Supplementary Material

Supplementary Table 1. Details of the treatment administered in the included studies.[1-41]

Study ID	Study type	Total Participants	Definition of symptomatic ICH	Type of EVT	Type of AAT	Dose of AAT	≥ 3 passes(%), mean±SD or median (IQR)	Rescue or Concurrent AAT
Anadani et al. 2019[1]	Prospective cohort	486	N/A	SR, CA	IA rtPA	3.0 - 5.0 mg up to 15 mg	≥3 passes: AAT 26.5% ST 37.3%	Rescue
Baik et al. 2021[2]	Retrospective	114	ECASS criteria	SR+CA	IA urokinase	20,000 - 60,000 IU	N/A	Rescue
Berkhemer et al. 2015[3]	Post hoc analysis RCT	191	ECASS criteria	SR	IA rtPA	5.0 mg single dose up to 30 mg	N/A	Rescue
Bracard et al. 2016[4]	Post hoc analysis RCT	139	ECASS criteria	SR, CA	IA rtPA	3.0 - 10.0 mg	N/A	Rescue
Cappellari et al. 2021[5]	Prospective cohort	506	ICH and NIHSS ≥1	SR, CA, SR + CA	IA rtPA	N/A	N/A	Concurrent
Collette et al. 2023[36]	Prospective cohort	2263	Heidelberg Bleeding Classification	SR, CA	IA urokinase/rtPA	Urokinase - 250000IU, rTPA - 20 mg	≥3 passes: AAT 36.2% ST 35.8%	Concurrent

Fischer et al. 2013[39]	Retrospective	169	PROACT-II criteria (ICH + NIHSS score increase ≥4)	SR	IA Urokinase	7500,000 IU	N/A	Rescue
Goyal et al. 2015[6]	Post hoc analysis RCT	165	Determined clinically at the study site	SR	IA tPA	1.0 - 7.0 mg	N/A	N/A
Gruber et al. 2019[7]	Retrospective	32	ECASS criteria	SR	IA tirofiban	10 µg/kg	N/A	Concurrent
Guo et al. 2022[8]	Retrospective	821	ECASS criteria	SR, CA	IA tirofiban	0.25 - 0.5 mg	N/A	Concurrent or Rescue
Heiferman et al. 2017[9]	Retrospective	40	Heidelberg Bleeding Classification	SR	IA rtPA	8.0 - 16.0 mg	N/A	Concurrent
Huo et al. 2020[10]	Retrospective	207	ECASS criteria	SR, CA	IA tirofiban	0.25 - 1.0 mg	N/A	Rescue
Huo et al. 2021[11]	Prospective	649	ECASS criteria	SR + CA	IA tirofiban	0.25 - 1.0 mg	N/A	Rescue
Jang et al. 2021[12]	Retrospective	314	N/A	SR + CA	IA tirofiban	0.5 - 2.0 mg	N/A	Concurrent or Rescue
Kaesmacher et al. 2020[13]	Prospective cohort	993	PROACT-II criteria (ICH + NIHSS ≥4 or	SR	IA urokinase	250,000 - 500,000 IU	N/A	Rescue

			1-point increase in consciousness level on NIHSS)					
Kim et al. 2020[14]	Retrospective	118	N/A	SR + CA	IA tirofiban	0.5 - 2.0 mg	N/A	Rescue
Kohli et al. 2022[15]	Prospective cohort	271	N/A	SR + CA	IA rtPA	variable between 0 to >10mg	≥3 passes: AAT 11.5% ST 39.2%	Concurrent or Rescue
Ma et al. 2021[16]	Prospective	201	Heidelberg Bleeding Classification	SR, CA	IA tirofiban	0.25-1.0 mg	AAT: 2.5±1.8 ST: 2.7±1.5	Rescue
Ma et al. 2022[37]	Prospective cohort	892	Heidelberg Bleeding Classification	N/A	IA eptifibatide	135-180 micrograms/kg	AAT: 1 (1-2) ST: 2 (2-3)	Rescue
Mujanovic et al. 2023[40]	Retrospective	459	ECASS criteria	N/A	IA Urokinase	250,000 IU	N/A	Rescue
Noh et al. 2022[17]	Retrospective	69	ECASS criteria	SR	IA tirofiban	0.5 - 1.0 mg	N/A	Rescue
Pan et al. 2022[18]	Retrospective	130	ECASS criteria	N/A	IA tirofiban	0.25-1.0 mg	N/A	Concurrent or Rescue
Quan et al. 2019[19]	Retrospective	159	ECASS criteria	SR, CA	IA tirofiban	N/A	N/A	Concurrent

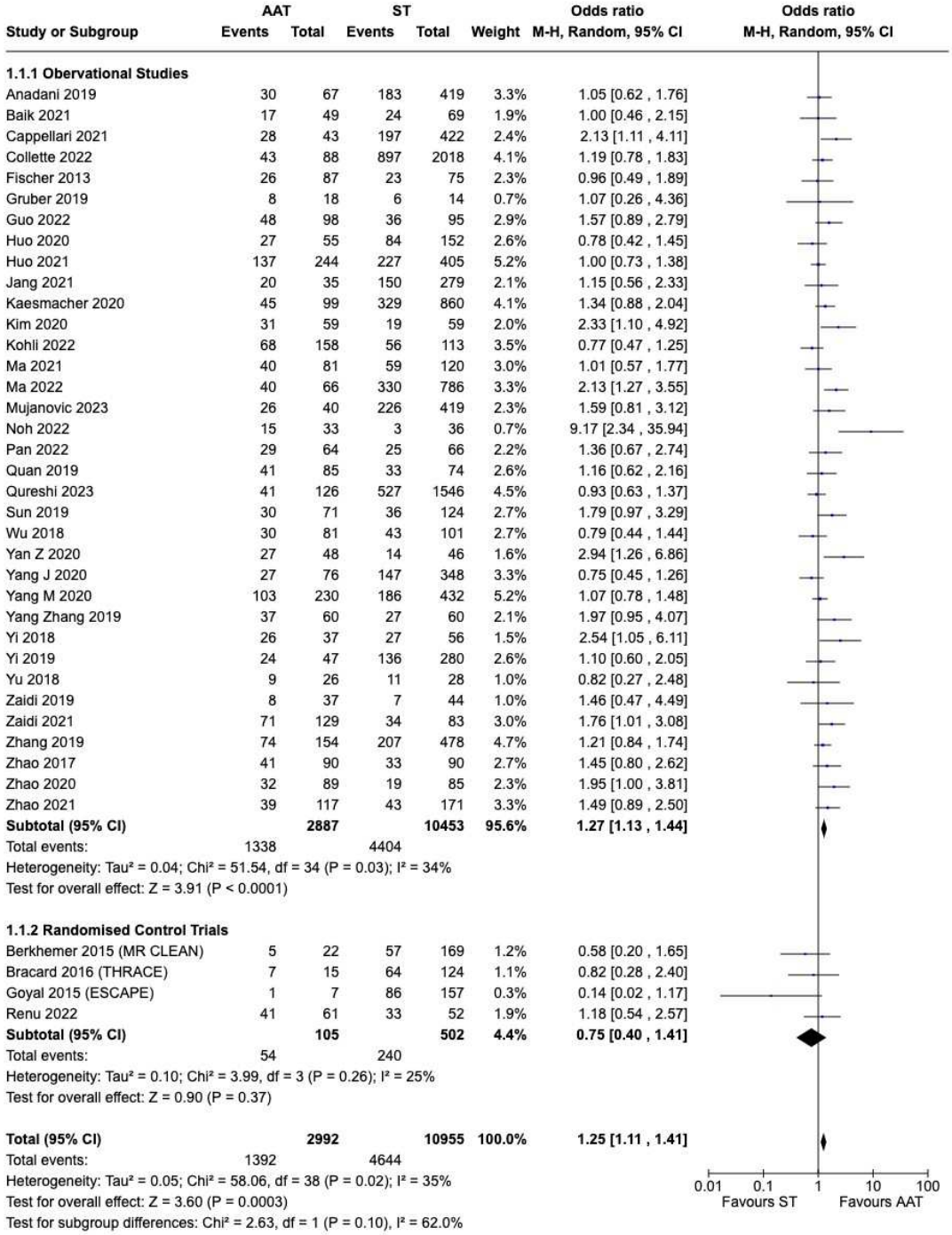
Qureshi et al. 2023[41]	Retrospective	1672	ECASS criteria	SR, CA	IA urokinase/rtPA	N/A	N/A	Rescue
Renu et al. 2022[38]	RCT	113	ECASS criteria	SR, CA, SR + CA	IA rtPA	0.225 mg/kg (max dose 22.5 mg)	N/A	Concurrent
Singer et al. 2013[20]	Retrospective	733	ECASS criteria	SR	IA rtPA	N/A	N/A	Concurrent
Sun et al. 2019[21]	Prospective	195	ECASS criteria	SR	IA tirofiban	0.25 - 0.5 mg	N/A	Rescue
Wu et al. 2018[22]	Prospective	218	ECASS criteria	SR	IA tirofiban	50 µg/mL (max dose 10 µg/kg)	≥3 passes: AAT 17.9% ST 20.2%	Concurrent
Yan et al. 2020[23]	Retrospective	98	Heidelberg Bleeding Classification	SR	IA tirofiban	0.4 - 0.5 mg	AAT: 2 (1-2) ST: 2 (1-2)	Rescue
Yang J et al. 2020[24]	Prospective cohort	433	ECASS criteria	SR	IA tirofiban	10 µg/kg	≥3 passes: AAT 31.6% ST 25.3%	Rescue
Yang M et al. 2020[25]	Prospective cohort	662	ECASS criteria	SR, CA	IA tirofiban	0.25 - 1.0 mg	≥3 passes: AAT 10.0% ST 6.1%	Rescue
Yang Z et al. 2019[32]	Prospective	120	N/A	SR	IA tirofiban	N/A	N/A	Rescue

