Supplementary Materials

Is Different Anterior Circulation Stroke from Posterior Circulation Stroke in Relation to Outcome after Thrombolysis? A Systematic Review and Meta-analysis

Supplementary Methods

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I. Risk of bias depicted as colors (red: high-risk; green: low-risk; yellow: unclear).

II. Sensitivity analyses

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(F) Favorable outcome for ERT

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Each horizontal line indicates a repeated result from pooled analysis after sequentially excluding the corresponding study. Vertical dotted lines represent pooled estimates and its 95% confidence intervals (CIs) using all data from six, five or nine studies, respectively.

III. Publication bias for analysis.

(A) sICH for IVT

References list

I. Korea University Stroke Registry (KUSR) TPA/MT

The KUSR collects demographic, clinical, radiological, and laboratory data from acute stroke patients within seven days from the onset of symptoms. Three tertiary medical centers contribute to KUSR, including Korea University Anam Hospital in the northern part of Seoul, Korea University Guro Hospital in the southern part of Seoul, and Korea University Ansan Hospital in the southeastern part of the Gyeonggi province.

The treatment protocols in our three university hospitals generally follow the major guidelines for stroke management. Those treated with thrombolysis were grouped into TPA (intravenous thrombolysis) and MT (mechanical thrombectomy) with or without IV thrombolytics. At each center, neuro-interventionalists performed the intraarterial procedures. Functional status at follow-up was evaluated by patient′s visit or telephone interview from trained research nurse.

Supplementary Table 1. Baseline characteristics of included studies (IVT)

Study	Center & Contry	Study period	Design	Included patients	Time window, dose	Additional endovascular tx.	Age (ACS *vs.* PCS)	Initial NIHSS (ACS *vs.* PCS)	ONT (ACS *vs.* PCS)	sICH criteria
Förster A, 2011[1]	Single-/Germany	2004-2007	Prospective	198 *vs.* 30	<3hr, 0.9mg/kg	None	70±14.4 *vs.* 70.3±11.4	†13(7–16) *vs.* 8(4.75–13)	†141.1(30.7) *vs.* 156.2(23.2)	ECASSII
Breuer L‡, 2011[2]	Single-/Germany	2006-2010	Retrospective	398 *vs.* 21	<3hr, 0.9mg/kg	None	73(63-81) *vs.* 72(62.5-80)	†9(0–27) *vs.* 6.5(2–15)	NR	ECASSIII
Dorňák T, 2015[3]	Single-/ Czech Republic	2005-2014	Retrospective	777 *vs.* 100	<4.5hr, 0.9mg/kg	16%	†71.0 *vs.* 67.5	10 *vs.* 8	†160 *vs.* 175	ECASSI?
Sung SF, 2013[4]	4 centers/Taiwan	2007-2012	Retrospective	434 *vs.* 84	<4.5hr, 0.9mg/kg	None	67±12 *vs.* 68±12	13(8–19) *vs.* 11 (8–20)	NR	NINDS/ECASSII/ SITSMOST
Sarikaya H, 2011[5]	3 centers/Swiss	1998-2008	Retrospective	788 *vs.* 95	<4.5hr since 2008, 0.9mg/kg	Only 1 center available	†66.9±14.3 *vs.* 62.9± 15.1	†12.2±5.9 *vs.* 9.3± 7.9	160.0±40.0 *vs.* 169.0±54.5	NINDS/ECASSII
Tong XU, 2016[6]	67 centers/China	2007-2012	Retrospective	829 *vs.* 124	<4.5hr, 0.5~0.9mg/ kg	None	64±11 *vs.* 63±11	12(8–17) *vs.* 10(5–20)	170(140–200) *vs.* 165(132–190)	NINDS
Diaz-Otero F, 2011[7]	5 centers/Spain	2004-2009	Prospective	1051 *vs.* 78	NR, 0.9mg/kg	None	No difference	†14±6 *vs.* 11±7	†142±42.9 *vs.* 165 ±54	NR
Kozai Y, 2012[8]	Single-/Japan	NA	Retrospective	64 *vs.* 15	NR	None	73 *vs.* 66	11 *vs.* 7	NR	NR
Lorenzano S, 2014[9]	Multi-/Italian	NA	Prospective	2199 *vs.* 291	NR	None	†69 *vs.* 67	†12 *vs.* 8	†165 *vs.* 170	NINDS/ECASSII/ SITS-MOST
Savic Od, 2012[10]	Multi-/Serbia	2006-2011	Prospective	525 *vs.*82	NR	None	57±12.4 *vs.* 59.5±12.3	13.2±4.9 *vs.* 13.6± 10.4	NR	ECASSIII
Herzig R, 2017[11]	Multi-/ Eastern europe	2010-2015	Prospective	2375 *vs.* 363	NR	None	NR	NR	NR	NINDS
KUSR-TPA, 2019[12]	3 centers/ South Korea	2007-2017	Prospective	538 *vs.* 110	<4.5hr since 2009, 0.9mg/kg	None	†67.3±12.2 *vs.* 63.7± 13.4	†11±5.3 *vs.* 9.3±-6.4	†132±56 *vs.* 144± 45	NINDS/ECASSII/ ECASSIII/ SITS-MOST

