SUPPLEMENTAL MATERIAL

Data S1.

SUPPLEMENTAL METHODS Search strategy

Database: MEDLINE

((((("Carotid Stenosis"[MeSH Terms] AND "Carotid Artery, Internal" [MeSH Terms] OR (internal carotid [Text Word] OR ICA [Text Word]) AND (occlusion [Text Word] OR occluded [Text Word] OR ICAO [Text Word])) AND (acute stroke[MeSH Terms]) OR CVA [Text Word] OR "acute cerebrovascular accident" [MeSH Terms] OR stroke [Text Word] AND (thrombectomy[MeSH Terms]) OR MECHANICAL THROMBECTOMY [Text Word])) AND (stent [MeSH Terms] OR "TANDEM occlusion" [TEXT WORD]))) AND ("2015"[Date - Publication] : "2020"[Date - Publication])

Total: 572 references

Database: EMBASE

('internal carotid artery occlusion'/exp OR 'carotid artery disease'/exp OR 'tandem occlusion') AND ('cerebrovascular accident'/exp OR stroke:ab,ti) AND ('mechanical thrombectomy'/exp OR 'thrombectomy':ab,ti) AND [2015-2020]/py

Total: 699 references

Database: WEB OF SCIENCE

((TS=("carotid artery occlu*" OR "internal carotid*") AND (TS=("acute stroke" or "cerebrovascular accident")) AND (TS=("mechanical thrombectomy" OR "stent" or "thrombectomy")))) AND DOCUMENT TYPES: (Article OR Review) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=2015-2020

Total: 133 references

Table S1. Characteristics of the studies included in the systematic review.

Study ID	Design	Primary outcomes	N	Interventions	Endovascular approach	IV tpA	FU (%)	Antithrombotic regimen	Additional outcomes
Yilmaz, 2017, Germany	Retrosp, SC	SICH (ECASS II within 24h) mRS-DC	47	aCAS (n=47) DLS (20), SLS (27)	Antero	51 %	72h	Previous APT (-): 500mg IV ASA before stent. CPD at discretion.	Stent patency (by US): TF 37% SLS, 50% DLS.
Pfaff, 2019, MN (Europe)	Retrosp, MC (7)	SICH (ECASS II/III) mRS-DC. TICI	160	aCAS (n=160) DLS	Antero (73.1%) Retro (26.9%)	61 %	72h	Post procedural: ASA alone/ ASA+ CPD or ticagrelor.	Acute TF (20.6%) and occlusion at 72h and previous APT.
Maus, 2017, MN	Retrosp, MC (4), PCDB	SICH (≥4pts) mRS-DC - 90d. TICI	197	aCAS (n=197)	Antero (55.3%) Retro (44.7%)	58 %	90d (81 %)	APT differed between centers.	Effect of contralateral CS (-).
Lucena, 2016, Brazil	Retrosp, SC	SICH (SITS-MOST ≥4pts at 72h) mRS 90d TICI	20	aCAS (n=20)	Antero	60 %	90d 100 %	Dual APT started at 24h after CAS for 3m.	

Heck, 2015, Usa	Retrosp, SC, PCDB	SICH (SITS-MOST) mRS 90d TICI	23	aCAS (n=23)	Antero	30 %	90d 100 %	ACT or APT at discretion.	
Anadani, 2019, MN	Retrosp, MC, TITAN Registry, PCDB	SICH (ECASS II) mRS 90d. TICI	205	aCAS (n=205)	Antero (66.8%) Retro (33.2%)	60 %	90d	APT differed between centers. PO meds: NA	
Park, 2019, Korea	Retrosp, SC	SICH (ECASS III at 24h) mRS 90d TICI	42	aCAS (n=42)	Antero	69 %	90d	tPA (+): dual APT after 24h. tPA (-): dual APT load and maintenance.	Stenosis vs. complete occlusion of ICA.
Lockau, 2015, Germany	Retrosp, SC	SICH (≥4pts at 18±6 h) mRS 90d TICI	37	aCAS (n=37)	Antero (32%) Retro (67.6%)	54 %	90d	APT (-): bolus tirofiban, then for 24h. Dual APT load and for 3m.	Early neurological improvement.
Maus, 2018, Germany	Retrosp, MC (4) PCDB	SICH (≥4pts) mRS 90d. TICI	171	aCAS (n=165) (6 SRC after CAS, no MT)	Antero (59%) Retro (41%)	62 %	90d (88 %)	APT on each center. Used: tirofiban, ASA, abciximab.	Best first approach