Yi et al. 2018[27]	Retrospective	93	ECASS criteria	SR	IA rtPA	1.0 mg/min, max 5.0 mg	≥3 passes: AAT 46.4% ST 18.9%	Concurrent
Yi et al. 2019[26]	Retrospective	327	N/A	SR	IA tirofiban	0.25 mg	AAT: 2.8±1.1 ST: 1.7±0.9	Concurrent
Yu et al. 2018[28]	Retrospective	54	ECASS criteria	SR	IA tirofiban	0.2 - 0.5 mg	AAT: 2.3±1.4 ST: 2.1±1.8	Concurrent
Zaidi et al. 2019[30]	Prospective cohort	81	ECASS criteria	SR	IA rtPA	N/A	≥3 passes: AAT 13.6% ST 5.4%	Rescue
Zaidi et al. 2021[29]	Prospective cohort	212	N/A	SR	IA rtPA	2.0 - 12.0 mg	≥3 passes: AAT 49.4% ST 14.0%	Rescue
Zhang et al. 2019[31]	Prospective cohort	632	Heidelberg Bleeding Classification	SR	IA tirofiban	0.25 - 0.5 mg	AAT: 2 (1-3) ST: 2 (1-3)	Rescue
Zhao et al. 2017[34]	Retrospective	180	ECASS criteria	SR	IA tirofiban	0.25 - 0.5 mg	N/A	Concurrent or Rescue
Zhao et al. 2020[33]	Retrospective	174	ECASS criteria	SR	IA tirofiban	5.0 μg/kg	AAT: 2 (1-2) ST: 2 (1-3)	Concurrent or Rescue

Zhao et al. 2021[35]	Prospective	288	Heidelberg Bleeding Classification	SR	IA tirofiban	0.25 - 0.5 mg	AAT: 2 (1-3) ST: 2 (1-3)	Concurrent or Rescue

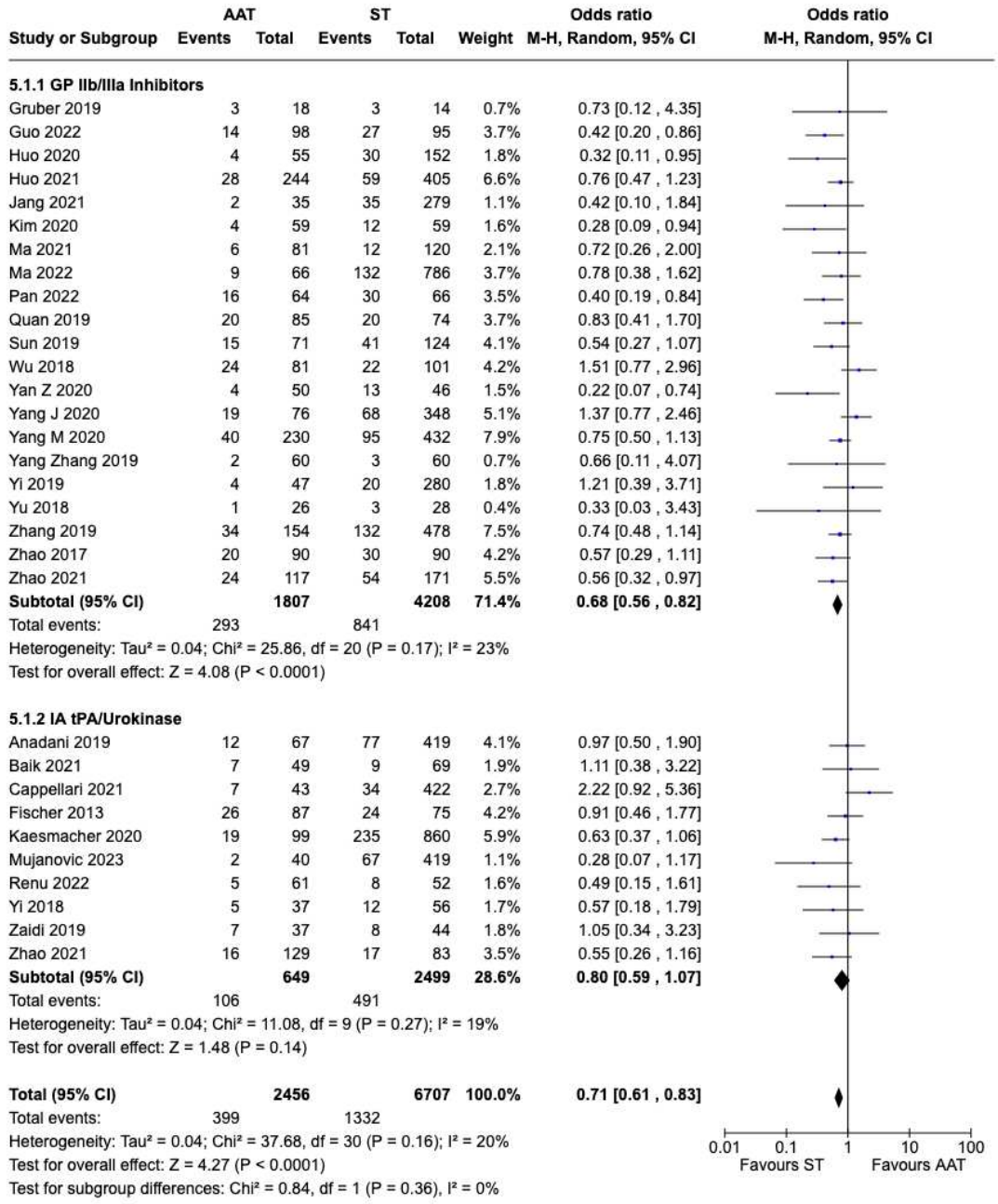
AAT = adjunctive antithrombotic therapy, ST = standard therapy, IA = intraarterial, EVT = endovascular thrombectomy, ECASS = European Cooperative Acute Stroke Study, ICH = intracranial haemorrhage, sICH = symptomatic intracranial haemorrhage, NIHSS = National Institutes of Health Stroke Scale, RCT = randomised controlled trial, SR =stent retriever, CA =contact aspiration, rtPA =recombinant tissue-type plasminogen activator, PROACT-II = Prolyse in Acute Cerebral Thromboembolism II, N/A = not available.
ECASS definition = intracranial haemorrhage with NIHSS increase ≥4; Heidelberg Bleeding Classification = Intracranial haemorrhage with any increase in NIHSS ≥4 or by ≥2 in any subcategory

Supplementary Figure 1. Forest plot comparing the odds ratio of functional independence at 90 days between AAT vs ST, grouped by observational studies or randomised studies.



