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A Prospective Pilot Study of Predictors of Acute Stroke in Emergency Department Patients with Dizziness

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Abstract

Objective—To prospectively examine undifferentiated Emergency Department (ED) patients with dizziness in order to identify clinical features associated with acute stroke.

Patients and Methods—We conducted a pilot study from November 1, 2009 to October 30, 2010 of adult patients with dizziness presenting to 3 urban academic ED's. Data collected included demographics, past medical history, presenting complaints, exam findings, clinician pre-test probability of stroke and neuro-imaging results. Logistic regression was used to identify variables with a significant association with acute stroke ($p < 0.05$).

Results—During the study period, we enrolled 473 patients, mean age 56.7±19.3 years, 60% female and 71% Caucasian. We found 30 (6.3%) acute, serious diagnoses (14 ischemic strokes, 2 subarachnoid hemorrhages, 7 mass lesions, 2 demyelinating lesions, 2 severe vertebral artery stenosis, 2 acute coronary syndrome, 1 hydrocephalus/ meningitis). We identified 6 clinical variables associated with stroke; age (OR 1.04; 95%CI 1.0–1.07), hyperlipidemia (3.62; 1.24–10.6) hypertension (4.91; 1.46–16.5), coronary artery disease (3.33; 1.06–10.5), abnormal tandem gait testing (3.13; 1.10–8.89) and high or moderate physician pretest probability for acute stroke (18.8; 4.72–74.5).

Conclusions—The vast majority of ED patients with dizziness do not have a serious cause for their symptoms. Though the small number of outcomes precluded development of a multivariate model, we did identify several individual high risk variables associated with acute ischemic stroke. Further study will be needed to validate the findings of this pilot investigation.

INTRODUCTION

Dizziness is a common Emergency Department (ED) complaint accounting for an estimated 7.5 million visits to ambulatory care settings each year.[1] Most episodes of dizziness are

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caused by benign conditions, but it is estimated that 30% of patients will have a serious cause for their symptoms.[2] Of these, a missed or delayed diagnosis of acute stroke, particularly in the posterior fossa, has the most serious potential consequences and dizziness may be the sole manifestation in as many as 10% of patients with cerebellar infarctions.[3] One systematic review of the accuracy and reliability of symptoms and neurologic findings found that non-orthostatic dizziness was one of the symptoms, along with changes in speech, vision, numbness and weakness, with a high agreement with the diagnosis of stroke.[4]

Recent reviews have concluded that misdiagnosis of cerebellar infarction is common[5] and that even neurologists may have difficulty in identifying cerebrovascular disease in the vertebrobasilar system.[6] One study assessing the impact of neurologists in the ED found that nearly 1 in every 4 stroke patients was given a false diagnosis and 22% of those patients were assigned a tentative diagnosis of vertigo.[7] In another study, patients discharged home from the ED with a diagnosis of vertigo or dizziness had a two-fold higher 3 year stroke or cardiovascular event risk than patients without these diagnoses.[8]

Nonetheless, in a survey of academic ED physicians, approximately half reported that they would not pursue a neurologic diagnosis in the setting of vague dizziness complaints in the absence of neurologic findings.[9] Despite this, there are very few prospective data guiding management decisions and dizziness remains a poorly understood and largely understudied problem.[9] Likely owing to this diagnostic uncertainty, patients with dizziness tend to consume greater health care resources than non-dizzy ED patients, including longer lengths of stay in the ED and higher rates of admission, cardiac monitoring and diagnostic imaging.[10–16]

To our knowledge, no group has prospectively enrolled and obtained follow-up on an undifferentiated population with dizziness symptoms. The primary goal of this pilot study was to study an “all-comer” population of ED patients with dizziness in order to identify high risk clinical variables associated with an acute stroke.

METHODS

Study Design

This is a prospective, multicenter observational pilot study of ED patients with dizziness. Informed consent was obtained from all study subjects and this study was approved by the Institutional Review Boards at the participating institutions.

Study Setting and Population

The study was conducted in the EDs at Beth Israel Deaconess Medical Center (primary), Massachusetts General Hospital and Brigham and Women’s Hospital in Boston Massachusetts from 11/1/09 to 10/30/10. These are Harvard Medical School-affiliated teaching hospitals and home to the 2 Harvard Affiliated Emergency Medicine residency training programs. The EDs have a combined annual patient census of 200,000 patients with 24 hour neurologic consultation and emergency neuro-imaging capabilities.

