Distinguishing Between Stroke and Mimic at the Bedside
The Brain Attack Study

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Background and Purpose—The bedside clinical assessment of the patient with suspected stroke has not been well studied. Improving clinical skills may accelerate patient progress through the emergency department. We aimed to determine the frequency and nature of stroke mimics and to identify the key clinical features that distinguish between stroke and mimic at the bedside.

Methods—Consecutive presentations to an urban teaching hospital with suspected stroke were recruited. A standard bedside clinical assessment was performed. The final diagnosis was determined by an expert panel, which had access to clinical features, brain imaging, and other tests. Univariate and multivariate analyses determined the bedside features that distinguished stroke from mimic.

Results—There were 350 presentations by 336 patients. The final diagnosis was stroke in 241 of 350 (69%) and mimic in 109 (31%). The mimics included 44 events labeled "possible stroke or TIA." Eight items independently predicted the diagnosis in patients presenting with brain attack: cognitive impairment and abnormal signs in other systems suggested a mimic, an exact time of onset, definite focal symptoms, abnormal vascular findings, presence of neurological signs, being able to lateralize the signs to the left or right side of the brain, and being able to determine a clinical stroke subclassification suggested a stroke.

Conclusions—The bedside clinical assessment can be streamlined substantially. This has important implications for teaching less experienced clinicians how to assess the patient with suspected stroke. **(*Stroke*. 2006;37:769-775.)**

Key Words: diagnosis ■ stroke, acute ■ stroke assessment

Stroke is a clinical diagnosis, supported in some cases, but not all, by an appropriate abnormality on brain imaging. Despite its limitations, the clinical assessment directs immediate management of the patient with suspected stroke. For patients to receive time-critical treatments (such as thrombolysis, medical or surgical treatment of intracerebral hematoma, reversal of anticoagulation), they must be brought to hospital rapidly, assessed quickly and accurately, and promptly sent for the appropriate investigation. Many studies show that stroke patients arrive at hospital early.[1,2] One of the major factors that explains the low proportion of patients who are treated with thrombolysis is the delay in processing acute stroke patients through the emergency department and to the scanner.[3–5] Delays may in part be attributable to the uncertainty of trainee doctors (the first contact point in emergency rooms) who lack confidence dealing with acute neurological patients.[6]

We may be able to improve our management of acute stroke by examining the first interaction between patient and medical staff: the bedside assessment. There have been few comprehensive studies of the clinical assessment.[7] We prospectively examined consecutive patients who presented to our hospital with suspected stroke. Our aims were to determine the frequency and nature of stroke mimics and to identify the key clinical features that distinguish between stroke and mimic at the bedside.

Materials and Methods

This was an observational, prospective study of consecutive patients admitted to hospital with possible stroke. It was based in an urban teaching hospital with a 16-bed acute stroke unit, an emergency department, and access to typical investigations (computed tomography [CT]/magnetic resonance, carotid ultrasound, echocardiography, etc). The local ethics committee approved the study, and all patients (or their relatives) provided informed consent.

Inclusion Criteria

We recruited consecutive patients admitted with possible stroke, which we called a "brain attack." This was defined as apparently focal brain dysfunction of apparently abrupt onset. Focal brain dysfunction could be a symptom or a sign. We wanted to study all

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patients with suspected stroke, so we did not set time limits for inclusion in the study. Subarachnoid hemorrhage was not considered to be a brain attack or stroke in this study.

The primary source of study patients came from the emergency department staff directly paging the research fellow when a suitable patient arrived. Other overlapping sources (admission registers of the emergency department, stroke unit, and neurology ward) were used to ensure that all patients with brain attack were identified.

Patient Assessment

A research fellow assessed patients as soon as possible after hospital presentation, before investigations were performed (or blind to the results). Four research fellows participated in the study. All were between 5 and 9 years postregistration and were undertaking a cerebrovascular fellowship; 2 were trained neurologists, and 2 were trainees in internal medicine.

