FERNE Update and Journal Club
ED Stroke Mimic and Chameleon Patient Care

Acute Ischemic Stroke Mimic and Chameleon Patients: Clinical Imperative

When evaluating patients with possible acute ischemic stroke (AIS), clinicians must consider two critical clinical questions:

“Can the clinician rapidly and safely distinguish true CNS ischemia from stroke mimic patients while preserving the speed necessary to provide timely reperfusion therapy for eligible AIS patients?”

“If a patient with a stroke mimic receives thrombolytic therapy because AIS cannot be excluded, or if a stroke chameleon patient is mistakenly diagnosed with a non-stroke condition, what are the clinical consequences for the patient and clinician, including untoward neurological disability?”

This is an important clinical situation for the following reasons:

- Stroke mimics patients often present with focal neurological deficits that resemble AIS.
- Stroke chameleon patients with true CNS ischemia presenting atypically which delays the diagnosis of AIS and the delivery of reperfusion therapies.
- Stroke chameleon patients with posterior circulation ischemia may present without weakness or aphasia and may initially have negative CT imaging.
- Emergency clinicians must balance diagnostic certainty with treatment urgency, especially thrombolytic therapies, during the time-critical stroke patient evaluation and reperfusion period.

FERNE Educational Content

This FERNE educational presentation examines the Emergency Department evaluation and management of patients with possible acute ischemic stroke (AIS) who may present as stroke mimic or stroke chameleon patients. The educational content reviews the clinical features, differential diagnosis, neuroimaging, and treatment considerations associated with CNS ischemia, stroke mimics, and patients presenting with atypical symptoms. Dr. Sloan also emphasizes posterior circulation ischemia and acute vestibular syndrome as important potential stroke chameleon presentations.

Stroke Mimic Patient Case Information

A 29-year-old woman with a history of epilepsy presents to the ED with sudden right arm and leg weakness and aphasia after witnessed rhythmic jerking movements at home. On arrival, she is confused but gradually improving. Her neurological deficits begin to improve during the ED evaluation. Exam reveals mild residual weakness and postictal confusion. Non-contrast CT (NCCT) neuroimaging is negative for hemorrhage.

If this patient eventually is diagnosed as a stroke mimic and the patient was provided thrombolytic therapy because of suspected acute ischemic stroke, will the mimic patient's outcome still be safe and optimal?

The answer, based on the published clinical evidence reviewed in this presentation, is generally yes. Stroke mimic patients who receive thrombolytic therapy usually have low complication rates, rare intracranial hemorrhage, and generally uncomplicated clinical courses.

The FERNE stroke mimic and stroke chameleon presentation listed below was updated using a **slide-by-slide, question-directed PubMed evidence review**. For each important clinical statement or older reference in the existing PowerPoint, we identified the specific clinical concept being taught and searched PubMed for the **best recent 2025–2026 publication that directly addressed that same concept**, rather than simply selecting the newest stroke publication. Each newer article was then reviewed for its methods, patient population, clinically important numerical findings, conclusions, and relevance to Emergency Department practice. The new evidence was compared directly with the original slide to determine whether the existing teaching point should be **kept, strengthened, modified, or replaced**, while the older foundational references were retained when they continued to provide useful support. Finally, the updated evidence was synthesized into practical clinical questions and recommendations emphasizing the bedside challenges of distinguishing AIS from stroke mimics, recognizing stroke chameleons—particularly posterior circulation ischemia—and preserving timely, appropriate reperfusion therapy despite diagnostic uncertainty.

The PPT presentation used is name:

FERNE Stroke Mimic Patient Rx Sloan Update 081126.

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24 Key Clinical Questions and Answers
ED Stroke, Mimic, and Chameleon Patient Care

1. What is the most important first principle when evaluating suspected AIS?

Treat an acute focal neurological syndrome as possible CNS ischemia until the evaluation establishes a more likely diagnosis.

Stroke is a clinical syndrome rather than a diagnosis, and several disorders can reproduce the findings of AIS. Conversely, true ischemic stroke may present atypically and become a stroke chameleon. No single historical feature, examination finding, or initial test reliably separates all strokes from mimics. The ED objective is therefore rapid probability-based diagnosis while preserving access to time-sensitive reperfusion therapy. (2,7,12)

2. How common are stroke mimics during suspected stroke evaluation?

Stroke mimics are common enough that every emergency physician evaluating acute stroke will encounter them regularly.

