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Title page

Title: IV thrombolysis in stroke mimics - Results from the SITS International Stroke Thrombolysis Register (SITS-ISTR).

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Abstract

Background and Purpose: Patients with stroke mimics, conditions with stroke-like symptoms, may risk harm if treated with intravenous thrombolysis (IVT). Current guidelines state low risk of intracranial hemorrhage (ICH) based on studies comprising a total of <400 stroke mimic cases. We aimed to compare safety and outcomes following IVT between patients with acute ischemic stroke and mimicking conditions.

Methods: We included IVT-treated ischemic stroke patients in the SITS International Stroke Thrombolysis Registry (SITS-ISTR) 2003–2017, examined with MRI 22-36 hours after treatment. Outcomes were parenchymal hematoma (PH) after treatment, symptomatic ICH (SICH) per SITS-MOST, ECASS II and NINDS criteria, death, and modified Rankin Scale score at 3 months.

Results: Of 10436 patients, 429 mimics (4.3%) were identified. The most common types were functional (30.8%), migraine (17.5%), and seizure (14.2%). Patients with mimics had fewer cerebrovascular risk factors and lower median NIHSS: 7 (IQR 5-10) vs 8 (5-14), p<0.001. Among mimics versus stroke patients, PH was seen in 1.2% vs 5.1%, p<0.001; SICH NINDS in 0.5% vs 3.9%, p<0.001; SICH ECASS II in 0.2% vs 2.1% p=0.007; and SICH SITS-MOST in 0% vs 0.5%, p=0.28. mRS 0-1 at 3 months was present in 84.1% vs

57.7% (p<0.001), and death within 3 months in 2.6% vs 5.4% (p=0.028) in mimics and stroke patients respectively.

Conclusions: This large observational study indicates that parenchymal hemorrhage and SICH following IVT in patients with stroke mimics are uncommon.

Introduction

The only approved medical therapy for acute ischemic stroke (AIS) is intravenous tissue plasminogen activator (IVT), with an effective treatment time window of 0-4.5 hours from symptom onset.[1] Earlier treatment is associated with a higher likelihood for good outcome.[2] However, very rapid assessment may lead to inadvertent treatment of non-stroke patients presenting with stroke-like symptoms, stroke mimics (SM), risking hemorrhagic complications, and incurring unnecessary costs.[3] In a stroke unit in London, stroke mimics accounted for 24.2% of admissions and 8.2–17.2% of bed occupancy.[4] Reported proportions of treated SM vary depending on diagnostic criteria. A multi-center European study on IVT in SM reported 100 mimics among 5518 treated patients (1.8%), defining SM as "patients with clinical details not suggesting a vascular etiology and an alternate diagnosis convincingly explaining their symptoms".[5] Higher proportions, 6.5-17.0%, have been shown in single-center studies using diffusion weighted MRI to distinguish AIS from SM.[6–9]

The risk of symptomatic intracerebral hemorrhage (SICH) after IVT treatment in SM has previously been shown to be low. The multi-center European study [5] found one case of SICH per the Second European Co-operative Stroke Study definition (ECASS II)[10] and one case of SICH per the National Institutes of Neurological Disorders and Stroke Study

definition (NINDS)[11]. Both patients recovered from the symptoms caused by the hemorrhage.[5] Current American Stroke Association guidelines refer to these data, stating that initiating IVT is preferred over delaying treatment and that the risk of SICH in SM is "quite low".[12] A meta-analysis of nine studies using the SICH definition "imaging evidence of intracerebral hemorrhage with an NIHSS increase of ≥4 points", found 2/392 (0.5%) such cases, compared to 417/8085 (5.2%) in the AIS group.[8] Given the paucity of published cases of SM with cerebral hemorrhagic complications, we sought to investigate the occurrence of parenchymal hematoma (PH) and SICH in patients with SM within the SITS International Stroke Thrombolysis Registry.

Our hypothesis was that frequencies of PH, SICH, and death within 3 months are lower, and that excellent and independent functional outcomes are more common, in patients with SM compared to AIS.

Methods

Study population and procedures

All patients treated with IVT (Alteplase) recorded in the SITS International Stroke Thrombolysis Register (SITS-ISTR) between February 2003 and September 2017, with data confirmed at baseline, 24 hours and discharge, were considered, N=100941. Patients who had undergone any endovascular intervention were excluded. Only patients with MRI follow-up 22-36 hours after treatment were included, as it has been shown that the vast majority of bleeding complications occur within this time window.[13] MRI was used due to its higher sensitivity and specificity in the diagnosis of AIS in comparison with CT. This led to a risk of selection bias, via preferential exclusion of patients with severe or deteriorating AIS at

elevated risk for SICH, in whom CT imaging could have been seen as more suitable. The AIS+MRI comparator group could then be predicted to have milder stroke, and better outcomes, than unselected patients treated with IVT for AIS. A sensitivity analysis was conducted to address this, comparing AIS patients treated with IVT having CT follow-up at 22-36 hours with the original SM group with MRI follow-up.