The research fellow performed a complete bedside assessment of each patient and recorded details on a standard data form. Information collected included: (1) past medical history, including vascular risk factors, previous stroke or transient ischemic attack (TIA), risk factors for a stroke mimic (cognitive impairment, migraine, epilepsy, malignancy, and psychological disturbance); (2) history of the present event, including nature of the neurological symptoms, timing of symptom onset, change in symptoms over time; (3) general examination, including level of consciousness, vascular status, signs in other systems; (4) neurological examination, including the National Institutes of Health Stroke Scale (NIHSS); and (5) diagnostic formulation, including stroke or stroke mimic, Oxfordshire Community Stroke Project (OCSP) subclassification.[8]

Determination of the Final Diagnosis

We used the consensus opinion of a panel of stroke experts to determine the final diagnosis of the event, which was assigned after reviewing anonymized clinical details, brain imaging, and other relevant investigations. The panel comprised ≥1 stroke neurologist, 2 stroke physicians, a neuroradiologist, and 2 research fellows.

A definite nonstroke was diagnosed when the clinical details did not suggest a vascular etiology, and another convincing explanation for the symptoms was discovered (often requiring supportive investigations, eg, tumor). A definite stroke was diagnosed when the history and examination were considered to be completely typical of a vascular brain event, and there was supportive or noncontradictory brain imaging. A definite TIA required full resolution of symptoms within 24 hours. A probable stroke had clinical features consistent with a vascular etiology, with no alternative explanation. A possible stroke had clinical features that were less convincing, and an alternative explanation for the clinical syndrome may have been present, but there was no definite proof of a nonstroke. A possible TIA was a possible stroke that resolved within 24 hours.

Statistical Analysis

We dichotomized the final diagnosis into stroke or mimic to permit analysis of the clinical features that distinguished between the 2 conditions. Definite and probable stroke (or TIA) were classed as stroke, whereas definite nonstroke and possible stroke (or TIA) were classed as mimic.

Differences between the 2 groups were assessed using descriptive statistics and standard tests of significance (as indicated). The odds ratio (OR) with 95% CIs was calculated for univariate analyses. Analyses were performed on either the total number of episodes or the total number of patients depending on the nature of the data collected (because the same patient could be recruited into the study multiple times, each hospital admission was defined as an episode).

Forward stepwise multiple logistic regression was performed to determine the clinical factors that independently predicted the diagnosis. To ensure that modeling produced reliable results, we conformed to strict methodological principles.[9,10] Only the first recruiting event was used for this analysis. The outcome was a final diagnosis of stroke or mimic, and predictor variables were dichotomized wherever possible. We eliminated predictor variables with too much missing data, in which the event rate was low, the reliability of the item was poor or moderate (Hand et al, unpublished data, 2005), or that duplicated other items and combined several variables to create composite variables. The performance of the model produced by the multivariate analysis was assessed by: (1) the Hosmer and Lemeshow test, which measures goodness of fit of the model to the data set (when the significance is low [$P<0.05$], the model does not fit the data set); (2) the accuracy of the predictions of the model; and (3) the area under the receiver operating characteristic (ROC) curve, which measures the discrimination of the model (area under the curve can range from 0.5 (no discrimination) to 1.0 (perfect discrimination).

Analyses were performed using Microsoft Excel (version 97 SR-2), SPSS (version 11.0.0) and Confidence Interval Analysis software (Martin J. Gardner and British Medical Journal, 1989).

Sample Size Calculation

Reliable multivariable statistical analysis requires that there are ≥10 outcome events for each variable modeled.[10] Assuming 20% to 30% frequency of mimics, a sample size of 350 to 400 would recruit 80 mimics, thus permit logistic regression modeling with 8 variables.

Results

We studied 350 consecutive presentations with brain attack in 336 patients; 8 patients presented twice, and 3 patients presented 3 times. An exact time of onset could be determined in 247 episodes (71%), an approximate time could be established in all but 5 episodes, and in 31%, the symptoms were first noted on waking. A total of 116 presentations (33%) were within 3 hours of symptom onset, but the study clinicians saw only 32 (9%) within 3 hours. Table 1 describes the baseline demographic data for the patients recruited. At the time of examination by the research fellow, 47 of 350 (13%) presentations had no neurological signs.