Spiotta, 2015, USA	Retrosp, SC	SICH mRS 90d. TICI	16	aCAS (n=16)	Antero	50 %	90d 100 %	IA Abciximab (0.25 mg/ kg) at CAS. Dual APT load and maintenance.	
Yoon, 2015, China	Retrosp, MC (2) PCDB	SICH (≥4pts) mRS 90d TICI	42	aCAS (n=42) (7 SRC after CAS)	Antero	64 %	90d	45% URK in MT Dual APT by NGT immediately PO, for 3m.	Predictors for favorable outcome. In-stent thrombosis (1).
Mpotsaris, 2017, Germany	Retrosp, SC	SICH (ECASS 18±6 h). mRS 90d	63	aCAS (n=63)	Antero (27%) Retro (73%)	52 %	90d (97 %)	Abciximab bolus, followed by dual APT for 3m after 12–24h NCCT	
Steglich-Arnholm, 2015, Denmark	Retrosp, SC	SICH (≥4pts at 24h) mRS 90d TICI	62	aCAS (n=47) 15 SRC after CAS	NA	85 %	90d	Load of IV ASA and/or GPIIb/IIIa (eptifibatide or abciximab). Dual APT after FU imaging.	Stent patency: 8 TF, 4 occlusions at 90d Early clinical improvement 72h.
Behme, 2015, Germany	Retrosp, MC (4) PCDB	SICH (ECASS) mRS 90d TICI	170	aCAS (n=170)	Antero (89%) Retro (11%)	72 %	90d	APT on each center.	Risk factors for SICH

Cohen, 2015, Israel	Retrosp, SC	SICH (≥4pts at 36h) mRS 90d and 6 months TICI	24	aCAS (n=24)	Antero	42 %	90d (77 %) 6 m 90%	Previous APT (-): ASA 300mg. After (-) CT, added CPD 300mg. dual APT for 2m.	
Sadeh-Gonik, 2018, France	Retrosp, SC PCDB	SICH (≥4pts at 24h) mRS 90d TICI	46	aCAS (n=12)	Retro	76 %	90d (93 %)	NA	
Fahed, 2016, France	Retrosp, SC	SICH (ECASII at 24h and 72h) mRS 90d. TICI	70	aCAS (n=37) No stent (n=33)	NA	49 %	90d (96 %)	CAS: IV ASA bolus followed by a dual APT if (-) 24h NCCT	NIHSS at 24h and 7d
Bucke, 2018, Germany	Retrosp, SC PCDB	SICH (SWIFT PRIME at 24h) mRS 90d TICI	107 1LVO 222 TO	aCAS (n=222) LVO MT (n=849)	Antero	24 %	90d	IV dual APT or Ticagrelor load prior to CAS (at discretion)	

Rodriguez-Lopez, 2018, Spain	Retrosp, SC	mRS 90d TICI	66	aCAS (n=33) MT alone (33)	Retro	54 %	90d	NA	
Runck, 2019, Germany	Retrosp, SC	SICH (ECASS) TICI	66	aCAS+ MT (45) aCAS not TO (21)	Antero (80%) Retro (20%)	64 %	DC	APT (-): ASA after CAS and PO tirofiban. At 4h before cessation of the infusion, a ticagrelor load, then for min 6w and ASA for 6m.	In-stent thrombosis (22%).
Maurer, 2015, Germany	Retrosp, SC	SICH (24h) mRS DC TICI	43	aCAS (n=38), BA (n=5)	Antero	88 %	DC	Loading dose of CPD or ticagrelor	
Lescher, 2015, Germany	Retrosp, SC	SICH mRS 90d TICI	39	aCAS (n=09), BA (n=30)	Retro	74 %	90d	CPD load before CAS. Maintenance dual APT the next day.	
Akpinar, 2017, Turkey	Retrosp, SC PCDB	SICH (≥4pts) mRS TICI	15	BA (n=15), Delayed 7-10d CAS (n=10)	Antero	53 %	7–10, 30 and 90 days	CAS (+): dual APT 5d before CAS.	
Slawski, 2018, USA	Retrosp, SC PCDB	SICH (≥4pts) mRS 90d. TICI	45 TO. 39 Tx	aCAS (n=27), CEA (n=12)	Retro	46 %	90d	CAS: Dual APT before EPD. Low-dose heparin (2000-3000 U).	Re-occlusion 3/12. In-stent thrombosis (US 24h)