In a contemporary cohort, 19.1% of patients evaluated for suspected stroke/TIA were ultimately diagnosed with a stroke mimic. (14) Among patients with minor but disabling symptoms who received thrombolysis, 29% were subsequently classified as mimics. (1) The exact percentage varies substantially with patient selection, stroke activation criteria, and treatment population. Mimics should therefore be expected rather than regarded as rare diagnostic errors. (1,9,10,14,16)

3. What demographic characteristics help distinguish AIS from stroke mimics?

Older age and vascular risk factors increase the probability of AIS, while younger age favors a mimic—but demographics should never exclude stroke.

Stroke/TIA patients in Sørensen were older than mimics, with median ages of 74 versus 67 years. (14) In Klimbytė, AIS patients averaged 70.2 years compared with 57.4 years among mimics and more commonly had hypertension, diabetes, and atrial fibrillation. (9) However, Brunser found that true AIS patients presenting as chameleons were younger than readily recognized stroke patients, 59 versus 70 years. (4) Demographics should therefore modify pretest probability rather than determine the diagnosis.

4. Does abrupt symptom onset reliably distinguish AIS or TIA from a mimic?

Abrupt onset supports CNS ischemia but does not reliably distinguish ischemia from a stroke mimic.

Sudden onset occurred in 59.3% of stroke/TIA patients and 51.3% of mimics in the contemporary Sørensen cohort. (14) Thus, the traditional sudden-onset vascular pattern remains useful but lacks sufficient specificity to make the diagnosis independently. Seizure, migraine, metabolic disorders, and other mimics may also produce abruptly recognized deficits. The clinician should integrate onset with the type of deficit, evolution, examination, vascular territory, risk factors, and imaging.

5. Which symptoms most strongly favor true CNS ischemia?

Abrupt negative focal neurological deficits—particularly unilateral loss of motor function—should increase concern for CNS ischemia.

Limb weakness occurred in 48.0% of stroke/TIA patients compared with 23.9% of mimics. (14) Difficulty controlling an extremity occurred in 35.7% versus 16.8%, respectively. (14) Facial weakness, limb weakness, sensory loss, dysarthria, gaze abnormalities, and visual-field abnormalities also made AIS more readily recognizable in the Brunser chameleon study. (4) The absence of these classic findings, however, should prompt consideration of an atypical stroke rather than automatically favoring a mimic.

6. Can a low NIHSS safely exclude AIS?

A low or even zero NIHSS does not exclude clinically important AIS, particularly mild disabling and posterior circulation stroke.

Stroke chameleons in Brunser had a median NIHSS of only 1, and 82.5% had NIHSS scores ≤5. (4) Afzal specifically examined patients with NIHSS ≤5 and disabling symptoms; 71% ultimately had true ischemic stroke despite their low scores. (1) NIHSS incompletely captures gait, balance, vertigo, some cranial nerve abnormalities, and other posterior circulation findings. The emergency physician should therefore assess whether a deficit is disabling rather than allowing the numerical NIHSS alone to determine clinical importance.

7. How should seizure and Todd's paralysis be approached?

Seizure and Todd's paralysis are important mimics, but seizure-associated focal deficits still require evaluation for CNS ischemia.

Epilepsy strongly favored a mimic in Klimbytė, with an OR of 31.11, and Todd's paralysis accounted for 8.1% of mimics. (9) Seizure accounted for 17% of mimics in Afzal and 19% in the Loggini telestroke population. (1,10) Postictal weakness, aphasia, or sensory deficits may closely reproduce an acute vascular syndrome. Because ischemic stroke itself may provoke seizure, the clinician should determine the temporal sequence rather than assuming seizure proves a nonvascular diagnosis.

8. Why should glucose and metabolic disorders be evaluated immediately?

Identify glucose and other important metabolic abnormalities early because they are treatable causes of stroke-like neurological deficits.

Toxic-metabolic encephalopathy represented 40% of thrombolysed telestroke mimics in Loggini. (10) It accounted for 27% of mimics among Afzal's patients receiving thrombolysis for minor but disabling suspected AIS. (1) Rapid bedside glucose testing can identify an immediately reversible abnormality without delaying the remainder of the stroke evaluation. Persistent focal neurological deficits after correction should prompt continued investigation for concomitant CNS ischemia.

9. How important is migraine with neurological aura?

Migraine with neurological aura remains a major stroke mimic, particularly in younger patients, but migraine history cannot independently exclude AIS.

A history of migraine independently favored a mimic in Klimbytė with an OR of 8.47, and migraine accounted for 24.3% of mimics. (9) Migraine accounted for 50% of mimics in Afzal's minor disabling deficit population. (1) Sørensen found migraine in 11.5% of mimics, while complex migraine represented 5% of telestroke mimics in Loggini. (10,14) Sequential evolution and positive spreading symptoms may favor migraine, but an otherwise convincing ischemic syndrome still requires stroke evaluation.

