

# Stroke and Stroke Mimics



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# Stroke mimics

- Prevalence 1.4% - 38% of admissions for suspected acute ischemic stroke
- Rate of mimics treated with iv tPA 1%-20%

		Diagnosis at discharge	
		Stroke	Not a stroke
Diagnosis in the emergency room	Stroke	True positive	Mimic
	Not a stroke	Chameleon	True negative

J Emerg Med. 2017;52:176-183.  
Neuroimag Clin N Am 2018;28:537-549.  
Curr Opin Neurol 2019;32:54-59.



# Topics

- Safety and outcome of IV tPA
  - IV thrombolysis in Stroke mimics
  - Stroke mimics via telestroke
  - Seizure & stroke mimics
- AHA/ASA 2019 Guideline and stroke mimic
- Complication of IV tPA and treatment

## Acute Ischemic Stroke (AIS)

- Time critical
- Early management key to optimizing outcomes
- New evidence has produced major changes in treatment

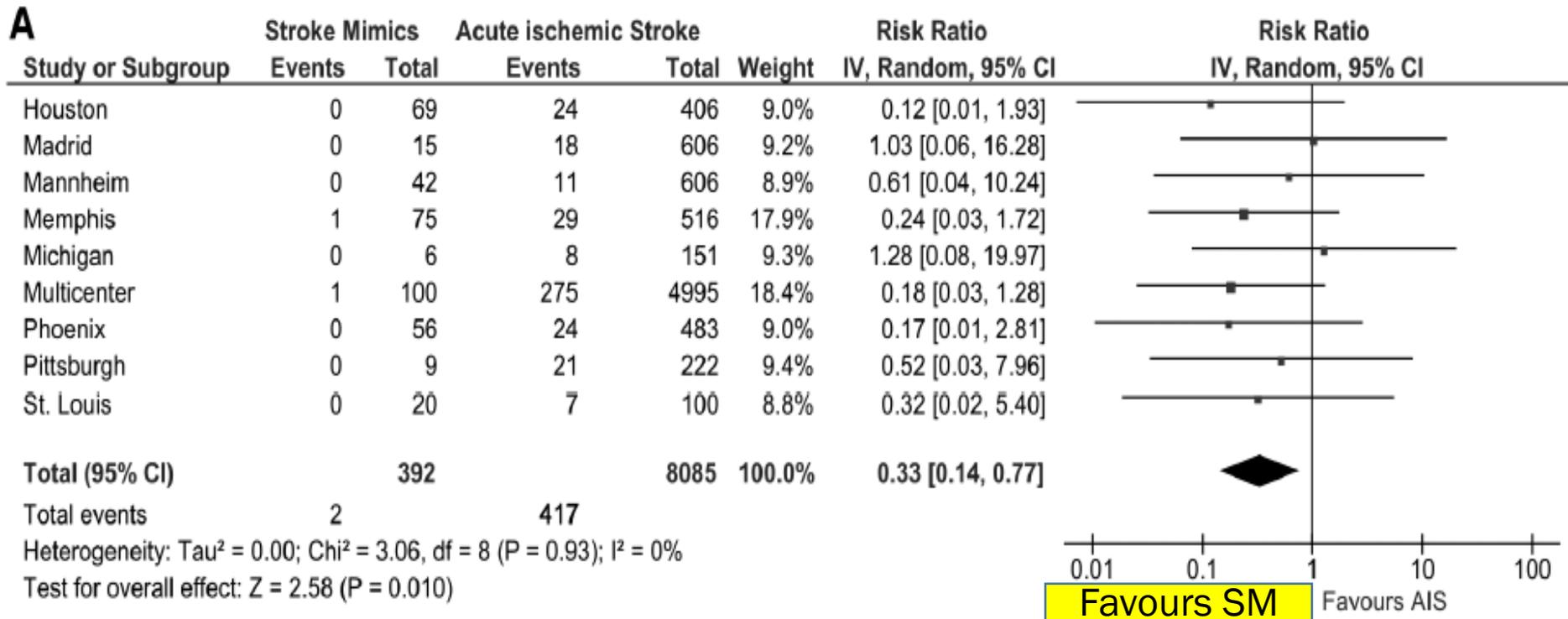


# IV Thrombolysis in Stroke Mimics



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# Meta-Analysis of 9 studies (8942 IVT): the symptomatic intracranial hemorrhage (sICH)