								CEA: ASA and a heparin bolus (5000 U).	
Poppe, 2019, Canada	RCT pilot study. SC	SICH (ECASS II at 24h) mRS 90d TICI	24	aCAS (n=11), BA (n=02)	Antero (18%) Retro (82%)	75 %	90d 100 %	No strict rec. tpA(+): ASA if (-) APT or CPD if (+) Dual APT after imaging at 6–24h. tpA(-): dual APT immediately PO.	PO stenosis
Kim, 2019, Korea	Retrosp, MC (17) PCDB	SICH mRS 90d TICI	955 MT, 75 TO	aCAS (n=56), BA (n=19)	Antero (90%) Retro (10%)	56 %	90d	CAS: PO APT on each center.	Re-occlusion (9%) Factors of success TICI
Papanagiotou, 2018, MN	Retrosp, MC (18) TITAN registry	SICH (≥4pts at 24h) mRS 90d TICI	482	aCAS (n=322), BA (n=52) MT alone (108)	Antero	61 %	90d	APT depended on each center.	Efficacy and safety outcomes according to APT type.
Jadhav, 2018, USA	Retrosp, MC (55) PCDB STRATIS	SICH (SWIFT PRIME at 24h) mRS 90d	147	aCAS (n=80), BA (n=43), delayed CAS (n=24)	Antero (47%) Retro (53%)	74 %	90d (93 %)	NA	Predictors of good outcomes in TO, and predictors of aCAS.

	Registry	TICI							
Labeyrie, 2018, France	Retrosp, SC PCDB	ICH (ECASS > 1 at 48h) mRS 90d TICI	49	aCAS (n=16), BA (n=9). Coils (n=12), Medical (n=13)	NA	67 %	90d (86 %)	Before stent positioning: IV ASA + CPD by NGT, then for 3m *additional IV anti-GP IIb/IIIa at discretion.	Early embolic recurrence (9/64). Stroke recurrence at 30 days.
Kang, 2019, Korea	Retrosp, SC PCDB	SICH (≥4pts at 24h) mRS 90d TICI	62	aCAS (n=40), BA (n=22)	Antero (22%) Retro (78%)	40 %	90d 1y	Neurologist's discretion: Immediate/ delayed (>1h) Dual /single APT	Long-term stent patency
Vu Dang, 2020, Vietnam	Retrosp, SC	ICH (Heidelberg 18±6 h) mRS 90d TICI	17	aCAS (n=10), BA (n=07)	Antero	59 %	90d	4000 UI heparin at CAS. Dual APT for 3m, then ASA.	Early clinical improvement at 24h
Li, 2018, China	Retrosp, SC	SICH (Heidelberg at 36h) mRS 90d TICI	37	aCAS (n=19), BA (n=18)	NA	32 %	90d	tpA(+): dual APT after 24h and for min 3m. tpA(-): dual APT load and maintenance.	In-stent stenosis at 3m (1/11)

Walloch a, 2019, Germany	Retrosp, SC PCDB	SICH (≥4pts) mRS 90d TICI	163	aCAS (n=149), BA (n=14)	Antero (52%) Retro (48%)	55 %	90d-5y (97 %)	CAS: IV ASA. IV heparin in some procedures. CPD 24h after. Dual APT for 4w, followed by mono-APT	Stent patency: acute re-occlusion 5.4%
Eker, 2018, Switzerland	Retrosp, MC (2) PCDB	SICH (≥4pts at 24h) mRS 90d TICI	121 TO 456 LVO	aCAS (n=98), BA (n=9), delayed CAS (n=14)	Antero (38%) Retro (62%)	52 %	90d (97 %)	IV ASA prior to CAS. Dual APT after (-) NCCT within 24h	Acute in-stent thrombosis (2/98)