10. How should functional neurological disorder be approached?

Diagnose functional neurological disorder from positive clinical findings while continuing to appropriately evaluate the possibility of CNS ischemia.

Functional/conversion disorder accounted for 35% of thrombolysed telestroke mimics in Loggini. (10) Functional neurological disorder represented 24.3% of mimics in Klimbytė. (9) Findings such as give-way weakness or other internally inconsistent neurological signs may support FND but may be more difficult to assess remotely. Psychiatric history alone should never be used to terminate an AIS evaluation.

11. What diagnoses belong in a practical ED stroke-mimic differential?

Prioritize seizure, migraine, toxic-metabolic disease, FND, systemic illness, peripheral vestibular disease, infection, and structural CNS lesions.

The established mimic differential also includes hypoglycemia, transient global amnesia, encephalitis, venous thrombosis/infarction, tumors, Bell's palsy, and peripheral nerve disorders. (2,12) Peripheral vertigo accounted for 24.7% of mimics in the contemporary Sørensen population. (14) CNS tumors accounted for 8.1% of mimics in Klimbytė. (9) The differential should be driven by the patient's specific syndrome rather than approached as a generic checklist.

12. What exactly is a stroke chameleon?

A stroke chameleon is true CNS ischemia presenting atypically enough that the initial diagnosis of stroke may be missed.

Among 1,197 confirmed AIS patients in Brunser, 63—5.2%, or approximately 1 in 20—were stroke chameleons. (4) These patients tended to have less obvious focal neurological findings and lower NIHSS scores. Chameleons are fundamentally different from mimics: the mimic does not have AIS, whereas the chameleon does. (4,7) The clinical danger of a chameleon is delayed recognition of genuine ischemia and potential loss of treatment opportunity.

13. Which findings should specifically trigger concern for a stroke chameleon?

Mild deficits, atypical symptoms, altered consciousness, transient symptoms, posterior findings, and atrial fibrillation should increase vigilance for a chameleon.

Stroke chameleons had a median NIHSS of 1 compared with 3 among immediately recognized AIS patients. (4) Altered level-of-consciousness components were strongly associated with chameleon presentation. (4) Atrial fibrillation was independently associated with chameleon presentation, with an OR of 2.22 in the ED clinical model. (4) An atypical presentation should therefore stimulate more careful localization and reassessment rather than provide reassurance.

14. Why is posterior circulation ischemia particularly important?

Posterior circulation ischemia is a major source of stroke chameleons because dizziness, imbalance, and subtle neurological deficits may occur without classic hemiparesis or aphasia.

Posterior circulation involvement produced approximately threefold greater odds of a chameleon presentation in Brunser, OR 3.02. (4) Tysland notes that approximately 3%–5% of acute dizziness presentations are attributable to posterior circulation stroke and that some posterior strokes may present with isolated dizziness. (15) Vertigo occurred in 25.7% of patients with true stroke/TIA in Sørensen despite also being common among mimics. (14) Posterior symptoms therefore require localization rather than reflex assignment to a benign peripheral vestibular disorder.

15. How should acute vestibular syndrome be evaluated for possible stroke?

Assess gait, truncal ataxia, nystagmus, hearing, and associated neurological findings, using HINTS+ appropriately when performed by trained clinicians.

Tysland emphasizes that bedside neuro-ophthalmological assessment remains important because posterior stroke may be difficult to recognize with routine stroke assessment. (15) HINTS and related structured bedside approaches have high diagnostic accuracy when correctly applied by trained providers. (15) A normal or very low NIHSS does not adequately evaluate many vestibular and posterior circulation abnormalities. Advanced neuroimaging is appropriate when the clinical evaluation continues to suggest central ischemia.

16. Can initially negative CT or CTA exclude AIS?

Normal early NCCT and absence of an arterial occlusion on CTA do not exclude acute cerebral ischemia.

Klimbytė studied 330 thrombolysed patients with no early ischemic NCCT findings and no arterial occlusion on CTA; 293 were ultimately classified as AIS and only 37 as mimics. (9) NCCT is indispensable for detecting hemorrhage but may remain normal during early ischemia. CTA identifies important vascular pathology but cannot identify every ischemic event. Imaging must therefore be interpreted within the neurological syndrome rather than used as an isolated stroke/no-stroke test.