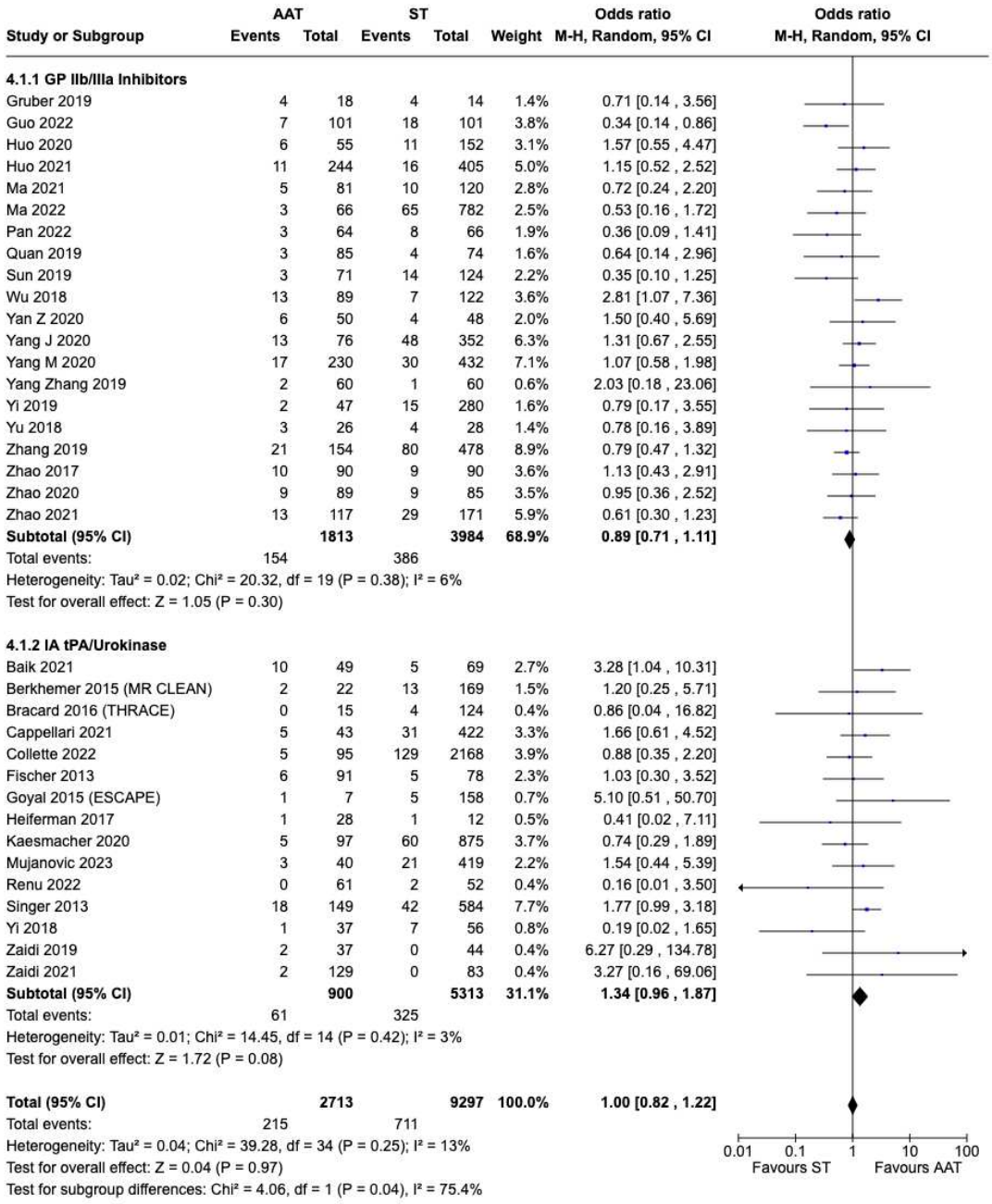
SD=standard deviation, CI=confidence interval, ST = standard therapy, AAT = adjunctive anti-thrombotic therapy, vs=versus, I2=heterogeneity index.

Supplementary Figure 2. Forest plot comparing the odds ratio of mortality rates at 90 days between AAT vs ST groups based on the type of drug used (GPIIb/IIIa, IA-tPA or urokinase).



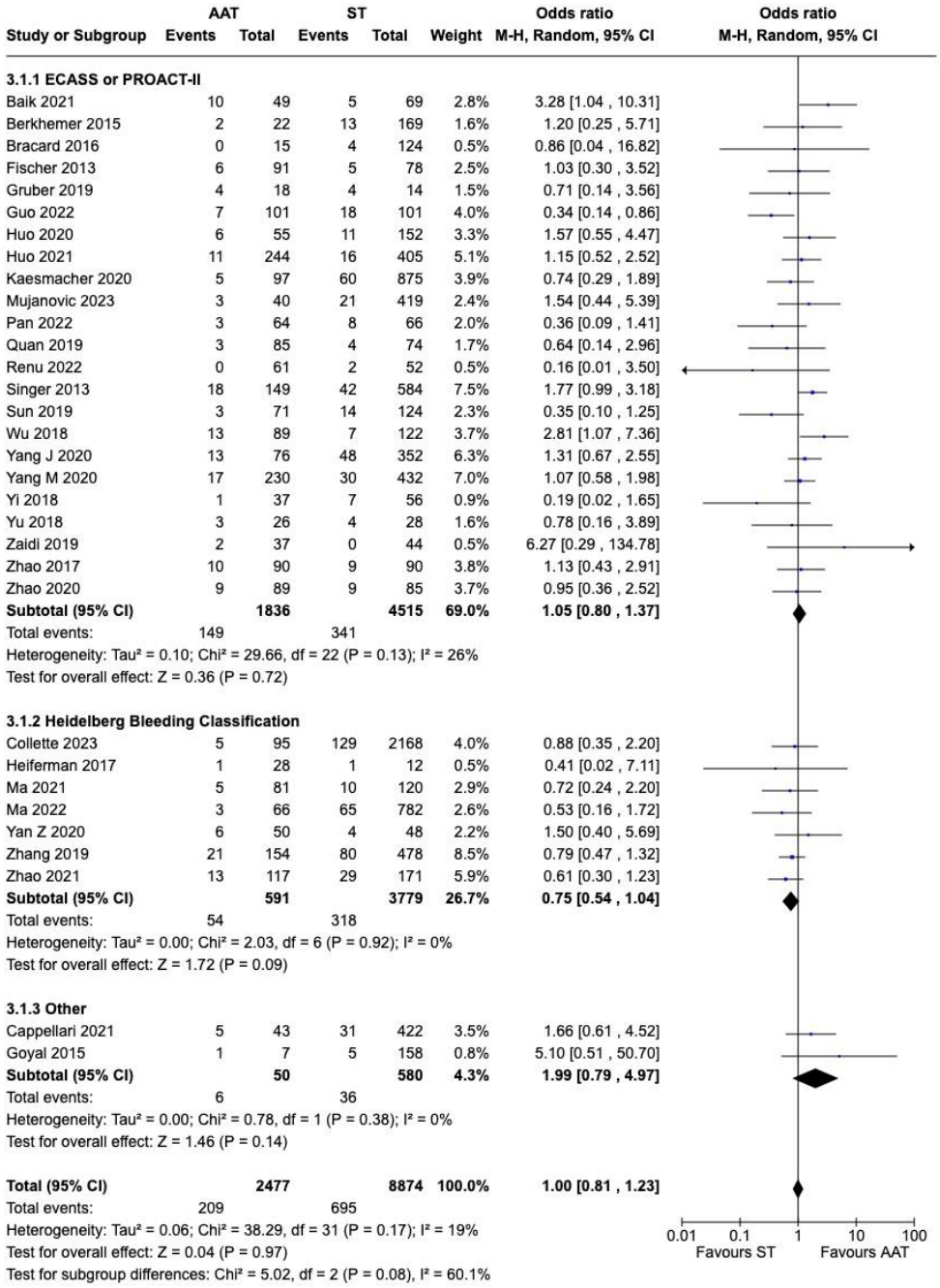
SD=standard deviation, CI=confidence interval, ST = standard therapy, AAT = adjunctive anti-thrombotic therapy, GPIIb/IIIa =glycoprotein IIb/IIIa, IA-tPA= intraarterial tissue plasminogen activator, vs=versus, I2=heterogeneity index.