aCAS stands for acute carotid artery stenting; ACT, anticoagulation therapy; Antero, anterograde; APT, antiplatelet therapy; ASA, acetylsalicylic acid; ATS, atorvastatin; BA, balloon angioplasty; CEA, carotid endarterectomy; CPD, clopidogrel; CS, carotid stenosis; d, days; DC, discharge; DLS, dual layer stent; ECASS II, European Cooperative Acute Stroke Study II; EPD, embolic protection device; FU, follow up; h, hours; IA, intra-arterial; IV, intravenous; LVO, large vessel occlusion; m, months; MC, multicenter; min, minimum; MN; multinational; mRS, Modified Rankin Scale; MT, mechanical thrombectomy; NA, not available; NCCT, non-contrast computerized tomography; NGT, nasogastric tube; NIHSS, The National Institutes of Health Stroke Scale; PCDB, prospectively collected database; PO, post-operative; RCT, randomized controlled trial; rec, recommendations; retro, retrograde; Retrosp, retrospective; SC, single center; SICH, symptomatic intracranial hemorrhage; SITS-MOST, Safe Implementation of Thrombolysis in Stroke-Monitoring Study; SLS, single layer stent; SRC, spontaneous recanalization; SWIFT PRIME, Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment trial; TF, thrombus formation; TICI, thrombolysis in cerebral infarction; TO, tandem occlusion; tpA, tissue plasminogen activator; Tx, treatment; U, units; URK, urokinase; US, ultrasound; w, weeks; and y, year.

Table S2. Risk of bias assessment of studies included in the systematic review without control group.

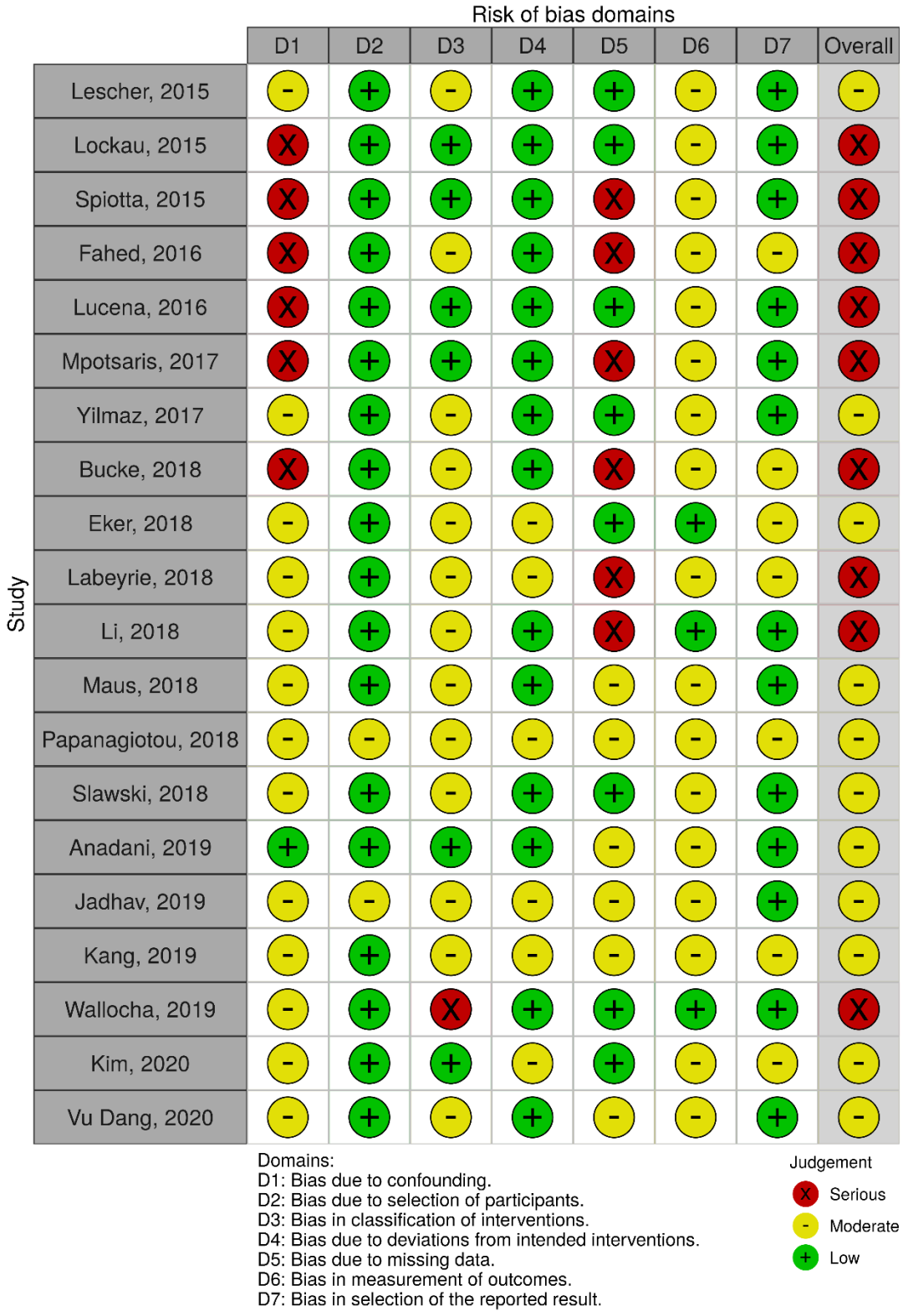
National Institute of Health Quality Assessment Tool for before-after (pre-post) Studies	
Study ID	Quality rating
Akpinar, 2017	Fair
Pfaff, 2019	Fair
Heck, 2015	Fair
Park, 2019	Fair
Maus, 2017	Good
Yoon, 2015	Good
Runck, 2019	Fair
Rodriguez-Lopez, 2018	Fair
Steglich-Arnholm, 2015	Fair
Sadeh-Gonik, 2018	Fair
Maurer, 2015	Fair
Behme, 2015	Good
Cohen, 2015	Poor