17. Can a negative early DWI MRI exclude ischemic stroke?

Negative early DWI decreases the probability of infarction but does not completely eliminate AIS, especially when the clinical syndrome suggests posterior ischemia.

Afzal included patients ultimately classified as true stroke despite negative DWI, including posterior circulation presentations. (1) The updated presentation therefore appropriately emphasizes that negative DWI should not automatically override a compelling neurological syndrome. Small lesions, early imaging, and posterior location may contribute to diagnostic difficulty. Continued focal symptoms or recurrent deficits warrant reassessment rather than automatic diagnostic closure.

18. What is the significance of recurrent stereotyped transient deficits?

Recurrent stereotyped transient motor or sensory deficits can represent unstable cerebral ischemia and should not be dismissed because they completely resolve.

Shariff's capsular warning syndrome case illustrates recurrent transient face, arm, and leg deficits followed by persistent neurological dysfunction and MRI-confirmed infarction. (13) These episodes may repeatedly resolve before a completed stroke develops. The presentation can be mistaken for seizure, migraine, or another transient neurological disorder. Recurrent stereotyped focal deficits therefore warrant urgent stroke evaluation and repeated neurological reassessment.

19. How safe is IV thrombolysis when the patient ultimately proves to be a mimic?

Contemporary studies show a very low rate of serious hemorrhagic complications when stroke mimics inadvertently receive IV thrombolysis.

Afzal reported no symptomatic ICH, asymptomatic ICH, extracranial bleeding, or thrombolysis-related adverse events among 18 mimics. (1) Klimbytė reported no intracranial hemorrhage among 37 thrombolysed mimics, with 92% having mRS 0 at discharge. (9) Loggini reported no symptomatic ICH among 43 thrombolysed telestroke mimics, and 86% were discharged home; the larger Zinkstok experience likewise established a substantially lower sICH risk in mimics than in true ischemic stroke. (10,16) These data support a favorable safety profile but should not be interpreted as indicating zero risk.

20. Should concern about a possible mimic delay otherwise indicated IV thrombolysis?

When AIS remains clinically likely and the patient is otherwise eligible, uncertainty about a possible mimic should not unnecessarily delay indicated thrombolysis.

The older thrombolysis experience demonstrated that inadvertent treatment of mimics generally produced few serious complications. (3,11,16) Contemporary Afzal, Klimbytė, and Loggini data reinforce that finding in modern stroke populations. (1,9,10) Clinical prediction tools and demographic features are not sufficiently reliable to eliminate diagnostic uncertainty before every treatment decision. The bedside goal is rapid evidence-based treatment of eligible patients—not absolute diagnostic certainty before thrombolysis.

21. Does transfer for thrombectomy change the approach to IV thrombolysis?

Provide indicated IV thrombolysis promptly in eligible patients even when transfer for possible endovascular thrombectomy is being arranged.

The drip-and-ship experience demonstrates that transferred thrombolysed populations may include more mimics than patients evaluated initially at a stroke hub. (11) Mehta reported a **22% mimic rate among drip-and-ship patients compared with 5.4% among patients treated at the hub hospital**. (11) Importantly, the mimics in that experience did not experience ICH and were discharged home. The possibility of later diagnostic revision or transfer should therefore not itself become a reason to withhold otherwise indicated time-sensitive therapy.

22. What does methotrexate-induced leukoencephalopathy teach the emergency physician?

In a patient receiving methotrexate, an acute stroke-like syndrome with diffusion restriction may represent treatment-related leukoencephalopathy rather than arterial ischemia.

The earlier Gosavi case described a 17-year-old with ALL receiving intrathecal methotrexate who developed recurrent reversible paresthesias and clumsiness with MRI abnormalities resembling AIS. (8) This demonstrates that chemotherapy-related neurotoxicity can produce both focal symptoms and imaging findings capable of mimicking ischemic stroke. Medication and oncologic treatment history should therefore be obtained during the acute neurological assessment whenever feasible. The diagnosis requires a high index of suspicion because the presentation may look strikingly vascular. (8)

23. What does the newer methotrexate leukoencephalopathy case add?

Methotrexate neurotoxicity can produce a dramatic acute aphasic encephalopathy with diffusion restriction sufficiently convincing to result in thrombolysis.

Duong described a 16-year-old with ALL receiving high-dose methotrexate who developed sudden dysphasia and cognitive slowing progressing to global aphasia and altered consciousness. (6) MRI demonstrated bilateral diffusion restriction initially suggesting acute ischemia, and IV alteplase was administered before methotrexate toxicity was recognized. (6) Methotrexate was withheld and supportive care resulted in complete neurological recovery within three days. (6) The practical lesson is to include recent chemotherapy exposure in the differential when the clinical or MRI distribution is unusual for a vascular territory.