The SITS-ISTR is a prospective, academic-driven, multinational, observational register for hospitals treating patients with acute stroke. Data was retrieved and analyzed retrospectively. The SITS-ISTR methodology, including procedures for data collection and management, patient identification and verification of source data, has been described previously.[14,15]

We collected baseline and demographic characteristics, stroke severity per the National Institute of Health Stroke Scale (NIHSS), time logistics, medication history, and imaging data on admission and follow-up, as well as death and functional outcome per the modified Rankin Scale (mRS) at 3 months. Patients with a discharge diagnosis of ischemic stroke and patients with a non-stroke diagnosis formed the AIS and SM groups respectively. The non-stroke patients were further classified into 14 diagnostic categories based on free text description of the case available in the register, see table 2. Ambiguous cases were classified after email contact with registry coordinators at individual centers.

Ethics approval and data monitoring

Ethics approval was obtained from the Stockholm Regional Ethics Committee for this project as part of the SITS-MOST (Safe Implementation of Thrombolysis in Stroke Monitoring Study) II framework. The SITS International Coordination Office monitored the SITS-ISTR data online and checked individual patient data monthly to identify errors or inconsistencies.

Outcomes

The main outcome measure was intracerebral parenchymal hematoma (PH), defined as any contiguous, (non-petechial) intra-parenchymal bleeding, as evidenced on imaging after treatment with IV-tPA at any timepoint during the acute in-hospital stay.

Secondary outcomes were SICH per SITS-MOST[14], ECASS II and NINDS-definitions, death within 3 months, excellent functional outcome (mRS 0-1) and functional independence (mRS 0-2), and the full-range mRS at 3 month follow-up. SICH events were adjudicated centrally by the SITS International Coordination Office based on submitted clinical and imaging reports; images were not available for review. Assessments of clinical parameters, imaging, and outcomes, as well as choice of MR protocols for imaging follow-up, were done according to clinical routine at participating centers.

Statistical analysis

We performed descriptive statistics for baseline data and outcomes, comparing patients with stroke mimics and ischemic stroke. For continuous variables, median and interquartile range values were calculated. For categorical variables, we calculated percentage proportions by dividing the number of events by the total number of patients, excluding missing or unknown cases, as in previous SITS publications.[16,17] Continuous variables were compared using the Mann-Whitney U-test and dichotomized variables using the Pearson χ^2 or Fisher's exact method as appropriate. P-values <0.05 (two-tailed) were considered significant. Statistical analyses were performed in Stata 15.1.

Results

Of 100941 patients enrolled in the SITS-ISTR between February 2003 and September 2017, 10436 were found eligible for analysis. Stroke mimics comprised 429 (4.3%) of cases (see fig. 1). The study cohort originated from 560 centers in 43 countries. Table 1 presents baseline demographic, clinical, and laboratory characteristics of SM and AIS patients. There were significant differences in most baseline characteristics. SM patients were younger (52 vs 65 years), more commonly female (53.8% vs 41.4%) and fewer had atrial fibrillation (2.3% vs 40.7%). Among major risk factors for SICH, SM patients had lower NIHSS scores (7 vs 8) and baseline systolic blood pressure (140 vs 150 mmHg) compared to AIS. In SM, onset to treatment time was longer (175 vs 155 minutes) than in AIS. The proportion of patients examined with MRI at baseline was 4.5% in the SM group vs 15.8% in the AIS group. The most common SM categories were functional (30.8%), migraine (17.5%) and seizure (14.2%) (Table 2). Safety and functional outcome data are shown in table 3. There were 5 cases of PH in the SM group (1.2% vs 5.1%, $p<0.001$), no cases of SICH per SITS-MOST (0% vs 0.5%), 1 case per ECASS II (0.2% vs 2.1%), and 2 cases per NINDS (0.5% vs 3.9%) definitions. No death was due to SICH per any definition in the SM group. Figure 2 shows a comparison of mRS scores 0-6 between SM and AIS. The two mimic patients with SICH, (one fulfilling both ECASS II and NINDS criteria and one only NINDS criteria) belonged to the subgroup with an unspecified mimic diagnosis. Of the five patients with PH, two belonged to the seizure category, and one each to the brain tumor, migraine and unspecified categories. No SM patients with a previous stroke suffered bleeding complications.

