MEDICAL SCIENCE MONITOR

REVIEW ARTICLES

e-ISSN 1643-3750
© Med Sci Monit, 2014; 20: 2117-2124
DOI: 10.12659/MSM.892259

Received: 2014.08.17
Accepted: 2014.09.03
Published: 2014.11.02

Safety and Outcome of Thrombolysis in Mild Stroke: A Meta-Analysis

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Source of support: Self financing

Background: Whether patients presenting with mild stroke should or should not be treated with intravenous rtPA is still controversial. This systematic review aims to assess the safety and outcome of thrombolysis in these patients.

Material/Methods: We systematically searched PubMed and Cochrane Central Register of Controlled Trials for studies evaluating intravenous rtPA in patients with mild or rapidly improving symptoms except case reports. Excellent outcome (author reported, mainly mRS 0-1), symptomatic intracranial hemorrhage (sICH) and mortality were analyzed.

Results: Fourteen studies were included (n=1906 patients). Of these, 4 studies were comparative (2 randomized and 2 non-randomized). The remaining were single-arm studies. On the basis of 4 comparative studies with a total of 1006 patients, the meta-analysis did not identify a significant difference in the odds of excellent outcome (OR=0.86; 95% CI: 0.64–1.15; I^2=0) between IV rtPA-treated minor stroke and those without rtPA treatment. Eleven studies involving 1083 patients showed the pooled rate of excellent outcome was 76.1% (95% CI: 69.8–81.5%, I^2=42.5). Seven studies involving 378 patients showed the mortality rate was 4.5% (95% CI: 2.6–7.5%, I^2=1.4). Twelve studies involving 831 patients showed the pooled rate of sICH was 2.4% (95% CI: 1.5–3.8, I^2=0).

Conclusions: Although efficacy is not clearly established, this study reveals the adverse event rates related to thrombolysis are low in mild stroke. Intravenous rtPA should be considered in these patients until more RCT evidence is available.

MeSH Keywords: **Intracranial Thrombosis • Meta-Analysis • Stroke**

Abbreviations: **sICH** –symptomatic intracranial hemorrhage; **IV rtPA** – intravenous thrombolysis with recombinant tissue plasminogen activator; **mRS** – Modified Rankin Scale; **NIHSS** – National Institute of Health Stroke Scale; **RCT** – randomized controlled trials; **IST-3** – The Third International Stroke Trials; **ECASS III** –European Cooperative Acute Stroke Study

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Background

Intravenous thrombolysis with recombinant tissue plasminogen activator (IV rtPA) applied within 3 hours or 4.5 hours is efficacious in acute ischemic stroke patients [1–3]. However, few ischemic stroke patients are treated with IV rtPA due to the narrow time window for treatment [4,5]. However, even patients who would generally be eligible are often not treated because of mild stroke or clinical improvement, perceived protocol exclusions, emergency department referral delay, and significant comorbidity [5]. It is very common to not treat patients with mild or rapidly improving symptoms because of an uncertain risk-benefit ratio. In studies evaluating eligibility for thrombolysis, up to 43% of patients with mild or improving stroke symptoms do not receive thrombolytic therapy [6].

However, according to recent reports, 15–31% of patients with mild or rapidly improving symptoms are dependent or dead during hospital admission without thrombolysis [4–7]. In contrast, some researchers have reported that mild stroke patients also benefited from IV thrombolysis, and up to 94% achieved excellent 3-month outcome (modified Rankin Scale, mRS 0–1) [8–10]. At present, no one has truly tested the effectiveness of IV rtPA in mild stroke versus placebo. Studies evaluating intravenous rtPA in mild stroke patients are limited by small sample sizes and non-controlled comparison groups. Until more RCT evidence is available, a systematic review of all studies can provide useful information on the odds for benefits and risks of IV rtPA in patients with mild or rapidly improving symptoms and help decision-making for individual treatment. We therefore conducted this systematic review to assess the safety and outcome of thrombolysis in these patients.

Material and Methods

Search strategy and Eligibility Studies

We systematically searched PubMed (from its earliest date to April 2013), Embase (1980 to May 2013), and Cochrane Central Register of Controlled Trials (The Cochrane library 2013, issue 3) for studies evaluating thrombolysis in patients with mild or rapidly improving symptoms. The terms 'Minor stroke', 'Mild deficit', 'Mild symptom', 'Mild stroke', 'Stroke with rapidly improving symptoms', 'Thrombolysis', 'Intravenous tissue plasminogen activator', and 'rt-PA' were combined using 'And' or 'Or' for searching relevant studies. The bibliographies of relevant articles were screened. Studies were included if the following criteria were fulfilled: (1) we considered both comparative (randomized or nonrandomized) and single-arm studies; (2) all patients had been treated for IV rtPA; (3) at least 10 patients were enrolled; (4) at least 1 of following outcomes was reported: functional outcome, mortality, or sICH. Articles were excluded if they were case reports. In case of multiple publications from the same study population, only the report with the most complete data was included.

