Published in final edited form as:
J Stroke Cerebrovasc Dis. 2013 November ; 22(8): . doi:10.1016/j.jstrokecerebrovasdis.2013.04.018.

Predictors of acute stroke mimics in 8,187 patients referred to a stroke service

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Abstract

Background—Some patients seen by a stroke team do not have cerebrovascular disease but a condition that mimics stroke. The purpose of this study was to determine the rate and predictors of stroke mimics in a large sample.

Methods—This is an analysis of data from consecutive patients seen by the NIH Stroke Program over 10 years. Data were collected prospectively as a quality improvement initiative. Patients with a cerebrovascular event or a stroke mimic were compared with the Student t or Pearson's chi-square test as appropriate and logistic regression was done to identify independent predictors.

Results—The analysis included 8,187 patients: 30% had a stroke mimic. Patients with a stroke mimic were younger and the proportion of patients with a stroke mimic was higher among women, patients without any risk factors, those seen as a code stroke or who arrived to the emergency department via personal vehicle, and those who had the onset of symptoms while inpatients. The proportion of patients with a stroke mimic was marginally higher among African Americans than Caucasians. Factors associated with the greatest odds of having a stroke mimic in the logistic regression were lack of a history of hypertension atrial fibrillation, or hyperlipidemia.

Conclusions—A third of the patients seen by a stroke team over 10 years had a stroke mimic. Factors associated with a stroke mimic may be ascertained by an emergency physician before calling the stroke team.

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Conflicts of Interest

The authors do not have any relevant conflicts of interest to report.

Keywords

Acute stroke; emergency medicine; stroke mimics

Introduction

Stroke teams are often asked to see patients who have an abrupt onset of a neurological deficit —and thus possibly an ischemic or hemorrhagic stroke— but in whom the final diagnosis is not a cerebrovascular event.(1, 2) Patients without a cerebrovascular etiology for their symptoms are considered to have a stroke mimic, and several small studies report that as many as a third of patients evaluated acutely by a stroke team, and up to 15% of patients treated with intravenous t-PA, have such stroke mimics; potential etiologies include subdural hematoma, migraine, seizures, tumors, infections, multiple sclerosis, delirium, peripheral nerve injuries and conversion disorders.(3–13) Several studies have evaluated the stroke mimic rate in different settings and have identified clinical and imaging features associated with a final diagnosis of stroke mimic, including clinical symptoms, vital signs, neurological signs, stroke severity, and even neurological impairment at discharge.(3, 7, 10–14) Most of these factors, however, cannot be easily ascertained by the referring physician, often the emergency room doctor, before calling the stroke team. The purpose of this study was to answer two questions: What proportion of patients who are seen by an acute stroke team have a stroke mimic? What variables, if any, that are known by a referring physician before calling the stroke team (demographics, acuity, and past medical history) can predict whether a patient has a stroke mimic? The answers to these questions may serve as a benchmark when assessing stroke team consult and response rates and may help determine the best allocation of a stroke team's human resources.

Methods

Patients

This is an analysis of data from consecutive patients referred for evaluation of suspected stroke to the NIH Stroke Program at two hospitals in the Washington, D.C. metropolitan area –Suburban Hospital (SH) and Medstar Washington Hospital Center (WHC)– between January 1, 2001 and December 31, 2010. The NINDS Intramural Stroke Branch established an NIH Stroke Program at these hospitals to conduct acute stroke clinical research. The NIH Stroke Program staffs the stroke team at both hospitals and provides clinical coverage for most patients with suspected acute stroke. SH is a community hospital (238 beds) in Bethesda, MD. When the NIH Stroke Program at SH was established in 1999 the stroke team only evaluated patients who were eligible for thrombolysis or candidates for enrollment in a clinical trial but on January 1, 2001 the NIH Stroke Program expanded coverage to all patients with suspected stroke, regardless of time of symptom onset. WHC is the largest private teaching hospital (926 beds) in the District of Columbia and serves a socioeconomically diverse population. The NIH Stroke Program at WHC was established in 2004, and from the onset the stroke team evaluated all patients with suspected stroke. Both hospitals are primary stroke centers certified by The Joint Commission. The same group of board-certified vascular neurology attending physicians and fellows staff the stroke team at both hospitals.