A sensitivity analysis was conducted, comparing baseline characteristics (Table I online-only) and outcomes (Table II online-only) of the same stroke mimic patients, to AIS patients with a CT follow-up at 22-36 hours (n=85664). The differences between SM and AIS patients regarding age (52 vs 72 years, $p<0.001$) and NIHSS scores (7 vs 11) were larger.

Differences in all outcomes followed the pattern from the main analysis and remained statistically significant.

Discussion

This large, multi-center, observational study has shown that IVT in patients with stroke mimics is reasonably safe. Mimic patients had a much lower risk of parenchymal hemorrhage than those with AIS. rare occurrences of SICH per ECASS II and NINDS, and no instance of the most severe type, SICH per SITS-MOST. This is consistent with the large difference in mRS scores and death within 3 months, all in favor of the SM group. The three most common mimicking conditions were functional symptoms, migraine and seizure. The longer onset-to-treatment time with no difference in door-to-needle time in the SM group possibly reflects a diagnostic uncertainty in the pre-hospital setting.

The proportion of patients with mimics was 4.1%, in line with the 4.4% reported in a recent meta-analysis by Tsivgoulis, et al.[8] This is higher than the 1.8% in the European multi-center study by Zinkstok, et al, which did not require MRI, used strict mimic criteria, and was conducted at highly experienced academic stroke centers.[5,18]

Six single-center studies using MRI have shown a wide range of proportions of SM among IVT-treated patients, between 3.7% and 14.5%, with varying criteria for defining mimics.[6–9,19,20]The proportion of mimics in our study is at the lower end of this range. However, our data was collected at 560 centers participating in the SITS-ISTR, which is known to have highly varying patient volumes and experience in stroke thrombolysis across hospitals.[16]

In our study, the bleeding rates in the AIS group with MRI follow-up were surprisingly low. Compared to previous SITS studies of unselected IVT patients, the AIS group with MRI follow-up had lower median NIHSS, age and burden of co-morbidities. This likely explains the fewer hemorrhagic complications in our AIS group with MRI follow-up, since these factors are associated with SICH.[14,21]

There are several limitations to this study, in addition to those inherent to observational registry studies. Due to few cases of PH and SICH, we were precluded from performing logistic regression analysis to adjust for the major differences in baseline parameters between the groups. The requirement for MRI follow-up was set to ascertain that the diagnosis of stroke mimic was as well-established as possible, but there was no way to ascertain whether any DWI negative AIS patients could have been misdiagnosed as having a mimic. Detailed data on MRI protocols used were not available. Furthermore, we lacked detailed data regarding the diagnostic work-up, which was done according to clinical routine at participating hospitals. This could explain why 14% of the mimic patients had an unspecified mimicking condition. Both mimic patients with SICH in our study had an unspecified diagnosis, which remained despite attempts to contact the treating centers for clarifications. While we have addressed the potential exclusion of severe or unstable stroke cases from routine MRI follow-up in a sensitivity analysis, we cannot know whether the MRI criterion may have excluded any mimic cases with massive SICH, deteriorating so rapidly that MRI follow-up would be contraindicated. Meanwhile, this would be a limitation in any study of stroke mimics using MRI. Three-month outcome data was missing in 14% of cases. Nevertheless, our results on functional outcome and death in patients with SM are consistent with previous studies.[5,8,22]

Despite these limitations, our study has provided new knowledge on clinical characteristics and outcomes of stroke mimic patients treated with IVT. We have demonstrated the frequency of parenchymal hematoma after IVT in SM in addition to SICH, providing additional information on bleeding complications that do not meet SICH criteria. Furthermore, no cerebral hemorrhagic complications in the mimic category with functional neurological symptoms, together with previous publications, indicates a high degree of treatment safety in this group. While previous studies have reported bleeding complications in mimics with Todd's paralysis, to our knowledge, this is the first study to report an ICH after thrombolysis in a patient with migraine stroke mimic.

Conclusion

This large, multi-center study has shown that IVT in patients with stroke mimics, especially with functional neurological symptoms, is reasonably safe in terms of cerebral parenchymal hematoma and symptomatic intracerebral hemorrhage. While efforts should be made to identify stroke mimics before IVT,[9] this study lends support to the AHA/ASA guidelines in that IVT should not be withheld for fear of treating a mimicking condition.