24. What does spontaneous spinal epidural hematoma teach us about stroke mimics?

Sudden hemiparesis accompanied by prominent neck or cervical pain should trigger consideration of spinal epidural hematoma before thrombolysis.

Castelo-Pablos described a young patient with sudden cervical pain followed by acute hemiparesis and sensory deficits that initially suggested AIS; the initial brain CT was unremarkable. (5) Cervicothoracic MRI subsequently demonstrated an epidural hematoma extending from C3 to T2 with spinal cord compression. (5) Surgical decompression and hematoma evacuation were performed, with complete neurological recovery within one month. (5) The bedside lesson is that **acute neck/back pain plus hemiparesis or an examination suggesting spinal localization is a critical red flag for a dangerous structural stroke mimic before thrombolysis.**

Overall Clinical Take-Home

Recognize common mimics, actively search for chameleons, distrust false reassurance from low NIHSS or early negative imaging, and preserve timely reperfusion therapy when AIS remains clinically likely.

The 16 references collectively reinforce that mimics are common and diagnostically challenging, but serious complications from inadvertent thrombolysis of mimics are uncommon. Posterior circulation disease, mild deficits, transient symptoms, and atypical presentations deserve particular attention because these are settings in which true ischemia may be missed. The unusual case reports add an equally important counterbalance: medication toxicity and spinal structural disease can sometimes reproduce both the clinical and imaging appearance of AIS. The emergency physician therefore needs **rapid treatment coupled with disciplined diagnostic vigilance**, rather than either indiscriminate thrombolysis or excessive delay in pursuit of diagnostic certainty.

Clinical Action Steps
ED Stroke, Mimic, and Chameleon Patient Care

1. **Treat an acute focal neurologic syndrome as possible AIS until adequately evaluated.**
   Begin the stroke pathway promptly while simultaneously considering important mimics and chameleons.
2. **Establish last-known-well and symptom evolution immediately.**
   Determine whether symptoms were sudden, progressive, fluctuating, recurrent, or completely resolved.
3. **Identify the disabling neurologic deficit—not simply the NIHSS score.**
   Aphasia, visual loss, severe ataxia, or dominant-hand weakness may be disabling despite a low NIHSS.
4. **Perform and document a focused, complete neurologic examination.**
   Assess consciousness, language, speech, gaze, vision, face, motor, sensory, coordination, gait, and balance.
5. **Check bedside glucose early.**
   Hypoglycemia and other metabolic abnormalities are common, treatable stroke mimics.
6. **Use demographics and vascular risk factors to modify probability—not exclude AIS.**
   Younger age and fewer vascular risks favor mimics, but true stroke and chameleons still occur in these patients.
7. **Actively consider the common stroke mimics.**
   Specifically consider seizure/Todd paralysis, migraine, FND, toxic-metabolic disease, systemic illness, and peripheral vestibular disease.
8. **Ask specifically about seizure activity and postictal symptoms.**
   Todd paralysis can closely resemble AIS, while AIS itself may precipitate a seizure.
9. **Ask about migraine history and symptom evolution.**
   Positive or spreading neurologic phenomena favor migraine aura, whereas abrupt negative deficits favor ischemia.
10. **Look for positive findings of functional neurological disorder.**
    Diagnose FND from characteristic examination findings rather than psychiatric history or demographic assumptions.

11. **Actively search for stroke chameleons when the presentation seems atypical.**
    Mild, transient, fluctuating, unusual, or poorly localizing symptoms may still represent genuine cerebral ischemia.

12. **Do not allow a low or zero NIHSS to falsely reassure you.**
    Mild disabling and posterior circulation strokes may have NIHSS scores of 0–5.

13. **Take recurrent stereotyped focal deficits seriously.**
    Repeated transient face-arm-leg weakness or sensory loss may represent unstable ischemia such as capsular warning syndrome.

14. **Maintain heightened suspicion for posterior circulation ischemia.**
    Vertigo, dizziness, imbalance, diplopia, dysarthria, ataxia, or difficulty walking may be the predominant stroke manifestations.

15. **Evaluate acute vestibular syndrome systematically.**
    Assess gait/truncal ataxia, nystagmus, hearing, and associated neurological findings; use HINTS+ appropriately when trained.

16. **Use imaging to support—not replace—clinical judgment.**
    Normal early NCCT, absence of CTA occlusion, and occasionally negative early DWI do not completely exclude AIS.