Abbreviations: NR = not reported, NIHSS = National Institutes of Health Stroke Scale, ONT = onset to needle time, IV tPA = intravenous alteplase, sICH = symptomatic intracerebral hemorrhage, ECASS-II = European Co-operative Acute Stroke Study-II, SITS-MOST = Safe Implementation of Thrombolysis in Stroke-Monitoring Study, AF = atrial fibrillation, NINDS = The National Institute of Neurological Disorders and Stroke. KUSR-TPA = Korea University Stroke Registry TPA. †statistically significant, ‡ included only supratentorial PCA infarction. Results are expressed as column %, mean±SD, or median (range) as appropriate.

Supplementary Table II. Baseline characteristics of included studies (IAT)

Study	Center & Contry	Study period	Design	Included patients (ACS *vs.* PCS)	Time criteria	Thrombolytic agent/ time window	Mechanical devices/additional angioplasty or stenting	Age (ACS *vs.* PCS)	Initial NIHSS (ACS *vs.* PCS)	Occlusion site	ONT (ACS *vs.* PCS), min	OGT (ACS *vs.* PCS), min	ORT/OCT /procedure time (ACS *vs.* PCS), min	Recanalization rate	sICH criteria
Dorn F, 2012[13]	Single-/ Germany	2008-2009	Retrospective	81 *vs.* 23	NR	46.2%, IV-tPA, 30.8%, IA-tPA/ <4.5hr	Solitare, Phenox, MERCI, Penumbra/ +	65.8 *vs.* 72.8	15.3±5.1 *vs.* 16.1±11.2	BA, VA	NR	NR	265(56–1,031)/-/NR	79%	Increase of 4 points on NIHSS
Burnell AL, 2018[14]	3 centers/ New Zealland	2011-2018	Retrospective	260 *vs.* 52	If possible <6hr for ACS, <12hr for PCS	62%, IV-tPA 0.9mg/kg or IV tenecteplase 0.25mg/kg	Solitare, Trevo, aspiration devices/ +	64(16-92) *vs.* 64(18-82)	18(3–40) *vs.* 20(3–38)	BA	123(47–425) *vs.* 148(90–330)	200(65–923) *vs.* 266(90–985)	-/261(110–1,065) *vs.* 345(125–1,105) /NR	87%	SITS-MOST
Singh RK, 2017†[15]	Multi-/India	2014-2016	Retrospective	112 *vs.* 25	NR	50.4%, IV-tPA	Solitaire/ +	57.85± 12.52 *vs.* 56.4±9.19	15.5±4.32 *vs.* 19±5.5	BA	220±80.6 *vs.* 326 ±191.8	NR	NR/NR/ 39.5±14.1 *vs.* 42.20±19.4	91.2%	ECASSII
Alawieh A, 2018[16]	Single-/USA	2013-2017	Retrospective	380 *vs.* 56	Mainly <10hr or judgement based on DWI if >10hr	39.4%, IV-tPA; 17%, IA-tPA/ <4.5hr	ADAPT± Solitare/ +	67.28± 14.47 *vs.* 67.3±14.9	15.3±7.0 *vs.* 17.4±11.0	BA,VA, PCA	NR	492±812 *vs.* 480±846	NR/-/28.1±24 *vs.* 26.3±20	92.9%	PH2 on ECASS
Hu SY, 2017†[17]	Single-/ South Korea	2013-2016	Retrospective	137 *vs.* 24	<8hr for ACS, <12hr for PCS	45.3%, IV-tPA/ <4.5hr	Solitare, Trevo/ +	65.5(22-87) *vs.* 65.7(32-85)	†10.4 *vs.* 14.2 as mean	BA	NR	†216(IQR36-612) *vs.* 268(59-552)	†333(90-870) *vs.* 390(137-675)/-/ 116(27-360) *vs.* 122(40-285)	80.1%	NR
Daou B, 2015[18]	Single-/USA	2012-2014	Retrospective	80 *vs.* 9	~12hr?	48.3%	Solitare/NR	63	16(3-35)	Vertebro-basilar artery	NR	6.7hr(3-21)	8hr(4-2)/58min	84.9	NR
Alonso de Lecinana M, 2017†[19]	Multi-/Spain	2012-2016	Prospective	427 *vs.* 52	<8hr for ACS <12hr for PCS, <24hr, if fluctuating or progressing stroke	50%, IV-tPA/ <4.5hr?	Mechanical thrombectomy / NR	†70(60-77) *vs.* 64(50-74)	†18 IQR(14–21) *vs.* 11 IQR(6–23)	BA	†120(IQR95–150) *vs.* 140(IQR125–180)	280(212–365) *vs.* 312(225–510)	†315(IQR240–415) *vs.* 385(IQR320–540)/-/ †60(39–90) *vs.* 100 (40–130)	83.1%	SITS-MOST
Weber R, 2018[20]	Multi-/Germany	2012-2013	Prospective	961 *vs.* 139	Mainly <12h, >12hr in minor portion	60.3%, IV-tPA/ <4.5hr	Solitare, Trevo, REVIVE, pREset, Penumbra/ NR	†69.0±13.9 *vs.* 65.4± 15.8	†15(12–19) *vs.* 12(6–21)	BA,VA, PCA	†105(76–150) *vs.* 115(90–214)	†195±197 *vs.* 225±235 for DAS imaging time	†274(210–362) *vs.* 329(249–543)/-/-	74.1%	Any ICH with increase of 4 points on NIHSS
KUSR-MT, 2019[12]	3 centers/ South Korea	2007-2017	Prospective	105 *vs.* 14	<12hr	45.4%, IV-tPA/ <4.5hr	Solitare, Penumbra/ +	†67.3±12.2 *vs.* 63.7± 13.4	15.4±4.4 *vs.* 16±8.9	BA, VA, PCA	228±216 *vs.* 240 ±156	356±210 *vs.* 444±336	252±126 *vs.* 222 ±144/-/-	58%	NINDS/ ECASSII / ECASSII I/ SITS-MOST