What Conditions Cause Brain Attack?

The expert panel determined the final diagnosis as definite stroke in 186 (53%), definite TIA in 17 (5%), and probable stroke in 34 (10%). A definite nonstroke was diagnosed in 65 (19%), possible stroke in 35 (10%), and possible TIA in 13 (4%). Of the 48 presentations of brain attack labeled possible stroke/TIA, there was an alternate, plausible nonstroke diagnosis in all but 4. The dichotomized final diagnosis was stroke in 241 of 350 (69%) and mimic in 109 (31%).

Of the 106 patients (109 episodes) who presented with a stroke mimic, 44 (42%) had experienced a previous stroke (with symptoms completely resolved in 19 of 44), and 27 (26%) were known to have cognitive impairment. The causes of stroke mimic are detailed in Table 2, which is subdivided by time of patient presentation. A total of 62 of 109 (57%) mimics were neurological conditions, and in an additional 20 mimics (syncope, confusional state, dementia), neurological conditions were among the differential diagnoses. The most frequent site of sepsis was the chest, and the most common toxic/metabolic disturbance was hypoglycemia.

Features Distinguishing Stroke From Mimic at the Bedside

Table 1 describes the clinical features of patients recruited into the study, subdivided into stroke and mimic. Univariate

TABLE 1. Characteristics of the Study Population, Subdivided Into Stroke and Mimic

Feature	All Patients n=350 Episodes; n=336 Patients	Stroke n=241 Episodes; n=237 Patients	Mimic n=109 Episodes; n=106 Patients
Median age (range, in years)*	76.3 (17.4–98.7)	76.3 (24.8–98.7)	77.0 (17.4–97.0)
Male gender*	163 (49%)	118 (50%)	48 (45%)
Median time from onset to presentation (hours)	4.71	4.47	4.67
Number presenting†			
0–6 h	189 (56%)	129 (54%)	60 (55%)
6–12 h	51 (15%)	38 (16%)	13 (12%)
>12 h	96 (29%)	63 (26%)	33 (30%)
Vascular risk factors‡			
Hypertension	159/325 (49%)	121/233 (52%)	45/99 (45%)
Ischemic heart disease	100/322 (31%)	79/231 (34%)	22/98 (22%)
Smoker (past or present)	172/326 (53%)	123/214 (57%)	50/95 (53%)
Atrial fibrillation	62/321 (19%)	47/229 (21%)	18/99 (18%)
Diabetes mellitus	40/327 (12%)	26/233 (11%)	15/101 (15%)
Peripheral vascular disease	33/307 (11%)	29/218 (13%)	4/96 (4%)
Past history of stroke*	129/323 (40%)	87/231 (38%)	48/99 (48%)
Risk factors for stroke mimic			
Cognitive impairment	54/326 (17%)	28/229 (12%)	27/103 (26%)
Migraine	16/336 (5%)	11/237 (5%)	5/106 (5%)
Epilepsy	12/336 (4%)	7/237 (3%)	8/106 (8%)
Known malignancy	33/336 (10%)	22/237 (9%)	11/106 (10%)
Psychological disturbance†	28/336 (8%)	17/237 (7%)	11/106 (10%)
Patient could walk independently before admission	309/332 (93%)	221/234 (94%)	95/105 (90%)
Presenting event‡			
Woke from sleep with symptoms	75/242 (31%)	64/191 (34%)	14/62 (23%)
Loss of consciousness	50/316 (16%)	25/234 (11%)	28/94 (30%)
Vomited	43/321 (13%)	25/230 (11%)	19/105 (18%)
Headache	97/300 (32%)	78/216 (36%)	22/95 (23%)
Patient could walk after symptom onset‡	136/332 (41%)	84/238 (35%)	56/108 (52%)
Examination findings‡			
BP ≥150/90	123/335 (37%)	97/241 (40%)	31/109 (28%)
Atrial fibrillation	69/336 (21%)	55/241 (23%)	17/109 (16%)
GCS=15	227/336 (68%)	163/241 (68%)	73/109 (67%)
Confusion¶	89/246 (36%)	61/172 (35%)	31/84 (37%)
No neurological signs	44/336 (13%)	18/241 (7%)	29/109 (27%)
NIHSS			
Mean	7.34	8.56	4.65
Median	4.0	5.0	3.0
Clinical classification‖			
TACS	60 (17%)	57 (24%)	3 (3%)
PACS	108 (31%)	77 (32%)	31 (28%)
LACS	59 (17%)	54 (22%)	5 (5%)
POCS	42 (12%)	31 (13%)	11 (10%)
Unsure/no signs	81 (23%)	22 (9%)	59 (54%)
Number with brain imaging	304 (87%)	232 (96%)	72 (66%)
MRI brain	57 (16%)	53 (22%)	4 (4%)