Data were collected prospectively as a quality improvement initiative. Office of Human Subjects Research (OHSR) exemptions and local Institutional Review Board (IRB) approvals were obtained for use of clinical and research data. Over the last 10 years the NIH Stroke Team's staff and policies changed but these changes were minor. Any member of the hospital staff may activate a code stroke if they suspect the patient may be indeed having a

stroke based on the history or examination. Usually, when a patient with a potential stroke is identified in the emergency department or an inpatient service at either hospital, the referring physician or nurse pages the stroke team, regardless of the time of onset of symptoms. After answering the call, the stroke team's responder (a vascular neurology fellow or attending) determines whether the symptoms are consistent with a possible cerebrovascular event (sudden onset of neurological deficits) and if so, how urgently the patient will be seen. Patients are seen immediately (as a code stroke) if they are within the time window for standard intravenous thrombolysis, are a candidate for an endovascular or another acute intervention, or are eligible for enrollment in a clinical trial. They are seen with less urgency, but as soon as possible, if these criteria are not met. If the clinical presentation is not consistent with a cerebrovascular event, the stroke team does not see the patient. The stroke team also does telephone consultations and accepts transfers from other hospitals.

The data analyzed in this study include: age, sex, race, acuity of the consult (code stroke vs. not code stroke), mode of arrival in the emergency room (via personal vehicle vs. EMS, excluding patients transferred from other hospitals), location of the patient when the call to the stroke team was made (emergency department vs. inpatient service), and history of any of the following stroke risk factors known at the time of presentation: hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease, atrial fibrillation, carotid artery stenosis, intracerebral hemorrhage, and ischemic stroke. The final diagnosis was established after the completion of the evaluation by the NIH Stroke Team taking into account all clinical, imaging and ancillary data and the diagnostic categories include definite, possible or probable acute ischemic cerebrovascular syndrome (AICS)(15), intracerebral hemorrhage, or non-cerebrovascular event (i.e. stroke mimic). The etiology of the stroke mimic was not routinely recorded.

Statistical Analysis

Continuous variables were compared with the Student t-test or the Mann-Whitney test after assessing for normality with the Kolmogorov-Smirnov test. Categorical variables were compared using Pearson's chi-square or, when appropriate, Fisher's exact test. A forced entry logistic regression was done to identify independent factors associated with a stroke mimic, and odds ratios (OR) were calculated using stroke mimic (yes/no) as the dependent variable and the variables that were significant in the univariate model ($p<0.05$) as the covariates. Variables that were not available for at least 70% of the sample were excluded from the analysis.

Results

Over a 10-year period the NIH Stroke Team evaluated 8,194 patients in person: 5,066 (62%) had definite, probable or possible AICS, 667 (8%) had an intracranial hemorrhage, and 2,454 (30%) had a non-cerebrovascular etiology for the symptoms –a stroke mimic. In seven patients the diagnosis was not recorded in the database. The analyses in this study are limited to the 8,187 patients in whom the diagnosis (AICS, hemorrhagic stroke or stroke mimic) was known. The NIH Stroke Team saw 4,587 patients at SH (56%) and 3,600 patients at WHC (44%). The mean age of the patients was 68.6 years (SD ± 15.9) and the median age was 71 years (interquartile range [IQR], 57–81). The oldest patient was 104 years, and only 13 patients were younger than 18. The median NIHSS score in the 6,241 patients for whom it was available was 4 (IQR 1–11, range 0–42). Over half the patients (55%) were women. Most patients were Caucasian (56%) or African American (38%) and only 6% were Asian, Native American, Pacific Islander or other. Information about Hispanic ethnicity is not reliably available. Over the 10 years, 6,121 patients (75%) arrived directly to the emergency room at one of the two hospitals (60.6% were brought by EMS and 39.4% by

personal vehicle) while 803 patients (10%) were transferred from other hospitals (53.6% by ambulance and 46.4% by helicopter) and 1,263 patients (15%) had the onset of symptoms while they were inpatients. The acuity of presentation (code stroke status) is known for 5,729 patients. The stroke team physician answering the stroke page thought that 46% of these patients were within the time window for standard thrombolysis, an endovascular intervention, or enrollment in a clinical trial and saw these patients as a code stroke; the proportion of patients who met the code stroke criteria varied by location (36.4% of inpatients, 48.4% of ER patients, and 51.8% of transfer patients; $p<0.0001$). Information about the presence of known risk factors at the time of initial evaluation is available for 6,987 patients. More than three quarters of these patients (78.4%) had a known vascular risk factor: 66.1% had hypertension, 24.7% diabetes mellitus, 38.1% hyperlipidemia, 22% coronary artery disease, 15.5% atrial fibrillation, 4.2% carotid artery stenosis, 22.6% prior ischemic stroke, and 2.2% (of 6,287 patients) prior intracranial hemorrhage.