Abbreviations: ACS = anterior circulation stroke, PCS = posterior circulation stroke, NR = not reported, NIHSS = National Institutes of Health Stroke Scale, ONT = onset to needle time, OGT = onset to groin puncture time, ORT = onset to recanalization time, OCT =onset to closure time, BA = basilar artery, VA = vertebral artery, sICH = symptomatic intracerebral hemorrhage, IV = intravenous, IA = intraa-rterial, tPA = tissue plasminogen activator, ADAPT = direct aspiration first pass technique endovascular clot retrieval, PH2 = parenchymal hematoma type 2, DWI = diffusion-weighted image, ECASS-II = European Co-operative Acute Stroke Study-II, SITS-MOST = Safe Implementation of Thrombolysis in Stroke-Monitoring Study, NINDS = National Institute of Neurological Disorders and Stroke, KUSR-MT = Korea University Stroke Registry – mechanical thrombectomy. †statistically significant. Results are expressed as column %, mean±SD, or median (range or interquartile range [IQR] as appropriate).

Supplementary Table III. Subgroup analyses in IVT

		No.	OR	95% CI	*P* value	I^2
sICH						
Publication status	Published studies	6	0.3	0.15-0.59	0.0005	0%
	Gray literature	6	0.33	0.19-0.57	<.0001	0%
Study center	Single-center	5	0.33	0.13-0.83	0.02	0%
	Multi-center	7	0.31	0.19-0.51	<.0001	0%
Thrombolysis type	IVT only	10	0.35	0.22-0.54	<.0001	0%
	IVT + IAT	2	0.16	0.04-0.56	0.004	0%
