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BRIEF REPORT

Code Stroke: Multicenter Experience With In-Hospital Stroke Alerts

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Between 2.2% and 17% of all strokes have symptom onset during hospitalization in a patient originally admitted for another diagnosis or procedure. A response system to rapidly evaluate inpatients with acute neurologic symptoms facilitates evaluation and treatment of stroke developing during hospitalization. The National Stroke Association implemented an in-hospital stroke quality-improvement initiative from July 2010 to June 2011 in 6 certified stroke centers from Michigan, South Carolina, Pennsylvania, Colorado, Washington, and North Carolina. Three hundred ninety-three in-hospital stroke alerts were examined over a 1-year period. Of the alerts, 42.5% were for ischemic stroke, 8.7% probable or possible TIA, 2.8% intracranial hemorrhage, and 46.1% were stroke mimics. The most common stroke mimics were seizure, hypotension, and delirium. Participating hospitals had an alarm rate for diagnoses other than acute cerebrovascular events ranging from 28.0% to 66.7%. Of 194 in-hospital stroke/transient ischemic attack cases, 8.2% received intravenous thrombolysis alone, 10.3% received intra-arterial/mechanical thrombolysis alone, and 1% received both. No patient with a stroke mimic received thrombolysis. Our findings suggest that in-hospital response teams need to be prepared to respond to a range of acute medical conditions other than ischemic stroke. *Journal of Hospital Medicine* 2015;10:179–183. © 2014 Society of Hospital Medicine

Acute change in neurologic status in a hospitalized patient is an emergency requiring timely coordinated evaluation. To address this need, many hospitals have created a mechanism for in-hospital stroke alerts utilizing generalized rapid response teams or specialized stroke teams.[1–3] The common purpose is to quickly diagnose new ischemic stroke within the time window for thrombolytic therapy.

Even when acute change in neurologic status is not due to brain ischemia, it may represent a new metabolic disturbance or reflect developing serious systemic illness. Sepsis, hypoglycemia, cardiac arrhythmia, respiratory failure, severe electrolyte disturbances, seizures, or delirium may first manifest as a change in neurologic status.

Prior research on stroke alerts has largely focused on patients who present from the community to the emergency department (ED).[4–8] Patients who develop acute neurologic symptoms during hospitalization have different risk factors and exposures compared to patients in the community.[9] This study represents the experience of a multistate quality improvement initiative for in-hospital stroke. We characterize etiologies for symptoms triggering in-hospital stroke alerts and thrombolytic treatment for in-hospital strokes.

PATIENTS AND METHODS

The National Stroke Association's (NSA) initiative, Improving In-Hospital Stroke Response: A Team-based Quality Improvement Program, included data collection for all in-hospital stroke alerts over a 12-month period.[10] Six Joint Commission certified primary stroke centers from Michigan, South Carolina, Pennsylvania, Colorado, Washington, and North Carolina completed the 1-year quality improvement initiative. One additional site withdrew from the program after the first quarter and was not included in this analysis. Sites prospectively reported deidentified patient-level data on all adult in-hospital stroke alerts from July 2010 to June 2011 to the NSA. At all sites, any provider could activate the in-hospital stroke response system. Stroke alerts were evaluated by a rapid response team with stroke training. The providers on the stroke rapid response team varied between sites. A nurse with stroke training was 1 of the first responders on the stroke response team at all sites.

The NSA in-hospital stroke-alert criteria included the following symptoms occurring in the last 24-hours, even if they resolved: (1) sudden numbness or weakness of the face, arm or leg, especially on 1 side of the body; (2) sudden confusion, trouble speaking or understanding; (3) sudden trouble seeing in 1 or both eyes; (4) sudden trouble walking, dizziness, loss of balance or coordination; and (5) sudden, severe headache with no known cause. Hospitals reported location, service, age, sex, race, symptoms triggering the stroke alert, free text entry of final clinical

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TABLE 1. Final Diagnosis Following In-Hospital Stroke Alert

Diagnosis	No. (N = 393)	%
Ischemic stroke	167	42.5%
TIA (definite, probable, or likely)	27	6.9%
TIA (possible or "versus" a mimic)	7	1.8%
Syncope, hypotension, presyncope, bradycardia	23	5.9%
Seizure	23	5.9%
Delirium/encephalopathy/acute confusional state/dementia	23	5.9%
Stroke mimic NOS	21	5.3%
Other (examples include Parkinson's crisis, musculoskeletal, primary ophthalmologic diagnosis, or cardiovascular ischemia)	17	4.3%
Final diagnosis uncertain	16	4.1%
Medication effect (sedation due to narcotics, limb weakness due to epidural anesthetic, pupil dilation from ipratropium)	15	3.8%
Metabolic (hypoglycemia, electrolyte abnormality, hypercarbia, acid/base disorders, respiratory failure)	12	3.1%
Intracranial hemorrhage (intraparenchymal hemorrhage, subarachnoid hemorrhage, subdural hematoma)	11	2.8%
Conversion disorder/psychiatric/functional/medically unexplained symptoms	7	1.8%
Old deficit due to remote stroke	6	1.5%
Peripheral neuropathy (Bell's palsy, cranial nerve palsy, compression neuropathy)	6	1.5%
Sepsis/infection	5	1.3%
Migraine	4	1.0%
Peripheral vestibular dysfunction	3	0.8%