17. **Look for red flags suggesting an unusual structural or toxic mimic.**
    Severe neck/back pain may suggest spinal epidural hematoma, while recent methotrexate or other neurotoxic therapy should raise concern for treatment-related encephalopathy.

18. **Provide indicated IV thrombolysis promptly when AIS remains clinically likely.**
    Diagnostic uncertainty about a possible mimic should not unnecessarily delay treatment in an otherwise eligible patient.

19. **Proceed with appropriate thrombectomy evaluation and transfer while preserving timely thrombolysis.**
    When indicated, initiate IV thrombolysis and rapidly arrange transfer/endovascular evaluation rather than treating these as competing strategies.

20. **Reassess, document your reasoning, and revise the diagnosis as new information arrives.**
    Record why AIS, TIA, mimic, or chameleon is suspected; reassess after treatment, imaging, symptom evolution, and additional clinical data.

Key Clinical Facts
ED Stroke, Mimic, and Chameleon Patient Care

Emergency Department Patients with Suspected AIS

1. Acute ischemic stroke remains fundamentally a clinical diagnosis supported—not replaced—by imaging. (1,2)

The emergency physician must integrate onset, focal deficits, neurological localization, risk factors, and imaging. Waiting for absolute diagnostic certainty can sacrifice the time-dependent benefit of reperfusion.

2. Sudden symptom onset supports AIS but does not reliably distinguish stroke from a mimic. (14)

Sudden onset occurred in **59.3% of stroke/TIA patients versus 51.3% of mimics**, which was not significantly different. The nature and localization of the neurological deficit are therefore more useful than onset alone.

3. Loss of neurological function is more characteristic of cerebral ischemia than many positive neurological phenomena. (12,14)

Stroke/TIA patients more often reported weakness, impaired limb control, facial weakness, and speech difficulty than mimics. Negative deficits such as loss of strength, speech, sensation, or vision should therefore heighten concern for ischemia.

4. Limb weakness substantially increases the probability that a suspected stroke syndrome represents true stroke/TIA. (14)

Limb weakness occurred in **48.0% of stroke/TIA patients versus 23.9% of mimics**. Difficulty controlling an extremity was also more common with stroke/TIA.

5. Multiple BE-FAST findings favor true stroke/TIA but cannot establish the diagnosis. (14)

At least two BE-FAST symptoms occurred in **58.9% of stroke/TIA patients versus 36.3% of mimics**. A classic multidomain focal syndrome therefore raises ischemic probability, but atypical strokes remain important.

6. A low NIHSS does not mean that a neurological deficit is clinically unimportant or nonischemic. (1,4)

Among patients with NIHSS ≤5 and disabling symptoms in Afzal, **71% ultimately had true ischemic stroke**. The clinician should determine whether the deficit is disabling rather than using the NIHSS number alone to decide its significance.

7. Normal early NCCT does not exclude AIS. (2,9)

Klimbytė evaluated thrombolysed patients without early ischemic NCCT findings or arterial occlusion on CTA, yet most ultimately had AIS. NCCT's immediate role is particularly important for excluding hemorrhage rather than proving that ischemia is present.

8. Absence of an arterial occlusion on CTA does not exclude clinically important cerebral ischemia. (9)

In Klimbytė's cohort of **330 thrombolysed patients with no early NCCT ischemic changes and no CTA occlusion, 293 were ultimately classified as AIS and 37 as mimics**. Small-vessel, recanalized, and other non-LVO ischemic events remain possible despite negative vascular imaging.

9. Negative early DWI should not automatically override a compelling ischemic neurological syndrome. (1,4)

Some patients ultimately classified as true stroke in Afzal were DWI-negative, including posterior circulation presentations. Brunser similarly cautions that neurological symptoms in a patient with atrial fibrillation deserve continued stroke consideration even with negative DWI.

10. The ED objective is rapid probability-based diagnosis—not elimination of every possible mimic before treatment. (1,3,9,10,16)

Stroke and mimics overlap sufficiently that some diagnostic uncertainty will remain during the thrombolysis window. The appropriate response is disciplined clinical evaluation while preserving timely treatment for eligible patients.

Stroke Mimic Patients

11. Stroke mimics are common among patients entering an acute stroke pathway. (1,9,10,14)

Sørensen found **113 mimics among 592 suspected stroke/TIA patients—19.1%**. Mimic frequency varies substantially depending on whether the population includes all stroke alerts or only patients selected for thrombolysis.

12. Stroke mimics tend to be younger than patients with true stroke/TIA, but age cannot exclude AIS. (9,14)

Sørensen found median ages of **67 years for mimics versus 74 years for stroke/TIA**. Klimbytė similarly found mean ages of **57.4 versus 70.2 years**, respectively.

