Table S1. Studies included in the review

Author	Total sample size	Mean age for total sample	Male % for total sample	Imaging modality	Country
Larrue V, et al, 1997 [1]	609, ECASS 1	65	55.4%	CT	14 European countries
Fiorelli M, et al, 1999 [2]	ECASS 1	Not given	Not given	CT	Europe, Australia, New Zealand
Molina CA, et al, 2001 [3]	53	73.7	32%	CT	Spain
Montaner J, et al, 2001 [4]	39	77.6 [4]	50%	CT	Spain
Larrue V, et al, 2001 [5]	ECASS 2	Not given	Not given	CT	Europe, Australia, New Zealand
Hermier M, et al, 2003 [6]	58	63	43.1%	MRI	France
Montaner J, et al, [7]	41	70+/-10.6	39%	CT	Spain
Montaner J, et al, 2003 [8]	61	71+/-9.3	44.3%	CT	Spain
Celik Y, et al, 2004 [9]	86 Consecutive MCA pts, no antithrombotic tx	68.1	47.7%	CT	Turkey
Castellanos M, et al, 2004 [10]	87	67	69.8%	CT	Spain
Ribo M, et al, 2004 [11]	77	70	60%	CT	Spain
Rodriguez-Yanez M, et al, 2006 [12]	200	72.5	51.5%	CT	Spain
IMS study group, 2006 [13]	80	Not given	Not given	CT	USA
Dzialowski I, et al, 2007 [14]	954	67.1	55%	CT	Canada
Millan M, et al, 2007 [15]	134	67	65.7	CT	France, Spain
Thomalla G, et al, 2007 [16]	152	64	61.2%	CT/MRI	Germany
Paciaroni M, et al, 2008 [17]	1125 consecutive AIS pts	76	55.9%	CT	Italy
Kimura K, et al, 2008 [18]	51	73	43%	MRI	Japan
Hjort N, et al, 2008 [19]	33	68	Not given	MRI	Denmark
Mendioroz M, et al, 2009 [20]	119	71.8	59%	CT	Spain
Aviv RI, et al, 2009 [21]	41	70.3+15.4	63%	MRI	Canada
Butcher K, et al, 2010 [22]	97, EPIPHET RCT	71.2+14	55%	MRI	Canada, Australia, New Zealand
Campbell BCV, et al, 2010 [23]	91, EPIPHET RCT	71.4	53.8%	MRI	Australia, UK, New Zealand, Belgium

Kim JH, et al, 2010 [24]	184 consecutive MCA AIS pts	65.7	53.8%	MRI	USA S Korea
Prodan CI, et al, 2010 [25]	115	64.6	71%	CT/MRI	USA
Hernandez-Guillamon M, et al, 2010 [26]	141	Not given	Not given	CT	Spain
Sobrino T, et al, 2010 [27]	79	66.7	54.4%	CT	Spain
Ko Y, et al, 2010 [28]	786 consecutive AIS pts	70	60.6%	CT/MRI	S Korea
Choi KH, et al, 2012 [29]	752 consecutive first AIS pts	65.9	59.9%	MRI	Korea
Leira R, et al, 2012 [30]	161	70.6	Not given	MRI	Spain
del Rio-Espínola A, et al, 2012 [31]	885	Not given	75.5%	CT	Spain
El-Khawas HM, et al, 2012 [32]	324 consecutive AIS pts.	60.5	Not given	MRI	Egypt
Costello CA, et al, 2012 [33]	206	71	68.4%	CT	Australia
Takahashi W, et al, 2013 [34]	187	74	40.1%	CT/MRI	Japan
Jain AR, et al, 2013 [35]	83 consecutive AIS pts	72	55.4%	CT/MRI	USA
Kufner A, et al, 2013 [36]	109	71.3+-12.5	50%	MRI	Germany
Lee JG, et al, [37]	770 consecutive AIS pts.	70.3	56.1%	MRI	Korea
Yassi N, et al, 2013 [38]	132	74	Not given	CT/MRI	Australia
Pereira VM, et al, 2013 [39]	202, STAR clinical trial	72	40%	CT/MRI	Europe, Canada, Australia
Rodriguez-Gonzalez R, et al, 2013 [40]	129	66.5	56.7%	CT	Spain
Jickling GC, et al, 2013 [41]	44, CLEAR trial	68.7	63.6%	CT	USA
Cortijo E, et al, 2014 [42]	69	71.8	52%	CT	Spain
Hong JM, et al, 2014 [43]	75	66.2	59%	CT	S Korea
Llombart V, et al, 2014 [44]	186	71.5	53.8%	CT	Spain
Öcek L, et al 2015 [45]	171	71.2	55%	CT/MRI	Turkey
d'Esterre C, et al, 2015 [46]	55	67.3	41.8%	CT	Canada, Italy
Renú A, et al, 2015 [47]	132 endovascular therapy	67	47.7%	CT/MRI	Spain
Liu C, et al, 2015, [48]	87	67.3	56.3%	MRI	China
Guo Y, et al, 2015 [49]	362	67.7	63.2%	CT/MRI	China