Selection of studies and data extraction

One reviewer independently screened the titles and abstracts of every record. The full articles were obtained when the information given in the title or abstracts conformed to the selection criteria outlined previously. Two reviewers independently performed data extraction and compared the results. The data extraction form included contents as follows: (1) general characteristics of studies and patients, (2) sample size, (3) the diagnostic criteria for mild stroke, (4) outcome measurements (mRS, Mortality, sICH). Articles that met all inclusion criteria but in which specific data extraction was not possible were marked as "NG" (not given). Discrepancies were resolved by consensus.

Statistical methods

For comparative studies, results for dichotomous outcomes were expressed as odds ratios (OR) with 95% confidence intervals (CI) and we also obtained the pooled proportions for excellent outcome, mortality, and sICH, including both comparative and single-arm studies. We considered p-values less than 0.05 to be statistically significant.

We evaluated heterogeneity among included studies using the I^2 test. We considered a value greater than 50% to indicate substantial heterogeneity. Regardless of the size of heterogeneity, a random effects model was used for statistical analysis. We conducted the meta-analysis using Cochrane RevMan 5.1 software and Meta-analyst (version 3.13beta; Tufts Medical Center) [11].

Results

Studies identified

The selection of studies is depicted in Figure 1. The initial literature search identified 461 relevant articles. After reading titles and abstracts, we retained 32 studies for further assessment; of these, we excluded 20 studies [12–31]. Two additional studies were included by reference list screening. Ultimately, 14 studies, containing 1906 patients, were included in this systematic review [8–10,32–42]. Two studies were subgroup analyses from previous RCTs (NINDS 1995 and IST-3) [9,37]. The remaining studies were observational studies (single-arm), of which 2 studies had a concurrent control group. Thus, 4 studies (2 randomized and 2 nonrandomized) contributed data to both the rtPA group and the non-rtPA group. The number of participants ranged from 19 to 535 (Table 1).

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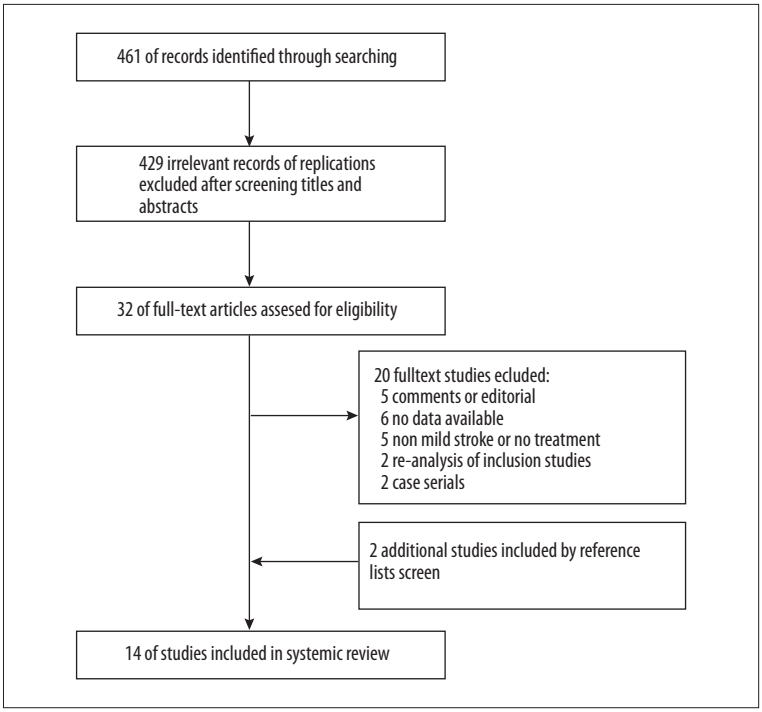

Figure 1. Flow chart of literature screening and selection process.

Characteristics of included studies

The mean age of participants ranged from 59 to 70 years. The proportion of male participants was 55.6-78.9% among these trials. Most of studies enrolled patients treated within 3 hours. All studies except 1 used NIHSS as criteria for mild stroke. Usual cut-off to define mild stroke was NIHSS 4, 5, or 6. More details are given in Tables 1 and 2.