Supplementary Figure 3. Forest plot comparing the odds ratio of symptomatic intracranial haemorrhage rates between AAT vs ST groups based on the type of drug used (GPIIb/IIIa, IA-tPA or urokinase).



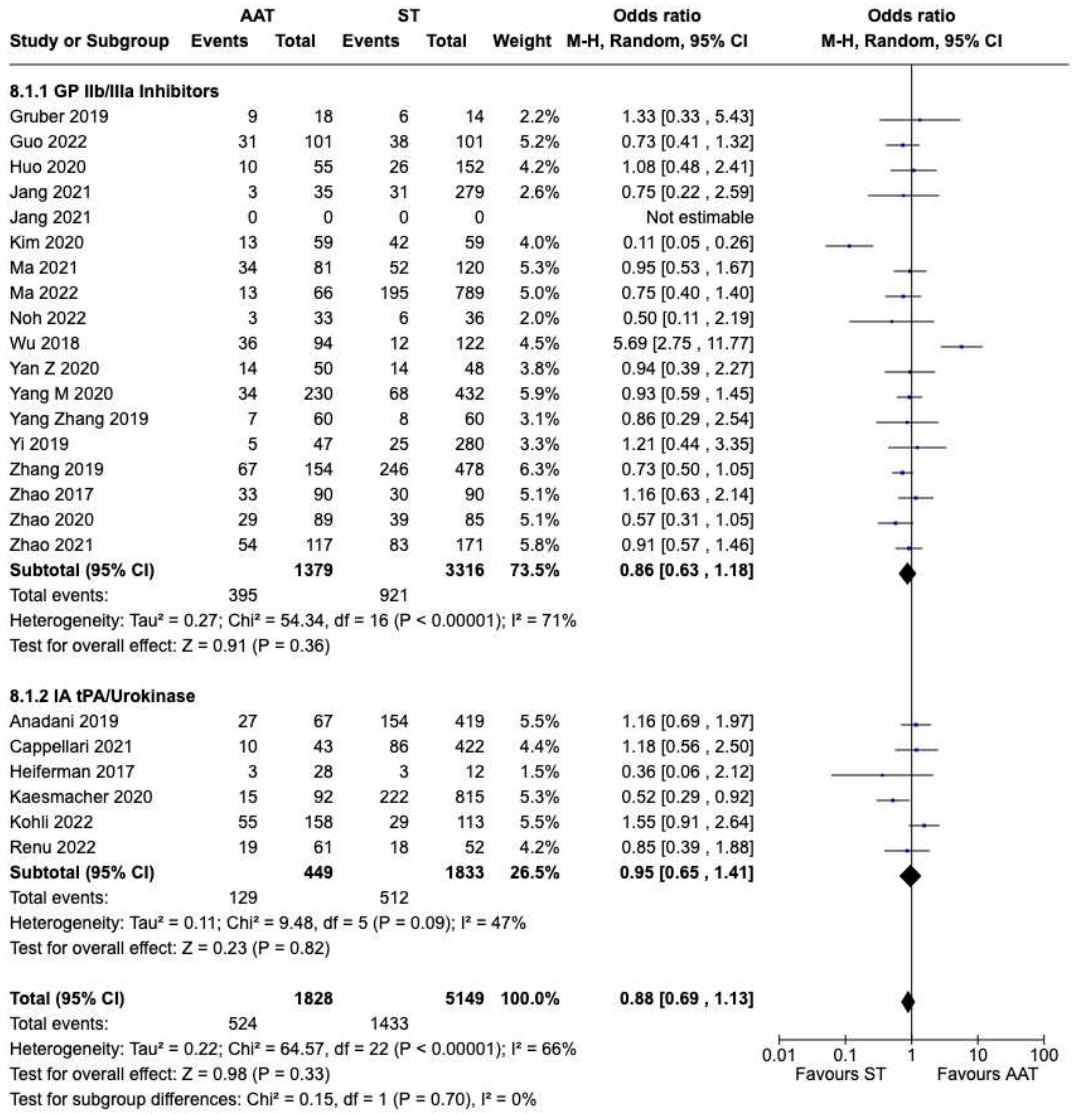
SD=standard deviation, CI=confidence interval, ST = standard therapy, AAT = adjunctive anti-thrombotic therapy, GPIIb/IIIa =glycoprotein IIb/IIIa, IA-tPA= intraarterial tissue plasminogen activator, vs=versus, I2=heterogeneity index.

Supplementary Figure 4. Forest plot comparing the odds ratio of symptomatic intracranial hemorrhage (sICH) rates at 90 days between AAT vs ST groups based on the criteria used to define sICH (ECASS or PROACT-II, Heidelberg Bleeding Classification or other).



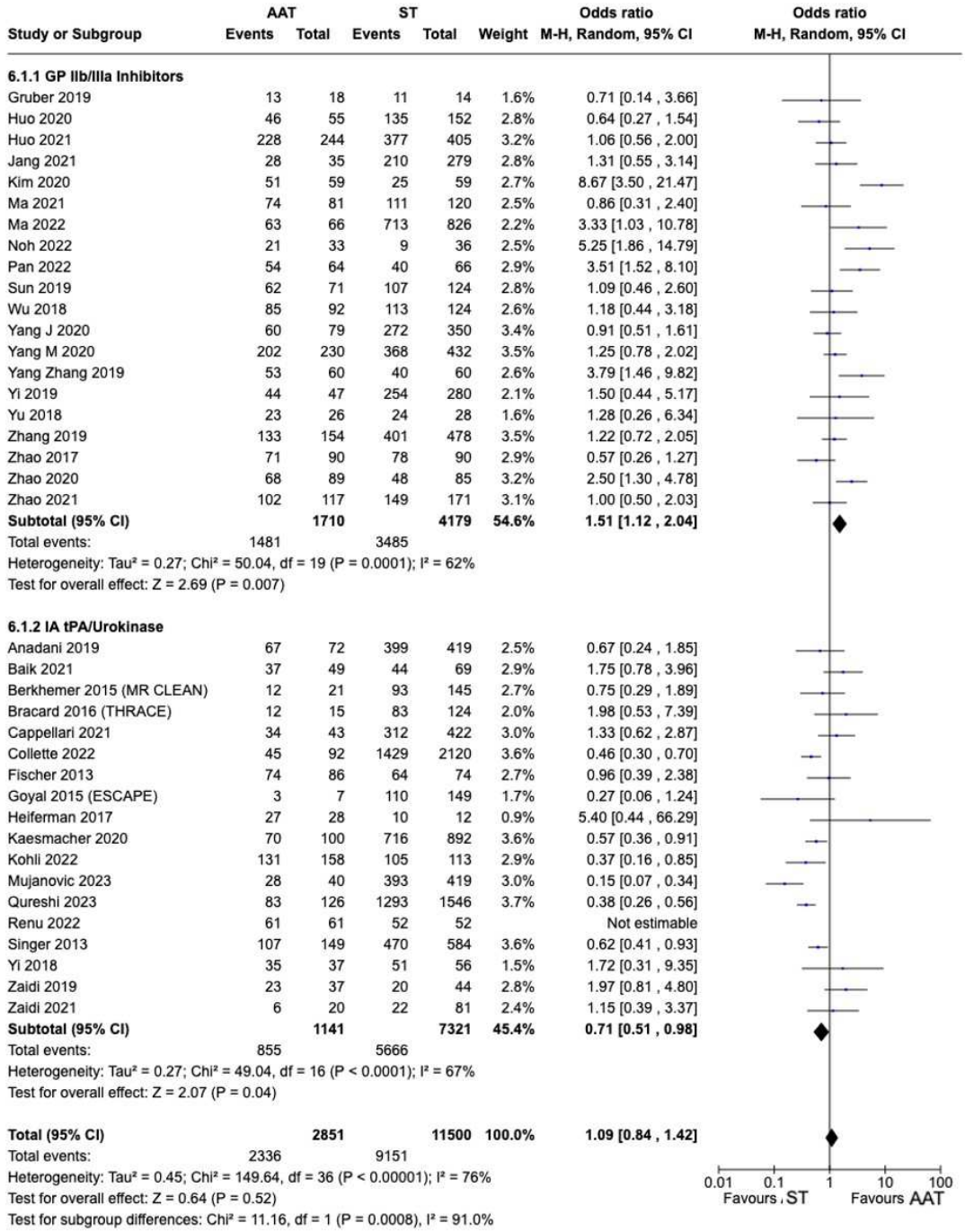
SD=standard deviation, CI=confidence interval, ST = standard therapy, AAT = adjunctive anti-thrombotic therapy, ECASS = European Cooperative Acute Stroke Study, PROACT-II = Prolyse in Acute Cerebral Thromboembolism II, vs=versus, I2=heterogeneity index.

