Received: 30 March 2023 | Accepted: 4 September 2023

DOI: 10.1111/ene.16066

european journal of neurology
the official journal of the european academy of neurology

ORIGINAL ARTICLE

Do monosymptomatic stroke patients with dizziness present a vestibular syndrome without nystagmus? An underestimated entity

Florence Nikles[1] | Hassen Kerkeni[2] | Ewa Zamaro[1] | Athanasia Korda[1] | Franca Wagner[3] | Thomas C. Sauter[4] | Roger Kalla[2] | Miranda Morrison[1] | Georgios Mantokoudis[1]

[1]Department of Otorhinolaryngology, Head and Neck Surgery, Inselspital, University Hospital Bern and University of Bern, Bern, Switzerland

[2]Department of Neurology, Inselspital, University Hospital Bern and University of Bern, Bern, Switzerland

[3]University Institute of Diagnostic and Interventional Neuroradiology, Inselspital, University Hospital Bern and University of Bern, Bern, Switzerland

[4]Department of Emergency Medicine, Inselspital, University Hospital Bern and University of Bern, Bern, Switzerland

Correspondence
Georgios Mantokoudis, University Department of Otorhinolaryngology, Head and Neck Surgery, Inselspital Bern and University Hospital Bern, University of Bern, 3010 Bern, Switzerland.
Email: georgios.mantokoudis@insel.ch

Website: http://hno.insel.ch

Funding information
Schweizerischer Nationalfonds zur Förderung der Wissenschaftlichen Forschung

Abstract

Background and purpose: Vestibular symptoms are common in emergency department (ED) patients and have various causes, including stroke. Accurate identification of stroke in patients with vestibular symptoms is crucial for timely management. We conducted a prospective cross-sectional study from 2015 to 2019 to determine stroke prevalence and associated symptoms in ED patients with vestibular symptoms, aiming to improve diagnosis and outcomes.

Methods: As part of the DETECT project, we screened 1647 ED patients with acute vestibular symptoms. Following a retrospective analysis of 961 head and neck magnetic resonance imaging (MRI) scans, we included 122 confirmed stroke cases and assessed them for vestibular signs and symptoms.

Results: Stroke prevalence in dizzy patients was 13% (122/961 MRI scans). Most patients (95%) presented with acute vestibular symptoms with or without nystagmus, whereas 5% had episodic vestibular syndrome (EVS). Nystagmus was present in 50% of stroke patients. Eighty percent had a purely posterior circulation stroke, and nystagmus was absent in 46% of these patients. Seven patients (6%) had lesions in both the anterior and posterior circulation. Vertigo was experienced by 52% regardless of territory.

Conclusions: A stroke was identified in 13% of ED patients presenting with acute vestibular symptoms. In 5%, it was EVS. Most strokes were in the posterior circulation territory; vertigo occurred with similar frequency in anterior and posterior circulation stroke, and absence of nystagmus was common in both.

KEYWORDS
anterior circulation, nystagmus, posterior circulation, stroke, vertigo

Florence Nikles and Hassen Kerkeni contributed equally to this work.

INTRODUCTION

Approximately 10%–20% of all patients [1] seen in the emergency department (ED) will present with acute vestibular syndrome (AVS), consisting of continuous dizziness/vertigo, nausea, vomiting, nystagmus, gait disturbance, and motion intolerance. Up to 11% of these patients will have a vestibular stroke defined as an acute onset of vertigo, dizziness, or postural imbalance due to stroke [2]. Diagnosing dizzy patients and in particular diagnosing those patients who are at risk of stroke is a challenge. Fifty percent of patients with AVS do not have any focal neurological signs [3]. Younger patients lacking risk factors or who have nondiagnostic neuroimaging are at risk of being misdiagnosed [4, 5]. The proportion of dizzy stroke patients presenting with episodic (short duration or repeated episodes) vertigo is still unknown. That a large proportion of patients will present to the ED with headache and vestibular symptoms a few days prior their admission for stroke [6] might reflect the number of strokes that were misdiagnosed on first admission.