Study Protocol

Adult ED patients with dizziness identified via ED triage or by the clinical team were screened for study eligibility by trained clinical research assistants at the 3 enrollment sites, on average for 16 hours a day during the week and 8 hours on weekends. Patients were screened continuously via the ED triage dashboards at the participating institution and study eligibility was confirmed with the clinical team.

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Inclusion Criteria—Patients with a primary or secondary complaint of dizziness or a related triage complaint (vertigo, lightheadedness, weakness, syncope/ nearsyncope, gait instability, difficulty walking or imbalance) were screened for study eligibility. Patients were study-eligible only if they had not had any neuro-imaging prior to identification by the research team in order to obtain an unbiased clinician pre-test probability for stroke.

Exclusion Criteria—Patients were excluded from the study if they had a clearly defined cause for dizziness symptoms at ED screening including a new focal motor neurologic finding defining stroke at presentation (hemiparesis/plegia, dysarthria, facial droop), acute ST segment elevation myocardial infarction, active hemorrhage, hypotension or orthostasis, diarrheal illness with clinical dehydration, hypoglycemia (finger stick blood glucose less than 60 mg/dL) or were acutely intoxicated.

Measures

Data collection points were determined prior to study initiation and included all clinical variables associated with index hospitalization including patient demographics, past medical history, presenting complaints, associated symptoms and character of dizziness symptoms (Tables 1 and 2). Data were collected by trained research assistants on a standardized data collection instrument following direct patient interview, discussion with the treating clinicians and review of concomitant ED documentation. Physical exam findings including nystagmus, dysmetria, gait testing, ataxia, and oculomotor test results were recorded directly by the examining clinician. In addition, treating clinicians reported their own assessments of pretest probability for acute stroke as low, moderate or high prior to any neuro-imaging. Follow up was performed at 14 days via telephone or electronic medical record query if unreachable by telephone. Follow up data collection included questions about symptom resolution or progression, further evaluation, testing or hospitalization for dizziness and any new diagnoses. Data were recorded on a separate form.

Outcomes—The primary outcome was an acute stroke identified by either CT or MRI of the brain. All neuro-imaging findings were confirmed as new and causative lesions by Neurology documentation.

Data Analysis

All data were entered into a StudyMaker database (StudyMaker LLC, Version 2.11, copyright 2009) and imported into SAS 9.2 Software for data analysis. (SAS Institute Inc., copyright 2008, Cary, NC, USA). Logistic regression was used to assess the relationship between the primary outcome, acute stroke, and the presence or absence of individual clinical variables. P values are reported for each variable (Chi square for age, Fisher's exact for all others) in Table 1 and Table 2. Odds ratios and 95% confidence intervals (95% CI) are reported for each variable with a significant association with the primary outcome. (Table 3)

RESULTS

We enrolled 473 patients. Table 1 shows the demographics of the population. Average age was 56.7±19.3; 60% were female, 71% Caucasian and 16% African American and 6% Hispanic. We found 30 (6.3%) acute, serious diagnoses in our undifferentiated ED population with dizziness. Overall, there were 14 (3%) patients with an acute ischemic stroke. Patients with stroke were aged 68.5 ±17 years. Table 2 shows the distribution of clinical variables among patients with and without stroke. In addition to the 14 stroke diagnoses, there were 2 subarachnoid hemorrhages, 7 new mass lesions, 2 new

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demyelinating lesions, 2 cases of severe vertebral artery stenosis, 2 cases of acute coronary syndrome and 1 case hydrocephalus/ meningitis in our dizzy population.

We identified several variables associated with the primary outcome: age (OR 1.04; 95%CI 1.0–1.07), hyperlipidemia (3.62; 1.24–10.6), hypertension (4.91; 1.46–16.5), coronary artery disease (3.33; 1.06–10.5) and abnormal tandem gait testing (3.13; 1.10–8.89). Emergency physician pretest probability when assessed as high (n= 8) or medium (n= 4) as compared to low (n= 2) also reliably predicted stroke (18.8; 4.72–74.5). (Table 3)