Outcome rates

Four comparative studies evaluated the effect of IV rtPA on excellent outcome. On the basis of these studies with a total of 1006 patients, the meta-analysis did not identify a significant difference in the odds of excellent outcome (OR=0.86; 95% CI: 0.64–1.15; I^2=0) between IV rtPA-treated minor stroke and those without rtPA treatment (Figure 2).

We also calculated the pooled proportions for excellent outcome, mortality, and sICH, including both comparative and single-arm studies in patients with mild stroke receiving IV rtPA. The excellent outcome was available for 11 studies (1083 patients). It was reported to range from 57.6% to 100%. The pooled proportion of excellent outcome was 76.1% (95% CI: 69.8–81.5%, I^2=42.5) (Figure 3). Seven studies involving 378 patients showed the risk of mortality rate ranged from 0% to 8%, with a pooled 90-day mortality rate of 4.5% (95% CI: 2.6–7.5%, I^2=1.4) (Figure 4). Regarding the definition of sICH, 4 studies defined it as clinical neurological deterioration temporally related to ICH [9,10,33,36] and 2 defined it as a ≥4-point increase in NIHSS associated with ICH [8,38]; 1 defined clinical neurological deterioration or a ≥4-point increase in NIHSS associated with ICH [41]; the definition was unclear in the remaining studies [32,34,35,40]. The risk of sICH was reported to range from 0% to 5.1%. Twelve studies involving 831 patients showed the pooled rate of sICH was 2.4% (95% CI: 1.5–3.8, I^2=0) (Figure 5).

Discussion

Thrombolysis is often withheld in patients with mild symptoms, so little is known about its efficacy and safety in these patients. Our study suggests that there are no significant differences for excellent outcome after 3 months of IV rtPA-treated minor stroke compared with those without rtPA treatment. The pooled estimates associated with IV rtPA were 76.1% for excellent outcome, 4.5% for mortality rate, and 2.4% for sICH.

In previous studies, the proportion of poor outcome (mRS 2-6) in mild patients who do not receive IV rtPA varied from 15% to 31%. Our study showed the pooled proportion of excellent outcome (mRS 0-1) was 76.1% for mild patients receiving IV rtPA, which is similar to the results mentioned above. A post hoc subgroup analysis of the NINDS study with small group of patients suggested that the risk-to-benefit ratio for using t-PA in patients with minor stroke favored treatment in eligible patients [9]. However, the subgroup analysis of the IST-3 trial did not show a significant effect of rt-PA in patients with mild stroke [37]. This may be due to the treatment effect being

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Table 1. Characteristics and outcome of studies on minor stroke treated with intravenous tissue plasminogen activator.