sICH criteria	NINDS	6	0.30	0.16-0.53	<.0001	23%
	ECASSII	5	0.32	0.11-0.95	0.04	44%
	ECASSIII	3	0.43	0.14-1.30	0.13	0%
	SITS-MOST	3	0.28	0.09-0.84	0.02	0%
	Others	3	0.24	0.08-0.71	0.01	0%
aICH						
Publication status	Published studies	4	0.34	0.20-0.59	0.0001	32%
	Gray literature	2	0.45	0.25-0.80	0.007	29%
Study center	Single-center	3	0.40	0.17-0.95	0.04	51%
	Multi-center	3	0.39	0.25-0.62	<.0001	29%
Mortality						
Publication status	Published studies	4	1.02	0.5-2.06	0.96	53%
	Gray literature	4	0.73	0.53-1.02	0.07	0%
Study center	Single-center	4	0.89	0.54-1.48	0.66	0%
	Multi-center	4	0.84	0.49-1.44	0.52	63%
Thrombolysis type	IVT only	7	0.92	0.62-1.36	0.67	36%
	IVT + IAT	1	0.63	0.3-1.34	0.23	NA
Time point	Discharge	2	0.78	0.22-2.79	0.7	48%
	3 month	4	0.75	0.33-1.74	0.51	64%
Functional outcome						
Publication status	Published studies	2	1.55	1.09-2.22	0.02	0%
	Gray literature	5	1.32	0.99-1.76	0.05	70%
Study center	Single-center	2	1.00	0.66-1.52	1	0%
	Multi-center	5	1.44	1.12-1.87	0.005	65%
Good outcome	mRS 0-1	5	1.49	1.12-1.97	0.005	54%

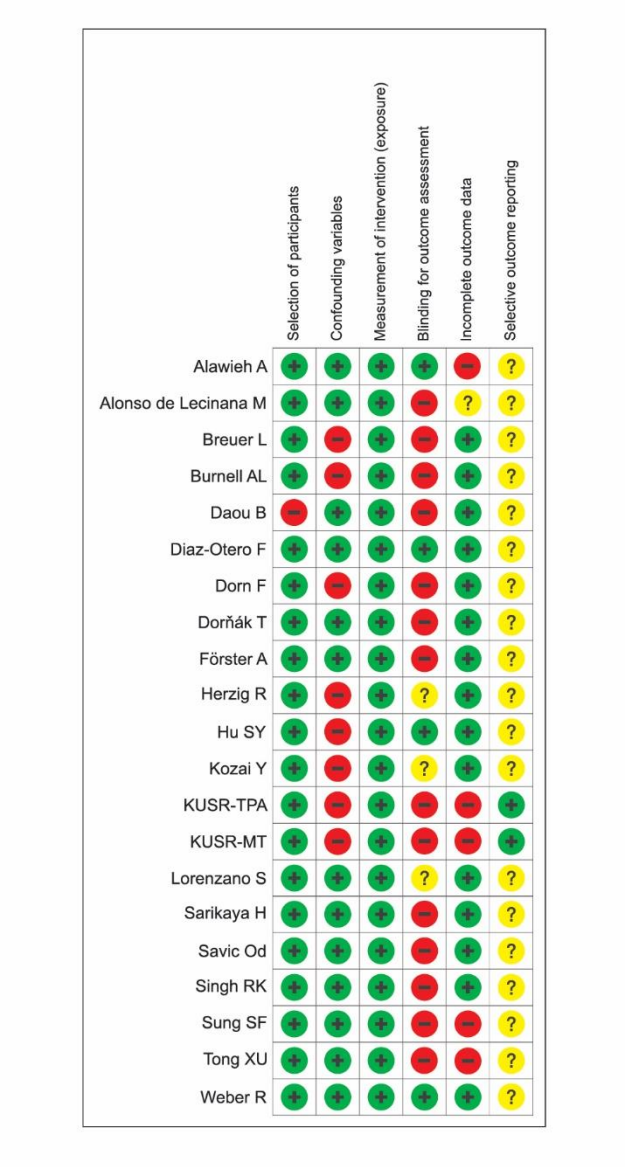
Abbreviations: No = number, OR = odds ratio, IVT = intravenous thrombolytics, IAT = intra-arterial thrombolysis, NA = not applicable, NINDS = National Institute of Neurological Disorders and Stroke, ECASS = European Co-operative Acute Stroke Study, SITS-MOST = Safe Implementation of Thrombolysis in Stroke-Monitoring Study.