There were no presenting complaints that were significantly associated with the primary outcome, though 12 of our 14 stroke patients complained of feeling off balance or unsteady with walking (OR 3.7; 0.93–14.5). However, neither ataxia nor a positive Romberg test predicted acute stroke in our sample: there were 3 patients with an acute stroke who had documented ataxia while 8 did not have ataxia and 3 were not tested compared to 70 non-stroke patients with ataxia of 344 tested (104 not tested) (OR 1.06; 0.58–1.9). Similarly, there were 3 patients of 9 tested in the stroke group who had a positive Romberg test while 28 non-stroke patients of 247 tested had a positive Romberg (OR 0.97; 0.57–1.7). Ninety-three percent of our patients were tested for nystagmus and a total of 93 patients had positive findings (71 horizontal, 12 vertical and 10 direction-changing), and 5 of those were stroke patients (3 horizontal, 2 direction-changing). Eight of our patients with stroke had no nystagmus noted on exam and 1 was not reported (p=0.17).

There were 149 patients who had Dix Hallpike testing performed including 3 stroke patients, all of whom had a negative test and 65 non-stroke patients with a positive Dix Hallpike test (OR 0.18; 0.01–3.6). Similarly, 64 patients had head thrust testing, 3 were stroke patients, all with a negative head thrust exam while 12 non-stroke patients had a positive head thrust test (OR 0.57; 0.02–13.1).

In total, 217 (45.9%) patients with dizziness were admitted to the hospital. 375 (79.3%) patients had an EKG performed; of these, 4 (1%) had acute findings (2 new atrial fibrillation, 1 bradycardia, 1 new right bundle branch block). A total of 341 (72.1%) patients had cardiac enzymes tested and only 1 had an initial elevation diagnostic of acute coronary syndrome. There were 158 specialty consultations obtained on ED dizzy patients including 122 neurology and 16 cardiology consults. There were 13 minor discrepancies noted between the ED physician and the neurology consult and 2 of these occurred in patients with acute stroke. Both discrepancies involved nystagmus; in one case, the ED physician reported nystagmus that was not observed by the neurology consult and in the second case, the converse was true.

We obtained complete follow-up on 94% of our patients. There were 208 (44%) patients who reported a follow up appointment within the 2 weeks after the index ED visit. Approximately 25% of those (10% overall) neurology visits. Of the 13 patients who returned to an ED following the initial visit, one was hospitalized but did not have a new diagnosis related to dizziness. There were 57 (12%) patients who had subsequent imaging. There were no new stroke diagnoses identified in the follow up period.

DISCUSSION

In this pilot investigation, we prospectively enrolled and studied a representative and undifferentiated population of patients with dizziness at risk for stroke. As a result, we were able to collect data that most reliably mimics the real world ED setting in which decisions about care and further testing are made. We were also able to capture data on the nature of dizziness symptoms and related complaints which have been lacking in prior studies that have relied on large databases and longitudinal outcomes. We had a much lower rate of

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stroke (3%) and overall serious diagnoses (6.3%) than reported in past dizziness studies. However, these numbers do not reflect the overall incidence of posterior circulation stroke at our institutions as we excluded patients with new focal motor findings or with any neuro-imaging prior to study enrollment in order to collect reliable data on physician pretest probability for stroke in this population.

In our study, patients with stroke were significantly older than those without stroke and we found a 4 percent increase in stroke risk with each additional year of age. Kerber et al found similar results in their population based study which limited its analysis to patients with dizziness over age 44,[17] whereas Putaala et al found a similar predictive profile for recurrent stroke among patients who had a first time stroke at age < 50 years.[18] Although increasing age is clearly a risk factor for stroke, it may paradoxically lead to misdiagnosis. In one small series of misdiagnosed cerebellar strokes, half of the patients were aged < 50 years.[19] Posterior fossa strokes were also more common in the younger patients in a much larger series of strokes presenting in patients < 50 years old.[20] Not surprisingly, we found that cardiovascular risk factors were associated with stroke in our population of patients with dizziness. Lee at al reported similar findings in their population level study of ED patients discharged with a diagnosis of vertigo or dizziness.[8]