13. Peripheral vestibular disease is a major contemporary stroke mimic. (14,15)

Peripheral vertigo accounted for **24.7% of mimics** in Sørensen. Because posterior circulation ischemia can produce nearly identical dizziness and vertigo, the distinction requires careful neurological and vestibular examination.

14. Migraine remains one of the most important neurological stroke mimics. (1,9,10,12,14)

Migraine represented **50% of mimics in Afzal**, 24.3% in Klimbytė, and 11.5% in Sørensen. A migraine history increases mimic probability but cannot independently exclude new cerebral ischemia.

15. A history of migraine strongly increases the probability of a mimic in selected thrombolysis populations. (9)

Klimbytė found migraine history independently associated with stroke mimic diagnosis, **OR 8.47**. This is useful probabilistically but is not sufficiently discriminatory to withhold treatment from an otherwise eligible patient.

16. Seizure and Todd paralysis remain important stroke mimics. (1,9,10,12)

Epilepsy strongly predicted mimic status in Klimbytė, **OR 31.11**, while seizure accounted for **19% of thrombolysed telestroke mimics** in Loggini. Stroke itself can precipitate seizure, so the sequence of seizure and neurological deficit remains critical.

17. Toxic-metabolic encephalopathy can produce neurological deficits convincing enough to trigger thrombolysis. (1,10)

Toxic-metabolic encephalopathy accounted for **40% of mimics** in Loggini and **27% in Afzal**. This reinforces the importance of rapid glucose measurement, medication review, laboratory assessment, and identification of reversible metabolic abnormalities.

18. Functional neurological disorder is a common and clinically convincing stroke mimic. (1,9,10)

Functional/conversion disorders represented **35% of mimics in Loggini** and **24.3% in Klimbytė**. Diagnosis should depend on positive functional findings rather than psychiatric history or demographic assumptions.

19. Structural CNS and spinal disorders can occasionally produce striking stroke-like syndromes. (5,9)

CNS tumors accounted for **8.1% of mimics** in Klimbytė, while Castelo-Pablos demonstrated that cervical spinal epidural hematoma can present as acute hemiparesis. Prominent neck/back pain, absent cranial findings, or spinal localization should prompt consideration of spinal imaging.

20. Medication-related neurotoxicity can mimic both the clinical and MRI appearance of AIS. (6,8)

Gosavi and Duong demonstrate that methotrexate neurotoxicity can produce focal deficits and restricted diffusion that initially appear ischemic. Recent chemotherapy exposure and nonterritorial, shifting, or reversible MRI abnormalities should raise suspicion for toxic leukoencephalopathy.

Stroke Chameleon Patients

21. A stroke chameleon is true cerebral ischemia that initially appears to be another disorder. (4,7)

This is the conceptual opposite of a stroke mimic: the patient truly has ischemic stroke, but the presentation obscures the diagnosis. Chameleons are particularly dangerous because missed recognition can prevent reperfusion and appropriate stroke-unit care.

22. Stroke chameleons are clinically important—not exceptional curiosities. (4,7)

In Brunser's contemporary cohort, **63 of 1,197 confirmed AIS patients—5.2%, approximately 1 in 20—were stroke chameleons**. Emergency physicians should therefore deliberately search for atypical manifestations of genuine ischemia.

23. Stroke chameleons commonly have mild neurological deficits. (4)

The median NIHSS among chameleons was only **1**, compared with 3 in immediately recognized AIS. Mild examination findings should therefore not produce premature diagnostic closure.

24. Most contemporary stroke chameleons have NIHSS scores ≤5. (4)

Brunser found **82.5% of chameleons had NIHSS ≤5**. This is clinically important because the patient most easily dismissed as “too mild to be stroke” may actually represent missed AIS.

25. Younger patients with genuine AIS are more likely to become diagnostic chameleons. (4)

Chameleon patients averaged approximately **59 years compared with 70 years** among readily recognized AIS patients. Younger age should therefore decrease—but never eliminate—the probability of ischemia.

26. Posterior circulation ischemia is one of the most important stroke-chameleon presentations. (4,15)

Posterior circulation involvement was independently associated with approximately **threefold greater odds of chameleon presentation, OR 3.02**. Dizziness, vertigo, imbalance, ataxia, and subtle ocular findings deserve particularly careful evaluation.

27. Vertigo increases the probability of a mimic but cannot exclude posterior circulation ischemia. (14,15)

Vertigo occurred in **42.5% of mimics but also 25.7% of true stroke/TIA patients** in Sørensen. The clinician therefore cannot safely translate “vertigo” into “peripheral disease.”