Supplementary Table Ⅳ. Subgroup analyses in IAT

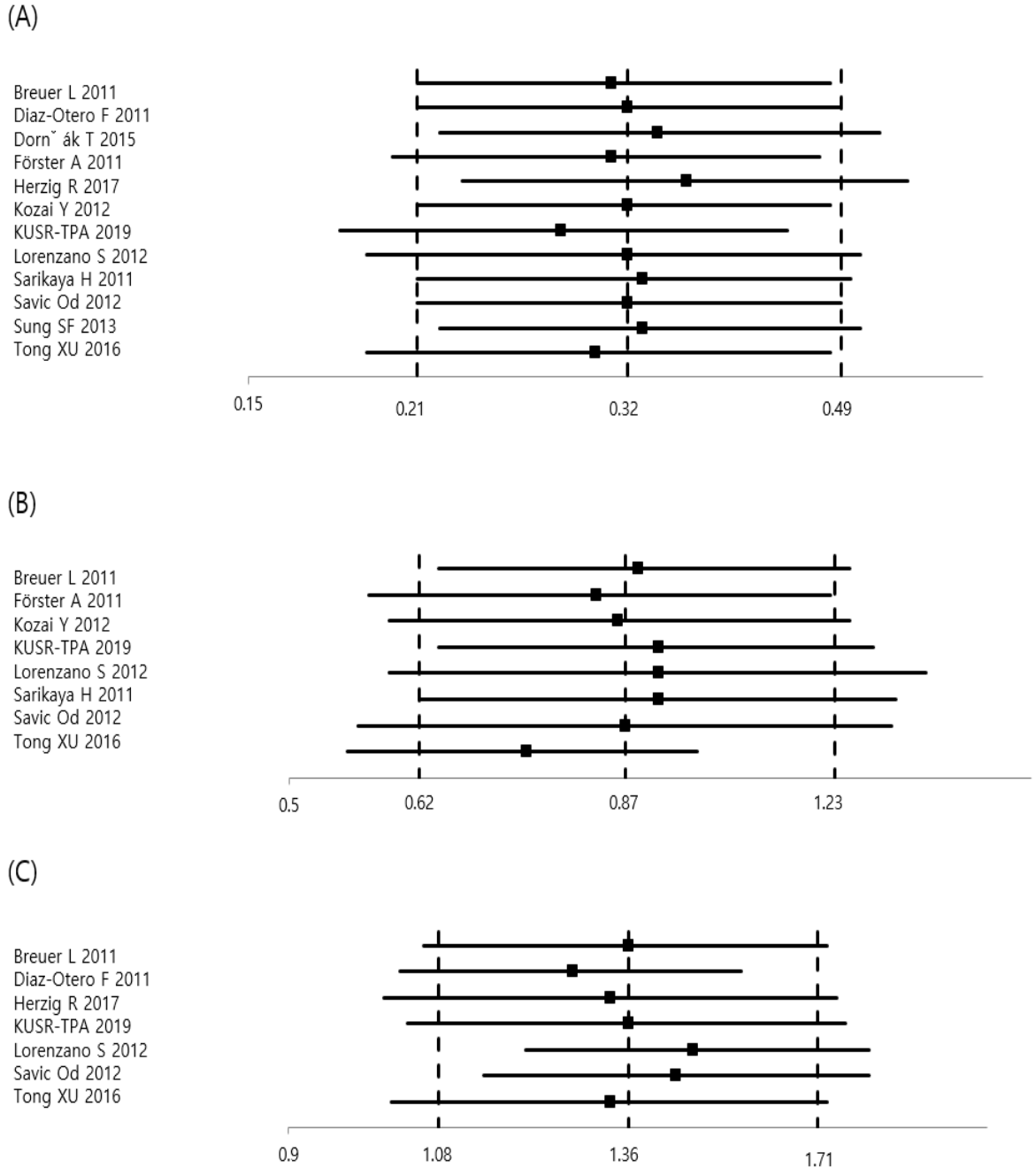
		No	OR	95% CI	*P* value	I^2
sICH						
Publication status	Published studies	6	0.61	0.29-1.3	0.2	0%
	Gray literature	1	0.54	0.7-4.51	0.57	NA
Study center	Single-center	3	0.92	0.38-2.21	0.84	0%
	Multi-center	4	0.29	0.09-0.94	0.04	0%
Type of thrombectomy	Stent retriever only	3	0.64	0.20-2.02	0.45	0%
	Inclusion of aspiration device	4	0.59	0.24-1.44	0.24	0%
Relevant artery	BA only	5	0.55	0.22-1.35	0.19	0%
	Inclusion of other PC artery	2	0.46	0.05-4.65	0.51	59%
sICH criteria	NINDS	1	0.54	0.07-4.51	0.57	NA
	ECASSII	2	0.47	0.08-2.61	0.39	0%
	ECASSIII	1	0.82	0.10-7.01	0.86	NA
	SITS-MOST	3	0.66	0.23-1.89	0.44	0%
	Others	3	0.57	0.17-1.89	0.36	20%
Mortality						
Publication status	Published studies	7	2.15	1.37-3.39	0.0009	56%
	Gray literature	1	1.08	0.22-5.36	0.92	NA
Study center	Single-center	4	2.33	1.44-3.68	0.0005	19%
	Multi-center	4	1.72	0.78-3.78	0.18	68%
Type of thrombectomy	Stent retriever only	3	1.88	1.04-3.39	0.04	0%
	Inclusion of aspiration device	5	2.16	1.17-3.98	0.01	70%
