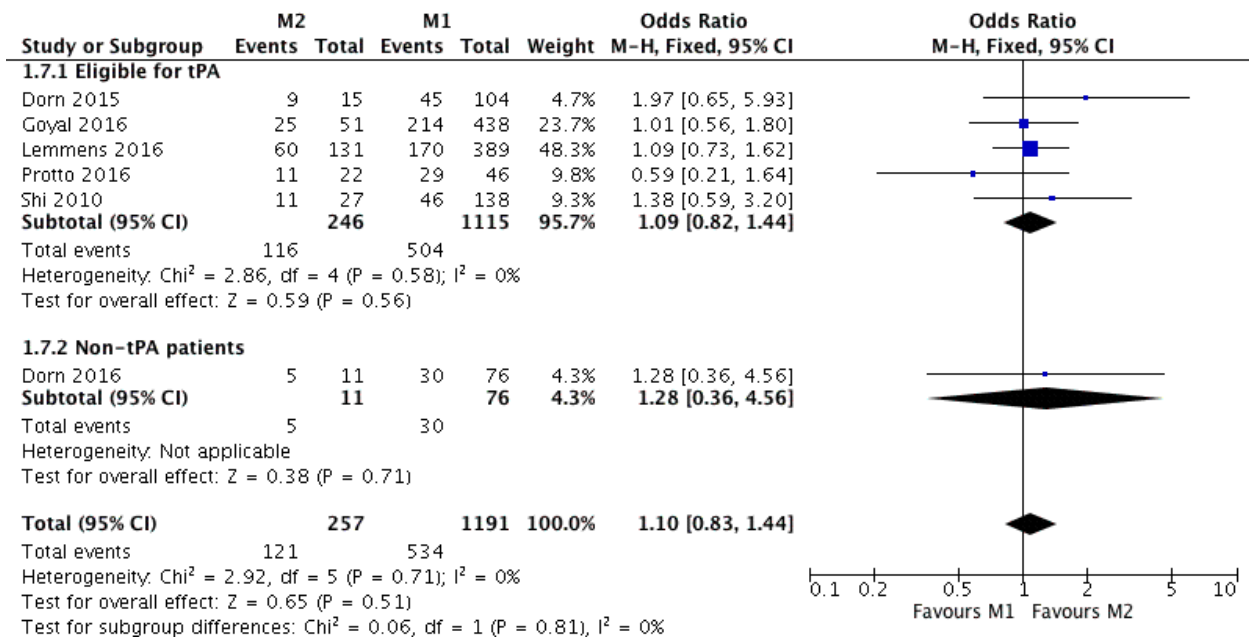
Supplemental Figure I

(a) Procedural complications in patients undergoing mechanical thrombectomy for M1 and M2 occlusions

Good Clinical Outcome

See figure 1A

(b) Good clinical outcome (mRs ≤ 2) at 90 days stratified by neurothrombectomy device type*



Supplemental Figure II

(c) Good clinical outcome (mRs ≤ 2) at 90 days stratified by patient eligibility for intravenous tPA.

Excellent Clinical Outcome

See figure 1C

- (d) Excellent clinical outcome (mRs \leq 1) at 90 days stratified by neurothrombectomy device type*
- (e) Excellent clinical outcome (mRs \leq 1) at 90 days in patients eligible for intravenous tPA.

Mortality at 3 months

See figure 2D

- (f) Mortality at 90 days stratified by neurothrombectomy device type*
- (g) Mortality at 3 months in only patients eligible for intravenous tPA.

Successful Recanalization

See figure 3A

- (h) Successful recanalization rates stratified by neurothrombectomy device type*
- (i) Successful recanalization rates in only patients eligible for intravenous tPA (total)

Significant Intracranial Hemorrhage

See figure 3B

- (j) Significant intracranial hemorrhage stratified by neurothrombectomy device type*
- (k) Significant intracranial hemorrhage in only patients eligible for intravenous tPA.

(*Protto 2016 & Dorn 2015 values represented by parenchymal hematoma, not symptomatic ICH)

* Non-MERCI devices: Second generation neurothrombectomy devices; MERCI devices: Data including MERCI and other types of neurothrombectomy devices