In 2,454 patients (30%) the acute neurological symptoms had an etiology other than acute cerebrovascular disease. (i.e. they had a stroke mimic) There was no statistically significant difference in the proportion of stroke mimics at either hospital (30.1% vs. 29.8%, $p=0.77$) or throughout the 10 years (range 24.3% to 31.7%, $p=0.23$). Compared with patients with cerebrovascular events, patients with stroke mimics were younger than those with AICS or intracerebral hemorrhage (mean age 65.20 (±17.09) vs. 69.99 (±15.19); $p<0.0001$). The proportion of patients with a stroke mimic was higher among women than men, African Americans than Caucasians, patients without any risk factors of stroke than patients with these risks, patients seen as a code stroke than those seen with less acuity, patients who arrived to the ED via personal vehicle rather than ambulance (excluding transfers from other hospitals), and among inpatients rather than patients referred from the ED (Table 1). In our sample the characteristics of the patients and the prevalence of risk factors varied by age (Online Table); after adjusting for age, African American race was no longer associated with a stroke mimic diagnosis (Table 1).

In the logistic regression, demographic factors (age and race), symptom acuity (code stroke), location where the symptoms started (inpatient) and past medical history (lack of history of hypertension, hyperlipidemia or atrial fibrillation) were associated with having a stroke mimic. The patient characteristics associated with a stroke mimic diagnosis were slightly different for patients initially seen in the ED and those who had symptom onset while they were in the hospital (Table 2).

Discussion

In a third of the patients with suspected stroke seen acutely by a stroke team at two hospitals serving a multi-racial and socioeconomically diverse population over 10 years, the presenting symptoms were due to conditions other than a cerebrovascular event (i.e. they had a stroke mimic). Several patient characteristics that the referring physician can ascertain before calling the stroke team were associated with increased odds of having a stroke mimic, including demographic information, acuity of the presenting symptoms, location (inpatient vs. otherwise) of the patient when the symptoms were identified, and the presence of some known vascular risk factors. It is important to note that the lack of a history of hypertension, hyperlipidemia, atrial fibrillation, diabetes and coronary artery disease are stronger predictors of a stroke mimics than demographic or clinical features.

This is the largest study to date of stroke mimics. The prevalence of stroke mimics in this study was similar to what has been described in smaller series of unselected patients. The stroke mimic rate was 27% in a series of 487 consecutive patients who were directly admitted to a stroke service over 6 months. (4) Among 350 consecutive patients with focal

brain dysfunction of sudden onset presenting to an urban teaching hospital, 31% had a stroke mimic.(7) A recent series from a single stroke center found that 26.8% of patients referred from the ED as a stroke code did not have a cerebrovascular disorder, and the proportion of inpatients with a stroke mimic was even higher.(14) Other studies found a lower stroke mimic rate, but in these, the patient sample was not representative of the general population at risk. In a study of 411 consecutive patients presenting to the emergency room only 19% had a stroke mimic, but the emergency room physicians were specifically trained to identify stroke features because they were participating in an acute intervention trial.(3) In another study that also enrolled 411 patients for whom a code stroke was activated, 25.3% did not have an ischemic stroke and 18.5% did not have cerebrovascular disease.(8) The stroke mimic rate was only 4.8% in a sample of 637 patients who were admitted to a stroke department after an initial evaluation by a neurologist that included CT imaging.(9) In a study of 143 children referred to the stroke team for evaluation, 21% did not have a stroke. (6)