Supplementary Figure 5. Forest plot comparing the odds ratio of any intracranial hemorrhage rates between AAT vs ST groups based on the type of drug used (GPIIb/IIIa, IA-tPA or urokinase).



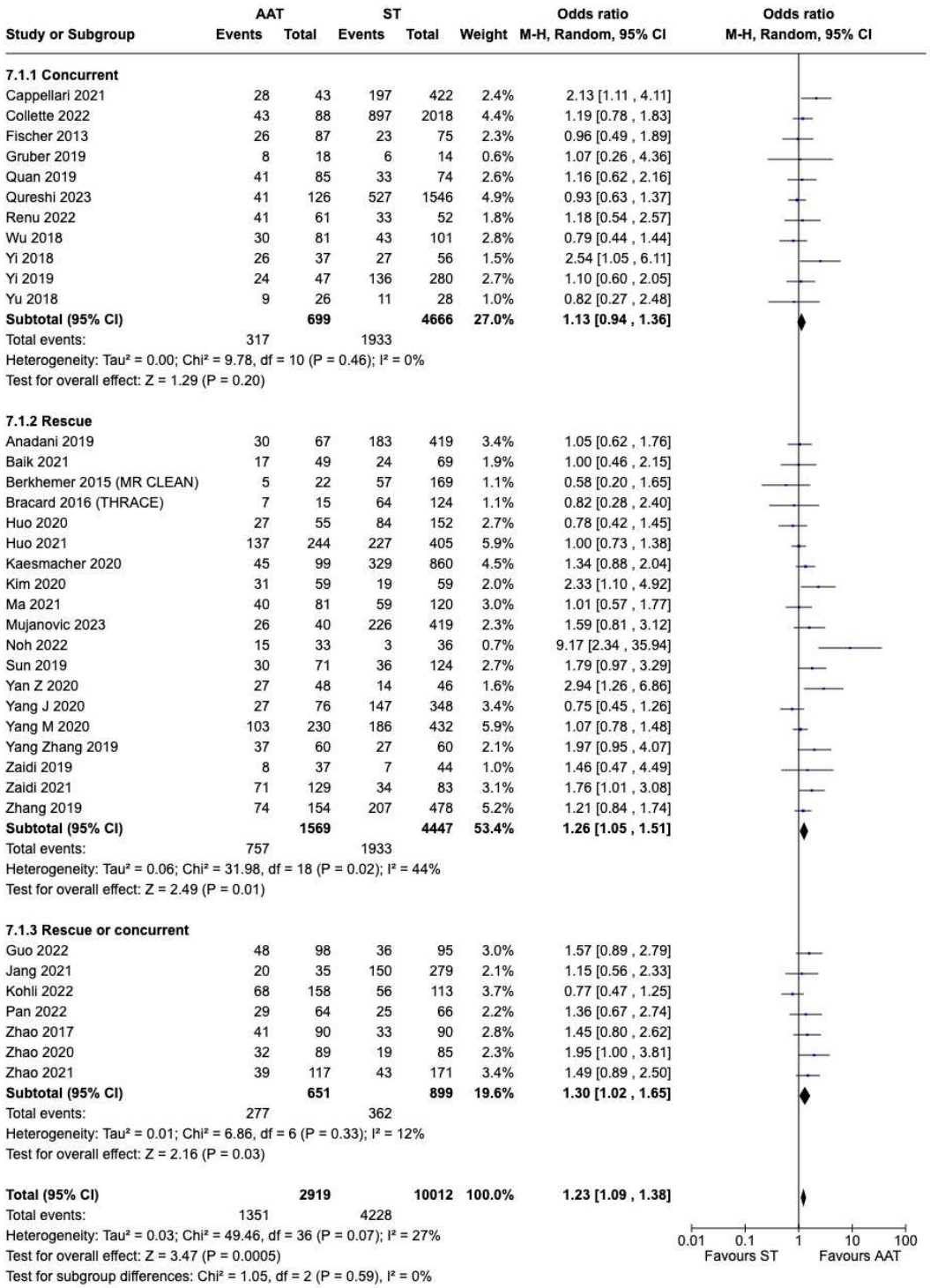
SD=standard deviation, CI=confidence interval, ST = standard therapy, AAT = adjunctive anti-thrombotic therapy, GPIIb/IIIa =glycoprotein IIb/IIIa, IA-tPA= intraarterial tissue plasminogen activator, vs=versus, I2=heterogeneity index.

Supplementary Figure 6. Forest plot comparing the odds ratio of successful recanalisation (TICI ⩾2b) rates between AAT vs ST groups based on the type of drug used (GPIIb/IIIa, IA-tPA or urokinase).



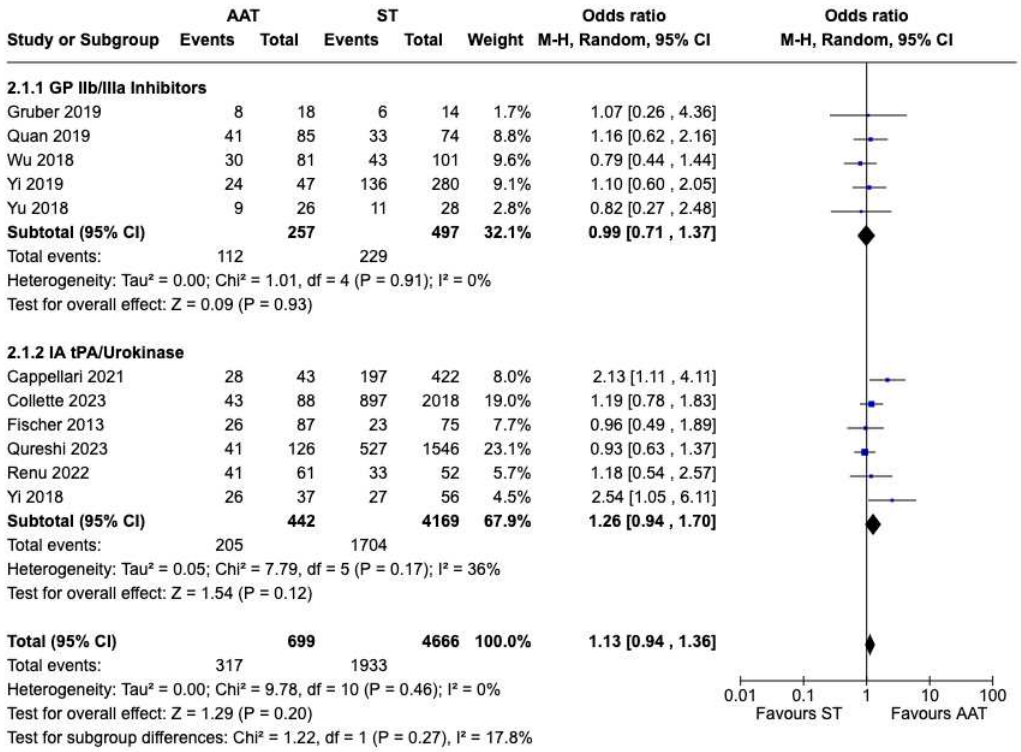
SD=standard deviation, CI=confidence interval, ST = standard therapy, AAT = adjunctive anti-thrombotic therapy, GPIIb/IIIa =glycoprotein IIb/IIIa, IA-tPA= intraarterial tissue plasminogen activator, TICI=thrombolysis in cerebral infarction, vs=versus, I2=heterogeneity index.