Study	Study type	N	Definition	Time	Age	Male,%	NIHSS	Functional outcome	sICH	Mortality 90
Comparative studies										
Khatri, 2010	RCT post hoc analysis	42	NIHSS ≤5	3 hours	NG	NG	NG	mRS 0–1 (90-day) 33/42, 78.6%	1/42, 2.4%	NG
Sandercock, 2012	RCT post hoc analysis	304	NIHSS ≤5	6 hours	NG	NG	NG	OHS 0–2 (6-month) 221/304, 72.7%	NG	NG
Huisa, 2012	Prospective Stroke registry	59	NIHSS ≤5	3 hours	66.5 (16.4)	61%	3.4 (1.4)	mRS 0–1 (90-day) 34/59,57.6%	3/59, 5.1%	3/59, 5.1%
Urra, 2013	Prospective Stroke registry	119	NIHSS ≤5	4.5 hours	68.8 (13.8)	68.9%	Median 3 (2–4)	mRS 0–1 (90-day) 99/119, 83%	0	2/119, 1.7%
Single arm studies										
Steffenhagen, 2009	Prospective Stroke registry	77	NIHSS ≤5	3 hours	65 (12)	48, 62%	Median 4	mRS 0–1 (90-day) 58/77, 75%	2.6%, 2/77	6/77, 8%
Strbian, 2012	Prospective thrombolysis registry	58 194 236 252 488	NIHSS 0–2 NIHSS 3–4 NIHSS 5–6 NIHSS 0–4 NIHSS 0–6	3 hours	62 (58–73) 65 (56–74) 68 (59–76)	30/58, 51.7% 116/194, 59.8% 137/236, 58.1% 146/252, 57.9% 283/488, 58.0%	0 (0–2) 1 (0–3) 2 (1–4)	45/58, 77.6% 116/194, 59.8% 130/236, 55.1% 161/252, 63.9% 291/488, 59.6%	0 5, 2.6% 5, 2.1% 5, 2.0% 10, 2.0%	NG
Kohrmann, 2009	Prospective Stroke registry	32	NIHSS<5	2 (1–12)	69.5 (42–92)	24/32, 75%	Median 3.5 (1–4)	mRS 0–1 (90-day) 30/32, 93.8%	0	0
Baumann, 2006	Prospective thrombolysis registry	19	RIE*	3 hours	59 (13)	15/19, 78.9%	Median 5 (4–6)	mRS 0–1 (90-day) 15/19, 78.9%	0	1/19, 5.3%
Nesi, 2014	Prospective Stroke registry	47	NIHSS ≤6	3 hours	NG	NG	NG	mRS 0–1 (90-day) 41/47, 87.2%	0	0
Joshua Z, 2011	Prospective database	535	NIHSS ≤5	3 hours	NG	NG	NG	NG	NG	Mortality discharge 10/535, 1.9%
Mittal, 2012	Stroke Center database	25	NIHSS ≤5	3 hours	66.5 (12.5)	NG	NG	NG	1/25, 4%	Death/ Hospice (disharge) 2/25, 8%
Desilles 2011	Prospective database	25	NIHSS ≤4	NG	NG	NG	4 (0–4)	mRS 0–2 (90-day) 25	0	0
Hassan, 2010	Retrospective study	27	NIHSS ≤6	3 hours	62.4 (14.3)	15/27, 55.6%	Mean 4.52 (1.25)	mRS 0–1 (90-day) 25/27, 92.6%**	1/27, 3.7%	NG
Wendt, 2013	Hospital thrombolysis database	107 65	NIHSS ≤4 NIHSS ≤3	NG NG	71 (64–78) 71 (63–78)	66/107, 62% 36/65, 55%	NG NG	mRS 0–1 (90-day) 79/107, 74% mRS 0–1 (90-day) 48/65, 74%	1/107, 0.9% 0	NG NG

* RIE: Rapid early improvement of neurological deficit (defined as regression of neurological symptoms between stroke onset and evaluation by the treating neurologist); ** 7–10 days or discharge; OHS – Oxford Handicap Score; RCT – randomised controlled trial; NIHSS – National Institutes of Health Stroke Scale; mRS – modified Rankin Scale; sICH – symptomatic Intracranial Hemorrhage; NG – not given.

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Table 2. Subgroup analyses of outcomes according to different time and NIHSS.

Subgroup	Number of study and participants	Excellent outcome OR 95%CI	Number of study and participants	Mortality OR 95%CI	Number of study and participants	sICH OR 95%CI
Time						
≤3 hours	6, 496	0.727 (0.634–0.805) I^2=41.4	4, 202	0.060 (0.033–0.107) I^2=0	8, 548	0.028 (0.016–0.046) I^2=0
≤6 hours	1, 304	0.727(0.674–0.774)	–	–	–	–
NIHSS						
≤3	1, 65	0.738 (0.619–0.831)	–	–	1, 65	0.015 (0.002–0.101)
≤4	4, 416	0.891 (0.519–0.984) I^2=46	2, 57	0.017 (0.002–0.111) I^2=0	4, 416	0.017 (0.008–0.036) I^2=0
≤5	5, 601	0.740 (0.659–0.808) I^2=41.4	3, 255	0.047 (0.020–0.105) I2=31.5	5, 322	0.032 (0.015–0.063) I^2=0
≤6	2, 535	0.750 (0.401–0.930) I^2=47.8	1, 47	0.01 (0.001–0.146)	1, 27	0.037 (0.005–0.221)

NIHSS – National Institutes of Health Stroke Scale; sICH – symptomatic intracranial hemorrhage.