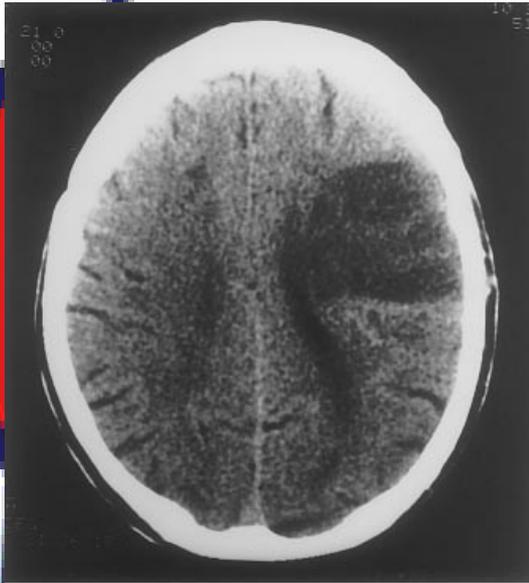
In meta-analysis of 9 studies (8942 IVT),  
 -among 392 patients with SM treated with IVT  
 -the pooled rates of sICH 0.5% (95% CI, 0%–2%)  
 -orolingual edema 0.3% (95% CI, 0%–2%)

Stroke. 2015;46:1281-1287.