Supplementary Figure 7. Forest plot comparing the odds ratio of functional independence at 90 days between AAT vs ST groups based on the treatment indication (rescue, concurrent, rescue or concurrent).



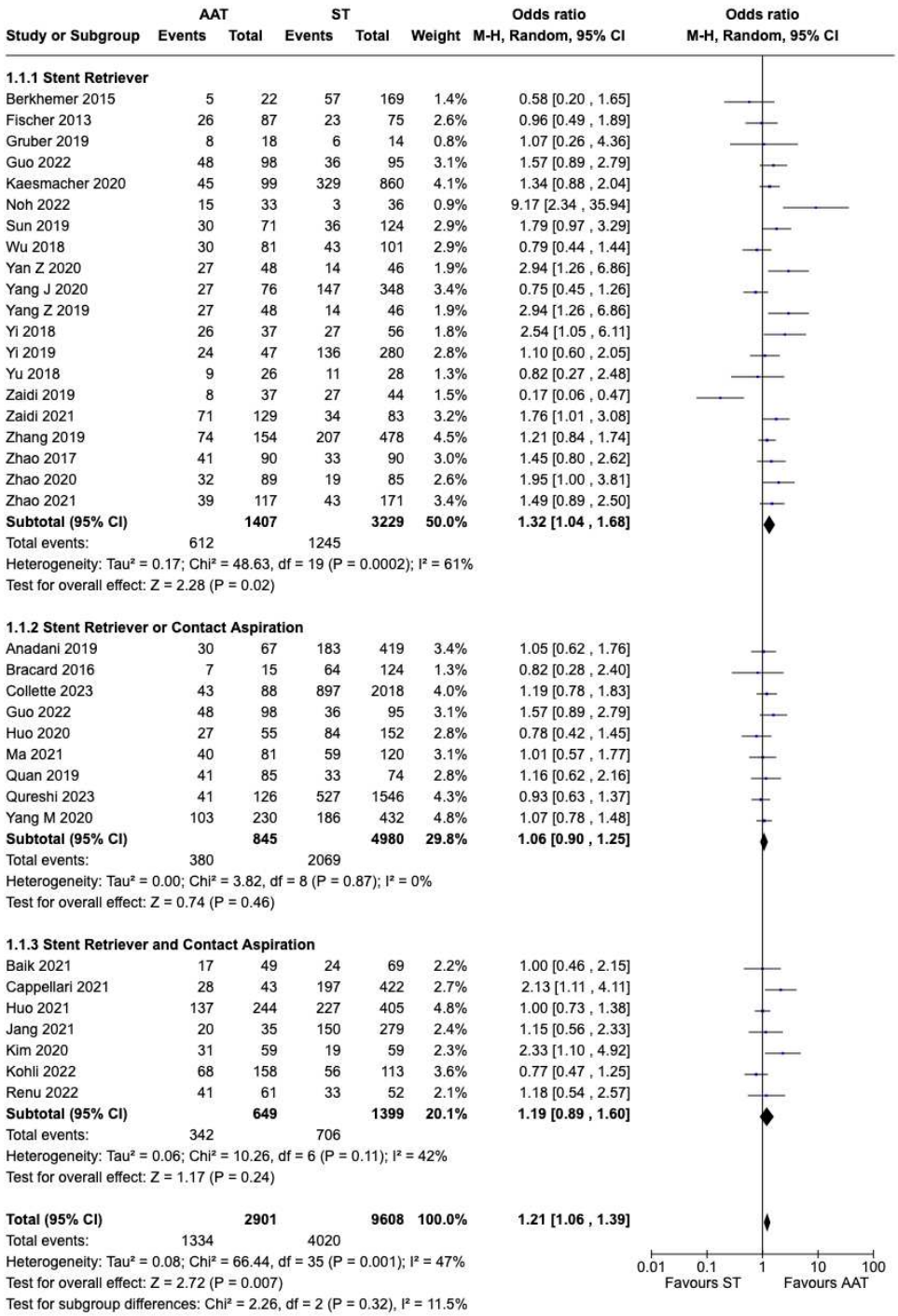
SD=standard deviation, CI=confidence interval, ST = standard therapy, AAT = adjunctive anti-thrombotic therapy, vs = versus, I2 = heterogeneity index.

Supplementary Figure 8. Forest plot comparing the odds ratio of functional independence at 90 days between AAT vs ST groups based on the type of drug used as concurrent treatment (GPIIb/IIIa or IA-tPA).



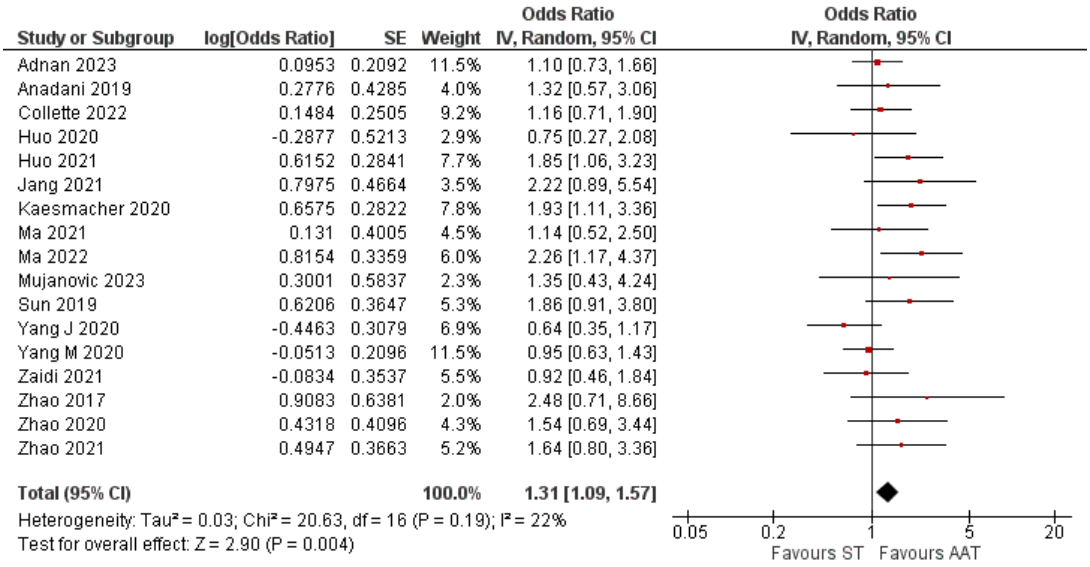
SD=standard deviation, CI=confidence interval, ST = standard therapy, AAT = adjunctive anti-thrombotic therapy, GPIIb/IIIa=glycoprotein IIb/IIIa, IA-tPA= intraarterial tissue plasminogen activator, vs=versus, I^2=heterogeneity index.

Supplementary Figure 9. Forest plot comparing the odds ratio of functional independence at 90 days between AAT vs ST groups based on the type of endovascular thrombectomy technique used (stent retriever, contact aspiration).



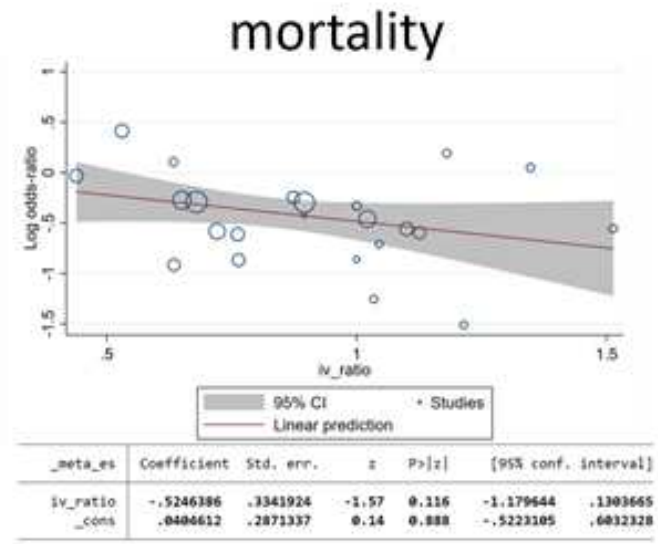
SD=standard deviation, CI=confidence interval, ST = standard therapy, AAT = adjunctive anti-thrombotic therapy, vs=versus, I2=heterogeneity index.