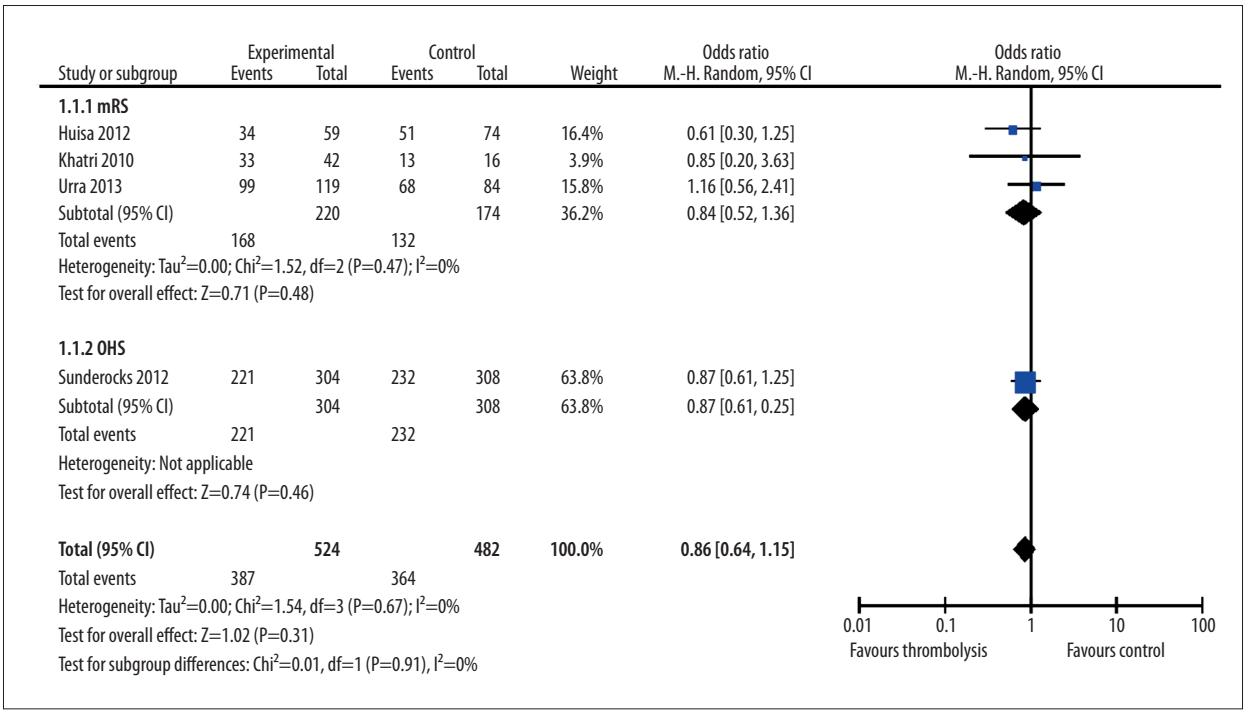

Figure 2. Odds ratio for 'Excellent outcome' after 3 months of intravenous rtPA-treated minor stroke compared with those without rtPA treatment.

too small to be detected, and would require a very large sample. A second reason why IST may not have shown a benefit of rt-PA in mild strokes is because the treatment window was 6 hours and this was a criterion for inclusion into the trial.

The main reason of the exclusion from thrombolysis in patients with mild symptoms is the fear that rtPA will present a potential risk for cerebral hemorrhage. Our results demonstrated that the rate of sICH in IV rt-PA treated patients with mild stroke (2.4%) was similar to the rate of hemorrhage in the control group (1.8%) from a recently updated meta-analysis of rtPA for acute ischemic stroke (12 trials, 7012 patients) and lower than in treated patients (7.7%) [43]. It is also lower than the result of SITS-MOST containing 6483 treated

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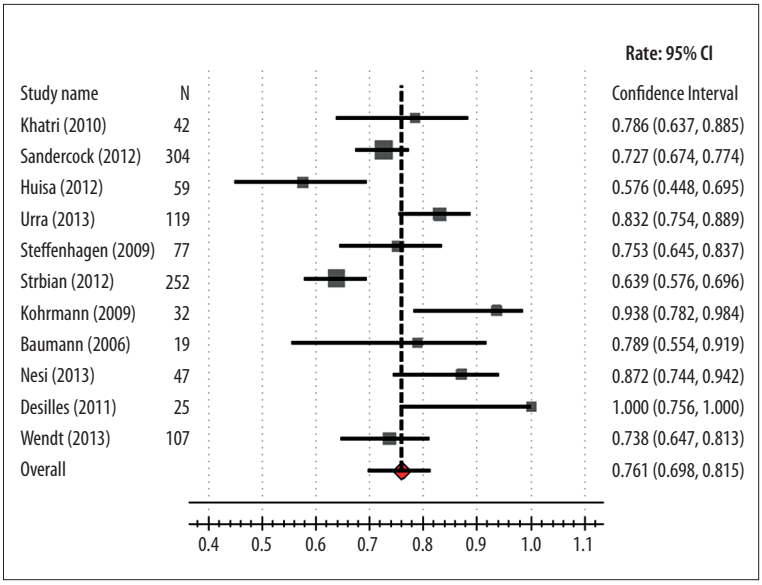

Figure 3. Pooled proportion of excellent outcome at the end of 3 months.