Jia W, et al, 2015 [50]	904	63.6	38.3%	CT	China
Maeshima S, et al, 2016 [51]	165	Not given	38.1%	CT	Japan
Shi ZS, et al, 2016 [52]	206 endovascular therapy	66.8	42.2%	CT/MRI	Korea
Bivard A, et al, 2016 [53]	229	68	Not given	MRI	Australia and China
Cappellari M, et al, 2016 [54]	147	79	38%	CT	Italy
Purrucker J, et al, 2016 [55]	28	74	54%	CT/MRI	Germany
Gioia L, et al, 2016 [56]	66	71	67%	MRI	Canada
Heo J, et al, 2016 [57]	289 EUREKA RCT	64.5	59.9%	MRI	Korea
Liu J, et al, 2016 [58]	130	68.15	43.1%	MRI	China
Ho BL, et al, 2016 [59]	241 TTT-AIS Study	65.8	60.2%	CT	Taiwan
Guo Z, et al, 2016 [60]	189	65	65%	CT	China
Bas DF, et al, 2016 [61]	180	63.1	62%	CT	Turkey
Chen X, et al, 2017 [62]	316	66.3	62.3%	CT	China
Wei CC, et al, 2017 [63]	251	68.5	39.4%	MRI	China
Castro P, et al, 2017 [64]	46	73	54%	CT	Portugal
Purrucker JC, et al, 2017 [65]	231	77.4	53.2%	CT/MRI	Germany

Table S2. Studies Included in Individual Analyses.

Study Characteristics	**Number**
Number of studies analyzing HT with CT	**34**
Number of studies analyzing HT with MRI	18
Number of studies analyzing HT with a combination of CT and MRI	13
Number of studies published before 2000	3
Number of studies published after 2000	62
Number of studies including data from East Asia	19
Number of studies including data from Europe	35
Number of studies including data from North America	11
Number of studies including data from the Middle East (Egypt)	1