Although vestibular symptoms (dizziness/vertigo and imbalance) are known to be the most common presenting symptom (47%–75%) in patients with posterior circulation strokes [7, 8], the prevalence of anterior circulation strokes in dizzy patients is less well studied [9]. Many supratentorial cortical areas (anterior and middle cerebral circulation) such as the parietoinsular vestibular cortex (PIVC; including the insular gyrus, inferior parietal lobule, intraparietal sulcus, middle frontal gyrus, middle temporal gyrus, superior temporal gyrus, precentral gyrus, cingulate gyrus, hippocampus, putamen, and thalamus) have been identified as playing an important role in the vestibular system [10]. The proportion of patients with lesions in these areas who develop a typical vestibular syndrome remains unclear [11, 12]. In this cross-sectional study, we sought to investigate the prevalence of stroke in patients with vestibular symptoms visiting the ED. The aim was to identify the symptoms and signs of these patients stratified by anterior versus posterior strokes and by the presence of spontaneous nystagmus (SN).

MATERIALS AND METHODS

Study design and population

We initially conducted a prospective cross-sectional study from February 2015 to October 2019 of all patients presenting with vestibular symptoms at the ED of a tertiary referral care center as part of the larger ongoing DETECT project (Dizziness Evaluation Tool for Emergent Clinical Triage in AVS Patients) [3, 13–15]. In this larger study, 1647 patients with acute onset of vestibular symptoms with or without nystagmus were prospectively screened by trained research staff during office hours and by emergency physicians outside of office hours. Research staff used Frenzel goggles (blocked visual fixation) to screen for nystagmus in all gaze directions. ED physicians assessed dizzy patients with or without Frenzel goggles as part of the standard care. We retrospectively analyzed clinical data (symptoms and signs) from all patients presenting with a new onset of vestibular symptoms in the ED, including patients with non-AVS-related vestibular symptoms, who were screened but not enrolled in the initial DETECT study.

We reassessed all dizzy patients who underwent diagnostic neuroimaging (magnetic resonance imaging [MRI]) for stroke or suspected stroke either on the day of admission to the ED or 3–10 days after enrollment in the initial study. A blinded experienced board-certified senior consultant in neuroradiology reassessed all MRIs. Our final study sample included all dizzy patients with an MRI-confirmed stroke diagnosis. In participants who presented with lesions in multiple vascular territories, each lesion was counted separately. Figure 1 shows the screening and inclusion process. All patients were classified into one of three categories of vestibular syndromes based on predefined criteria [16]: (i) AVS (state of continuous dizziness and additional symptoms and signs such as nausea, vomiting, SN, head motion intolerance, or new gait/balance disturbance); (ii) episodic vestibular syndrome (EVS; short duration of <24 h or repeated episodes of vertigo); and (iii) acute imbalance syndrome (AIS) if patients did not fulfill all the criteria of a vestibular syndrome (e.g., acute vestibular symptoms such as vertigo, dizziness, postural symptoms, vestibulovisual symptoms with no recorded nystagmus). Thus, patients with acute onset of vestibular symptoms and no recorded nystagmus who could therefore not be classified as having AVS were classified as AIS [17].

Stroke prevalence was calculated as the proportion of strokes among all screened patients receiving an MRI.

HINTS acronym stands for Head Impulse Test, Nystagmus and Test of Skew. A “central HINTS” was recorded if either a gaze-evoked or direction-changing nystagmus, and/or a skew deviation and/or an absence of corrective saccades on the head impulse test could be detected. The head impulse test was not taken into consideration if the patient did not have SN. A "peripheral HINTS" was recorded if there was no gaze-evoked direction-changing nystagmus, no skew deviation, and an abnormal head impulse test in patients showing SN.

Magnetic resonance protocol

The patients were scanned in one of our six magnetic resonance (MR) scanners: either on a 1.5-T scanner (Magnetom Avanto and Magnetom Aera, Siemens Medical Solutions) or on a 3-T scanner (Magnetom Verio, Siemens Medical Solutions). Our standard MRI protocol for all patients included axial diffusion-weighted imaging (DWI) with apparent diffusion coefficient (ADC; 5-mm slice thickness [SL]), axial fluid-attenuated inversion recovery (5-mm SL), axial susceptibility-weighted imaging (1.6-mm SL), and three-dimensional time of flight MR angiography (MRA; 0.5-mm SL). Optionally, and depending on the clinical symptoms, axial brainstem DWI with ADC (3-mm SL) and axial T2-weighted imaging over the brainstem (3-mm SL) were added. After administration of intravenous gadobutrol (Gadovist; Bayer Schering Pharma) in an antecubital vein with a 5-mL/s injection rate, we acquired a standard dynamic susceptibility contrast MRI perfusion (5-mm SL) as well as a contrast-enhanced T1 turbo spin echo-weighted sequence (5-mm SL). Finally,