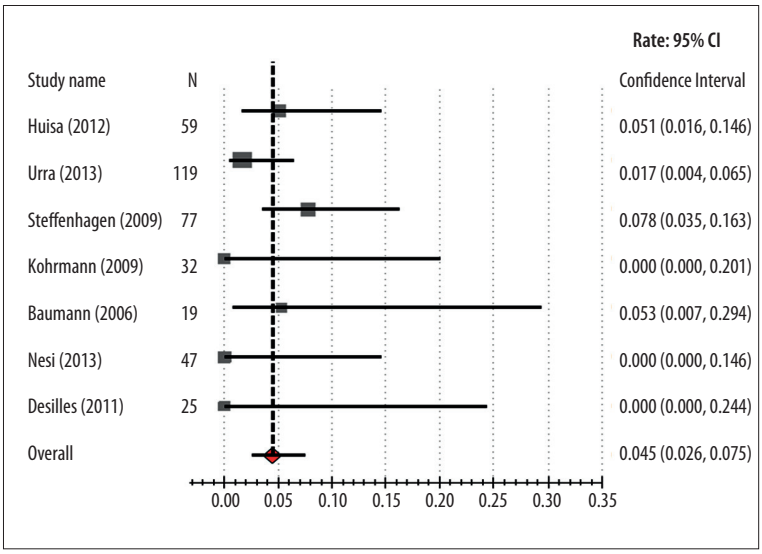

Figure 4. Pooled mortality at the end of 3 months.

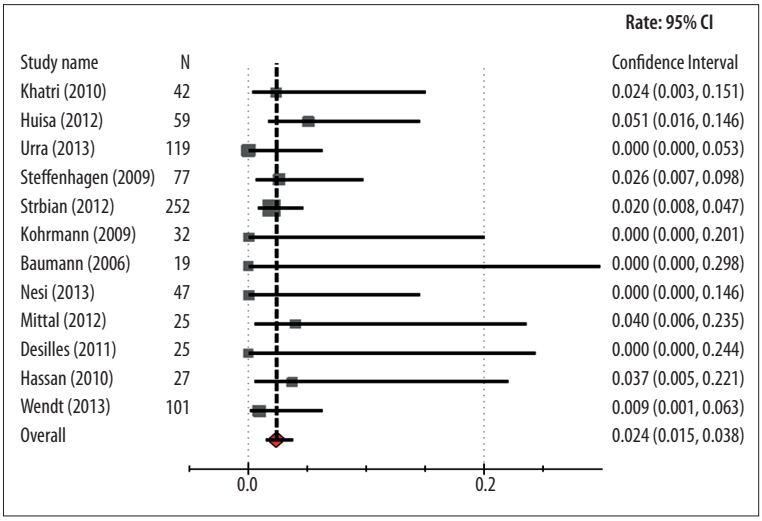

Figure 5. Pooled rate of symptomatic intracranial hemorrhage.

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patients, which assessed the safety profile of Alteplase in clinical practice [44].

The main limitation of this study is that most of the included studies that described the outcome either used historical controls or no control group and the patient count was low. A further limitation in this combined analysis is lack of adjustment on baseline differences. In addition, there is no consensus definition of minor stroke. The NINDS t-PA study and the ECASS III [1,2] both excluded patients with mild stroke, but they failed to clearly define a threshold for mild stroke. So far, although there are no identical variates for predicting the poor outcome of patients with minor stroke, future studies are needed to focus on how to really identify minor stroke patients with poor outcome by clinical features combined with imaging features. Previous studies found that mild stroke patients with large-vessel occlusion were at high risk for early neurological deterioration or poor outcome [45]. Imaging with advanced MRI is a possibility to guide treatment decision-making in mild stroke [27,34,36]. However, the decision-making process regarding these techniques seems to be rather sophisticated. These issues should be addressed in further randomized controlled clinical trials.

Conclusions

Although efficacy is not clearly established, this study reveals that the adverse event rates related to thrombolysis are low in mild stroke. Intravenous rtPA should be considered in these patients until more RCT evidence is available.

Competing interests

The authors declare that they have no competing interests.