28. NIHSS 0 does not exclude posterior circulation stroke. (4,15)

Posterior circulation deficits are incompletely represented in the NIHSS, particularly gait, balance, vestibular, and some ocular findings. Tysland reinforces the need for a targeted neuro-ophthalmological and vestibular examination in acute dizziness.

29. Atrial fibrillation should sustain concern for ischemia even when initial imaging is unrevealing. (4)

Atrial fibrillation independently increased the odds of chameleon presentation in Brunser, **OR 2.22**. The authors specifically caution that neurological symptoms in a patient with AF and negative DWI should still be carefully evaluated as possible stroke.

30. Recurrent stereotyped transient deficits can represent unstable cerebral ischemia rather than a benign mimic. (12,13)

Capsular warning syndrome can produce repeated face-arm-leg motor or sensory episodes with complete recovery between attacks before completed infarction. These patients warrant urgent stroke evaluation and repeated neurological reassessment rather than reassurance based on transient resolution.

IV Thrombolytic Therapy: Safety with Mimics & Diagnostic Uncertainty

31. Serious hemorrhagic complications are uncommon when stroke mimics inadvertently receive IV thrombolysis. (1,3,9,10,11,16)

This finding is remarkably consistent across older multicenter experience and the newer 2025 cohorts. Clinically, this matters because demanding absolute diagnostic certainty before treatment risks delaying therapy in true AIS.

32. Afzal observed no thrombolysis-related adverse events among 18 treated stroke mimics. (1)

There were **0 symptomatic ICH, 0 asymptomatic ICH, 0 extracranial bleeding events, and no other reported thrombolysis-associated adverse events**. In contrast, the true-stroke group had one symptomatic ICH and two asymptomatic ICHs.

33. Most thrombolysed mimics in Afzal had excellent short-term functional outcomes. (1)

Sixteen of 18 mimics—89%—had discharge mRS <1, compared with 39% of true-stroke patients. Mimics also had shorter hospital stays, although treatment still consumes substantial stroke-system resources.

34. Klimbytė found no intracranial hemorrhage among 37 thrombolysed stroke mimics. (9)

In addition, **92% of the mimics had mRS 0 at discharge**, compared with 19% of AIS patients. This contemporary cohort strongly reinforces the favorable safety profile of inadvertent mimic thrombolysis.

35. Telemedicine thrombolysis inevitably includes some patients ultimately diagnosed as mimics. (10)

Among **171 thrombolysed telestroke patients, 43—25%—were ultimately stroke mimics**. Rapid remote treatment therefore requires acceptance of some diagnostic uncertainty.

36. Clinical prediction tools are not reliable enough to safely eliminate all mimics before thrombolysis. (10)

The TeleStroke Mimic score had a **c-statistic of only 0.61** in Loggini. The investigators concluded that the identified clinical variables were insufficient to define a subgroup in whom thrombolysis could safely be withheld.

37. Most thrombolysed telestroke mimics had favorable disposition. (10)

Loggini found **86% of mimics were discharged home versus 55% of patients with cerebrovascular disease**. This supports the generally favorable clinical course observed among inadvertently thrombolysed mimics.

38. The drip-and-ship model can produce a higher proportion of thrombolysed mimics than treatment at the stroke hub. (11)

Mehta reported a **22% mimic rate in drip-and-ship patients compared with 5.4% among patients treated at the hub hospital**. This reflects the diagnostic tradeoff inherent in initiating time-sensitive treatment before transfer rather than waiting for tertiary-center reassessment.

39. Older multicenter evidence and contemporary studies reach the same practical conclusion: thrombolysed mimics have substantially lower hemorrhagic risk than true AIS patients. (3,16)

Brunser 2013 and Zinkstok 2013 established the earlier safety signal that is now reinforced by Afzal, Klimbytė, and Loggini. The consistency across eras and clinical settings strengthens confidence that inadvertent treatment of occasional mimics is an expected consequence of a rapid stroke system rather than evidence that the system has failed.

40. The appropriate response to mimic risk is better diagnosis—not delaying indicated thrombolysis until diagnostic uncertainty disappears. (1,3,9,10,11,16)

No bedside characteristic, imaging strategy, or mimic score completely separates AIS from mimics during the treatment window. For an otherwise eligible patient whose presentation remains clinically consistent with disabling AIS, the evidence supports **rapid assessment, appropriate IV thrombolysis, and continued diagnostic reassessment rather than unnecessary treatment delay**.

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