In this study, we recorded real-time physical exam findings and physician pretest probability for stroke, prior to any neuro-imaging. Here, we found that a moderate or high physician pretest probability was associated with a stroke outcome as 86% of stroke patients were deemed to have moderate to high risk as compared to only 21% of non-stroke patients. While pretest probability has been established as a predictor in other emergent conditions like pulmonary embolism,[21] we are unaware of any prior ED based investigation establishing the value of clinical suspicion for stroke in a similar patient population. In terms of physical exam findings, we found that abnormal tandem gait testing (found in 8 of our 14 stroke patients) was strongly associated with stroke; 4 patients had an abnormal exam and 4 others were recorded as too symptomatic to perform the exam – one additional patient had testing deferred due to baseline ambulatory dysfunction. Of interest, we had only two stroke patients for whom physician pretest probability was reported as low. The first of these patients was a 30 year old female with no past medical history found to have a vertebral artery dissection while the second was an 85 year old with hypercholesterolemia and hypertension found to have a cerebellar infarct. In both cases, there were no abnormal exam findings reported but neither patient had gait testing (the latter was the patient not tested due to baseline ambulatory dysfunction). While we cannot definitively say that gait testing would have altered pretest suspicion for stroke for these patients, the association of abnormal gait testing with stroke in our population without their inclusion further reinforces the notion that all dizzy patients should have a gait exam.

We did not find any significant differences in presenting complaints or symptom characterization that may reliably be used to distinguish between patients with and without stroke. We examined data on the number of episodes, onset, duration and potential triggers that have historically been used as reassurance of a benign etiology. It is important to note that we did not give our physicians any specific training; rather, physicians recorded historical data according to their normal practice. Because of this, it is certainly possible that we missed associations with various timing and triggers characteristics of the patients' dizziness. Though no presenting complaint was independently associated with acute stroke, we did find a trend toward significant association with a complaint of imbalance (OR 3.7; 0.93–14.5). This has been observed in prior retrospective work from our group and from others.[17,22] In fact, Kerber found nearly 4 times higher rate of stroke with a complaint of imbalance as compared to dizziness and, more recently, in a retrospective chart review of

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ED patients presenting with dizziness, Navi et al found that a chief complaint of imbalance was strongly predictive of a serious neurologic outcome.[23]

In addition, we did not find any association between nystagmus, Dix Hallpike and head thrust testing and stroke outcomes. Several studies have reported that various components of oculomotor testing are diagnostic or strongly suggestive of central versus a peripheral cause of the acute vestibular syndrome (AVS).[24,25] ED physicians routinely use the Dix Hallpike test, but may be less familiar with more detailed vestibulo-ocular testing as is suggested by the small percentage of patients who had head thrust testing in our study.[26] Kattah et al have reported results of a combination of oculomotor testing in patients presenting with the AVS.[27] They found 100% sensitivity if at least one of the three tests was abnormal (HINTS – Head Impulse test, direction-changing Nystagmus, Test of Skew) which performed better than MRI with diffusion weighted imaging in the first 24 hours. However, the tests in this study were performed by trained neuro-ophthalmologists. Among our stroke patients, the only discrepancies reported between neurology and ED examinations involved 2 cases of nystagmus. It is possible that the finding would wax and wane or be present intermittently, but this may underscore the importance of characterizing the quality of the nystagmus, not just its presence or absence.

At present, there are no evidence-based guidelines for ED management of the dizzy patient and a reliable testing strategy distinguishing benign peripheral and central ischemic etiologies has yet to be established. This has resulted in considerable practice variability within and between specialties as well as high resource utilization. In a recent study utilizing the NHAMCS database, Saber Tehrani et al reported that healthcare costs for ED patients with dizziness and vertigo are rising, which they attributed to both increasing numbers of ED visits and increasing utilization of imaging in the pursuit of a possible stroke diagnosis.[12] Further, in an international survey, emergency physicians ranked the identification of central or serious vertigo as number 2 in their 10 top clinical priorities for clinical decision rules.[28] These factors, coupled with the frequent poor outcomes of missed posterior fossa strokes, suggest that there is a strong need for focused research in this area.[19] We do note that one recent report suggested the ABCD2 score might help ED clinicians identify those dizzy patients who had a cerebrovascular cause.[29] Additionally, we believe that validating the use of the HINTS strategy by non-neuro-otologists is needed. There are also goggles on the market that may help to record these tests and objectify the results, which might render them more usable by the average front-line clinician.[30]

As a pilot study, we attempted to be as broadly inclusive as possible to avoid any potential ‘missed diagnoses’. However, we excluded a large segment of patients who were transferred to our sites for neurologic evaluation or had already had neuro-imaging performed. Consequently, our study had a low number of strokes which limited our ability to create a multivariate model. As an observational investigation, we did not mandate a study-specific imaging protocol and did introduce any educational intervention. As a result, not every data point was acquired on every patient and imaging practices may have varied somewhat between the enrollment sites.