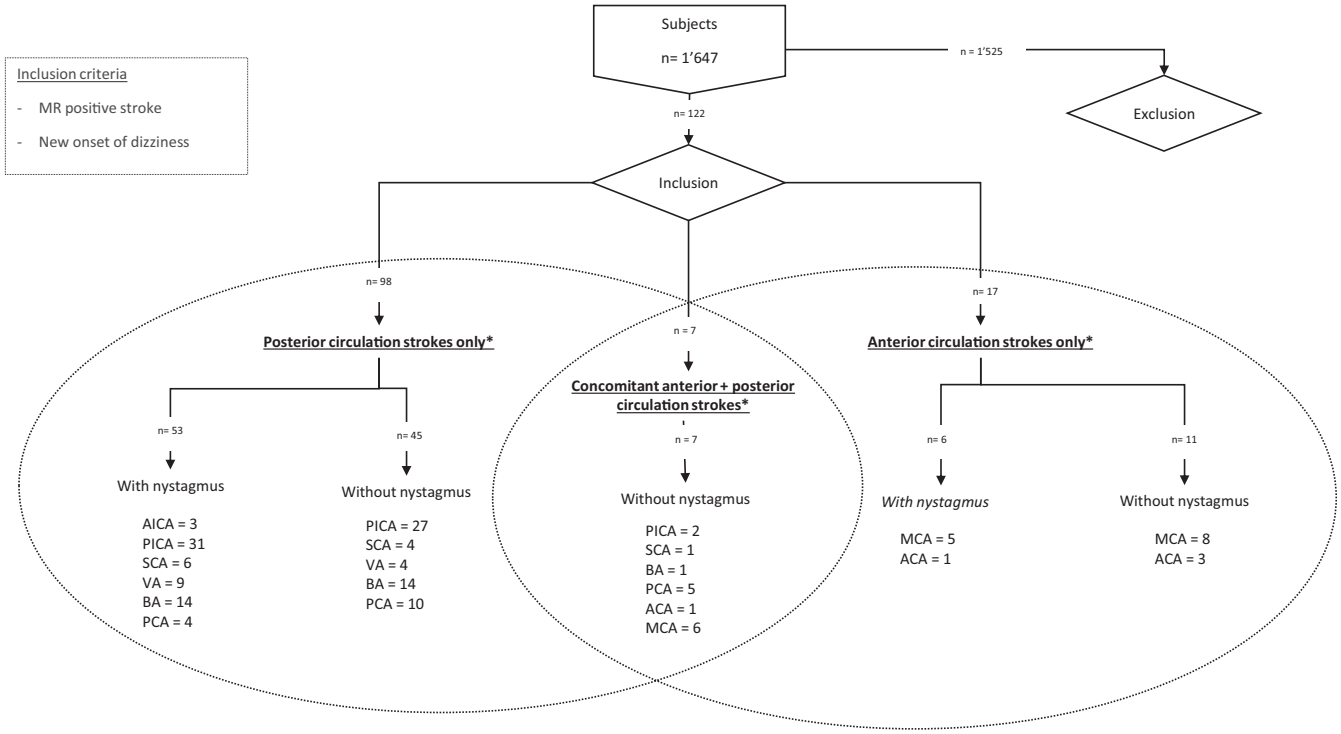

FIGURE 1 Presentation of stroke distribution in regard to the vascular territory, more precisely the clogged artery, as well as presence of nystagmus. *It is important to note that one subject could have multiple concomitant strokes, each individually shown in the listed artery strokes, with "*n*" representing the number of subjects. ACA, anterior cerebral artery; AICA, anterior inferior cerebellar artery; BA, basilar artery; MCA, middle cerebral artery; MR, magnetic resonance; PCA, posterior cerebral artery; PICA, posterior inferior cerebellar artery; SCA, superior cerebellar artery; VA, vertebral artery.

contrast-enhanced MRA of the head and neck vessels was acquired after injection of a second bolus of gadobutrol with a 3-mL/s injection rate. If indicated, the follow-up MRI was performed using the same scanner and field strength with the same MRI protocol or a short native variant of the MR protocol without acquisition of the sequences with contrast.