Relevant artery	BA only	5	2.38	1.48-3.81	0.0003	13%
	Inclusion of other PC artery	3	1.95	0.94-4.05	0.07	72%
Time point	Discharge	4	2.97	1.51-5.86	0.002	6%
	3 month	5	1.65	0.89-3.06	0.11	74%
Functional outcome						
Publication status	Published studies	5	0.71	0.55-0.93	0.01	0%
	Gray literature	1	1.44	0.46-4.46	0.53	NA
Study center	Single-center	2	0.76	0.43-1.33	0.34	42%
	Multi-center	4	0.72	0.52-1.0	0.05	5%
Type of thrombectomy	Stent retriever only	3	0.66	0.39-1.11	0.12	14%
	Inclusion of aspiration device	3	0.78	0.57-1.07	0.12	9%
Relevant artery	BA only	4	0.60	0.42-0.87	0.007	0%
	Inclusion of other PC artery	2	0.89	0.62-1.26	0.5	0%
Recanalization rate						
Publication status	Published studies	8	0.80	0.61-1.05	0.11	2%
	Gray literature	1	1.35	0.42-4.3	0.61	NA
Study center	Single-center	5	1.14	0.69-1.88	0.61	0%
	Multi-center	4	0.72	0.52-1.0	0.05	4%
Type of thrombectomy	Stent retriever only	4	1.18	0.60-2.32	0.63	17%
	Inclusion of aspiration device	5	0.75	0.56-1.00	0.05	0%
Relevant artery	BA only	5	0.91	0.51-1.63	0.76	44%
	Inclusion of other PC artery	4	0.82	0.58-1.15	0.25	0%