Table S3. Baseline Patient Characteristics

Variable		HT vs non-HT	PH vs non-PH	PH vs HI
Baseline patient characteristics				
Age **HG**	W/O tPA	0.1 (-0.124–0.325) 3 studies [12, 25, 30]	0.121 (-0.516–0.758) 1 study [30]	0.115 (-0.56–0.791) 1 study [30]
	With tPA	0.3 (-0.249–0.849) 4 studies [10, 18, 26, 41]	**0.271** (0.037–0.505) 5 studies [20, 26, 27, 40, 59] 102 vs 552	NG
	Total pts. included	**0.125** (0.048–0.202) 15 studies [1, 9, 10, 12, 18, 22, 24-26, 30, 32, 37, 41, 52, 62] 968 vs 2512	**0.215** (0.087–0.344) 10 studies [1, 20, 22, 24, 26, 27, 30, 40, 52, 60] 273 vs 1729	**0.267** (0.084–0.45) 5 studies [1, 22, 24, 30, 52] 161 vs 386
Male **OR**	W/O tPA	1.71 (0.55–5.33) 3 studies [3, 12, 25]	5.07 (0.48–54.02) 1 study [8]	4.16 (0.33–50) 1 study [8]
	With tPA	0.89 (0.7–1.14) 5 studies [10, 12, 14, 25, 26]	1.37 (0.78–2.40) 7 studies [9, 13, 14, 26, 27, 40, 60]	1.08 (1.92–0.61) 2 studies [14, 26]
	Total pts. included	1.07 (0.88–1.31) 18 studies [1, 3, 10, 12, 14, 17, 18, 23-26, 29, 37, 41, 52, 56, 62, 64] 744/1282 vs 2568/4527	**1.50 (1.07–2.11)** 14 studies [1, 7, 9, 13, 14, 17, 23, 24, 26, 27, 29, 40, 52, 60] 281/431 vs 2395/4263	**1.43 (1–2)** 9 studies [1, 7, 14, 17, 23, 24, 26, 29, 52] 204/326 vs 352/640
Chronic hypertension **OR**	W/O tPA	1.67 (0.52–5.32) 4 studies [3, 12, 30, 45]	1.74 (0.54–5.54) 2 studies [30, 45]	2.69 (0.85–8.53) 3 studies [7, 30, 45]
	With tPA	1.74 (0.85–3.55) 2 studies included [14, 26]	**1.51 (1.10–2.07)** 6 studies [14, 20, 26, 27, 40, 60] 124/194 vs 745/1414	1.54 (0.96–2.48) 2 studies [14, 26] 64/108 vs 97/199
	Total pts. included	1.21 (0.86–1.71) 11 studies [1, 3, 12, 14, 17, 24, 26, 29, 30, 38, 45] 562/996 vs 2170/3485	**1.29 (1.04–1.61)** 12 studies [1, 14, 17, 20, 24, 26, 27, 29, 38, 40, 45, 60] 248/392 vs 2665/4350	1.31 (0.87–1.96) 8 studies [1, 14, 17, 24, 26, 29, 30, 38] 192/310 vs 340/649
Previous Diabetes **OR**	W/O tPA	1.41 (0.66–3.03) 5 studies [3, 12, 25, 30, 45]	NG	2.4 (0.96–6.02) 3 studies [7, 30, 45]
	With tPA	0.97 (0.69–1.38) 4 studies [14, 18, 26, 41]	NG	1 (0.1–9.91) 2 studies [14, 26]
	Total pts. included	1.23 (0.97–1.56) 21 studies [1, 3, 9, 12, 14, 17, 18, 22-26, 28-30, 37, 38, 41, 45, 62, 63] 339/1466 vs 1318/5571	NG	**1.66 (1.05–2.61)** 11 studies [1, 7, 14, 17, 23, 24, 26, 29, 30, 38, 45] 83/323 vs 117/680
Hyperlipidemia **OR**	W/O tPA	**0.53 (0.31–0.93)** 3 studies [3, 30, 45]	0.81 (0.29–2.26) 2 studies [30, 45]	1.14 (0.37–3.46) 3 studies [7, 30, 45]