*Number of patients; †incomplete numbers because inpatient strokes were not included; ‡the denominator excludes those patients in whom the feature was unknown; §one or more episodes of psychological disturbance severe enough to warrant medication; ¶made ≥1 errors on tests for confusion (orientation and attention); ‖OCSP clinical classification[8].

TACS indicates total anterior circulation syndrome; PACS, partial anterior circulation syndrome; LACS, lacunar syndrome; POCS, posterior circulation syndrome; GCS, Glasgow Coma Score.

TABLE 2. Causes of Stroke Mimics (n=109)*, Subdivided by Time to Presentation

Condition	Total Number (%)†	Mimics Presenting	
		Within 6 Hours	After 6 Hours
Seizure	23 (21.1%)	18 (29.0%)	5 (10.6%)
Sepsis	14 (12.8%)	6 (9.7%)	8 (17.0%)
Toxic/metabolic	12 (11.0%)	6 (9.7%)	6 (12.8%)
Space occupying lesion	10 (9.2%)	3 (4.8%)	7 (14.9%)
Syncope/presyncope	10 (9.2%)	9 (14.5%)	1 (2.1%)
Acute confusional state	7 (6.4%)	3 (4.8%)	4 (8.5%)
Vestibular dysfunction	7 (6.4%)	3 (4.8%)	4 (8.5%)
Acute mononeuropathy	6 (5.5%)	4 (6.5%)	2 (4.3%)
Functional/medically unexplained symptoms	6 (5.5%)	4 (6.5%)	2 (4.3%)
Dementia	4 (3.7%)	2 (3.2%)	2 (4.3%)
Migraine	3 (2.8%)	2 (3.2%)	2 (4.3%)
Spinal cord lesion	3 (2.8%)	- (0%)	3 (6.4%)
Other	3 (3.7%)	2 (3.2%)	1 (2.1%)
Total	109 (100%)	62 (100%)	47 (100%)

*Includes the 65 brain attacks definitely attributable to a mimic and the 44 brain attacks labeled as possible stroke/TIA in which there was a highly plausible alternate diagnosis.

There were 4 presentations diagnosed as possible stroke/TIA with no plausible alternate diagnosis (these patient episodes have not been included).

†Expressed as a proportion of the 109 mimics; ‡expressed as a proportion of those presenting within or after 6 hours.

analyses are shown in Figure 1 (only the significant relationships have been shown). A mimic was more likely if there was a known history of cognitive impairment, the patient lost consciousness or had a seizure at onset, the patient could still walk, there were no lateralizing symptoms, and the examination revealed confusion, signs in other nonvascular systems (eg, chest crackles) and no neurological signs ($P<0.05$ for all). A mimic was also more likely if the signs were inconsistent with the symptoms or did not conform to known vascular territory.

Strong bedside pointers to the diagnosis of stroke included definite focal symptoms, the patient was well in the last week, and an exact time of onset could be determined. Stroke was more likely if the patient had almost any focal neurological symptom or sign, although the frequency of the item was often low (eg, the OR for eye deviation was 11.5 [95% CI, 1.53 to 86.3], but it was observed in only 23 patients with stroke). Symptoms and signs suggesting a brain stem lesion, such as vertigo and lower limb ataxia, were not significant predictors because these features were also observed in peripheral vestibular disorders (a common stroke mimic).