Supplementary Figure 10. Forest plot of the adjusted odds ratios of functional independence at 90 days of the observational studies comparing AAT and ST.

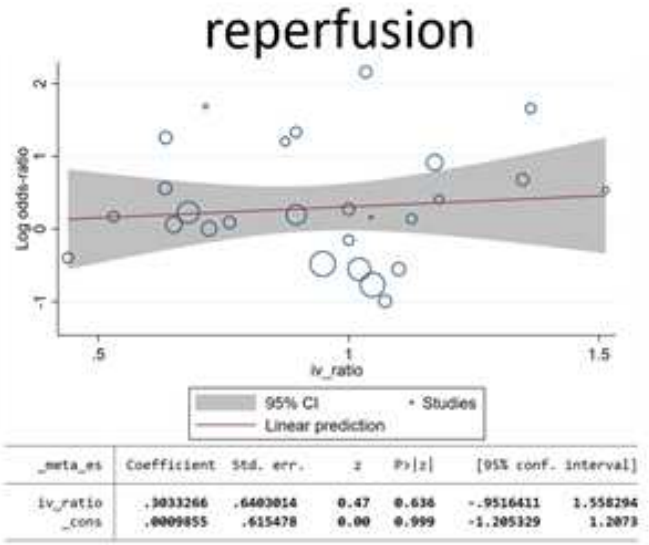


ST = standard therapy, AAT = adjunctive anti-thrombotic therapy, vs=versus, I2=heterogeneity index, SE=standard error, CI=confidence interval, I2=heterogeneity index.

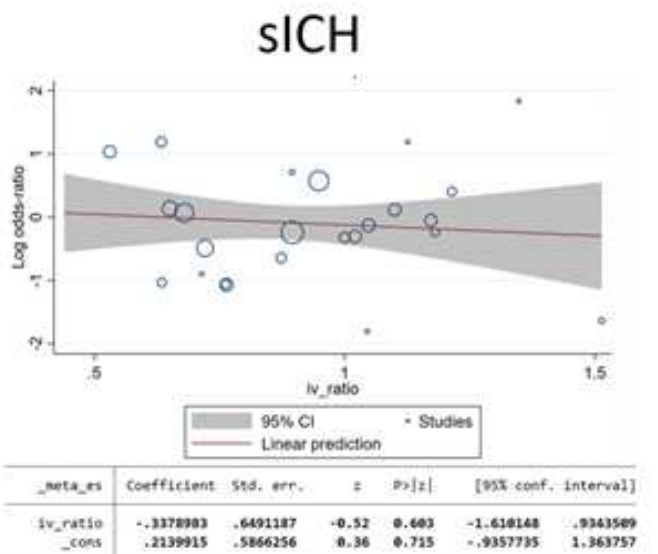
Supplementary Figure 11. Bubble plot and meta-regression of ratio of proportion of patients in adjunctive intraarterial antithrombotic therapy (AAT) arm to standard therapy (ST) arm who received intravenous thrombolysis on mortality, reperfusion, symptomatic intracranial haemorrhage (sICH) and any intracranial haemorrhage (ICH).



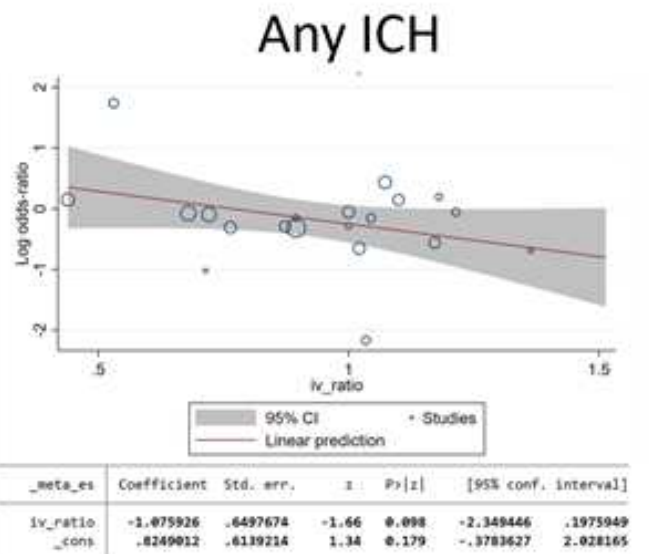
_meta_es	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
iv_ratio	-.5246386	.3341924	-1.57	0.116	-1.179644	.1303665
_cons	.0406612	.2871337	0.14	0.888	-.5223105	.6032328



_meta_es	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
iv_ratio	.3033266	.6403014	0.47	0.636	-.9516411	1.558294
_cons	.0009855	.615478	0.00	0.999	-1.205329	1.2073

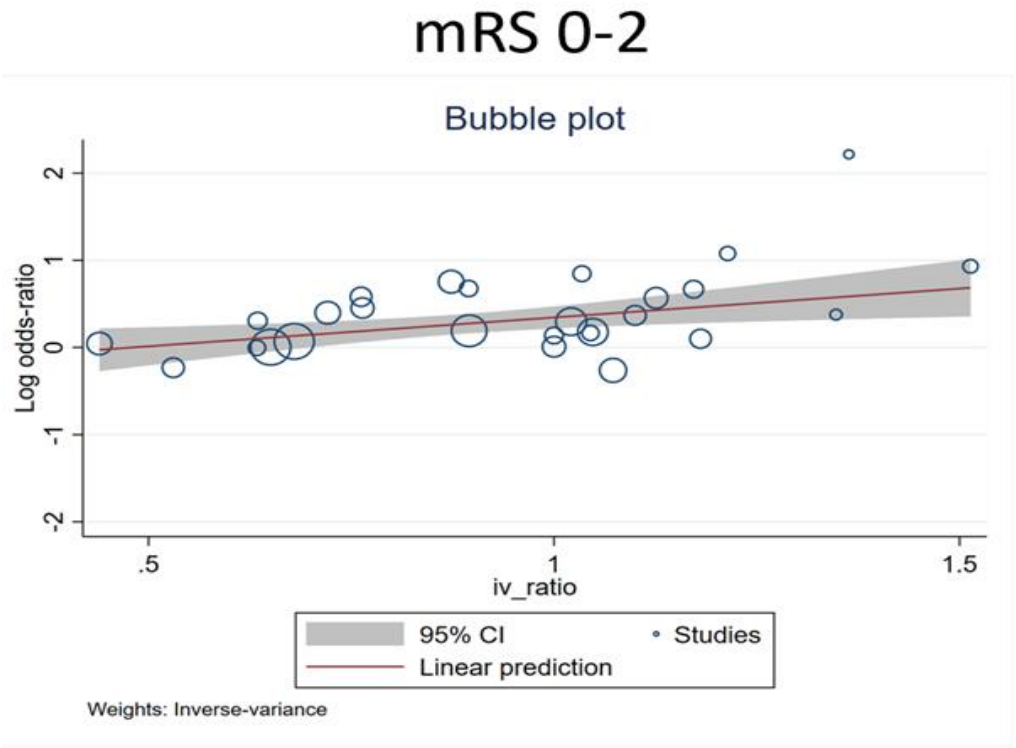


_meta_es	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
iv_ratio	-.3378983	.6491187	-0.52	0.603	-1.610148	.9343509
_cons	.2139915	.5866256	0.36	0.715	-.9357735	1.363757