Table S3. Risk of bias assessment, RoB2 tool

Cochrane risk of bias in randomized trials (RoB 2)- Poppe, 2019	
Domain	Classification
Randomization process	Low
Deviations from intended interventions	Some concerns
Missing outcome data	Low
Measurement of the outcome	Some concerns
Selection of the reported result	Low
Overall Bias	Some concerns

Figure S1. Risk of bias assessment of studies included in the systematic review and meta-analysis – ROBINS I (A) summary per study. (B) summary per domain.

A



B

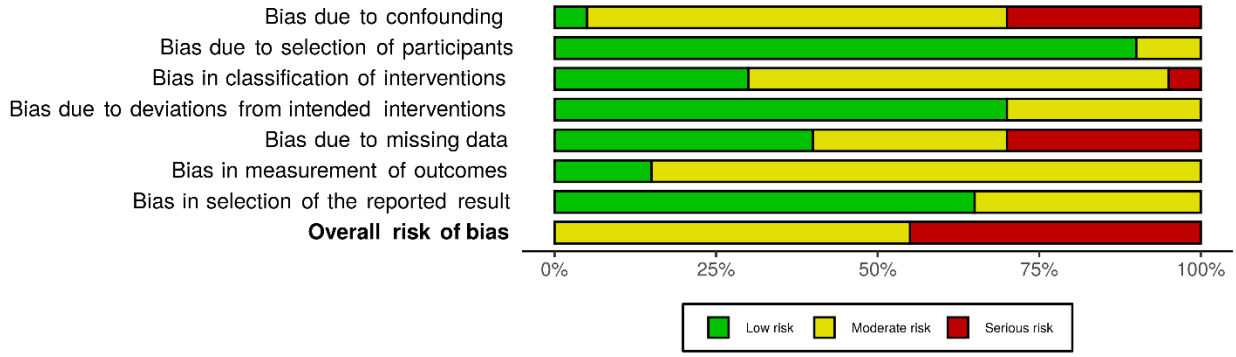


Figure S2. Meta-analysis of Symptomatic intracranial hemorrhage (sICH) in patients with acute stenting with of intravenous tissue plasminogen activator (IV tpA) versus without IV tpA.

