Original Article

Incidence and Predicting Factors of Cerebellar Stroke in Patients with Acute Vestibular Syndrome in Songklanagarind Emergency Department: A Preliminary Study

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Objective: To determine the incidence of stroke among patients with acute vestiular syndrome [AVS] and find factors that can predict stroke.

Materials and Methods: A prospective, observational study was conducted between March 1 and November 30, 2016. Patients with AVS underwent constructive history taking and physical examination. Final diagnoses were made by imaging or clinical follow-up with specialists.

Results: The present study enrolled 394 patients (73% age ≥50; 68% female). The incidence of stroke was 3% (12/394). The predicting factors for cerebellar stroke were identified as male gender (OR 6.79, 95% CI 1.81 to 25.55), systolic blood pressure (OR 1.03, 95% CI 1.01 to 1.06), diastolic blood pressure (OR 1.06, 95% CI 1.01 to 1.1), medical history of stroke/transient ischemic attack (OR 6.37, 95% CI 1.59 to 25.46), duration of symptoms greater than 24 hours (OR 6.66, 95% CI 2.91 to 22.04), symptoms of imbalance (OR 5.96, 95% CI 1.76 to 20.23), disproportionate symptoms (OR 11.32, 95% CI 3.45 to 37.21), GCS of less than 15 at presentation (OR 76.2, 95% CI 6.37 to 911.03), deficit CN examination (OR 76, 95% CI 6.36 to 908.64), positive tandem gait (OR 25.13, 95% CI 6.97 to 90.62), positive truncal ataxia (OR 33.27, 95% CI 9.24 to 119.75), and positive finger-to-nose test (OR 63, 95% CI 9.35 to 424.34).

Conclusion: Only 3% of AVS in the emergency department [ED] was due to cerebellar stroke. The small number of outcomes precluded a multivariate analysis, but several clinical factors were identified.

Keywords: Acute vestibular syndrome, Cerebellar stroke, Posterior circulation stroke, Emergency department

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Acute vestibular syndrome [AVS] presents with symptoms of vertigo, dizziness, unsteady gait, and feeling of imbalance that usually occurs abruptly and within 24 hours[1]. Approximately 2.6 to 4 million patients presented annually with vertigo and dizziness in ambulatory care settings in the United States, and marked one of the most common principal complaints in the emergency department [ED][2]. A survey in Siriraj Hospital, Bangkok, showed 1,566 annual visits of AVS in the ED[3]. According to Songklanagarind Hospital medical records in the audit year of 2013 to 2014, there were approximately 1,400 visits with the chief complaint of AVS in the ED.

The most common causes of AVS are benign and usually from vestibular systems, such as vestibular neuritis, labyrinthitis, and benign paroxysmal positional vertigo. These are self-limited and required only supportive treatment. It is estimated that 6% of these patients present with a life-threatening condition, which is cerebellar stroke[4]. Of these, a missed or delayed diagnosis has a mortality rate as high as 40%[5], but less than half of the patients diagnosed with stroke will show abnormal cerebellar signs. AVS may be the sole manifestation in as many as 10% of patients with posterior circulation stroke[6]. The sensitivity of computed tomography [CT] in hemorrhagic cerebellar stroke is as high as 93%[7] but only 16% in ischemic stroke[8]. Magnetic resonance imaging [MRI] is the investigation of choice to detect posterior circulation stroke but the use of MRI in the ED is rare[9].

The objective of the present study was to determine the incidence of cerebellar stroke and better characterize the clinical presentation, evaluation, diagnosis, and disposition of patients presenting with AVS in Songklanagarind Hospital. We also sought to identify the predicting factors to diagnose stroke among these patients.

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Materials and Methods

Study design and setting

We conducted a prospective, observational pilot study of consecutive patients presenting with vertigo, dizziness, or imbalance at Songklanagarind Hospital, Hat Yai, Thailand, which is a tertiary care university hospital. The ED annually receives 45,000 patients and is run 24 hours a day by interns, residents, and attending emergency physicians. The ED has 24-hour neurologic consultation and emergency CT brain capabilities.

Study population

All patients who were 18 years old or older with a chief complaint of vertigo, imbalance, spinning, or disequilibrium and visited the ED between March 1 and November 30, 2016 were included in the study. Patient triage complaints were documented by ED nurses. History taking and physical examinations were performed by interns and emergency medicine residents. Consent forms were obtained from all study subjects, and the present study was approved by the Institutional Ethics Committee.