The NIHSS was useful in distinguishing mimic from stroke (Figure 2). A low NIHSS predicted a mimic, but 19% of brain attacks with an NIHSS >10 were attributable to a mimic. These were often patients with a previous stroke who presented with an intercurrent infection or metabolic disturbance. The OCSP classification of a large anterior circulation or lacunar subtype predicted a stroke, and a mimic was likely if the OCSP subtype could not be determined (eg, patient presenting with dysarthria only).

After multivariate analyses, 8 items of the bedside assessment independently predicted the diagnosis (Table 3). The model created by multivariate analysis performed well. The model fitted the data set (Hosmer and Lemeshow test $P=0.746$), there were 83% correct classifications, and area under the ROC curve was 0.87 (95% CI, 0.83 to 0.91). Excluding the 30 events labeled possible or definite TIA, in which symptoms resolved within 24 hours, did not alter the findings on univariate and multivariate analyses.

Discussion

Although laboratory investigations and brain imaging can refine the diagnosis (and are essential for any decisions regarding treatment), the bedside clinical assessment remains important 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.[11] Despite the need for a rapid, confident clinical diagnosis in the thrombolysis era, the clinical assessment has received little formal study.[7]

Of the 350 consecutive presentations of brain attack in our study, ≈30% were stroke mimics. This figure is somewhat higher than many hospital-based studies (eg, 1.2%[12] to 5.0%[13]), but this may be explained by their more selective entry criteria. Less selective community-based studies reported higher proportions of mimics (eg, 25%,[14] 29%[15]), but they may not be as relevant to the hospital-based stroke physician. Libman et al[16] retrospectively identified all patients presenting with "sudden onset of a focal deficit" to a general hospital. A total of 78 of 411 (19%) had a stroke mimic, the same proportion as were diagnosed definite nonstroke in our study. Few studies report figure for possible stroke. This is curious; although some mimics will be definitively diagnosed (by brain imaging or other laboratory tests), it is a clinical reality that many cannot be diagnosed with certainty.

The stroke-mimicking conditions identified in our study were similar to previous reports. Many mimics are seen infrequently, such as transient global amnesia, demyelination, spinal cord lesions, and so on. A total of 82 of 109 (75%) mimics in our study were neurological disorders, yet many had normal brain imaging. Conversely, almost half (42%) of patients with a mimic had experienced a previous stroke, and many of these patients would have an abnormal brain scan. Because stroke is a clinical diagnosis, these data reinforce the need for neurologists, or stroke physicians with adequate neurological training, to be involved in the assessment of patients with brain attack. This has been argued by others since the 1950s[17–20] and remains relevant now.

We identified 47 clinical factors that significantly distinguished between stroke and mimic on univariate analysis. Libman et al[16] found that female gender, abnormal visual fields, diastolic blood pressure >90 mm Hg and atrial fibrillation increased the odds of stroke; and normal eye movements and an abnormal admission neurological examination increased the odds of a mimic. In our study, diastolic blood pressure >90 mm Hg and abnormal visual fields predicted stroke, but female gender, atrial fibrillation, and normal eye movements were not significant predictors, and an abnormal neurological examination actually suggested stroke (rather