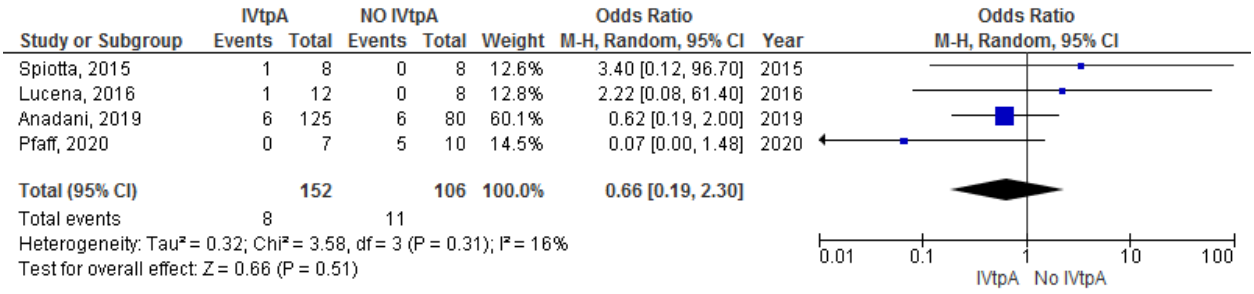
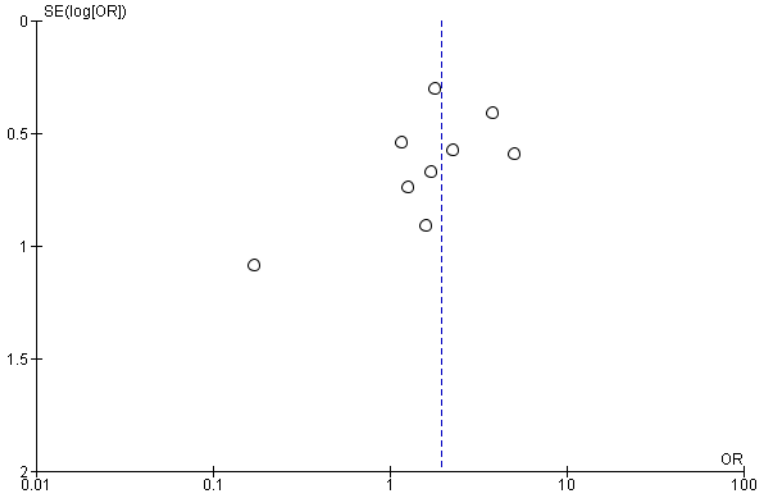
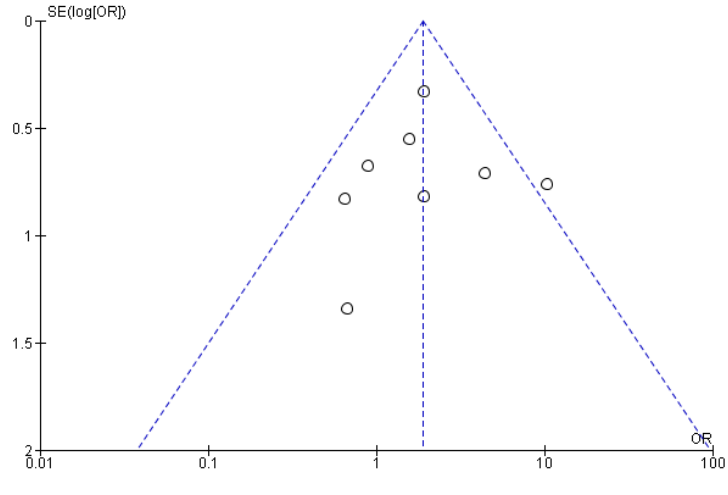


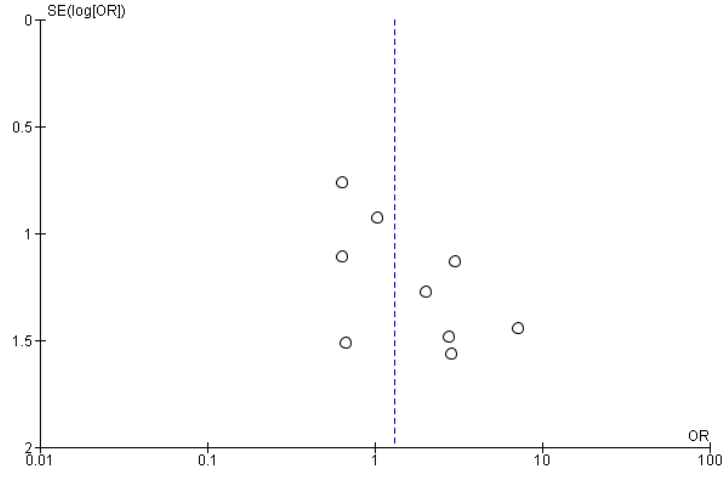
Figure S3. Funnel plots and Egger´s test results for (A) functional outcome at 90 days (modified Rankin Scale (mRS) score of 0–2), (B) good reperfusion status Thrombolysis in Cerebral Infarction (TICI) 2b-3, (C) Symptomatic intracranial hemorrhage (sICH), and (D) mortality as outcomes in acute stenting versus angioplasty studies showing no asymmetry.