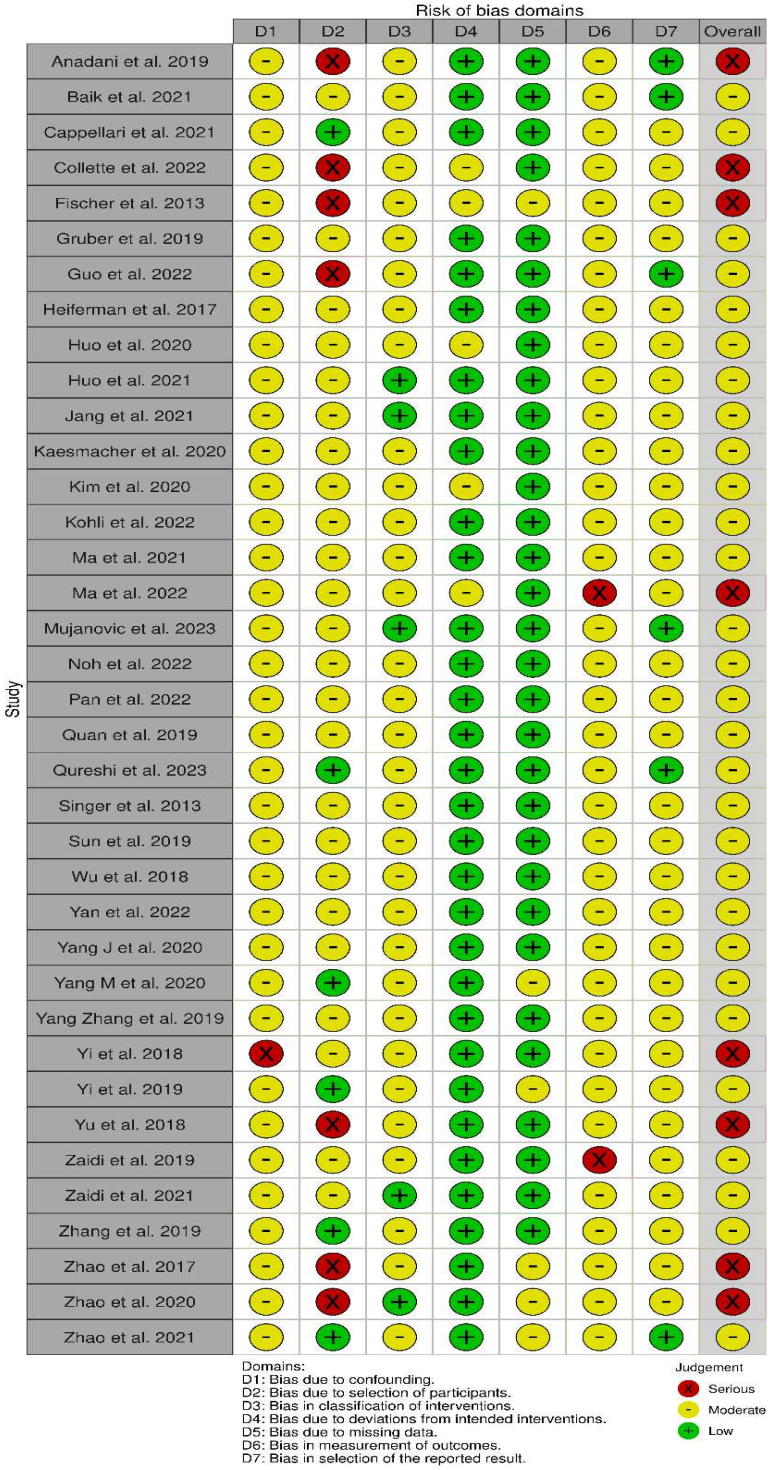
_meta_es	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
iv_ratio	-1.075926	.6497674	-1.66	0.098	-2.349446	.1975949
_cons	.8249012	.6139214	1.34	0.179	-.3783627	2.028165

Supplementary Figure 12. Bubble plot and meta-regression of ratio of proportion of patients in adjunctive intra-arterial antithrombotic therapy (AAT) arm to standard therapy (ST) arm who received intravenous thrombolysis (IVT) on functional independence (modified Rankin Scale 0-2) at 90 days.

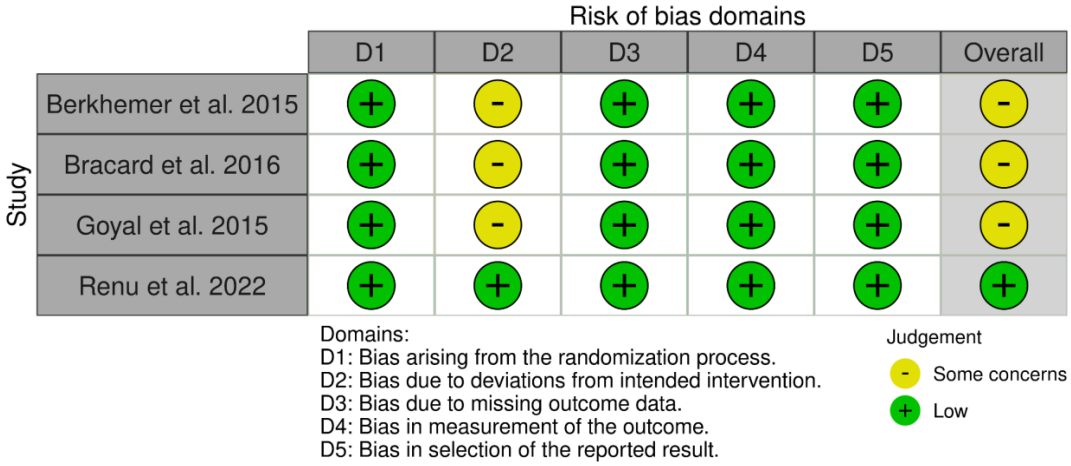


_meta_es	Coefficient	Std. err.	z	P>|z|	[95% conf.	interval]
iv_ratio	.6619404	.2495642	2.65	0.008	.1728036	1.151077
_cons	-.3176149	.2277989	-1.39	0.163	-.7640926	.1288628

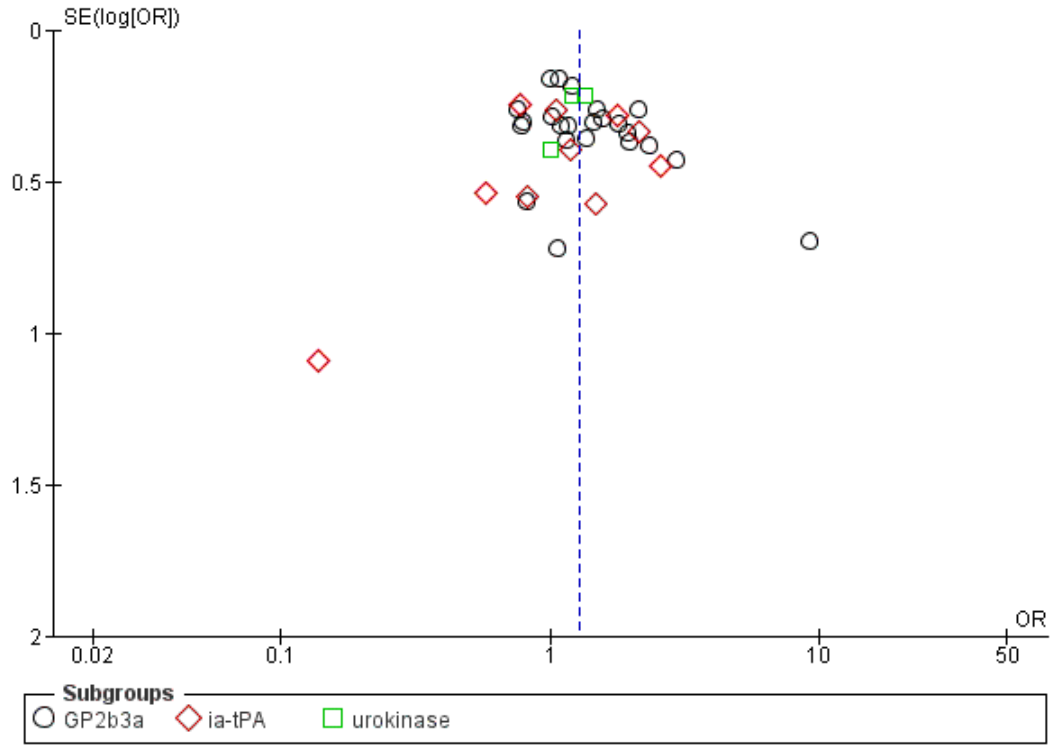
Supplementary Figure 13. Risk Of Bias In Non-randomised Studies of Interventions (ROBINS-I) assessment.



Supplementary Figure 14. Risk-of-Bias (RoB 2) assessment of randomised trials.



Supplementary Figure 15. Funnel plot for good clinical outcome in intraarterial adjunctive therapy (standard therpay vs adjunctive intraarterial antithrombotic therapy) by the type of the drug used; GP2b3a=glycoprotein IIb/IIIa, IA-tPA= intraarterial tissue plasminogen activator.



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