Abbreviations: No = number, OR = odds ratio, IVT = intravenous treatment, IAT = intra-arterial treatment with or without iv thrombolytics, NA = not applicable, NINDS = The National Institute of Neurological Disorders and Stroke, ECASS = European Co-operative Acute Stroke Study-II, SITS-MOST = Safe Implementation of Thrombolysis in Stroke-Monitoring Study.

Supplementary Figure I.



Supplementary Figure II.



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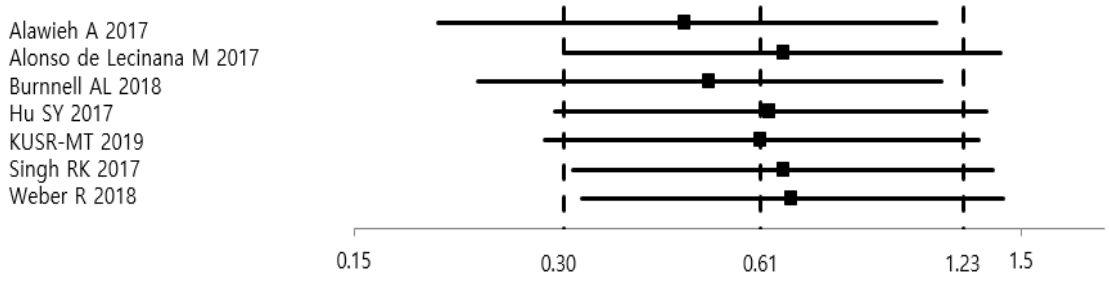
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Burnnell AL 2018
Hu SY 2017
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Weber R 2018
0.15
0.30
0.61
1.23
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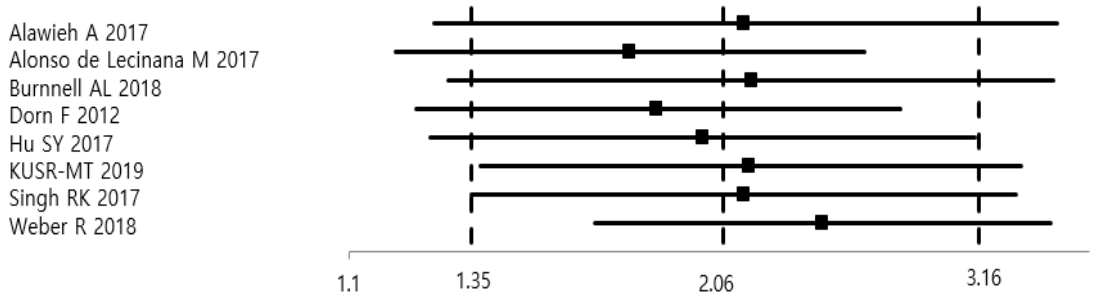
(E)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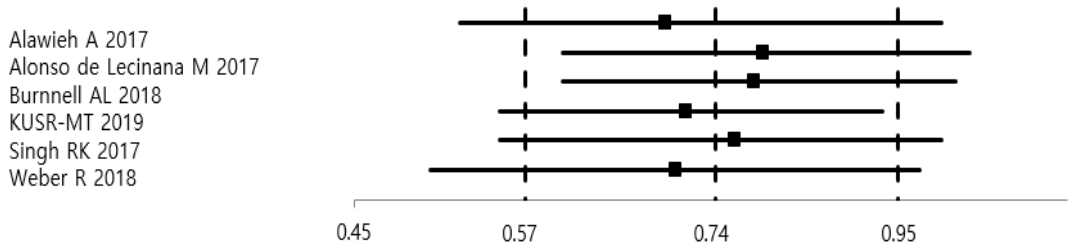
2.06
3.16

(F)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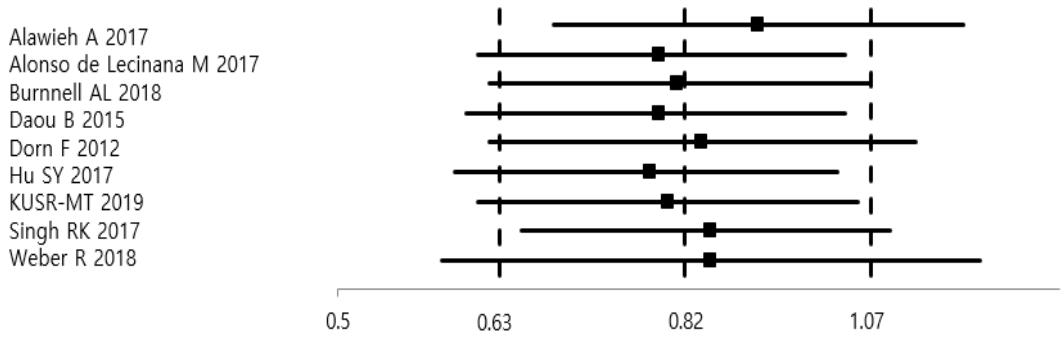
(G)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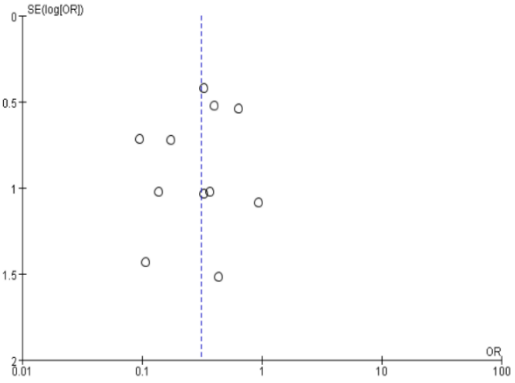
Supplementary Figure III.