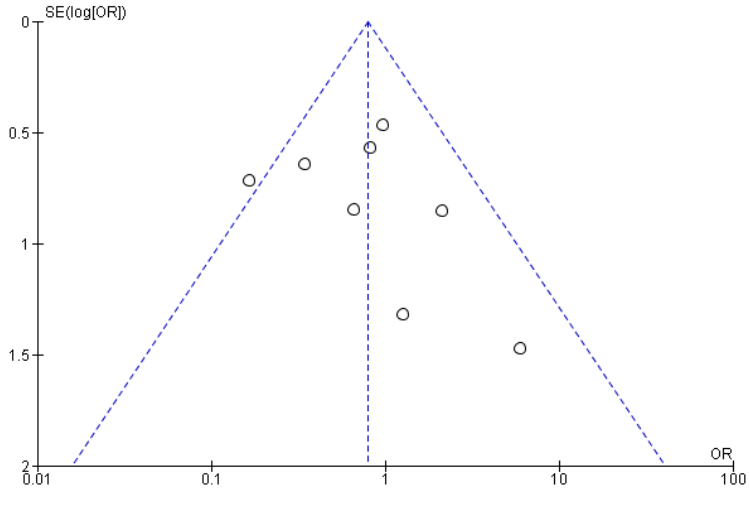
A Egger's test: p=0.27



B Egger's test: p=0.87

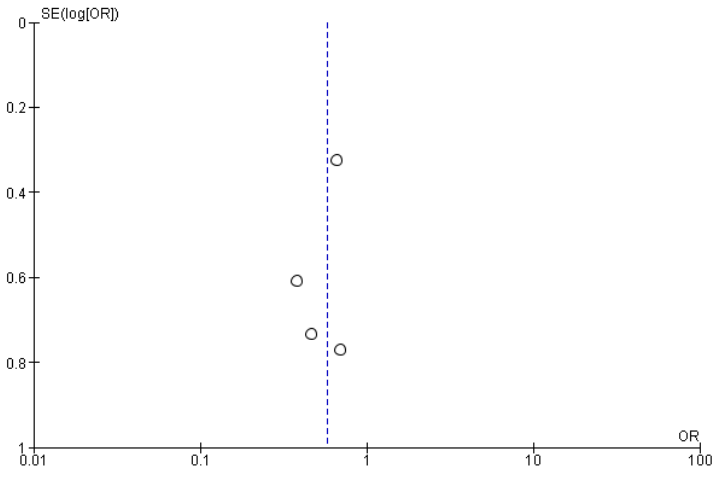


C Egger's test: p=0.06

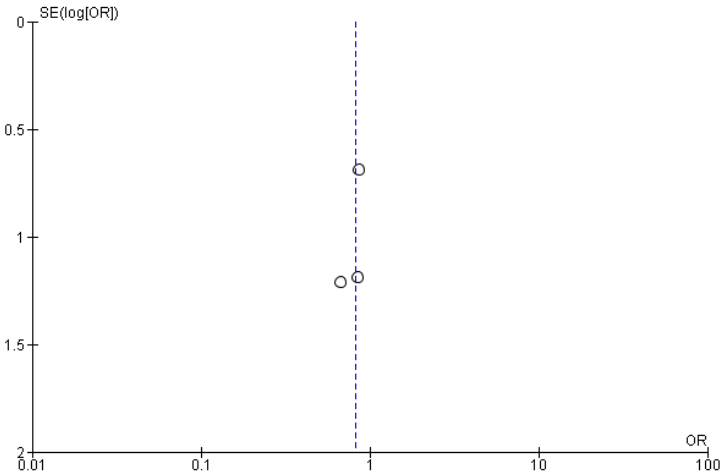


D Egger's test: p=0.54

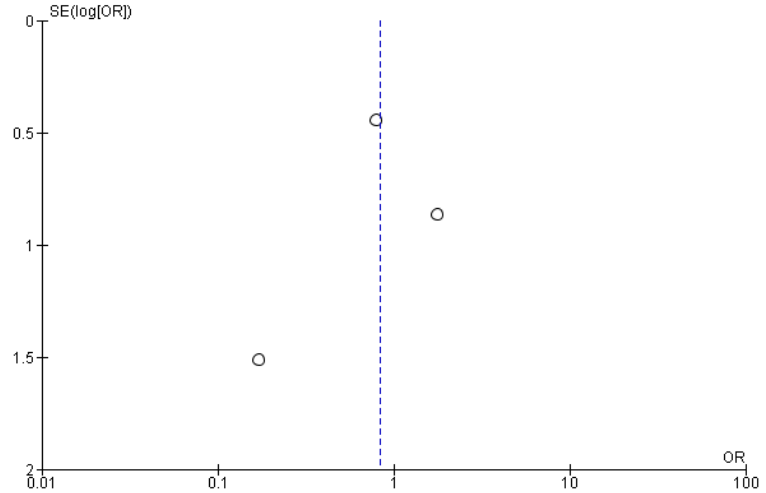
Figure S4. Funnel plots and Egger´s test results for (A) functional outcome at 90 days (modified Rankin Scale (mRS) score of 0–2), (B) Symptomatic intracranial hemorrhage (sICH), (C) mortality as outcomes in anterograde versus retrograde approach studies showing no asymmetry,