NOTE: **Abbreviations:** NOS, not otherwise specified; TIA, transient ischemic attack.

diagnosis following the completion of stroke alert evaluation, treatment with intravenous or intra-arterial/mechanical thrombolysis, and any contraindications to intravenous thrombolysis. We categorized stroke mimics using the responses in the "final diagnosis" field after the data collection period was complete. Strokes were categorized as ischemic stroke, transient ischemic attack (TIA), or intracranial hemorrhage (intraparenchymal, intraventricular, epidural, subdural, or subarachnoid). Stroke mimics were subdivided according to the categories in Table 1. Lack of certainty in the final diagnosis was handled by creating a category of "possible TIA," which includes alternative diagnosis versus TIA or the qualifier "possible" before TIA. Patients with final diagnoses unable to be determined were classified as stroke mimics. Institutional review board exemption was obtained for the deidentified prospective data registry of this quality-improvement program.

RESULTS

During the 12-month data collection period, 393 in-hospital stroke alerts were reported to the NSA. Hospitals reported an average of 65.5 in-hospital stroke alerts (range, 27–156; standard deviation 46.8) (Table 2). Median age was 70 years (range, 18 to >89 years, interquartile range [IQR], 62–80 years). Of the stoke alert patients, 52.8% were female, 81.7% were white, 12.7% were black, 2.9% were Hispanic, and 2.7% were other or were unable to be determined. The most common primary services were medicine/hospitalist (36.4%), cardiology (19.5%), cardiothoracic/vascular surgery (13%), and orthopedic surgery (8.6%).

Of the stroke alert patients, 167 (42.5%) were found to have ischemic stroke, 27 (6.9%) TIA, 11 (2.8%) intracranial hemorrhage, and 7 (1.8%) had TIA possible or considered along with a stroke mimic in the final diagnosis. The stroke mimic rate was 46.1%, with a confidence range of 42.0% to 47.8% depending on the true pathologic cause of the alerts in the categories "possible TIA" and "final diagnosis uncertain." Participating hospitals had an alarm rate for stroke mimics ranging from 28.0% to 66.7% (median, 45.8%; IQR, 32.9%–49.7%) (Table 2). The most common stroke mimics were seizure, hypotension, and delirium (Table 1). Data were available on symptoms that triggered the alert in 373 (94.9%) of cases. Eighteen alerts (4.8%) were for symptoms clearly not included in the NSA stroke alert criteria. The final diagnosis was acute ischemic stroke/TIA or intracranial hemorrhage in 4 of these 18 (22.2%) nonconforming alerts. If alerts called for a decrease in consciousness were also considered nonconforming, then 67 alerts (18.0%) could be categorized as nonconforming. However, 24 of these 67 alerts (35.8%) had a final diagnosis of acute ischemic stroke/TIA or intracranial hemorrhage.

For 194 patients with a final diagnosis of ischemic stroke or TIA, intravenous thrombolysis alone was used for 16 in-hospital stroke patients (8.2%), 20 received intra-arterial/mechanical thrombolysis alone (10.3%), and 2 patients received both (1%) (Table 3). No patient with a stroke mimic received thrombolysis.

DISCUSSION

Given the protean manifestations of brain ischemia, and significant symptom overlap with many mimics, stroke alert criteria casts a wide net in order not to miss or delay evaluation and treatment of true brain ischemia. Time is critical given the association of improved outcomes with more rapid delivery of treatment.[11] The inevitable consequence of the combination of time pressure and clinical uncertainty based solely on physical exam will be alerts due to stroke mimics. Our analysis reveals many of these alternative diagnoses also require urgent evaluation and treatment.