Data collection and processing

The variables were determined prior to the study and based on a systematic review by Tarnutzer et al[10]. The collected data included patient demographics, medical history, presenting complaints, associated symptoms, and cardiovascular risk factors (Table 1). The physical examination findings focused on the vital signs and neurological examinations, such as Glasgow coma scale [GCS] score, cranial nerves [CNs], motor power, sensory, and reflex. Bedside cerebellar signs such as tandem gait, truncal ataxia, finger-to-nose test, heel-to-knee-to-shin test, rapid alternating movements, head impulse test, nystagmus, and the skew deviation test were performed. CT was requested in each subject that favored a diagnosis of stroke. If the presentation was still questionable, a further MRI would be scheduled. The final diagnosis was made by specialists who were either neurologists or otolaryngologists in both inpatient and outpatient settings.

Outcome measurement

The primary outcome was the incidence of stroke among patients with AVS. The secondary outcome was the predicting factors from presentation and neurological examination that favored stroke.

Data analysis

All data were entered into Epidata software version 3.1 and the statistical analysis was performed using R software version 3.3.0 (R foundation for Statistical Computing, Vienna, Austria). Patient demographic data were presented as mean with standard deviation [SD] or as median, interquartile range [IQR], and percentage. Comparisons between stroke and non-stroke patients used the Student t-test or Wilcoxon rank-sum test depending on the results of the Shapiro-Wilk test. Categorical data were compared by Chi-square test or Fisher's exact test. Univariate logistic regression was used to assess the relationship between the primary outcome and the presence or absence of individual clinical variables. The odds ratio [OR] and 95% confidence interval [CI] were calculated for each significant variable. A *p*-value smaller than 0.05 was considered statistically significant.

Results

There were 425 subjects enrolled into the study. We included 394 patients who had complete data. Table 1 shows the demographics of the population. Most patients were older than 50 years old (73.4%) and 68% were females. Twelve (3%) patients had acute stroke among 394 patients with AVS, 8 out of

Table 1. Patient demographics

Variable	Non-stroke (n = 382)	Stroke (n = 12)	*p*-value
Age			0.195
<50 years	104 (27.2)	1 (8.3)	
≥50 years	278 (72.8)	11 (91.7)	
Gender			0.002
Female	265 (69.4)	3 (25.0)	
Male	117 (30.6)	9 (75.0)	
Blood pressure, median (IQR)			0.419
SBP	142 (128.8, 158)	166 (147.8, 178.8)	0.020
DBP	85 (76, 93)	92.5 (85.5, 107)	0.025
Smoking	6 (1.6)	0 (0.0)	1.000
Diabetes	53 (13.9)	3 (25.0)	0.390
Hypertension	127 (33.2)	6 (50.0)	0.231
Dyslipidemia	108 (28.3)	5 (41.7)	0.337
Arrhythmia	12 (3.1)	2 (16.7)	0.063
Medical history			
Preeclamsia/Eclampsia	1 (0.3)	0 (0.0)	1.000
Head trauma	10 (2.6)	0 (0.0)	1.000
Stroke/TIA	19 (5.0)	3 (25.0)	0.024
MI	13 (3.4)	0 (0.0)	1.000
Anticoagulant use	11 (2.9)	2 (16.7)	0.055

SBP = systolic blood pressure; DBP = diastolic blood pressure; IQR = interquartile range; TIA = transient ischemic attack; MI = myocardial infarction

Data are presented as n (%) unless indicated otherwise

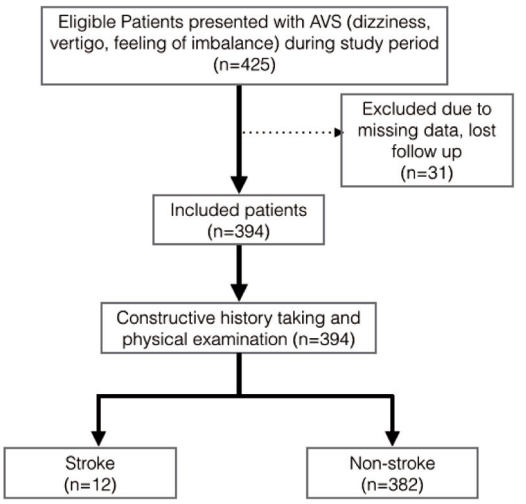

Figure 1. Flowchart of study participants.