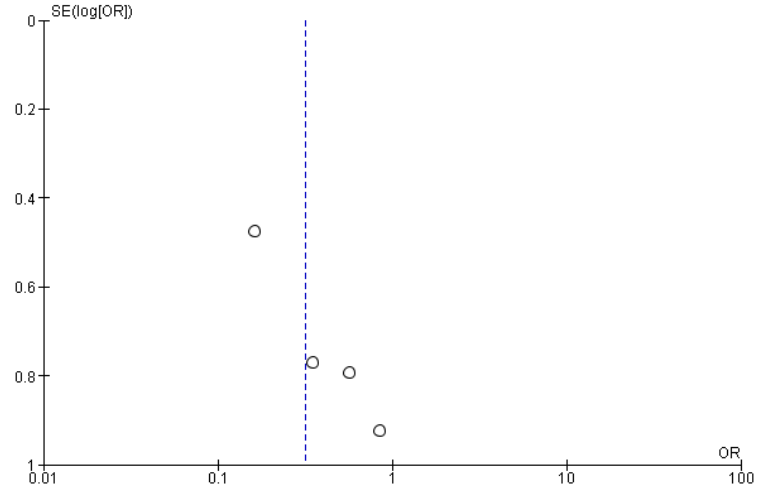
A Egger's test: p=0.43



B Egger's test: p=0.52



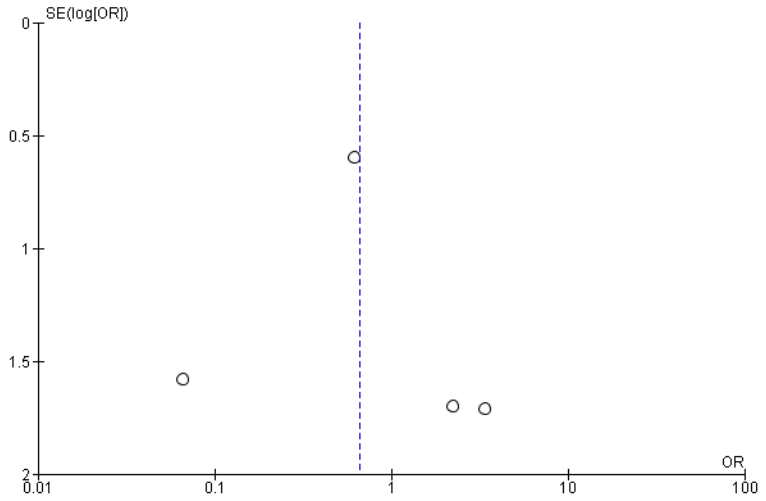
C Egger's test: p=0.79



D Egger's test: p=0.02

and (D) good reperfusion status Thrombolysis in Cerebral Infarction (TICI) 2b-3 showing asymmetry and possible bias.

Figure S5. Funnel plot and Egger´s test result for Symptomatic intracranial hemorrhage (sICH) as outcome in patients with acute stenting with of intravenous tissue plasminogen activator (IV tpA) versus without IV tpA showing no asymmetry.



Egger's test: p=0.88