Statistical analysis

Descriptive statistics were calculated (SPSS Statistics for Windows, version 25.0, IBM) for all variables of interest, and data are presented as counts and percentages. A two-sided exact chi-squared test (Fisher exact test) was performed in Excel and applied to compare the relationship of vestibular symptoms between anterior and posterior circulation strokes. We analyzed patients with lesions solely restricted to either the anterior or the posterior circulation.

Ethics

All enrolled patients gave written consent. This study was approved by the local ethics committee (Kantonale Ethikkommission Bern).

RESULTS

We screened 1647 patients presenting to the ED with vestibular symptoms and included 122 patients aged between 24 and 93 years (mean age = 67.3 years, SD = 15.6) with a confirmed stroke and new onset of vestibular symptoms. The initial examination was conducted predominantly by neurologists ($n = 107$, 88%) or internists ($n = 13$, 11%), whereas two stroke patients were initially examined by an ear, nose, and throat specialist ($n = 2$, 2%). Patients presented between 2 and 769 h after onset of symptoms (mean = 83 h, SD = 126.7) at our tertiary center ED.

Prevalence of stroke and vascular territories

The stroke period prevalence was 13% (122 of 961 patients who received an MRI). A total of 159 acute stroke lesions were identified (some patients presented with multiple concomitant lesions). The vascular territories identified included posterior inferior cerebellar artery ($n = 60$, 38%), basilar artery ($n = 29$, 18%), posterior cerebral artery ($n = 19$, 12%), middle cerebral artery ($n = 19$, 12%), superior cerebellar artery ($n = 11$, 7%), vertebral artery ($n = 13$, 8%), anterior cerebral artery ($n = 4$, 3%), and anterior inferior cerebellar artery ($n = 3$, 2%; Figure 1).

Of all subjects who received an MR scan based on clinical suspicion of stroke, 0.2% ($n=4$) had acute stroke lesions that were initially missed (not documented in the ED reports) and were detected on review of the MR images by our senior consultant in neuroradiology. MR-positive lesions restricted to the posterior circulation were found in 98 patients (80%), whereas lesions restricted to the anterior circulation were found in 17 patients (14%). Simultaneous lesions in the anterior and posterior circulation were found in seven patients (6%).

Regarding the diagnosis of the remaining 1525 patients, the most frequent diagnoses were benign paroxysmal positional vertigo (9.7%), acute unilateral vestibulopathy (9.6%), and transient ischemic attack (5%). The diagnosis remained unknown in 45% of the cases. A recent retrospective analysis of all screened patients showed a total of 26 missed strokes at the follow-up [17].

Type of vestibular syndromes caused by stroke

Most stroke patients presented with acute onset vestibular symptoms (95%) with or without nystagmus, whereas only 5% had EVS. The proportion of patients with EVS was low regardless of the underlying vascular territory (Table 1). Table 1 gives an overview of the distribution of vestibular syndromes stratified by anterior and posterior circulation strokes. Forty-five percent of the stroke patients (55/122) presented with acute vestibular symptoms (more than one symptom possible: postural symptoms $n=28$, 51%; dizziness $n=6$, 11%; vertigo $n=26$, 47%; vestibulovisual symptoms $n=1$, 2%; unspecified $n=12$, 22%) without nystagmus and were classified as AIS. Table 2 shows an overview of reported symptoms stratified by vascular territory. Only 48% of patients had vertigo regardless of whether the posterior or anterior circulation was involved. A small proportion of stroke patients reported dizziness (disorientation in space), which was predominantly seen in those with posterior circulation strokes (15% vs. 6%, $p=0.23$). The most frequent vestibular symptoms were postural (e.g., balance symptoms relative to maintenance of postural stability, which occur only while in the upright position [18]). There was a significant difference in reporting postural symptoms between patients with posterior circulation stroke and those with anterior circulation stroke (64% vs. 41%, $p<0.001$). The most notable contrast was observed in the occurrence of lateropulsion (25% vs. 12%, $p=0.2$).

Accompanying symptoms

Nausea was the most common accompanying symptom, with a slight predominance in the posterior stroke group (38% vs. 29%, $p=0.22$; Table 3). Vomiting was even more often present in the posterior circulation stroke group (39% vs. 6%, $p=.005$; Table 3). Table S4 gives an overview of accompanying symptoms in patients with no SN. Stroke patients without nystagmus ($n=61$, 50%) showed the same symptom distribution, with focal weakness (33%), headache (33%), vomiting (31%), dysphagia/dysarthria 26%, and nausea (26%; Table S4). Two patients presented with no accompanying symptoms or clinical signs other than nausea or vomiting.