the 12 were diagnosed by emergency CT at the ED. The other four were diagnosed with MRI as outpatient department [OPD] cases. Most of the patients with stroke were over 50 years old (91.7%) and were males (75%). The median (IQR) for systolic blood pressure [SBP] was 166 mmHg (147.8, 178.8) and the median (IQR) for diastolic blood pressure [DBP] was 88.8 mmHg (76, 107), which showed significance in stroke patients. Underlying disease was not associated with stroke. The only variable in the medical history that showed significance in stroke was a history of stroke/transient ischemic attack [TIA] (25%, p = 0.024). Table 2 shows the characteristics of the clinical variables among patients with and without stroke. The onset of symptoms and episode (single vs. multiple) showed insignificance between the non-stroke and stroke patients (p = 0.71). Duration of symptoms longer than 24 hours was significant in stroke patients (41.7%, p = 0.005). The associated symptoms with stroke were weakness and nausea/vomiting. There were two significant symptoms, imbalance (66.7%, p = 0.004), and the disproportionate symptoms between imbalance and nausea or vomiting. Stroke patients stated that gait or postural imbalance was more prominent than nausea or vomiting (50%, p<0.001).

Several physical examinations that included GCS of less than 15 (83.3%, p = 0.003) and deficit CN examination (83.3%, p = 0.04) determined stroke in AVS (Table 2). Two subjects who had deficit CN examination (CN IV and dysarthria) showed 100% of stroke. The important cerebellar examinations associated with stroke were positive tandem gait (54%, p<0.001), positive truncal ataxia (50%, p<0.001),

Table 2. Clinical characteristics of patients with and without stroke

Variable	Non-stroke (n = 382)	Stroke (n = 12)	*p*-value
Presenting complaint			
Onset			0.710
• Gradual	74 (19.4)	3 (25.0)	
• Abrupt	308 (80.6)	9 (75.0)	
Episode			0.834
• Single	163 (42.7)	6 (50.0)	
• Multiple	219 (57.3)	6 (50.0)	
Duration			0.005
• >24 hours	37 (9.7)	5 (41.7)	
• ≤24 hours	345 (90.3)	7 (58.3)	
Symptoms			
Neck pain	9 (2.4)	0 (0.0)	1.000
Diplopia	18 (4.7)	0 (0.0)	1.000
Dysphagia	2 (0.5)	0 (0.0)	1.000
Hoarseness	3 (0.8)	0 (0.0)	1.000
Weakness	2 (0.5)	1 (8.3)	0.089
Imbalance	96 (25.1)	8 (66.7)	0.004
Nausea/vomiting	238 (62.1)	5 (41.7)	0.226
Disproportionate symptoms	31 (8.1)	6 (50.0)	<0.001
Hearing loss	11 (2.9)	0 (0.0)	1.000
Physical examination			
GCS			0.003
• 15	381 (99.7)	10 (83.3)	
• <15	1 (0.3)	2 (16.7)	
CN			0.003
• Intact	381 (99.7)	10 (83.3)	
• Deficit	1 (0.3)	2 (16.7)	
Motor power			0.170
• Grade V all	377 (98.7)	11 (91.7)	
• Deficit	5 (1.3)	1 (8.3)	
Cerebellar examination			
Tandem gait			<0.001
• +ve	17 (4.6)	6 (54.5)	
• -ve	356 (95.4)	5 (45.5)	
Truncal ataxia			<0.001
• +ve	11 (2.9)	6 (50.0)	
• -ve	366 (97.1)	6 (50.0)	
Finger-to-nose			<0.001
• +ve	2 (0.5)	3 (25.0)	
• -ve	378 (99.5)	9 (75.0)	
Heal-to-knee-to-shin			-
• +ve	0 (0.0)	0 (0.0)	
• -ve	379 (100)	10 (100)	
Rapid alternating movement			1.000
• +ve	1 (0.3)	0 (0.0)	
• -ve	377 (99.7)	8 (100)	
HINTS			
Head impulse test			1.000
• +ve	10 (12.7)	1 (14.3)	
• -ve	69 (87.3)	6 (85.7)	
Nystagmus			1.000
• +ve	58 (24.3)	2 (20.0)	
• -ve	181 (75.5)	8 (80.0)	
Skew deviation test			1.000
• +ve	1 (1.4)	0 (0.0)	
• -ve	72 (98.6)	8 (100)	

GCS = Glasgow coma scale; CN = cranial nerve; HINTS = head impulse-nystagmus-test of skew

Data are presented as n (%)

and positive finger-to-nose test (25%, $p<0.001$). Two patients had missing data in the heal-to-knee-to-shin test and four patients had missing data in the rapid alternating test. Motor power deficit and the head impulse-nystagmus-test of skew [HINTS] examination were insignificant predictors in the present study (Table 2).