References:

1. Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. N Engl J Med, 1995; 333: 1581–87
2. Hacke W, Kaste M, Bluhmki E et al: Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med, 2008; 359: 1317–29
3. Maksimenko AV: Thrombolysis research – new objectives after a shift of accent. Med Sci Monit, 2002; 8(1): RA13–21
4. Ohara T, Nagakane Y, Tanaka E et al: Clinical and Radiological Features of Stroke Patients with Poor Outcomes Who Do Not Receive Intravenous Thrombolysis because of Mild Symptoms. Eur Neurol, 2013; 69: 4–7
5. Smith EE, Fonarow GC, Reeves MJ et al: Outcomes in mild or rapidly improving stroke not treated with intravenous recombinant tissue-type plasminogen activator: findings from Get With The Guidelines-Stroke. Stroke, 2011; 42: 3110–15
6. Khatri P, Conaway MR, Johnston KC: Ninety-day outcome rates of a prospective cohort of consecutive patients with mild ischemic stroke. Stroke, 2012; 43: 560–62
7. Barber PA, Zhang J, Demchuk AM et al: Why are stroke patients excluded from TPA therapy? An analysis of patient eligibility. Neurology, 2001; 56: 1015–20
8. Urra X, Arino H, Llull L et al: The outcome of patients with mild stroke improves after treatment with systemic thrombolysis. PLoS One, 2013; 8: e59420
9. Khatri P, Kleindorfer DO, Yeatts SD et al: Strokes with minor symptoms: an exploratory analysis of the National Institute of Neurological Disorders and Stroke recombinant tissue plasminogen activator trials. Stroke, 2010; 41: 2581–86
10. Kohrmann M, Nowe T, Huttner HB et al: Safety and outcome after thrombolysis in stroke patients with mild symptoms. Cerebrovasc Dis, 2009; 27: 160–66
11. Wallace BC, Schmid CH, Lau J et al: Meta-Analyst: software for meta-analysis of binary, continuous and diagnostic data. BMC Med Res Methodol, 2009; 9: 80
12. Ntaios G, Faouzi M, Michel P: The effect of thrombolysis on short-term improvement depends on initial stroke severity. J Neurol, 2012; 259: 524–29
13. Marler JR: Should stroke patients with mild or improving symptoms receive tissue plasminogen activator therapy? Nat Clin Pract Neurol, 2006; 2: 354–55
14. Ammerman JM: t-PA for mild ischemic stroke: we shouldn't be afraid to treat. South Med J, 2010; 103: 391
15. Tong DC: Avoiding thrombolysis in patients with mild stroke: is it SMART? Stroke, 2012; 43: 625–26
16. De Keyser J, Gdovinova Z, Uyttenboogaart M et al: Intravenous alteplase for stroke: beyond the guidelines and in particular clinical situations. Stroke, 2007; 38: 2612–18
17. Balucani C, Levine SR: Mild stroke and rapidly improving symptoms: it's not always a happy ending. Stroke, 2011; 42: 3005–7
18. Breuer L, Blinzler C, Huttner HB et al: Off-label thrombolysis for acute ischemic stroke: rate, clinical outcome and safety are influenced by the definition of 'minor stroke'. Cerebrovasc Dis, 2011; 32: 177–85
19. Meretoja A, Putaala J, Tatlisumak T et al: Off-label thrombolysis is not associated with poor outcome in patients with stroke. Stroke, 2010; 41: 1450–58
20. Bravata DM, Kim N, Concato J et al: Thrombolysis for acute stroke in routine clinical practice. Arch Intern Med, 2002; 162: 1994–2001
21. Lyden PD: Should all stroke patients receive tissue plasminogen activator therapy, despite mild or improving symptoms? Nat Clin Pract Cardiovasc Med, 2006; 3: 184–85
22. Machumpurath B, Davis SM, Yan B: Rapid neurological recovery after intravenous tissue plasminogen activator in stroke: prognostic factors and outcome. Cerebrovasc Dis, 2011; 31: 278–83
23. Solling C, Hjort N, Ashkanian M et al: Safety and efficacy of MRI-based selection for recombinant tissue plasminogen activator treatment: responder analysis of outcome in the 3-hour time window. Cerebrovasc Dis, 2009; 27: 223–29
24. Hassan AE, Zacharatos H, Hassanzadeh B et al: Does mild deficit for patients with stroke justify the use of intravenous tissue plasminogen activator? J Stroke Cerebrovasc Dis, 2010; 19: 116–20
25. Recombinant tissue plasminogen activator for minor strokes: the National Institute of Neurological Disorders and Stroke rt-PA Stroke Study experience. Ann Emerg Med, 2005; 46: 243–52
26. Garcia-Garcia J, Ayo-Martin O, Segura T: Is it justified to exclude patients with minor stroke from intravenous thrombolysis? Int J Stroke, 2013; 8: E4
27. Kruetzelmann A, Siemonsen S, Gerloff C et al: Thrombolysis targeting MRI defined tissue at risk in minor stroke. J Neurol Neurosurg Psychiatry, 2009; 80: 1156–58
28. Mishra NK, Lyden P, Grotta JC et al: Thrombolysis is associated with consistent functional improvement across baseline stroke severity: a comparison of outcomes in patients from the Virtual International Stroke Trials Archive (VISTA). Stroke, 2010; 41: 2612–17
29. Blinzler C, Breuer L, Huttner HB et al: Characteristics and outcome of patients with early complete neurological recovery after thrombolysis for acute ischemic stroke. Cerebrovasc Dis, 2011; 31: 185–90
30. Machumpurath B, Davis SM, Yan B: Rapid neurological recovery after intravenous tissue plasminogen activator in stroke: prognostic factors and outcome. Cerebrovasc Dis, 2011; 31: 278–83