Clinical signs

Nystagmus was present in 50% of all stroke patients. The National Institutes of Health Stroke Scale (NIHSS) score was zero in 23% of patients with posterior circulation stroke and in 18% of patients with anterior circulation stroke (Table 4). SN was noted in approximately half the patients in both groups (54% vs. 35%, $p=0.01$), although the nystagmus type and grade were not specifically described in most patients. From what was reported, patients with anterior circulation stroke and nystagmus presented different patterns such as (i) horizontal beating unidirectional nystagmus with a torsional component, (ii) horizontal SN grade 3 with a normal head impulse test, (iii) slight dysdiadochokinesis, (iv) unidirectional SN grade 3 accompanied by severe neurovegetative symptoms and tinnitus as well as ear fullness, (v) unidirectional horizontal SN grade 3 and NIHSS=2 (limb ataxia), and (vi) vertical diplopia before appearance of disbalance. NIHSS scores of >4 were recorded in 25% of patients without SN (Table 5). Cranial nerve pathologies were most frequent (44%) in these patients, followed by dysarthria (23%) and limb ataxia (20%). Facial palsy was the most frequent cranial nerve pathology encountered (26%). A small proportion of patients without nystagmus showed oculomotor pathologies such as ocular palsy (13%) and pathologic smooth pursuit (8%; Table 5). Table 5 shows details about the distribution of clinical signs in patients with and without SN and Table S5 those patients who had a stroke in the anterior or posterior circulation.

The full clinical beside HINTS examination was only performed by research personnel or ED physicians in 33% (Table 4) of cases. Overall, the HINTS results supported a central etiology in 29% of patients (30% in posterior circulation stroke and 24% in anterior

TABLE 1 Distribution of vestibular syndromes.

Vestibular syndromes	Total strokes, $n=122$	Posterior circulation stroke only, $n=98$	Anterior circulation stroke only, $n=17$	Anterior and posterior strokes simultaneously, $n=7$
AVS	61 (50%)	53 (54%)	6 (35%)	2 (29%)
AIS	55 (45%)	42 (43%)	9 (53%)	4 (57%)
EVS	6 (5%)	3 (3%)	2 (12%)	1 (14%)

Abbreviations: AIS, acute imbalance syndrome; AVS, acute vestibular syndrome; EVS, episodic vestibular syndrome.

TABLE 2 Distribution of vestibular symptoms.

Vestibular symptoms	Total, $n=115$[a]	Posterior circulation stroke only, $n=98$[b]			Anterior circulation stroke only, $n=17$[b]			p-Value (χ^2)[c]
		With nystagmus, $n=53$	Without nystagmus, $n=45$	Total, $n=98$	With nystagmus, $n=6$	Without nystagmus, $n=11$	Total, $n=17$	
Postural symptoms	70 (61%)	39 (74%)	24 (53%)	63 (64%)	2 (33%)	5 (45%)	7 (41%)	<0.001
Lateropulsion	26 (23%)	17 (32%)	7 (16%)	24 (25%)	0	2 (18%)	2 (12%)	0.20
Unsteadiness	35 (30%)	18 (34%)	13 (29%)	31 (32%)	2 (33%)	2 (18%)	4 (24%)	0.37
Balance-associated fall	11 (9%)	6 (11%)	3 (7%)	9 (9%)	0	2 (18%)	2 (12%)	0.76
Balance-associated near-fall	5 (4%)	4 (8%)	1 (2%)	5 (5%)	0	0	0	0.34
Vertigo	55 (48%)	23 (44%)	24 (53%)	47 (48%)	4 (67%)	4 (36%)	8 (47%)	0.95
Unspecified	32 (28%)	18 (34%)	8 (18%)	26 (27%)	2 (33%)	4 (46%)	6 (35%)	0.15
Dizziness	16 (14%)	9 (17%)	6 (13%)	15 (15%)	0	1 (9%)	1 (6%)	0.23
Vestibulovisual symptoms	6 (5%)	4 (8%)	1 (2%)	5 (5%)	1 (17%)	0	1 (6%)	0.54

[a]Patients with concomitant anterior and posterior stroke were not included in this table.

[b]Only magnetic resonance-positive strokes.

[c]Comparing anterior and posterior circulation strokes.