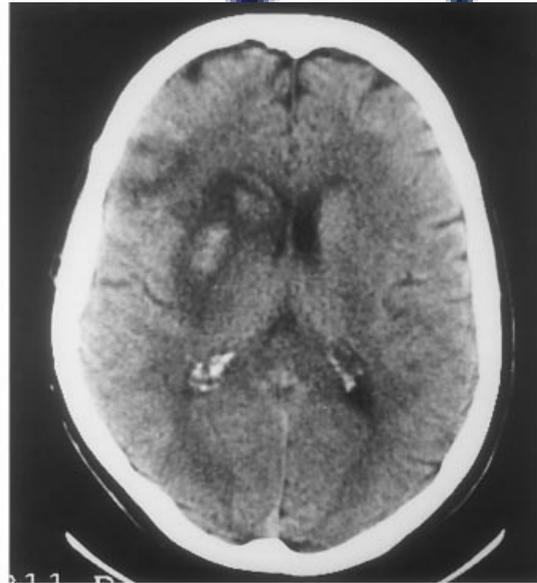


# Subtypes of hemorrhagic transformation

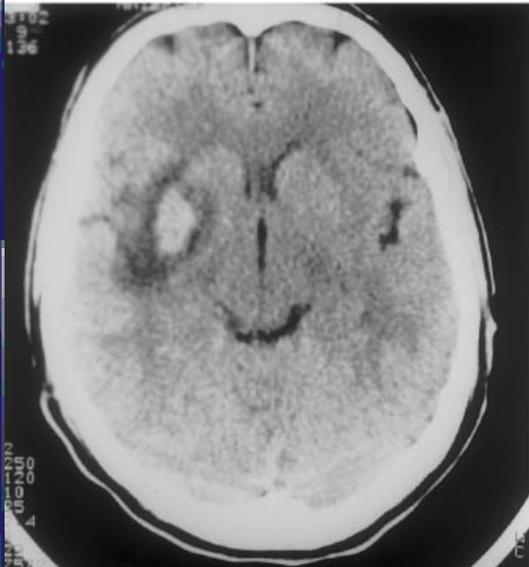
HI 1



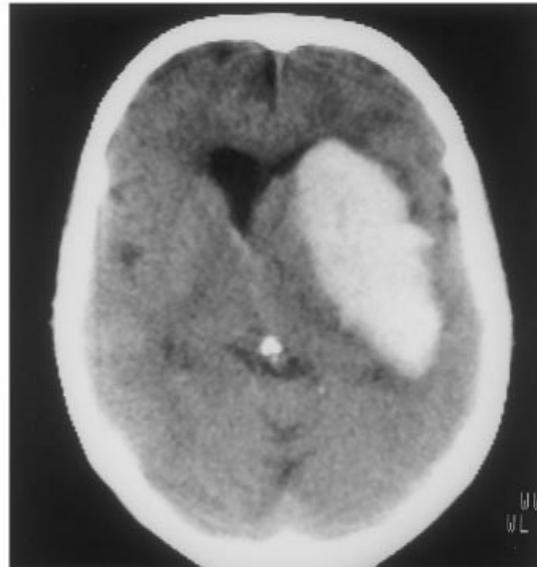
HI 2



PH 1



PH 2

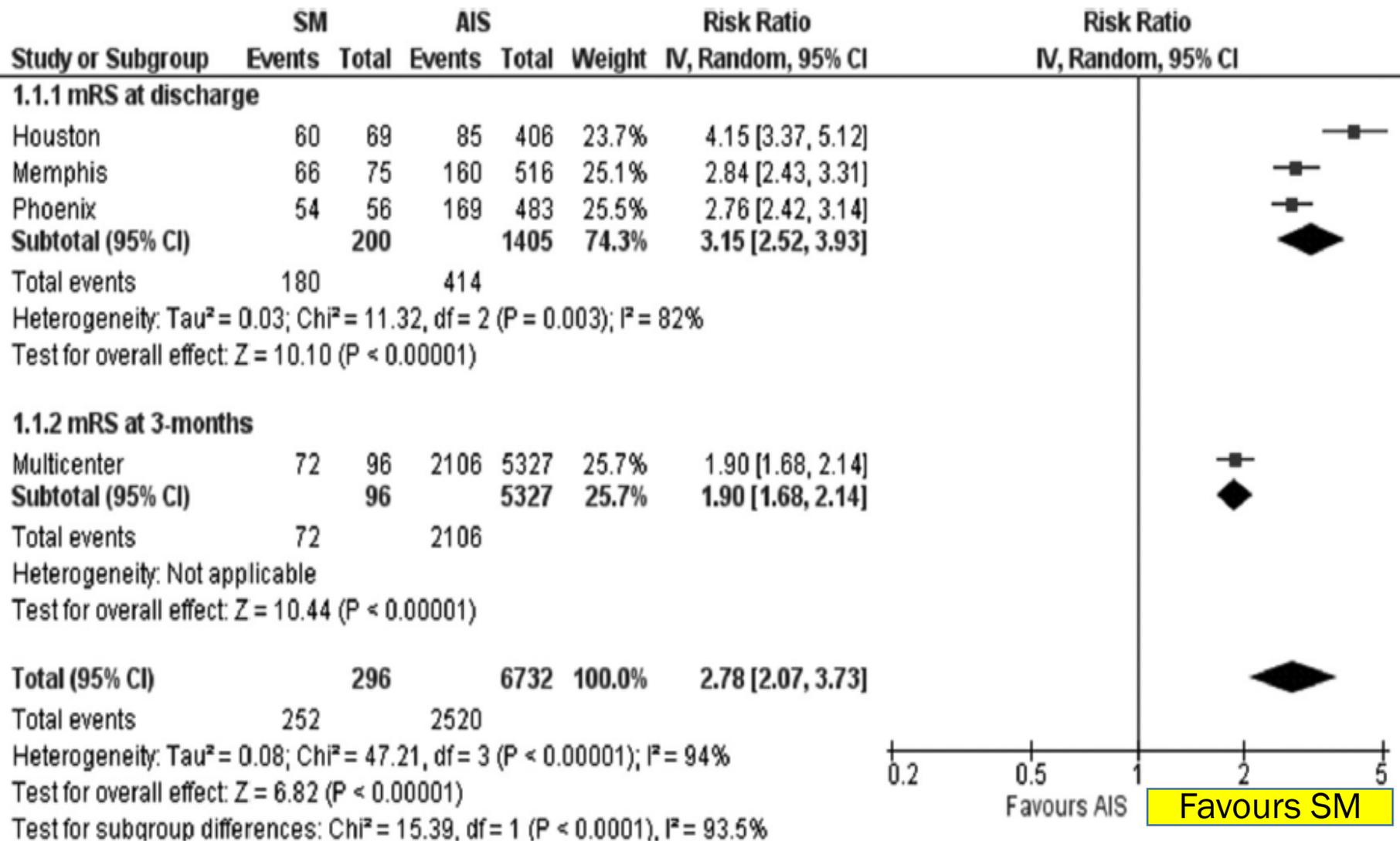


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# Meta-Analysis of 9 studies (89 IVT): favorable functional outcome at discharge and at 3-mo.



# Intravenous thrombolysis in stroke mimics: results from the SITS International Stroke Thrombolysis Register

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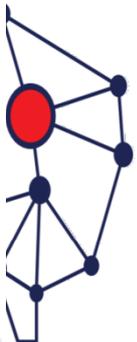
- the SITS International Stroke Thrombolysis Register 2003–2017
- MRI 22–36 h after IVT
- Outcome:
  - parenchymal hematoma (PH),
  - symptomatic intracerebral hemorrhage (SICH),
  - death
  - modified Rankin Scale score (mRS) at 3 months
- 10 436 patients, 429 mimics (4.1%)

# Baseline characteristic

Characteristic	SM with MRI follow-up ( <i>n</i> = 429)	Ischaemic stroke with MRI follow-up ( <i>n</i> = 10 007)	<i>P</i> -value
Patient history			
Age (years)	52 (39–65)	65 (54–75)	<0.001
Female	231/429 (53.8%)	4069/10 007 (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 score pre-IVT 0–1	382/422 (90.5%)	9033/9749 (92.7%)	0.099
Clinical parameters			
NIHSS score 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