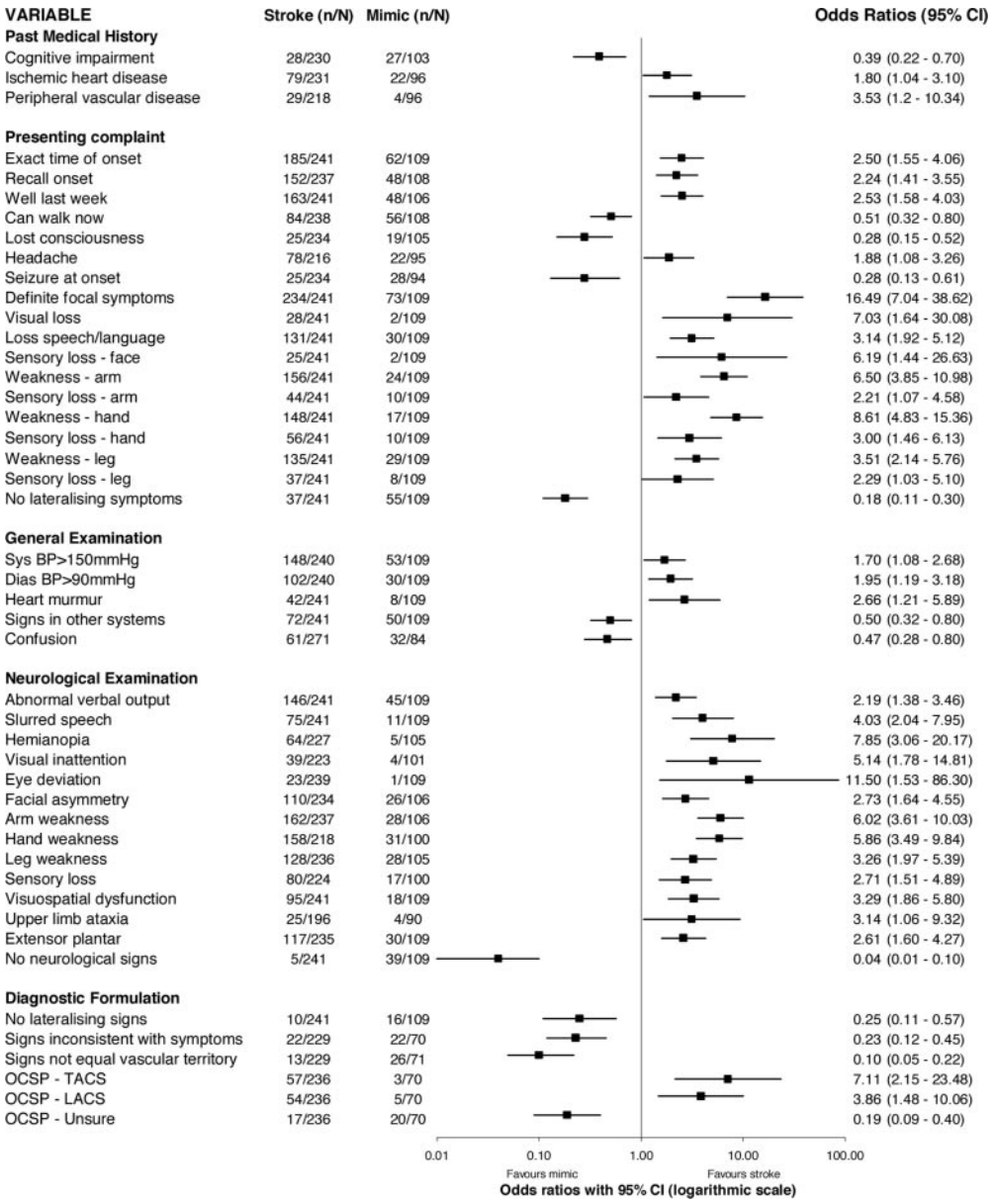

Figure 1. Items from the clinical assessment that were statistically significant in predicting the final diagnosis from univariate analyses. An OR >1 predicts a stroke; <1 predicts a mimic.

than mimic). Ferro et al[21] found that a mimic was more likely if the patient had no vascular risk factors, but we were unable to confirm this. Older studies[22,23] suggested that the temporal evolution of symptoms distinguished vascular from nonvascular events, but this is of little benefit in hyperacute assessment. In our study, an exact time of onset, the patient being able to recall exactly what he/she was doing at symptom onset, and being well in the last week were all strongly predictive of stroke, and all point to an abrupt onset.

We found that 8 items independently predicted the diagnosis in patients presenting with brain attack. The only other multivariate analysis identified just 2 independent predictors: decreased level of consciousness predicted a mimic, and angina predicted a stroke.[16] Our findings show that the bedside clinical assessment can be streamlined substantially. This has important implications for teaching the bedside assessment of suspected stroke to less experienced clinicians. Patients with acute neurological conditions can be daunting for an inexperienced clinician.[6] With better knowledge of the key features that reliably distinguish stroke from mimic, as identified in our study, the inexperienced clinician's assessment can be brief but more focused and assured.