CONCLUSIONS

While the limited number of stroke outcomes in our “all-comer” ED cohort precluded development of a decision rule, we did identify several risk factors strongly associated with stroke and other interesting trends on which future study can be focused. We found that traditional stroke risk factors (increasing age, hypertension, hyperlipidemia, coronary artery disease) were also associated with stroke in our population of patients with dizziness. In addition, abnormal tandem gait testing and treating physician assessment of stroke risk as

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moderate or high were also associated with stroke. Further prospective research is needed to validate the findings of this study and to develop a clinical decision tool to definitively identify high-risk patients in need of emergent stroke evaluation.

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ABBREVIATIONS

ED	Emergency Department
CT	computed tomography
MRI	magnetic resonance imaging

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Table 1

Patient Demographics

VARIABLE	Dizzy without Acute Stroke N = 459	Dizzy with Acute Stroke N= 14	P value
Age	56.3 ± 19 yrs	68.5 ± 17	***0.025***
Gender			0.17
Female	277	6	
Male	173	8	
Social History			
Illicit drug use	10	0	1.0
Tobacco use	83	1	0.48
Current pregnancy	10	0	1.0
Past Medical History			
None	106	1	0.21
Diabetes	57	2	0.69
Hypertension	184	11	***0.005***
Hyperlipidemia	148	9	***0.02***
Coronary artery disease	52	4	0.07
TIA or stroke	35	2	0.30
Arrhythmia	47	2	0.65
Atrial fibrillation	23	1	0.52
Malignancy	63	3	0.43
Multiple sclerosis	3	0	1.0
Vertigo	56	0	0.39

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Table 2

Clinical Characteristics of Patients with and without Stroke

VARIABLE	Dizzy without Acute Stroke N = 459	Dizzy with Acute Stroke N= 14	P value
Symptoms			
Upper respiratory infection	37	2	0.32
Ear pain	50	2	0.66
Tinnitus	42	1	1.0
Fever	9	0	1.0
Headache	160	5	1.0
Palpitations	26	1	0.54
Chest Pain	32	0	0.61
Presenting Complaint (s)			
Dizziness	376	11	0.73
Vertigo	168	7	0.40
Lightheaded	245	8	1.0
Imbalance	230	10	0.17
Syncope	154	4	0.78
Gait Instability	191	8	0.28
Fall	62	2	1.0
TIA or stroke	4	0	1.0
Visual Disturbance	93	4	0.50
Weakness (focal)	28	2	0.22
Weakness (generalized)	104	1	0.32
Nausea	205	6	1.0
Neck Pain	41	2	0.37
History of Present Illness			
Onset: sudden	288	9	1.0
Onset: gradual	92	2	1.0
Trigger: head movement	58	2	0.69
Trigger: general movement	78	2	1.0
Worsened by: head movement	74	1	0.71
Worsened by: general movement	105	3	1.0
Single episode	257	11	0.11
Multiple episodes	164	3	0.27
Physical Exam Findings			
Nystagmus (426 tested)	88	5	0.17
Dysmetria (383 tested)	15	1	0.43
Tandem gait: (266 tested)	186	9	***0.001***
Tested and abnormal	62	4	0.12

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VARIABLE	Dizzy without Acute Stroke N = 459	Dizzy with Acute Stroke N= 14	P value
Too symptomatic to test	73	4	0.26
Tandem gait abnormal or too symptomatic to test	135	8	**0.04**
Ataxia (355 tested)	70	3	0.80
Romberg (256 tested)	28	3	0.11
Dix Hallpike: positive (149 tested)	65	0	0.26
Head thrust: positive (64 tested)	12	0	1.0
Pretest probability for acute stroke: moderate-high (448 non-stroke (97.6%), 14 stroke (100%) tested)	94	12	***<0.001***

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Table 3

Variables Associated with Acute Stroke

VARIABLE	ODDS RATIO	95% CONFIDENCE INTERVAL
Age	1.04	1.00–1.07
Coronary artery disease	3.33	1.06–10.5
Hyperlipidemia	3.62	1.24–10.6
Hypertension	4.91	1.46–16.5
Tandem Gait (abnormal and too symptomatic only)	3.13	1.10–8.89
MD pretest probability	18.8	4.72–74.5