# Frequency of stroke mimic (SM) categories

SM category	<i>n</i>	% 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	



# Outcomes

Outcome	SM ( <i>n</i> = 429)	AIS ( <i>n</i> = 10 007)	<i>P</i> -value
PH	5/429 (1.2)	508/9993 (5.1)	<0.001
SICH (SITS-MOST)	0/429 (0.0)	52/10 001 (0.5)	0.28 <sup>†</sup>
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 score 0–1 at 3 months	276/328 (84.1)	5004/8668 (57.7)	<0.001
mRS score 0–2 at 3 months	303/328 (92.4)	6020/8668 (69.4)	<0.001
Death at 3 months	9/342 (2.6)	456/8518 (5.4)	0.028



# Stroke Mimics via Telestroke



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# Prehospital Stroke Management and Systems of Care

## Telemedicine

**Telemedicine solutions can help to improve care when on-site expertise is not available**



- **Teleradiology** shown to be useful for rapid image interpretation
- **Telestroke can be effective for IV alteplase decision making**
  - Meta-analysis comparing telestroke to stroke centers showed no difference in mortality or functional outcomes at 3 months
- **Telestroke may be reasonable for triaging patients for mechanical thrombectomy**
  - A single observational study showed similar rates of reperfusion and functional outcomes between telestroke patients and those admitted directly to a tertiary care center

# Stroke Mimics under the Drip-and-Ship Paradigm

J Stroke Cerebrovasc Dis. 2014;23(5):844-9.