Prior research has found a large proportion of in-hospital stroke alerts are not for cerebrovascular events.[1,4,12] We observed an average of 46.1% of in-hospital stroke alerts were due to mimics. This rate is substantially higher than described in studies of stroke mimics in the ED.[7,13,14] The largest analysis over a 10-year period from 2 hospitals in Washington found a 30% stroke mimic rate and concluded that in-hospital location for symptom onset was a statistically significant predictor of being a mimic rather than a cerebrovascular event.[4] One single-center trial in

TABLE 2. Participating Site Characteristics

	All Six Sites	Site A	Site B	Site C	Site D	Site E	Site F
No. of stroke alerts	393	156	72	50	49	39	27
Median age, y, (IQR 25th to 75th percentile), no. with data for this demographic	70.0 (62–80) 376	71.0 (63.0–81.0) 156	68.0 (58.8–79.3) 72	76.5 (65.5–85.0) 50	71.0 (63.0–78.5) 48	75.0 (58.5–84.5) 23	77.0 (66.0–84.5) 27
Sex, % female, no. with data for this demographic	52.8%, 377	48.7%, 156	63.9%, 72	52%, 50	49.0%, 49	52.2%, 23	55.6%, 27
Race, no. (%)							
White	308 (81.7%)	146 (93.6%)	40 (55.6%)	47 (94%)	39 (80.0%)	15 (65.2%)	21 (77.8%)
Black or African American	48 (12.7%)	3 (1.9%)	32 (44.4%)	1 (2%)	6 (12.2%)	0 (0%)	6 (22.2%)
Hispanic	11 (2.9%)	3 (1.9%)	0 (0%)	1 (2%)	1 (2.0%)	6 (26.1%)	0 (0%)
Other or unable to determine	10 (2.7%)	4 (2.6%)	0 (0%)	1 (2%)	3 (6.1%)	2 (8.7%)	0 (0%)
No. with data for this demographic	377	156	72	50	49	23	27
Service caring for patient, no. (%)							
General medicine	123 (36.4%)	44 (32.1%)	29 (40.3%)	21 (46.7%)	11 (22.9%)	7 (77.7%)	11 (40.7%)
Cardiology	66 (19.5%)	36 (26.3%)	11 (15.3%)	10 (22.2%)	9 (18.8%)	0 (0%)	0 (0%)
Cardiothoracic/vascular surgery	44 (13.0%)	21 (15.3%)	8 (11.1%)	3 (6.7%)	11 (22.9%)	0 (0%)	1 (3.7%)
Orthopedic surgery	29 (8.6%)	17 (12.4%)	4 (5.6%)	3 (6.7%)	2 (4.2%)	0 (0%)	3 (11.1%)
Family practice	13 (3.8%)	2 (1.5%)	1 (1.4%)	1 (2.2%)	0 (0%)	0 (0%)	9 (33.3%)
Pulmonology/critical care	11 (3.3%)	4 (2.9%)	4 (5.6%)	2 (4.4%)	1 (2.1%)	0 (0%)	0 (0%)
General surgery	11 (3.3%)	4 (2.9%)	1 (1.4%)	3 (6.7%)	2 (4.2%)	0 (0%)	1 (3.7%)
Other	41 (12.1%)	9 (6.6%)	14 (19.4%)	2 (4.4%)	12 (25.0%)	2 (22.2)	2 (7.4%)
No. with data for this demographic	338	137	72	45	48	9	27
In-hospital stroke alert mimic rate							
Percent stroke mimics(confidence range)*	46.1% (42.0%–47.8%)	48.7% (42.9%–51.3%)	50.0% (50.0%–50.0%)	28.0% (28.0%–30.0%)	42.9% (36.7%–46.9%)	66.7% (56.4%–66.7%)	29.6% (29.6%–29.6%)

NOTE: **Abbreviations:** IQR, interquartile range. *Lower limit of confidence range represents estimate if all "possible transient ischemic attack" and "final diagnosis unknown" represented true ischemic strokes. Upper limit of confidence range represents estimate if all "possible transient ischemic attack" and "final diagnosis uncertain" represented stroke mimics.

TABLE 3. In-Hospital Stroke Thrombolysis Rates and Contraindications

Treatment of stroke alerts with final diagnosis of ischemic stroke or TIA, no. (%), n = 194	
Treated with IV thrombolysis alone	16 (8.2%)
Treated with IA or mechanical thrombolysis alone	20 (10.3%)
Treated with both IV and IA/mechanical thrombolysis	2 (1.0%)
Contraindication to IV thrombolysis for patients not treated with IV thrombolysis, no. (%), n = 176*	
Multiple	42 (23.9%)
Time based	27 (15.3%)
Medical	25 (14.2%)
Contraindication not otherwise specified	24 (13.6%)
Surgical/procedural	20 (11.4%)
Minor or rapidly improving symptoms	19 (10.8%)
Anticoagulation	7 (4.0%)
Other	4 (2.3%)
Goals of care	3 (1.7%)
Data unavailable	3 (1.7%)
Seizure at onset of symptoms	2 (1.1%)

