Journal of Community Hospital Internal Medicine Perspectives

Volume 12 | Issue 4 Article 19

2022

A case-control study of distinguishing between stroke mimics and true strokes

Maya Gogtay
Department of Medicine, Saint Vincent Hospital, Worcester, MA, drgogtay@gmail.com

Yuvaraj Singh
Department of Medicine, Saint Vincent Hospital, Worcester, MA, yuvarajmle@gmail.com

Neha Varma
nehuvarma@gmail.com

Aakriti Soni
Department of Medicine, Saint Vincent Hospital, Worcester, MA

Pawina Subedi
Department of Medicine, Saint Vincent Hospital, Worcester, MA

See next page for additional authors

Recommended Citation

Gogtay, Maya; Singh, Yuvaraj; Varma, Neha; Soni, Aakriti; Subedi, Pawina; Sommer, David B.; Abraham, George M.; and George, Susan V. (2022) "A case-control study of distinguishing between stroke mimics and true strokes," *Journal of Community Hospital Internal Medicine Perspectives*: Vol. 12: Iss. 4, Article 19.
DOI: 10.55729/2000-9666.1076
Available at: https://scholarlycommons.gbmc.org/jchimp/vol12/iss4/19

A case-control study of distinguishing between stroke mimics and true strokes

Authors

Maya Gogtay, Yuvaraj Singh, Neha Varma, Aakriti Soni, Pawina Subedi, David B. Sommer, George M. Abraham, and Susan V. George

A Case–Control Study of Distinguishing Between Stroke Mimics and True Strokes

Maya Gogtay*, Yuvaraj Singh, Neha Varma, Aakriti Soni, Pawina Subedi, David Sommer, George M. Abraham, Susan V. George

St. Vincent Hospital, Department of Internal Medicine, 123 Summer Street, Worcester, MA 01608, USA

Abstract

This study was conducted with the primary aim to distinguish patients with a true stroke versus a stroke mimic based on clinical features and imaging. We conducted a retrospective case–control study on 116 adult patients who received alteplase (tPA) to treat acute stroke at our hospital. We further analyzed 79 patients with a normal computed tomography angiography (CTA). Based on their magnetic resonance imaging (MRI) of the brain, they were divided into cases (stroke mimics) and controls (true strokes).

Data were collected retrospectively by reviewing individual medical charts on the electronic medical record (EMR), including age, gender, history of stroke, seizure, hypertension, diabetes, atrial fibrillation, hyperlipidemia, presenting NIH Stroke Scale/Score, hemorrhagic conversion, history of migraine, history of depression, sidedness of symptoms and aphasia. Data were categorized to separate those who were later diagnosed to be stroke mimics by being- postictal, encephalopathic, in acute migraine, suffered post-stroke recrudescence (PSR) due to metabolic insult, or had conversion disorder when symptoms could not be attributed to any medical condition or mental illness.

Of the 79 study subjects, 48 (60%) were stroke mimics. The mean age of the cohort was 68.67 years, and 46.8% of the study subjects were females. Based on the multivariate logistic regression analysis, factors associated with being a stroke mimic were older age, history of migraine, and a history of prior stroke. In conclusion, increased attention to history and clinical examination as the first step can aid in the proper diagnosis of strokes versus stroke mimics.

Identifying stroke mimics early could help expedite hospital workup and prevent inadvertent investigations, reducing hospital occupancy during the ongoing COVID-19 pandemic. We could potentially avoid the administration of tPA to such patients, reducing both the cost and adverse effects of it. Every stroke can cause neurological deficits, but every deficit need not be a stroke.

Keywords: Stroke mimics, True stroke, Alteplase, NIH Stroke score, Migraine

1. Introduction

Stroke is a clinical diagnosis as endorsed by the World Health Organization (WHO), defined as rapidly developing clinical signs of focal or global disturbance in cerebral function lasting more than 24 hours or leading to death with no apparent cause other than a vascular origin.[1] It is ranked as the second leading cause of death worldwide, with an annual mortality of about 5.5 million.[2] It is a medical emergency, and an early diagnosis is of paramount importance. This entails judicious clinical assessment supported by neuroimaging studies to confirm the diagnosis. For patients to receive time-critical treatments such as thrombolytics, medical management, or surgical treatment of intracerebral hematoma and reversal of anticoagulation, patients must be brought to the hospital rapidly, assessed swiftly and accurately, and promptly undergo the appropriate imaging/investigations.[3,4]

Stroke mimics (SM) are certain disorders that can mimic clinical signs of a stroke, leading to misdiagnosis, delays, and inappropriate treatment. These are pathological conditions that resemble stroke-