The predicting variables associated with the primary outcome that underwent univariate analysis were male gender (OR 6.79, 95% CI 1.81 to 25.55), SBP (OR 1.03, 95% CI 1.01 to 1.06), DBP (OR 1.06, 95% CI 1.01 to 1.1), medical history of stroke/TIA (OR 6.37, 95% CI 1.59 to 25.46), duration of symptoms longer than 24 hours (OR 6.66, 95% CI 2.91 to 22.04), symptoms of imbalance (OR 5.96, 95% CI 1.76 to 20.23), disproportionate symptoms (OR 11.32, 95% CI 3.45 to 37.21), GCS smaller than 15 at presentation (OR 76.2, 95% CI 6.37 to 911.03), deficit CN examination (OR 76, 95% CI 6.36 to 908.64), positive tandem gait (OR 25.13, 95% CI 6.97 to 90.62), positive truncal ataxia (OR 33.27, 95% CI 9.24 to 119.75), and positive finger-to-nose test (OR 63, 95% CI 9.35 to 424.34) (Table 3).

Table 3. Variables associated with cerebellar stroke

Variable	OR (95% CI)	*p*-value
Gender		0.002
Female	1 [Reference]	
Male	6.79 (1.81 to 25.55)	
Blood pressure*		
SBP	1.03 (1.01 to 1.06)	0.01
DBP	1.06 (1.01 to 1.10)	0.015
Medical history		0.024
Never had stroke	1 [Reference]	
Prior stroke	6.37 (1.59 to 25.46)	
Associated symptoms		
Duration		0.005
• ≤24 hours	1 [Reference]	
• >24 hours	6.66 (2.91 to 22.04)	
Imbalance		0.003
• No	1 [Reference]	
• Yes	5.96 (1.76 to 20.23)	
Disproportionate symptoms		<0.001
• No	1 [Reference]	
• Yes	11.32 (3.45 to 37.21)	
Physical examination		
GSC		0.001
• 15	1 [Reference]	
• <15	76.20 (6.37 to 911.03)	
Deficit CN examination		0.001
• No	1 [Reference]	
• Yes	76.00 (6.36 to 908.64)	
Cerebellar examination		
Tandem gait		<0.001
• Negative	1 [Reference]	
• Positive	25.13 (6.97 to 90.62)	
Truncal ataxia		<0.001
• Negative	1 [Reference]	
• Positive	33.27 (9.24 to 119.75)	
Finger-to-nose test		<0.001
• Negative	1 [Reference]	
• Positive	63.00 (9.35 to 424.34)	

CI = confidence interval; SBP = systolic blood pressure; DBP = diastolic blood pressure; GCS = Glasgow coma scale; CN = cranial nerve

* Control variable

Discussion

In this preliminary investigation, the authors prospectively enrolled and studied an undifferentiated population of patients with AVS. As a result, we were able to collect data that mimicked other ED settings in which the decisions on care and further testing were made and we were also able to collect data on the nature of AVS and related complaints. The present study showed a 3% rate of stroke, which was similar to several prior studies[2,4,11]. This rate reflected the overall incidence of cerebellar stroke at our institution in a period of nine months.

The variables were set up from a systematic review by Tarnutzer et al[10] that presented a tool for collecting data (supplement 1). The data were collected by interns and emergency medicine residents from the first to third year of residency. The physical and neurological examination skills for residents were standardized by neurologists in the hospital, except the skills of rotating interns. We found that stroke patients were significantly older than those without stroke at age older than 50 years old, which was similar to the Norrving et al study[12]. Although increasing age is clearly a risk factor for stroke, it may paradoxically lead to a misdiagnosis. In one small series of misdiagnosed cerebellar stroke, half of the patients were less than 50 years of age[5]. Posterior circulation strokes were also more common in the younger patients in a much larger series of strokes presenting in patients younger than 50 years old[13]. We found that cerebellar stroke was predominant in males, which was similar to the study by Kerber et al[2], even though the majority of the included patients were female. Surprisingly, the only cerebrovascular risk factors associated with stroke in our population was a history of prior stroke or TIA, which was similar to the report by Kattah et al[1] that predicted patients with one or more vascular risk factors (smoking, hypertension, diabetes, dyslipidemia, atrial fibrillation, eclampsia, hypercoagulable state, cervical trauma,

prior stroke, and myocardial infarction) appeared to be at increased risk of stroke. Higher blood pressure was also associated with stroke diagnosis. The rates of strokes were 30% to 59% in patients with risk factors versus 10% to 20% in those without risk factors[1].