	With tPA	0.52 (0.25–1.06) 2 studies [26, 41]	1.25 (0.61–2.58) 5 studies [20, 26, 27, 40, 60]	0.82 (0.18–3.73) 1 study [26]
	Total pts. included	0.8 (0.62–1.03) 10 studies [3, 26, 28, 30, 37, 38, 41, 45, 62, 64] 101/452 vs 529/2167	1.02 (0.57–1.84) 8 studies [20, 26, 27, 30, 38, 40, 45, 60] 56/138 vs 338/980	0.76 (0.33–1.75) 5 studies [7, 26, 30, 38, 45] 9/56 vs 29/136
Alcohol Abuse **OR**	W/O tPA	1.47 (0.55–3.9) 1 study	1.97 (0.39–10.05) 1 study	1.62 (0.28–9.56) 1 study
	With tPA	NG	NG	NG
	Total pts. included	1.32 (0.92–1.88) 4 studies [17, 29, 30, 63] 56/342 vs 228/1947	1.02 (0.5–2.08) 3 studies [17, 29, 30] 10/78 vs 225/1960	1.15 (0.49–2.72) 3 studies [17, 29, 30] 10/78 vs 20/165
Prev. anticoagulation **OR**	W/O tPA	NG	NG	NG
	With tPA	NG	NG	NG
	Total pts. included	**2.47 (1.64–3.72)** 4 studies [17, 32, 37, 63] 40/378 vs 86/2092	**2.9 (1–8.55)** 1 study [17] 4/36 vs 46/1089	1.81 (0.42–7.74) 1 study [17] 4/36 vs 4/62
Prev. Antiplatelets **OR**	**W/O tPA**	0.64 (0.18–2.32) 1 study [25]	NG	NG
	With tPA	1.18 (0.84–1.66) 1 study [14]	**3.15 (1.39–7.17)** 4 studies [14, 27, 40, 60] 61/165 vs 237/1186	1.43 (0.8–2.57) 1 study [14]
	Total pts. included	1.01 (0.83–1.23) 8 studies [1, 17, 25, 32, 37, 55, 62, 63] 232/937 vs 1080/3527	**2.25 (1.26–4.02)** 6 studies [1, 14, 17, 27, 40, 60] 85/263 vs 630/2822	1.38 (0.66–2.87) 3 studies [1, 14, 17] 50/190 vs 78/414
Prev. Statins **OR**	**W/O tPA**	0.36 (0.45–1.29) (25)	NG	NG
	With tPA	NG	**3.58 (1.41–9.05)** 2 studies [27, 40]	NG
	Total pts. included	0.76 (0.45–1.29) 6 studies [17, 24, 25, 37, 57, 63] 54/440 vs 366/2294	2.15 (0.98–4.76) 4 studies[17, 24, 27, 40] 31/113 vs 146/1404	1.27 (0.2–8.15) 2 studies [17, 24] 10/68 vs 11/103
Atrial Fibrillation **OR**	**W/O tPA**	**4 (1.00–15.92)**	5.1 (0.69–37.86)	**4.27 (1.13–16.23)**
	With tPA	1.98 (0.55–7.14)	1.26 (0.83–1.9)	0.75 (0.41–1.38)
	Total pts. included	**2.85 (1.86–4.38)** 15 studies [1, 12, 14, 17, 18, 22, 23, 29, 30, 32, 38, 41, 45, 62, 64] 381/1039 vs 795/3943	**2.25 (1.47–3.44)** 12 studies [1, 14, 17, 22, 23, 27, 29, 30, 38, 45, 60] 146/359 vs 942/4156	**2.09 (1.26–3.48)** 9 studies [1, 14, 17, 22, 23, 29, 30, 38, 45] 118/286 vs 186/627
LDL level **HG**	**W/O tPA**	**-0.657 (-0.288– -1.03)** 1 study [45]	-0.089 (-0.673–0.496) 1 study [45]	0.234 (-0.442–0.909) 1 study [45]
	With tPA	NG	NG	NG
	Total pts. included	**-0.304 (-0.124– -0.483)**	-0.075 (-0.304–0.155)	0.018 (-0.259–0.296)

		5 studies [17, 24, 32, 45, 63] **356 vs 1699**	3 studies [17, 24, 45] 80 vs 1400	3 studies [17, 24, 45] 80 vs 128