Several clinical features that predict the presence of a stroke mimic have been identified, and some studies have noted that patients with mimics have a lower prevalence of stroke risk factors.(3, 5, 7, 10, 11, 13) Our study, however, is the first to explore factors the referring physician can ascertain during the initial evaluation of a patient before calling the stroke team. Recognizing patient characteristics that predict a stroke mimic may be useful when designing research studies that rely on pre-hospital evaluation and telephone triage of patients with potential stroke. (16) Our results may establish a benchmark against which stroke teams may compare their stroke mimic rate: if the rate of stroke mimics is low, the emergency room team may not be calling in all potential stroke patients; if the rate is higher, they may have too low a threshold and are considering that all patients with neurological symptoms may have a stroke. These data also put into perspective the complaints of stroke fellows and residents who may lament the calls they get from the ER to see patients who turn out to have a stroke mimics, as if this is an act of hostility or outrageous incompetence on the part of the ER. The results of our study, however, should not be the basis for triage decisions by emergency room physicians who should have a low threshold for consulting a stroke team to evaluate patients with potential stroke.

Our study has several strengths. The sample size is large and it includes all patients seen by a stroke team over 10 years, regardless of acuity or eligibility for treatment. Because we see patients from diverse socioeconomic backgrounds in a community hospital and a large urban teaching hospital, our sample is representative of a typical stroke center's population. The data were systematically recorded prospectively. The study also has limitations. The staff and the policies of the stroke team at both hospitals and the specific data points collected for quality purposes changed slightly over the years. Despite the changes, the proportion of patients with stroke mimics did not change significantly over time. In an exploratory analysis limiting the sample to 1,302 patients seen during a single academic year (July 1, 2009-June 30, 2010) the univariate predictors of stroke mimic status were the same as those observed in the 10-year sample, and the absence of risk factors was associated with the highest odds of being a stroke mimic in the logistic regression. Furthermore, to avoid biases due to changes in data collection policies we excluded from the logistic regression analysis of the entire sample those factors for which we have information from ≤70% of patients or that apply to ≤5% of patients. Another limitation is the fact that we do not have information about the final diagnosis of the patients with stroke mimics; how patients screened on the, phone by a fellow or an attending and the proportion who were not seen; or whether the patients who were not seen by the stroke team after the initial telephone conversation with the referring physician had a stroke. Some stroke mimics may have been in fact neurological emergencies with a cerebrovascular component and in these instances a code stroke activation may have been justified. In our study, the absence of vascular risk factors was the

strongest predictor of a patient having a stroke mimic. While this makes intuitive sense, there is a potential for bias as we may have selectively mislabeled patients without vascular risk factors as stroke mimics and not evaluated them further. In addition, while we were able to examine the sample by race, we do no not have ethnicity information (Hispanic vs. not Hispanic.)

In summary, a stroke team can expect that in up to a third of the patients that it sees, the presenting signs and symptoms are not due to a cerebrovascular event (i.e. these patients have a stroke mimic). Patients with a stroke mimic are more likely to be younger, have mild symptoms, arrive to the hospital by personal means rather than EMS and lack a history of vascular risk factors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This research was supported by the Intramural Research Program of the NIH, National Institute of Neurological Disorders and Stroke.

We would like to acknowledge the assistance of the NIH Stroke Teams at Suburban Hospital and Washington Hospital Center over the past 10 years in the performance of this study.

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J Stroke Cerebrovasc Dis. Author manuscript; available in PMC 2014 November 01.

Table 1

Univariate analysis of factors associated with having a stroke mimic.

Variable type	Variable	N	Mimic rate	p-value	Unadjusted OR (95% CI)	Age-adjusted OR (95% CI)
Demographics	Age					
	≥72	3999	25.3%			
	<72	4188	34.4%	<0.0001	1.55 (1.41–1.71)	
	Sex					
	Men	3700	26.0%			
	Women	4487	33.3%	<0.0001	1.42 (1.29–1.57)	1.51 (1.36–1.66)
	Race					
	Caucasian	4583	29.0%			
	African American	3129	31.9%	0.007	1.15 (1.04–1.27)	0.95 (0.85–1.05)
Acuity of symptoms	Code status					
	Not stroke code	3066	27.1%			
	Stroke code	2663	32.6%	0.0001	1.30 (1.16–1.46)	1.28 (1.14–1.53)
	Mode of arrival (ED only)					
	Ambulance	3707	27.8%			
	Automobile	2414	35.8%	<0.0001	1.45 (1.30–1.62)	1.30 (1.16–1.45)
Location when stroke team called	Location					
	ED	6108	31.0%			
	Inpatient	1263	34.0%	0.03	1.15 (1.01–1.30)	1.25 (1.10–1.42)
Past medical history	h/o hypertension					
	Yes	4620	11.4%			
	No	2367	42.9%	<0.0001	5.83 (5.16–6.57)	5.68 (5.01–6.43)
	h/o diabetes mellitus					
	Yes	1727	12.6%			
	No	5260	25.2%	<0.0001	2.33 (1.99–2.72)	2.35 (2.01–2.74)
	h/o hyperlipidemia					