Received 10 January 2022; revised 24 March 2022; accepted 30 March 2022.
Available online 4 July 2022

* Corresponding author at:
E-mail address: drgogtay@gmail.com (M. Gogtay), yuvarajmle@gmail.com (Y. Singh), nehuvarma@gmail.com (N. Varma), aakritisoni2122@gmail.com (A. Soni), pawina.subedi@stvincenthospital.com (P. Subedi), david.sommer@reliantmedicalgroup.org (D. Sommer), george.abraham@stvincenthospital.com (G.M. Abraham), susan.george@stvincenthospital.com (S.V. George).

https://doi.org/10.55729/2000-9666.1076

like clinical presentations. However, their etiology is not cerebrovascular.[5] There is widespread use of thrombolytic care in treating acute strokes in the modern era; evidence indicates that as many as 15% of patients treated with tissue plasminogen activator (tPA) are actually SM, for which the therapy is not an indication.[6] This results in unnecessary diagnostic tests, invasive procedures, extended hospital stays, and increasing patient care costs.[2]

Previous data from a multicentered European study describes the proportion of SM as high as 30% of all strokes.[7] Similarly, in sub-Saharan Africa, a hospital-based retrospective study conducted in Nigeria found that among 142 patients with a WHO clinical stroke diagnosis, 23.2% had SM, including brain tumors, brain abscess, subdural hematomas, hydrocephalus, and intracranial cysts.[8] Other described SM include seizures, syncope, metabolic encephalopathies (such as hypoglycemia, hyponatremia, uremia, and hepatic encephalopathy), infectious disorders including meningoencephalitis, and degenerative diseases, amongst other etiologies.[9,10] Although such conditions physiologically differ from actual strokes, the similarity of symptoms makes the diagnosis difficult.[9,11] Notable is that, in sub-Saharan Africa, stroke is readily diagnosed purely on clinical grounds with no confirmation due to limited access to brain imaging.[12] Lack of proper and timely diagnosis of stroke or stroke mimic can lead to irreversible complications. Hence, we undertook the present study, with the primary purpose of distinguishing stroke mimics and true strokes based on clinical features and imaging.

2. Methods and definitions

This retrospective case–control study was conducted after getting approval from the Institutional Review Board. We identified 116 patients who received alteplase (tissue plasminogen), 79 of the patients who had a negative computed tomography angiography (CTA) of their head were included for further analysis. The included patients were divided into cases (stroke mimics) and controls (true strokes) based on magnetic resonance imaging (MRI) of the brain. True strokes had relevant image findings on MRI, whereas stroke mimics did not.

When patients are brought in with possible stroke-like symptoms, a code stroke is activated either by the emergency medical services (EMS) or in the emergency room as per the hospital protocol. Rapid assessment of the patient followed by CT of the head without contrast and a CTA of the head and neck. If there is no intracranial hemorrhage or other contraindication to thrombolytic therapy and the patient is within 4.5 hours of symptom onset, the ER physician and the neurologist make a joint decision as to whether to administer tPA or transfer the patient for mechanical thrombectomy. Patients who receive tPA are monitored in the ICU for at least 24 hrs. All patients undergo an MRI to confirm the presence or absence of an actual stroke. All patients in our study followed this protocol.

Conversion disorder, also known as functional neurological symptom disorder, was defined as patients who presented with limb weakness or numbness or speech disturbances usually precipitated by acute psycho-social stressors with no organic etiology for neurological deficits. These patients were assessed and diagnosed by the neurologist. Post-stroke recrudescence (PSR) refers to the reappearance of previously resolved symptoms of a remote ischemic stroke, usually triggered by stressors, metabolic derangements, infection, or fatigue.

Data were collected retrospectively by reviewing individual medical charts on the EMR, including a history of stroke, seizure, hypertension, diabetes, atrial fibrillation, hyperlipidemia, presenting NIH Stroke Scale/Score, hemorrhagic conversion, seizure episode after tPA administration, history of migraine, history of depression, sidedness of symptoms and aphasia. Data were categorized to separate those who were later actually diagnosed to be stroke mimics by being- postictal, encephalopathic, PSR due to metabolic insult, or had conversion disorder when symptoms could not be attributed to any other medical condition.

2.1. Statistical analysis

All statistical analyses were performed in SAS version 9.4 software (SAS Institute, Cary, NC). We used a multivariate logistic regression model to assess the association between risk factors for being a stroke mimic. Continuous variables included in the model were age and NIHS score. Variables such as gender, history of migraine, prior stroke, gender, seizure history, and atrial fibrillation were included as dichotomous (yes or no) variables.