(A)



References

1. Förster A, Gass A, Kern R, et al. Thrombolysis in posterior circulation stroke: Stroke subtypes and patterns, complications and outcome. *Cerebrovasc Dis* 2011; 32: 349-353.
2. Breuer L, Huttner HB, Jentsch K, et al. Intravenous thrombolysis in posterior cerebral artery infarctions. *Cerebrovasc Dis* 2011; 31: 448-454.
3. Dorňák T, Kral M, Hazlinger M, et al. Posterior vs. Anterior circulation infarction: Demography, outcomes, and frequency of hemorrhage after thrombolysis. *Int J Stroke* 2015; 10: 1224-1228.
4. Sung SF, Chen CH, Chen YW, et al. Predicting symptomatic intracerebral hemorrhage after intravenous thrombolysis: Stroke territory as a potential pitfall. *J Neurol Sci* 2013; 335: 96-100.
5. Sarikaya H, Arnold M, Engelter ST, et al. Outcomes of intravenous thrombolysis in posterior versus anterior circulation stroke. *Stroke* 2011; 42: 2498-2502.
6. Tong X, Liao X, Pan Y, et al. Intravenous thrombolysis is more safe and effective for posterior circulation stroke: Data from the thrombolysis implementation and monitor of acute ischemic stroke in china (TIMS-China). *Medicine (Baltimore)* 2016; 95: e3848.
7. Diaz-Otero F, Alonso Leciñana M, Masjuan J, et al. Intravenous thrombolysis in anterior versus posterior circulation acute ischemic stroke: Is there any difference? *Cerebrovasc Dis* 2011: Supplement 2 (227-)
8. Kozai Y, Narai H, Manabe Y. Outcomes of intravenous thrombolysis in posterior versus anterior circulation stroke in our hospital. *Cerebrovasc Dis* 2012: Supplement 1 (71-).
9. Lorenzano S, Ahmed N, Wahlgren N, et al. Insight into differences and similarities in response to intravenous thrombolysis of posterior versus anterior circulation stroke: Results from sits-international stroke thrombolysis register. *Cerebrovasc Dis* 2014: Supplement 1 (662-).
10. Savic O, Jovanovic D, Budimkic SM, et al. Intravenous thrombolysis in posterior versus anterior circulation stroke. *Cerebrovasc Dis* 2012; 33: 598.
11. Herzig R, Belaskova S, Vitkova E, et al. Intravenous thrombolysis in posterior circulation stroke-risk of intracranial hemorrhage and clinical outcome: Results from the sits-east registry. *Eur J Neurol* 2017: Supplement 1 (88).
12. Eun MY, Jung Iloek, Lee SH, et al. Vascular territory (anterior vs. posterior circulation) can influence outcome after thrombolysis? In: *XXIV WCN* (world congress of neurology), Dubai, United arab emirates, 27-31 Oct. 2019.
13. Dorn F, Stehle S, Lockau H, et al. Endovascular treatment of acute intracerebral artery occlusions with the solitaire stent: Single-centre experience with 108 recanalization procedures. *Cerebrovasc Dis* 2012; 34: 70-77.
14. Burnell AL, Wu T, Fink J, et al. Endovascular clot retrieval for acute ischaemic stroke in new zealand. *N Z Med J* 2018; 26: 13-18.

15. Singh RK, Lalla RS, Panchal KC, et al. Acute ischemic stroke treatment using mechanical thrombectomy: A study of 137 patients. *Ann Indian Acad Neurol* 2017; 20: 211-216.
16. Alawieh A, Turner RD, Turk AS, et al. Equivalent favorable outcomes possible after thrombectomy for posterior circulation large vessel occlusion compared with the anterior circulation: The musc experience. *J Neurointerv Surg* 2018; 10: 735-740.
17. Hu SY, Lee DH, Hong JT, et al. Effectiveness and safety of mechanical thrombectomy with stent retrievers in basilar artery occlusion: Comparison with anterior circulation occlusions. *J Korean Neurosurg Soc* 2017; 60: 635-643.
18. Daou B, Chalouhi N, Starke RM, et al. Predictors of outcome, complications, and recanalization of the solitaire device: A study of 89 cases. *Neurosurgery* 2015; 77: 355-360.
19. Alonso de Lecinana M, Kawiorski MM, Ximenez-Carrillo Aet al. Mechanical thrombectomy for basilar artery thrombosis: A comparison of outcomes with anterior circulation occlusions. *J Neurointerv Surg* 2017; 9: 1173-1178.
20. Weber R, Nordmeyer H, Eyding J, et al; REVASK investigators. Thrombectomy in posterior circulation stroke: Differences in procedures and outcome compared to anterior circulation stroke in the prospective multicentre revask registry. *Eur J Neurol* 2019; 26: 299-305.