	Acute ischemic stroke, n = 100	Stroke mimics, n = 20	P value
Any intracerebral hemorrhage	24 (24%)	0	.01
Symptomatic intracerebral hemorrhage	7 (7%)	0	.22
Mortality	20 (20%)	0	.02
Discharge NIHSS, median (quartiles)	5 (2, 8)	0	<.0001
Discharge mRS, median (quartiles)	3 (2, 4)	0	<.0001
Discharge destination			<.0001
Home	24 (24%)	20 (100%)	
Acute rehabilitation facility	38 (38%)	0	
Skilled nursing facility	18 (18%)	0	

- 18 / 83 drip-and-ship pts (21.7%) were stroke mimic (SM)
- 2 / 37 directly to the hub hospital pts (5.4%) (P = 0.02)
- 14 conversion disorder, 2 migraine,
- 1 for: seizures, hypoglycemia, peripheral herpes zoster,
- and an exacerbation of an old stroke because of systemic infection

# Thrombolytic treatment to stroke mimic patients via telestroke

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- to compare the rate of pts receiving IVT with diagnosis of ischemic stroke as opposed to stroke mimic (SM) in TS network to those who presented to comprehensive stroke center (CSC)
- receiving IVT between August 2014 and June 2015 at CSC and TS network.
- 131 receiving IVT (74 CSC, 57 TS)
  - Rates of SM receiving IVT were similar
  - (CSC 12% versus 7% TS,  $p = 0.33$ ).



# Baseline and Clinical Characteristics by Diagnosis

	Stroke	Stroke mimic	P-value
N	118	13	
Age (Years)			0.10
Median (IQR)	73.5 (62-84)	61 (55-77)	
Me			
Numt			0.66
NIHSS			0.50
Me			
Onset			0.21
Me			
Hype			0.76
Dyslip			0.36
Diabe			>0.99
Atrial			0.51
Coronary artery disease/cardiomyopathy	39 (33%)	4 (31%)	>0.99
Previous Stroke/transient ischemic attack		5 (38%)	0.16
Nicotine abuse		3 (23%)	0.70
Alcohol abuse		2 (15%)	0.26
Migraine		3 (23%)	0.05
Cognitive impairment		3 (23%)	0.17
Epilepsy	5 (4%)	2 (15%)	0.14
Psychiatric illness	15 (13%)	7 (54%)	<0.01
Symptomatic intracerebral hemorrhage	1 (1%)	0	-
In-hospital mortality	3 (3%)	0	-
Discharge Destination			0.90
Home	64 (54%)	7 (54%)	
ARU	22 (19%)	3 (23%)	
Nursing Home	24 (20%)	3 (23%)	
Hospice	5 (4%)	0	
Morgue	3 (3%)	0	

**SM patients**

No sICH or in-hospital mortality

Discharge destination was similar

between stroke and SM patients

conversion dis-order (38%),  
migraine (23%),  
seizure (15%)

# Seizure at Onset and Stroke Mimics

# Intravenous Thrombolysis for Suspected Ischemic Stroke with Seizure at Onset

- Seizure at onset (SaO)
- Multicenter (9), IVT-registry-based study, TRISP
- assessed the association between SaO
  - sICH, (ECASS III), 3-mo mortality, 3-mo functional outcome (mRS)
- from 1998 to 2017 from 9 European stroke centers
- 10,074 IVT pts, 146 (1.5%) had SaO
  - ischemic stroke (89/146)
  - stroke mimics (57/146)
- SaO was not an independent predictor of poor prognosis either ischemic stroke or stroke mimics



# Summary of Studies Including 15 Patients Treated With Intravenous rtPA Who Had Seizures at Symptom Onset

Study	Study Design	Seizure/Total SMS, n	Average Initial NIHSS Score	Any ICH, n	sICH, n	mRS Score of 0–1, %
Winkler et al <sup>319</sup>	Retrospective of prospective registry	6/7	10*	0	0	86
Chernyshev et al <sup>334</sup>	Retrospective of prospective registry	26/69	7	0	0	87
Zinkstok et al <sup>294</sup>	Multicenter, observational cohort	81/100	6	NA	2	75
Tsivgoulis et al <sup>336</sup>	Retrospective of prospective registry	11/56	6	NA	0	96
Förster et al <sup>337</sup>	Retrospective of prospective registry	20/42	6.5	NA	0	NA
Chang et al <sup>338</sup>	Retrospective	6/14	6*	0	0	NA†