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

31. Stecksen A, Asplund K, Appelros P et al: Thrombolytic therapy rates and stroke severity: an analysis of data from the Swedish stroke register (Riks-Stroke) 2007–2010. Stroke, 2012; 43: 536–38
32. Baumann CR, Baumgartner RW, Gandjour J et al: Good outcomes in ischemic stroke patients treated with intravenous thrombolysis despite regressing neurological symptoms. Stroke, 2006; 37: 1332–33
33. Huisa BN, Raman R, Neil W et al: Intravenous tissue plasminogen activator for patients with minor ischemic stroke. J Stroke Cerebrovasc Dis, 2012; 21: 732–36
34. Desilles JP, Cho TH, Hermier M et al: Magnetic resonance imaging-guided thrombolysis in minor stroke. Int J Stroke, 2011; 6: 178
35. Mittal M, Rymer M, Lai SM: Should all patients with mild ischemic stroke be excluded from therapeutic stroke trials? J Clin Neurosci, 2012; 19: 1486–89
36. Steffenhagen N, Hill MD, Poppe AY et al: Should you thrombolyse all or any stroke patients with baseline National Institutes of Health stroke scale scores < or = 5? Cerebrovasc Dis, 2009; 28: 201–2
37. Sandercock P, Wardlaw JM, Lindley RI et al: The benefits and harms of intravenous thrombolysis with recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the third international stroke trial [IST-3]): a randomised controlled trial. Lancet, 2012; 379: 2352–63
38. Hassan AE, Hassanzadeh B, Tohidi V et al: Very mild stroke patients benefit from intravenous tissue plasminogen activator without increase of intracranial hemorrhage. South Med J, 2010; 103: 398–402
39. Wendt M, Tutuncu S, Fiebach JB et al: Preclusion of Ischemic Stroke Patients from Intravenous Tissue Plasminogen Activator Treatment for Mild Symptoms Should Not be Based on Low National Institutes of Health Stroke Scale Scores. J Stroke Cerebrovasc Dis, 2013; 22: 550–53
40. Nesi M, Lucente G, Nencini P et al: Aphasia predicts unfavorable outcome in mild ischemic stroke patients and prompts thrombolytic treatment. J Stroke Cerebrovasc Dis, 2014; 23: 204–8
41. Strbian D, Piironen K, Meretoja A et al: Intravenous thrombolysis for acute ischemic stroke patients presenting with mild symptoms. Int J Stroke, 2013; 8: 293–99
42. Willey JZ, Khatri P, Khoury JC et al: Variability in the use of intravenous thrombolysis for mild stroke: experience across the SPOTRIAS network. J Stroke Cerebrovasc Dis, 2013; 22: 318–22
43. Wardlaw JM, Murray V, Berge E et al: Recombinant tissue plasminogen activator for acute ischaemic stroke: an updated systematic review and meta-analysis. Lancet, 2012; 379: 2364–72
44. Wahlgren N, Ahmed N, Davalos A et al: Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST): an observational study. Lancet, 2007; 369: 275–82
45. Rajajee V, Kidwell C, Starkman S et al: Early MRI and outcomes of untreated patients with mild or improving ischemic stroke. Neurology, 2006; 67: 980–84
46. Thomalla G, Schwark C, Sobesky J et al: Outcome and symptomatic bleeding complications of intravenous thrombolysis within 6 hours in MRI-selected stroke patients: comparison of a German multicenter study with the pooled data of ATLANTIS, ECASS, and NINDS tPA trials. Stroke, 2006; 37: 852–58

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