The present study showed some significant differences in presenting complaints or symptom characteristics that may be used reliably to distinguish between patients with and without stroke. Duration of symptoms for longer than 24 hours suggested that stroke was contrary to the systematic review[10]. A duration of less than 24 hours already suggests a benign cause of vertigo such as benign paroxysmal positional vertigo or Meniere's disease. A duration longer than 24 hours supports stroke diagnosis but in literature search, a benign cause cannot be distinguished from stroke and basilar migraine[14,15]. In the present study, one patient presented with prolonged vertigo of more than 24 hours and was diagnosed as basilar migraine by neurologists. Patients with persistent symptoms also tended to have an imaging diagnosis at the ED. Symptoms of gait or postural imbalance together with dizziness and vertigo presented as abnormalities in the cerebellar system[16,17], which can predict stroke in our population along with the disproportionate symptoms (excessive gait or postural imbalance compared to nausea vomiting symptoms) similar to the study by Kase et al (n = 30 in 66 patients with cerebellar stroke)[18]. In contrast, an abrupt onset of dizziness predicted stroke[10,19]; however, it was insignificant in our study.

The results of the physical examinations were surprising in our study. A GCS of less than 15 and abnormal CN examination favored a diagnosis of stroke but according to a literature search, these two examinations did not show any significance. One patient diagnosed with cerebellar stroke at the ED presented with GCS of 14 and dysarthria. Another patient presented with deficit CN VI and another patient had GCS of 13. Unsurprisingly, the most important and reliable cerebellar examinations were abnormal tandem gait, truncal ataxia, and positive finger-to-nose test (p<0.001 all) These findings were similar to one recent study by Chase et al[20]. We can conclude that the use of gait testing could be included to distinguish between stroke and non-stroke patients in the setting of AVS in our ED. Interestingly, we did not find any association between the HINTS examination and stroke outcome. Several studies reported that various components of oculomotor testing were diagnostic and strongly suggestive of a central versus peripheral cause of AVS[1,10,21,22]. Kattah et al[1] reported results of a combination of oculomotor testing in patients presented with AVS. They found 100% sensitivity if at least one of the three tests was abnormal, which performed better than an MRI with diffusion weighted imaging in the first 24 hours. However, the tests in that study were performed by trained neuro-ophthalmologists[1]. In our study, the HINTS examination was standardized by neurologists but performed by interns and residents.

At present, there are no evidence-based guidelines for ED management of dizzy, vertigo patients and a reliable testing strategy to distinguish between benign peripheral and ischemic central etiologies. This has resulted in variable practice procedures and high resource utilization in the EDs worldwide. In a recent study, Saber Tehrani et al reported that healthcare costs for ED patients with dizziness and vertigo are rising, which they attributed to both an increasing number of ED visits and increasing utilization of imaging in the pursuit of a possible stroke diagnosis[23]. Further, in an international survey, emergency physicians ranked the identification of central or serious vertigo as number 2 in their top 10 clinical priorities for clinical decision rules[24]. These factors, coupled with frequently poor outcomes of missed posterior circulation strokes, suggest a strong need for focused research in this area. Additionally, we believe that validating the use of the HINTS strategy by non-neuro-otologists is needed. However, the supportive data of the HINTS examination in the Asian population is still unknown.

Limitations

As a preliminary study, we attempted to be as broadly inclusive as possible to avoid any potential 'missed diagnoses'. However, the number of patients was limited due to selective cases for inconclusive diagnosis in the ED as to either stroke or non-stroke. 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 educational intervention was not introduced to all examiners. As a result, the acquired data points in every patient may have varied somewhat.

Conclusion

The incidence of cerebellar stroke in patients who presented with AVS at the ED of Songklanagarind Hospital was found to be 3%. In our limited number of stroke outcomes, we identified several predicting factors that were strongly associated with stroke and other interesting trends, which can be the focus

of a future study. We found that male gender, high blood pressure, history of prior stroke/TIA, duration of symptoms longer than 24 hours, presenting of imbalance and disproportionate symptoms were the predicting factors. In addition, a GCS lower than 15, deficit CN examination, abnormal tandem gait, truncal ataxia, and finger-to-nose test were suggestive findings for stroke. Further prospective research is needed to validate the findings of the present study and to develop a clinical decision tool to definitively identify high-risk patients in need of emergent stroke evaluation.

What is already known on this topic?

The major causes of AVS are peripheral but central causes such as ischemic stroke or cerebellar hemorrhage can be fatal without close monitoring and prompt specialist consultation. Thus, patients whose AVS is mistakenly thought to be caused by peripheral etiology may appear to be clinically stable at the time of discharge from the ED, yet they may be at risk of complications days later.

What this study adds?

The authors report the incidence of cerebellar stroke in Thailand and state the predicting factors that help distinguish stroke through bedside history taking and physical examination. The HINTS examination was not favorable in this study even though it is well-known to determine stroke.

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Potential conflicts of interest

The authors declare no conflict of interest.

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