3. Results

116 patients received tPA, of which 79 patients that had a normal CTA were included in the study, and 39 patients with an abnormal head CTA were excluded. The MRI of these 79 patients were studied, and they were divided into 31 true strokes and 48 stroke mimics. The distribution of study subjects

Table 1. Distribution of study subjects based on demographics and history.

Patient Characteristics	Stroke mimic (N = 48) N (%)	True Stroke (N = 31) N (%)	Total (N = 79) N (%)	p-value
Age Mean (SD)	65.72 (17.8)	72.12 (12.7)	68.67 (16.07)	0.0813
Gender (Male)	27 (56.2)	15 (48.39)	42 (53.1)	0.4941
Prior stroke	15 (31.2)	2 (6.4)	17 (21.2)	0.0088*
Hypertension	32 (66.6)	26 (83.8)	58 (73.4)	0.0910
Diabetes	12 (25)	8 (25.8)	20 (25.3)	0.9358
Atrial fibrillation ^	6 (12.5)	2 (6.4)	8 (10.1)	0.4703
Hyperlipidemia	29 (60.4)	19 (61.9)	48 (60.7)	0.9381
NIHS Score Mean (SD)	5.85 (5.1)	6.39 (4.4)	6 (4.82)	0.1501
Hemorrhage conversion ^	2 (4.1)	4 (12.9)	6 (7.5)	0.2038
Seizure episode after tPa ^	3 (6.2)	0	3 (3.8)	0.2756
Aphasia	9 (18.7)	8 (25.8)	17 (21.5)	0.4561
Facial droop	12 (25)	15 (48.39)	27 (34.1)	0.0324*
History of seizures ^	10 (20.8)	1 (3.2)	11 (13.9)	0.0428*
Postictal ^	8 (16.6)	0	8 (10.1)	0.0196*
Depression	13 (27.0)	1 (3.2)	14 (17.7)	0.0067*
Encephalopathy	13 (27.0)	2 (6.4)	15 (18.9)	0.0224*
Migraine ^	9 (18.75)	1 (3.23)	10 (12.6)	0.0791
Functional disorder	16 (33.3)	1 (3.2)	17 (21.5)	0.0015*
Post-stroke recrudescence	14 (29.17)	2 (6.45)	16 (20.2)	0.0142*

*significance.
^ Fisher's exact test.

based on demographics and history was represented in Table 1.

For the continuous variable age, the mean (standard deviation) for study subjects in stroke mimic and true stroke groups was 65.7 (17.8) and 72.12 (12.7). Similarly, the mean (standard deviation) for NIHS score between the groups viz. stroke mimic & true stroke was 5.85 ± 5.1 and 6.39 ± 4.4, respectively.

The findings revealed as based on Fisher's exact test and chi-square, there was a statistically significant difference in the distribution of study subjects between the groups (stroke mimic & true stroke) as follows: facial droop (25%, p = 0.0324), prior stroke (31.25%, p = 0.0088), history of seizures (20.83%, p = 0.0428) and history of depression (27.08%, p = 0.0067). Other variables like post ictal state (16.6%, p = 0.0196), encephalopathy (27.08%, p = 0.0224), conversion disorder (33.3%, p = 0.0015) and post stroke recrudescence (29.17%, p = 0.0142) were also significant.

Logistic regression analysis showed that age greater than 65 years (OR 0.195, p = 0.087), history of prior stroke (OR 8.635, p = 0.0134), and history of migraine (OR 11.254, p = 0.0372) were positively associated with being a stroke mimic (see Table 2).

Table 2. Analysis of risk factors for stroke mimics with clinical signs of stroke.

Patient Characteristics	Odds Ratio (95% Confidence Interval)	p-value
Age >65 years	0.195 (0.058, 0.661)	0.0087*
Female Gender	0.694 (0.212, 2.277)	0.5466
NIHS Score <7	1.099 (0.296, 4.072)	0.8882
History of prior stroke	8.635 (1.563, 47.698)	0.0134*
History of Migraine	11.254 (1.154, 109.776)	0.0372*
Seizure History	6.132 (0.639, 58.862)	0.1161
Atrial Fibrillation	3.253 (0.416, 25.442)	0.2610

*p < 0.05.