References

1. Jauch EC, Saver JL, Adams HPJ, Bruno A, Connors JJB, Demaerschalk BM, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke J Cereb Circ. 2013 Mar;44(3):870–947.

2. Emberson J, Lees KR, Lyden P, Blackwell L, Albers G, Bluhmki E, et al. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials. Lancet Lond Engl. 2014 Nov 29;384(9958):1929–35.

3. Liberman AL, Liotta EM, Caprio FZ, Ruff I, Maas MB, Bernstein RA, et al. Do efforts to decrease door-to-needle time risk increasing stroke mimic treatment rates?. [Miscellaneous Article]. Neurol Clin Pract. 2015 Jun;5(3):247–52.

4. Dawson A, Cloud GC, Pereira AC, Moynihan BJ. Stroke mimic diagnoses presenting to a hyperacute stroke unit. Clin Med Lond Engl. 2016 Oct;16(5):423–6.

5. Zinkstok SM, Engelter ST, Gensicke H, Lyrer PA, Ringleb PA, Artto V, et al. Safety of thrombolysis in stroke mimics: results from a multicenter cohort study. Stroke J Cereb Circ. 2013;44(4):1080–4.

6. Chernyshev OY, Martin-Schild S, Albright KC, Barreto A, Misra V, Acosta I, et al. Safety of tPA in stroke mimics and neuroimaging-negative cerebral ischemia. Neurology. 2010;74(17):1340–5.

7. Tsivgoulis G, Alexandrov AV, Chang J, Sharma VK, Hoover SL, Lao AY, et al. Safety and outcomes of intravenous thrombolysis in stroke mimics: a 6-year, single-care center study and a pooled analysis of reported series. Stroke J Cereb Circ. 2011;42(6):1771–4.

8. Tsivgoulis G, Zand R, Katsanos AH, Goyal N, Uchino K, Chang J, et al. Safety of intravenous thrombolysis in stroke mimics: prospective 5-year study and comprehensive meta-analysis. Stroke J Cereb Circ. 2015 May;46(5):1281–7.

9. Forster A, Griebe M, Wolf ME, Szabo K, Hennerici MG, Kern R. How to identify stroke mimics in patients eligible for intravenous thrombolysis? J Neurol. 2012;259(7):1347–53.

10. Hacke W, Kaste M, Fieschi C, von Kummer R, Davalos A, Meier D, et al. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). Second European-Australasian Acute Stroke Study Investigators. Lancet Lond Engl. 1998 Oct 17;352(9136):1245–51.

11. National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med. 1995 14;333(24):1581–7.

12. Demaerschalk BM, Kleindorfer DO, Adeoye OM, Demchuk AM, Fugate JE, Grotta JC, et al. Scientific Rationale for the Inclusion and Exclusion Criteria for Intravenous Alteplase in Acute Ischemic Stroke: A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke J Cereb Circ. 2016 Feb;47(2):581–641.

13. Strbian D, Sairanen T, Meretoja AM, Pitkaniemi J, Putaala J, Salonen O, et al. Patient outcomes from symptomatic intracerebral hemorrhage after stroke thrombolysis. Neurology. 2011 Jul;77(4):341–8.

14. Wahlgren N, Ahmed N, Dávalos A, Ford GA, Grond M, Hacke W, 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 Lond Engl. 2007 Jan 27;369(9558):275–82.

15. Mazya MV, Cooray C, Lees KR, Toni D, Ford GA, Bar M, et al. Minor stroke due to large artery occlusion. When is intravenous thrombolysis not enough? Results from the SITS International Stroke Thrombolysis Register. Eur Stroke J. 2018 Mar 1;3(1):29–38.

16. Anani N, Mazya MV, Bill O, Chen R, Koch S, Ahmed N, et al. Changes in European Label and Guideline Adherence After Updated Recommendations for Stroke Thrombolysis: Results From the Safe Implementation of Treatments in Stroke Registry. Circ Cardiovasc Qual Outcomes. 2015 Oct;8(6 Suppl 3):S155-162.

17. Cooray C, Mazya M, Bottai M, Dorado L, Skoda O, Toni D, et al. External Validation of the ASTRAL and DRAGON Scores for Prediction of Functional Outcome in Stroke. Stroke. 2016;47(6):1493–9.

18. Nederkoorn PJ, Zinkstok SM, Engelter ST. Response to Letter Regarding Article, "Safety of Thrombolysis in Stroke Mimics: Results From a Multicenter Cohort Study". Stroke. 2013 Sep 1;44(9):e106–e106.