Variable type	Variable	N	Mimic rate	p-value	Unadjusted OR (95% CI)	Age-adjusted OR (95% CI)
	Yes	2664	11.1%			
	No	4323	28.8%	<0.0001	3.22 (2.81–3.70)	3.07 (2.67–3.53)
	h/o coronary artery disease					
	Yes	1536	11.7%			
	No	5451	25.0%	<0.0001	2.53 (2.14–2.99)	2.36 (1.99–2.79)
	h/o atrial fibrillation					
	Yes	1081	9.2%			
	No	5906	24.4%	<0.001	3.21 (2.59–3.98)	2.86 (2.30–3.56)
	h/o carotid artery disease					
	Yes	296	11.1%			
	No	6691	22.6%	<0.001	2.32 (1.61–3.35)	2.10 (1.45–3.03)
	h/o intracranial hemorrhage					
	Yes	137	10.9%			
	No	6150	14.7%	0.214	1.41 (0.82–2.42)	1.41 (0.82–2.41)
	h/o ischemic stroke					
	Yes	1573	15.8%			
	No	5392	23.7%	<0.0001	1.66 (1.43–1.93)	1.58 (1.36–1.84)

Table 2

Logistic regression including factors that were significant in the univariate analysis for entire sample and by location where the patient was initially identified.

Variable	All		Emergency Department		Inpatient onset	
	OR (95%CI)	p-value	OR (95%CI)	p-value	OR (95%CI)	p-value
Age <72 years (&)	0.94 (0.79–1.12)	0.48	1.06 (0.86–1.31)	0.57	0.67 (0.45–1.00)	0.05
Female sex	1.58 (1.34–1.86)	<0.000	1.49 (1.23–1.80)	0.000	1.32 (0.89–1.95)	0.17
African American	1.20 (1.01–1.43)	0.04	1.28 (1.04–1.58)	0.02	0.97 (0.64–1.47)	0.90
Code stroke	1.25 (1.07–1.46)	0.006	1.20 (0.99–1.44)	0.07	1.75 (1.17–2.61)	0.007
Arrival by automobile (ER patients only)	N/A *	0.001	1.41 (1.16–1.71)	0.001	N/A *	
Onset of symptoms as inpatient	0.75 (0.61–0.92)	0.005	N/A		N/A	
No history of hypertension	6.96 (5.81–8.33)	<0.000	6.93 (5.60–8.58)	0.000	8.17 (5.32–12.54)	0.000
No history of diabetes mellitus	1.07 (0.86–1.34)	0.56	1.04 (0.79–1.36)	0.79	0.86 (0.54–1.40)	0.55
No history of hyperlipidemia	2.14 (1.74–2.63)	0.000	2.33 (1.84–2.95)	0.000	1.95 (1.19–3.18)	0.008
No history of coronary artery disease	1.13 (0.88–1.45)	0.34	0.89 (0.66–1.20)	0.45	2.15 (1.28–3.6)	0.004
No history of atrial fibrillation	2.90 (2.11–3.99)	0.000	2.28 (1.58–3.31)	0.000	4.68 (2.34–9.33)	0.000
No history of carotid artery disease	1.14 (0.67–1.94)	0.63	0.91 (0.48–1.71)	0.76	3.43 (0.97–12.19)	0.06
No history of ischemic stroke	0.88 (0.71–1.09)	0.24	0.90 (0.70–1.15)	0.39	0.83 (0.48–1.44)	0.50

(&) The median age of the sample is 71.

* Arrival by automobile only applies to patients who were not inpatients at the time of onset of stroke and thus is not entered into the model that includes all variables.