4. Discussion

Although laboratory investigations and brain imaging can refine the diagnosis, the clinical assessment remains vital because it is the first step in the diagnostic pathway and often directs the speed at which more complex procedures are undertaken. Brain imaging, even diffusion-weighted MRI, is not infallible and may give confusing results.[13] Despite the need for a rapid and accurate clinical diagnosis in the thrombolysis era, the process of clinical assessment has received little formal study. Therefore, the present study was conducted with the primary aim to distinguish the patients with stroke mimics and true strokes based on clinical features and imaging.

The median age of the stroke mimic patients was 65.72 years. This figure is higher than many other studies,[14–17] and their selective entry criteria may explain this. The median NIHS score was 6.39 for stroke mimics. This result was similar to the Okano et al. study. They mentioned, "patients with stroke-like symptoms, wherein the NIHS score was

relatively low, and blood pressure was not elevated in the ED, should be treated carefully with the possibility of being a stroke mimic".[18]

Patients with a history of facial droop, prior stroke, known history of seizure, and history of depression had statistically significant differences between stroke mimics and true strokes. Furthermore, conversion disorder, encephalopathy, and post-stroke recrudescence from metabolic insults were significant for being stroke mimics. Stroke mimics had 10.1 times higher odds of having a history of stroke than true strokes. Similarly, stroke mimics are 12.9 times more likely to have a history of migraine than true strokes.

Stroke mimics have less clearly defined neurological symptoms that typically do not adhere to well-defined stroke syndromes.[19] The suddenness of onset is not always evident. Fluctuations in severity are common and systemic signs including drowsiness, confusion, agitation, and fever may be present.[20] Common symptoms include vertigo and dizziness, altered level of consciousness, paresthesia and numbness, monoplegia, speech dysfunction, limb ataxia, headache, and visual disturbances.

In case a patient with history of migraines, presents with headache, aura, and vertigo, it would be beneficial to treat the migraine with NSAIDs and antiemetics, conduct serial neurological examinations, or if possible, undergo an MRI rather than directly administering tPA. Also, since conversion disorder can be a stroke mimic, it would be beneficial to take a detailed psychiatric history and serial neurological examinations. In patients who have a history of stroke, presenting again with a negative CTA or a brain CT with no enlargement of the previous infarcted area, it might be helpful to assess whether presenting symptoms aren't residual from the past stroke, as this might be post-stroke recrudescence. It would be appropriate to work up electrolyte derangements and screen for infections by lab checks, chest x-ray, and urinalysis looking for insults that can worsen old neurological deficits in patients with a distant history of stroke.

For the future, we propose large sample size studies to be undertaken. Furthermore, a subgroup analysis on common stroke mimic risk factors should be done. Analysis with combining variables like female gender and depression or female gander and migraine or prior history of stroke and NIHS score should be attempted. This may give valuable information that a patient with these risk factors is more likely to be a stroke mimic than having a single risk factor. Given our limited sample size, we could not do the above subgroup analysis.

The treatment of stroke-mimics depends on the underlying condition outlined above, with common conditions mistaken for an acute stroke. Patients with inadvertently administered tPA should be stopped as soon as the diagnosis becomes apparent. According to protocol, if the drug has been infused, the patient will still require close observation for 24 hours. The diagnosis must be correctly recorded, especially in patients with conversion disorder with a high likelihood of repeated hospital visits. Recurrence is also likely with migraines, focal seizures, and patients with a pre-existing stroke (recrudescence). Treatment of the underlying conditions like infections, electrolyte derangements is vital to decrease the risk of recurrence and presentation of a stroke mimic again.

The average cost of hospitalization for a patient with stroke is >$20,000 ± $23,256 stay.[21] The difference is due to complications during the stay, hemorrhagic or ischemic stroke. According to leading reports, this, when compared to the cost of an MRI brain, is around $3000-$11000.

By incorporating above mentioned risk factors into the clinical exam and increasing awareness of stroke mimics, we intend to help reduce this burden on healthcare.

5. Conclusion

While not easy to confirm a stroke in the acuity of the emergency room or medical floors, the standard of care requires patients to undergo a CT stroke protocol before tPA administration. Aura before the onset of symptoms, headaches, or a prior history of depression might point away from a stroke when the CTA is normal.

Patients admitted with suspected stroke, end up undergoing extensive workup for etiology, risk stratification, judicious blood pressure management, lipid profile, and diabetes mellitus screening. They undergo evaluation for carotid artery disease, cardiac echocardiography to rule out a PFO and are monitored for arrhythmias on telemetry. They undergo evaluation by speech, physical and occupational therapy with a discharge plan to follow up with a neurologist.

Identifying stroke mimics early could help expedite hospital workup and prevent inadvertent investigations and use of hospital workforce, reducing hospital occupancy during the ongoing COVID-19 pandemic.