19. Uchino K, Massaro L, Hammer MD. Transient Ischemic Attack after Tissue Plasminogen Activator: Aborted Stroke or Unnecessary Stroke Therapy? Cerebrovasc Dis. 2010;29(1):57–61.

20. Winkler DT, Fluri F, Fuhr P, Wetzel SG, Lyrer PA, Ruegg S, et al. Thrombolysis in Stroke Mimics: Frequency, Clinical Characteristics, and Outcome. Stroke. 2009 Apr 1;40(4):1522–5.

21. Mazya M, Egido JA, Ford GA, Lees KR, Mikulik R, Toni D, et al. Predicting the risk of symptomatic intracerebral hemorrhage in ischemic stroke treated with intravenous alteplase: safe Implementation of Treatments in Stroke (SITS) symptomatic intracerebral hemorrhage risk score. Stroke J Cereb Circ. 2012 Jun;43(6):1524–31.

22. Kostulas N, Larsson M, Kall T-B, von Euler M, Nathanson D. Safety of thrombolysis in stroke mimics: an observational cohort study from an urban teaching hospital in Sweden. BMJ Open [Internet]. 2017 Oct 30 [cited 2017 Dec 5];7(10). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5665231/

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Table 1. Univariate analysis of baseline variables.

Characteristic	Stroke mimics with MRI follow-up n=429	Ischemic stroke with MRI follow-up n=10007	P-value
	Median (IQR) or Proportions (%)	Median (IQR) or Proportions (%)	
Patient history			
Age, years	52 (39-65)	65 (54-75)	<0.001
Women	231/429 (53.8%)	4069/10007 (41.4%)	<0.001
Atrial fibrillation	10/418 (2.3%)	1618/9898 (40.7%)	<0.001
CHF	11/426 (2.6%)	566/9897 (5.7%)	0.006
Hypertension	154/425 (36.2%)	5841/9918 (58.9%)	<0.001
Diabetes mellitus	48/428 (11.0%)	1613/9943 (16.2%)	0.004
Hyperlipidemia	83/423 (19.6%)	2976/9600 (31.0%)	<0.001
Smoking	128/415 (30.8%)	3422/9664 (35.4%)	<0.001
Previous stroke	47/426 (11.0%)	616/9432 (6.5%)	<0.001
Aspirin	73/428 (16.9%)	2567/9936 (25.8%)	<0.001
Clopidogrel	28/428 (6.5%)	445/9965 (4.5%)	0.044
Oral anticoagulants	3/375 (0.8%)	198/9233 (2.1%)	0.075
mRS pre-IVT 0-1	382/422 (90.5%)	9033/9749 (92.7%)	0.099
Clinical parameters			
NIHSS baseline	7 (5-10)	8 (5-14)	<0.001
OTT, min	175 (135-230)	155 (120-190)	<0.001
DNT, min	69 (45-103)	66 (45-95)	0.093
BPsys mmHg	140 (125-156)	150 (135-165)	<0.001
BPdia mmHg	80 (70-90)	81 (75-90)	<0.001
Glucose, mmol/L	5.94 (5.21-6.94)	6.44 (5.60-7.78)	<0.001
Weight, kg	75 (65-87)	75 (65-85)	0.85

Table 2. Frequency of SM categories

SM category	N	% of total
Functional	132	30.8%
Migraine	75	17.5%
Seizure	61	14.2%
Mimic (without further specification)	59	13.8%
Other specific neurological disease	22	5.1%
CNS infection	20	4.7%
Metabolic disorder	17	4.0%
Brain tumor	15	3.5%
Demyelinating disease	7	1.6%
Circulatory compromise	6	1.4%
Peripheral vestibulopathy	6	1.4%
Peripheral nerve palsy	4	0.9%
Spinal cord compression	3	0.7%
Delirium	2	0.5%
Total	429	

Table 3. Outcomes

Outcome	SM n=429 No./Total (%)	AIS n=10007 No./Total (%)	p-value
PH	5/429 (1.2)	508/9993 (5.1)	<0.001
SICH (SITS-MOST)	0/429 (0.0)	52/10001 (0.5)	0.28 †
SICH (ECASS II)	1/427 (0.2)	212/9918 (2.1)	0.007
SICH (NINDS)	2/427 (0.5)	383/9939 (3.9)	<0.001
mRS 0-1 3m	276/328 (84.1)	5004/8668 (57.7)	<0.001
mRS 0-2 3m	303/328 (92.4)	6020/8668 (69.4)	<0.001
Death 3m	9/342 (2.6)	456/8518 (5.4)	0.028