Table S4. Patient data upon admission

Variable		HT vs non-HT	PH vs non-PH	PH vs HI
Systolic BP	W/O tPA	-0.101 (-0.407–0.202)	-0.445 (-1.032–0.14)	**-0.759 (-0.063– -1.454)** **1 study [45]** **12 vs 25**
	With tPA	0.05 (-0.188–0.285)	**0.34 (0.11–0.569)** **4 studies [26, 27, 40, 60]** **89 vs 448**	NG
	Total pts.	0.043 (-0.056–0.141) 12 studies [3, 9, 10, 18, 22, 26, 28, 37, 41, 45, 63, 64] 547 vs 2035	**0.217 (-0.02–0.454)** **6 studies [22, 26, 27, 40, 45, 60]** **116 vs 689**	-0.227 (-1.24–0.786) 2 studies [22, 45] 27 vs 57
Diastolic BP	W/O tPA	-0.213 (-0.519–0.094)	-0.353 (-0.94–0.232)	-0.483 (-1.166–0.2)
	With tPA	0.08 (-0. 15–0.312)	-0.102 (-0.445–0.24)	NG
	Total pts.	0.031 (-0.073–0.136) 12 studies [3, 9, 10, 18, 22, 26, 28, 37, 41, 45, 63, 64] 597 vs 2034	-0.16 (-0.388–0.068) 5 studies [22, 26, 27, 40, 45] 88 vs 528	-0.37 (-0.823–0.082) 2 studies [22, 45] 27 vs 57
Glucose	W/O tPA	0.159 (-0.201–0.52)	0.409 (-0.177–0.995)	0.429 (-0.251–1.11)
	With tPA	0.284 (-0.048–0.617)	0.247 (-0.031–0.529)	NG
	Total pts.	**0.189 (0.085–0.293)** **13 studies [3, 9, 10, 17, 18, 22, 24, 26, 28, 37, 41, 45, 63]** **708 vs 3137**	**0.315 (0.146–0.483)** **7 studies [17, 22, 24, 26, 27, 40, 45]** **156 vs 1769**	**0.418 (0.163–0.673)** **4 studies [17, 22, 24, 45]** **95 vs 160**
NIHSS	W/O tPA	NG	NG	NG
	With tPA	**0.933 (0.358–1.510)**	NG	NG
	Total pts. included	**0.964 (0.477–1.45)** **6 studies [18, 23, 24, 32, 52, 62]** **321 vs 851**	**0.454 (0.217–0.691)** **3 studies [23, 24, 52]** **84 vs 382**	**0.438 (0.159–0.718)** **3 studies [23, 24, 52]** **84 vs 124**

Table S5. Prognostic follow-up of patients with hemorrhagic transformation

Variable		HT vs non-HT	PH vs non-PH	PH vs HI
mRS 5-6	W/O tPA	1.64 (0.93–2.9) 1 study [5]	2 (0.3–1.02) 1 study [5]	1.55 (0.39–6.12) 1 study [5]
	With tPA	**2.22 (1.7–2.92)** **2 studies [5, 14]**	**6.25 (3.2–12.3)** **2 studies [5, 14]**	**5.53 (2.28–13.40)** **2 studies [5, 14]**
	All patients	**2.16 (1.7–2.75)** **4 studies [1, 5, 14, 23]** **181/646 vs 207/1192**	**5.4 (3.2–9.1)** **4 studies [1, 5, 14, 23]** **88/165 vs 300/1673**	**4.25 (2.22–8.14)** **4 studies [1, 5, 14, 23]** **88/165 vs 93/481**
mRS 0-1	W/O tPA	NG	NG	NG
	With tPA	**0.48 (0.25–0.95)** **2 studies [14, 16]**	0.35 (0.10–1.28) 2 studies [14, 16]	0.5 (0.22–1.15) 2 studies [14, 16]
	All patients	**0.45 (0.28–0.71)** **3 studies [14, 16, 23]** **92/378 vs 342/819**	**0.35 (0.15–0.86)** **3 studies [14, 16, 23]** **18/120 vs 416/1077**	**0.5 (0.27–0.9)** **3 studies [14, 16, 23]** **18/120 vs 74/258**

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