- almost 300 patients with seizure at onset who received iv tPA for stroke-like symptoms
- sICH has been reported in only 2 patients

# AHA/ASA 2019 Guideline for Early Management of AIS

# AHA/ASA Guideline

## Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

*Endorsed by the Society for Academic Emergency Medicine and The Neurocritical Care Society*

AHA/ASA Guideline Stroke. 2019;50:e•••–e•••.



# Stroke mimics

- The risk of symptomatic intracranial hemorrhage in the stroke mimic population is quite low;
- thus, starting IV alteplase is probably recommended in preference over delaying treatment to pursue additional diagnostic studies. †
- (COR IIa; LOE B-NR)§



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# Complications of iv tPA and Treatment



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# Complications of rtPA therapy

- Intracerebral hemorrhage 3-6%
- Internal organ bleeding 0.4%
- Mild lingual angioedema 1.3%
- Anaphylaxis leading to intubation 0.001%

# Suspect intracranial haemorrhage if:

1. Acute neurological deterioration
2. New headache
3. Nausea or vomiting
4. Acute increase in BP

# If intracranial haemorrhage is suspected:

1. Discontinue rt-PA administration
2. Organise CT brain
3. Bloods: FBC, APTT, INR, fibrinogen, cross match
4. Request FFP, cryoprecipitate and platelets ??

# Management of sICH after IV Alteplase

COR IIb

LOE C-E0

Stop alteplase infusion

CBC, PT (INR), aPTT, fibrinogen level, and type and cross-match

Emergent nonenhanced head CT

**[redacted]** (includes factor VIII): 10 U infused over 10–30 min (onset in 1 h, peaks in 12 h); administer additional dose for fibrinogen level of <150 mg/dL

**[redacted]** 1000 mg IV infused over 10 min OR **[redacted]** 4–5 g over 1 h, followed by 1 g IV until bleeding is controlled (peak onset in 3 h)  
(Potential for benefit in all patients, but particularly when blood products are contraindicated or declined by patient/family or if cryoprecipitate is not available in a timely manner.)

Hematology and neurosurgery consultations

Supportive therapy, including BP management, ICP, CPP, MAP, temperature, and glucose control

# Management of Angioedema after IV Alteplase

COR IIb

LOE C-EO

## Maintain airway

Endotracheal intubation may not be necessary

Edema involving larynx, palate, floor of mouth, or oropharynx with rapid progression (within 30 min) poses higher risk of requiring intubation.

Awake fiberoptic intubation is optimal. Nasal-tracheal intubation may be required but poses risk of epistaxis after IV alteplase. Cricothyroidotomy is rarely needed and also problematic after IV alteplase.

Discontinue IV alteplase infusion and hold ACE inhibitors

Administer IV methylprednisolone 125 mg

Administer IV diphenhydramine 50 mg

Administer ranitidine 50 mg IV or famotidine 20 mg IV

If there is further increase in angioedema, administer epinephrine (0.1%) 0.3 mL subcutaneously or by nebulizer 0.5 mL

icatibant, a selective bradykinin B<sub>2</sub> receptor antagonist, 3 mL (30 mg) subcutaneously in abdominal area; additional injection of 30 mg may be administered at intervals of 6 h not to exceed a total of 3 injections in 24 h; and plasma-derived C1 esterase inhibitor (20 IU/kg) has been successfully used in hereditary angioedema and ACE inhibitor-related angioedema

Supportive care

# Conclusions

- IV tPA is safe, good outcome in stroke mimics
  - The risk of sICH in the stroke mimic is quite low
- starting IV alteplase is probably recommended over delaying treatment to pursue additional diagnostic studies for acute ischemic stroke confirmation





**THANK YOU**



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