This study had a number of limitations. The entry criteria may have been too restrictive (or overly inclusive) but were similar to many other studies.[16,24] We saw few patients within 3 hours, but our aim was to capture all events. Our cohort was older and the stroke severity was milder than other series,[25,26] which might make the bedside diagnosis more difficult. Our gold standard diagnosis was not independent of the research fellow's assessment, and most patients did not have MRI. It is difficult to determine

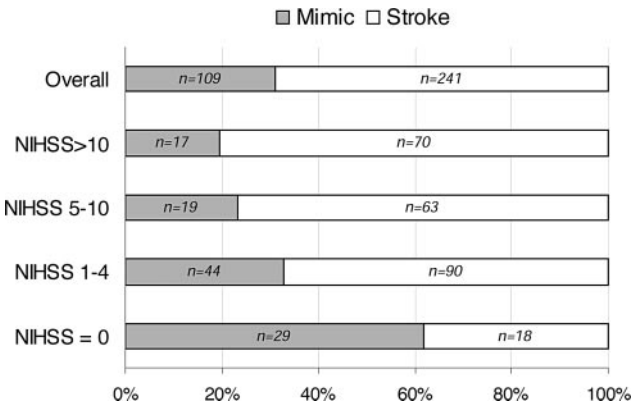

Figure 2. Proportion of brain attacks attributable to stroke or mimic subdivided by NIHSS score.

a gold standard for the diagnosis of stroke.[27] Fewer patients with a mimic were scanned, reflecting clinical reality but also introducing bias. Confounding factors included differences in experience and training of the research fellows, their improvement in clinical skills with time, and the inability to obtain key data in some situations (eg, aphasic patient with no relative). Finally, there are many well-described problems with logistic regression modeling, and internal validation does not imply that the model can be generalized to other cohorts of patients.[28] The results of our study need to be validated in further prospective studies.

Despite its limitations, our study provides numerical scientific data to support the "art" of the clinical assessment of patients with suspected stroke. Much of what we have shown would be familiar to the experienced stroke clinician. Knowing the stroke mimics and the key clinical features that help discriminate stroke from mimic (and the relative importance of each feature) means this can be taught to inexperienced doctors to help them gain knowledge and skill. The information from this study should be considered complementary to brain imaging and other laboratory tests. Our study provides a method for accelerating the patient's passage from the emergency department door to the acute stroke unit and treatment, via the CT or MRI scanner.

TABLE 3. Logistic Regression Model for Predicting the Diagnosis of Brain Attack

Variable	OR	95% CIs
Known cognitive impairment	0.33	(0.14–0.76)
An exact onset could be determined	2.59	(1.30–5.15)
Definite history of focal neurological symptoms	7.21	(2.48–20.93)
Any abnormal vascular findings*	2.54	(1.28–5.07)
Abnormal findings in any other system†	0.44	(0.23–0.85)
NIHSS=0‡		
NIHSS 1–4	1.92	(0.70–5.23)
NIHSS 5–10	3.14	(1.03–9.65)
NIHSS >10	7.23	(2.18–24.05)
The signs could be lateralized to the left or right side of the brain	2.03	(0.92–4.46)
OCSP classification was possible	5.09	(2.42–10.70)

The model gives a predicted probability of stroke (ranging from 0 to 1). The mathematical equation uses the coefficient for each variable plus a constant (not shown) to calculate the probability. The ORs provide a "weighting" for the importance of each variable (ie, NIHSS >10 and definite history of focal neurological symptoms are the most powerful predictive factors).

*Systolic blood pressure >150 mm Hg, atrial fibrillation, valvular heart disease, or absent peripheral pulses; †respiratory, abdominal, or other abnormal signs; ‡NIHSS=0 was entered as the reference group (therefore it does not have a coefficient).

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