NOTE: Abbreviations: IA, intra-arterial; IV, intravenous; TIA, transient ischemic attack; tPA, tissue plasminogen activator. *Definitions for IV exclusions. Multiple: any time more than 1 valid contraindication to IV tPA was listed. Examples would include: recent myocardial infarction on anticoagulation, out of time window and recent myocardial infarction, recent stroke, and advanced age with high National Institute of Health Stroke Scale, no clear onset time, and history of hemorrhagic stroke. Time based: if the sole listed contraindication related to time from onset of brain ischemia. Examples include "outside of treatment window," "time delay," subacute strokes on imaging, or unknown time last known normal. Medical contraindications: examples include arterial-venous malformation noted on computed tomography scan, history of recent stroke, history of recent myocardial infarction, gastrointestinal bleeding, or hematuria. Surgical/procedural: recent surgery such as femoral bypass, coronary artery bypass, orthopedic surgery, bowel resection, or invasive procedure such as thoracentesis, arterial puncture at noncompressable site, or cardiac catheterization. Contraindication not otherwise specified: contraindication to IV thrombolysis present but no specific contraindication listed. Minor or improving symptoms: examples include low scores on the National Institute of Health Stroke Scale or rapid improvement in symptoms. Anticoagulation: IV thrombolysis contraindicated due to use of anticoagulation product. Examples include use of warfarin with elevated international normalized ratio or treatment with therapeutic heparin or low-molecular-weight heparin. Other: if contraindication was listed but did not meet approved list of contraindications or if no contraindication to IV thrombolysis was listed but the patient was treated only with intra-arterial or mechanical thrombolysis. Examples include epistaxis or diabetic retinopathy or basilar artery thrombosis treated with IA thrombolysis. Goals of care: patient preferences or goals represent the reason for not considering thrombolysis or if patient/family declined thrombolysis. Examples include "comfort measures only" status or "family declined." Missing: field for contraindication left blank or notated as "unable to determine." Seizure at onset of symptoms: for patients with final diagnosis of stroke this would represent "onset seizures" rather than seizure mimicking stroke, but at the time of the initial stroke alert the seizure was felt to be a contraindication to thrombolysis.

North Carolina found markedly higher mimic rates for in-hospital stroke alerts (73%) versus ED stroke alerts (49%).[12] Assessment of neurologic symptoms is challenging in patients already hospitalized for acute medical conditions. The interaction of systemic illness, medications, and surgery seen in the hospital setting may make it more difficult to distinguish between cerebrovascular events and their many mimics.

Interpretation of NSA criteria for calling a stroke code likely varied within and between sites, and inter-rater reliability of physical signs was not assessed, which is a limitation of the data. Observed rates of stroke for alerts that did not conform to the NSA criteria suggest that clinical judgment remains valuable. Final diagnoses were assigned by the stroke programs, and reliability of this assessment was not evaluated. Sites were not asked to use a specific categorization scheme to group final diagnoses. This analysis was limited to stroke centers with existing infrastructure to respond to stroke alerts and participated in an explicit quality-improvement initiative on in-hospital stroke response. Mimic and thrombolysis treatment rates may be different for hospitals without this stroke expertise.

Clinical uncertainty as to final diagnosis was addressed with the inclusion of confidence intervals accounting for potential misdiagnosis of the events in the categories of "possible TIA" or in the cases where the final diagnosis was "unknown." Other studies have categorized "TIA versus an alternative diagnosis" as stroke mimic, and so our methodology is expected to yield a conservative estimate of the stroke mimic rate. Delirium is often a multifactorial phenomenon, so there may be an element of overlap between this category and other more specific mimic etiologies such as infection, hypotension, metabolic, or medication effect.

This initiative did not have the ability to assess the false negative rate of stroke team activation (failure to identify stroke symptoms in time for acute evaluation). It is not possible to calculate the sensitivity of stroke alerts in each center or conclude the "optimal" rate of false alarms. The finding of inter-institutional variability in stroke alerts due to true brain ischemia could be explained by differences in staff education, systematic differences in the patient populations cared for among hospitals, or variation in institutional acceptance of having activated the stroke response team for cases with lower pretest probability of stroke. Sensitivity of alert criteria is more important than specificity, given the consequences of missing a potentially treatable emergent condition.

In conclusion, in this multi-institution analysis of in-hospital stroke alerts, a substantial proportion of in-hospital strokes received thrombolytic therapy. Almost half of stroke alerts will not be for stroke or TIA. For many patients in our study, a change in neurologic status represented a harbinger of a change in general medical condition (hemorrhage, hypotension, hypoglycemia, or respiratory failure). Rapid response systems used for stroke in the hospital need to be trained and prepared to respond to a variety of acute medical conditions that extend beyond ischemic stroke.

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