Our study findings reiterate the importance of detailed history and clinical examination as the first step in improving an accurate diagnosis of a stroke mimic. This could potentially avoid the

administration of tPA to such patients, reducing both the cost and adverse effects of it. Every stroke can cause neurological deficits, but every deficit need not be a stroke.

Funding

There are no financial conflicts of interest to disclose.

Declaration of competing interest

All authors declare that they have no conflict of interest.

References

1. Farooq MU, Chaudhry AH, Amin K, Majid A. The WHO STEP wise approach to stroke surveillance. *J Coll Phys Surg Pakistan: JCPSP*. 2008;18(10):665.
2. Donkor ES. Stroke in the century: a snapshot of the burden, epidemiology, and quality of life. *Stroke Res Treat*. 2018;2018.
3. Harraf F, Sharma AK, Brown MM, Lees KR, Vass RI, Kalra L. A multicentre observational study of presentation and early assessment of acute stroke. *BMJ*. 2002 6;325(7354):17.
4. Lacy CR, Suh DC, Bueno M, Kostis JB. Delay in presentation and evaluation for acute stroke: stroke time registry for outcomes knowledge and epidemiology (STROKE). *Stroke*. 2001; 32(1):63−69.
5. Magauran BG, Nitka M. Stroke mimics. *Emerg Med Clin*. 2012; 30(3):795−804.
6. Merino JG, Luby M, Benson RT, et al. Predictors of acute stroke mimics in 8187 patients referred to a stroke service. *J Stroke Cerebrovasc Dis*. 2013;22(8):e397−403.
7. Zinkstok SM, Engelter ST, Gensicke H, et al. Safety of thrombolysis in stroke mimics: results from a multicenter cohort study. *Stroke*. 2013;44(4):1080−1084.
8. Onwuekwe I, Adikaibe BE, Ohaegbulam S, Chikani M, Amuta J, Uloh H. Stroke mimics-A study of CT images in Nigerian African stroke patients. *J Neurol Sci*. 2008;25(3).
9. Yew KS, Cheng EM. Diagnosis of acute stroke. *Am Fam Physician*. 2015;91(8):528−536.
10. Hosseininezhad M, Sohrabnejad R. Stroke mimics in patients with clinical signs of stroke. *Caspian J Int Med*. 2017; 8(3):213.
11. Demaerschalk BM. Diagnosis and management of stroke (brain attack). *Semin Neurol*. 2003;23(3):241−252.
12. El Husseini N, Goldstein LB. Code stroke": hospitalized versus emergency department patients. *J Stroke Cerebrovasc Dis*. 2013;22(4):345−348.
13. Engelter ST, Wetzel SG, Radue EW, Rausch M, Steck AJ, Lyrer PA. The clinical significance of diffusion-weighted MR imaging in infratentorial strokes. *Neurology*. 2004;62: 574−580.
14. O'Brien PA, Ryder DQ, Twomey C. The role of computed tomography brain scan in the diagnosis of acute stroke in the elderly. *Age Ageing*. 1987;16:319−322.
15. Besson G, Hommel M, Besson S, Guignier M, Robert C. Scoring systems for the differential diagnosis of ischemic and hemorrhagic stroke: response. *Stroke*. 1996;27:337−338.
16. Anderson CS, Jamrozik KD, Burvill PW, Chakera TM, Johnson GA, Stewart-Wynne EG. Ascertaining the true incidence of stroke: experience from the perth community stroke study, 1989 −1990. *Med J Aust*. 1993;158:80−84.
17. Ellekjaer H, Holmen J, Indredavik B, Terent A. Epidemiology of stroke in Innherred, Norway, 1994 to 1996. Incidence and 30-day case-fatality rate. *Stroke*. 1997;28:2180−2184.
18. Okano Y, Ishimatsu K, Kato Y, et al. Clinical features of stroke mimics in the emergency department. *Acute Med*. 2018;5(3): 241−248.
19. Sanossian N, Fu KA, Liebeskind DS, et al. Utilization of emergent neuroimaging for thrombolysis-eligible stroke patients. *J Neuroimaging*. 2017;27(1):59−64.
20. Moulin S, Leys D. Stroke mimics and chameleons. *Curr Opin Neurol*. 2019;32(1):54−59.
21. Wang G, Zhang Z, Ayala C, Dunet DO, Fang J, George MG. Costs of hospitalization for stroke patients aged 18-64 years in the United States. *J Stroke Cerebrovasc Dis*. 2014 May-Jun;23(5): 861−868.