TABLE 3 Distribution of accompanying symptoms (patient history).

Accompanying symptoms	Total, $n=115$[a]	Posterior circulation stroke only, $n=98$[b]			Anterior circulation stroke only, $n=17$[b]			p-Value (χ^2)[c]
		With nystagmus, $n=53$	Without nystagmus, $n=45$	Total, $n=98$	With nystagmus, $n=6$	Without nystagmus, $n=11$	Total, $n=17$	
Vomiting	39 (34%)	21 (40%)	17 (38%)	38 (39%)	1 (17%)	0	1 (6%)	0.005
Nausea	42 (37%)	24 (45%)	13 (29%)	37 (38%)	3 (50%)	2 (18%)	5 (29%)	0.22
Headache	33 (29%)	16 (30%)	12 (27%)	28 (29%)	0	5 (45%)	5 (29%)	0.55
Dysphagia, dysarthria	28 (24%)	17 (32%)	8 (18%)	25 (26%)	0	3 (27%)	3 (18%)	0.39
Abnormal vision/acuity	19 (16%)	9 (17%)	10 (22%)	19 (19%)	0	0	0	0.04
Focal weakness	27 (23%)	9 (17%)	10 (22%)	19 (19%)	2 (33%)	6 (54%)	8 (47%)	0.005
Double vision	18 (16%)	11 (21%)	6 (13%)	17 (17%)	1 (17%)	0	1 (6%)	0.19
Impaired sensation	21 (18%)	12 (23%)	5 (11%)	17 (17%)	1 (17%)	3 (27%)	4 (24%)	0.42
Tinnitus	3 (3%)	1 (2%)	1 (2%)	2 (2%)	1 (17%)	0	1 (6%)	NA
Hearing loss	1 (1%)	1 (2%)	0	1 (1%)	0	0	0	NA

Abbreviation: NA, not available.

[a]Patients with concomitant anterior and posterior stroke were not included in this table.

[b]Only magnetic resonance-positive strokes.

[c]Comparing anterior and posterior circulation strokes.

circulation stroke) and a peripheral pathology in 4% of patients (4% in posterior circulation stroke and 6% in anterior circulation stroke). There was only one patient without SN on whom all three tests were performed and who showed no gaze-evoked direction-changing nystagmus, no skew deviation, and no catch-up saccades on the head impulse test. This patient was classified neither as "central HINTS" nor as "peripheral HINTS".

Risk factors

Arterial hypertension was the most frequent risk factor encountered in this study's population (66%), and dyslipidemia was present in 39% of all stroke patients (Table S1). Most patients had a history of cardiovascular disease (66%). Almost 30% had a known central neurological disease, and up to 20% had an endocrinological disease

TABLE 4 Distribution of clinical signs comparing posterior and anterior circulation.

Clinical signs	Total, $n=115$[a]	Posterior circulation only[b]			Anterior circulation only[b]			p [χ^2][c]
		With nystagmus, $n=53$	Without nystagmus, $n=45$	Total, $n=98$	With nystagmus, $n=6$	Without nystagmus, $n=11$	Total, $n=17$	
Spontaneous nystagmus	59 (51%)	53 (100%)			6 (100%)			0.01
Vertical nystagmus	6 (5%)	6 (11%)			0			NA
Horizontal nystagmus	27 (23%)	23 (43%)			4 (67%)			NA
Unspecified nystagmus direction	26 (23%)	24 (45%)			2 (33%)			
NIHSS = 0	26 (23%)	8 (15%)	15 (334%)	23 (23%)	0	3 (27%)	3 (18%)	0.60
NIHSS = 1–3	51 (44%)	29 (55%)	18 (40%)	47 (48%)	1 (17%)	3 (27%)	4 (24%)	0.07
NIHSS ≥ 4	28 (24%)	12 (23%)	11 (24%)	23 (23%)	0	5 (45%)	5 (29%)	0.60
NIHSS unspecified	10 (9%)	4 (8%)	1 (2%)	5 (5%)	5 (83%)	0	5 (29%)	
Central HINTS[d]	33 (29%)	21 (21%)	8 (18%)	29 (30%)	4 (67%)	0	4 (24%)	0.62
Peripheral HINTS[d]	5 (4%)	4 (40%)	0	4 (4%)	1 (17%)	0	1 (6%)	0.62
Unspecified HINTS	77 (67%)	28 (53%)	37 (82%)	65 (66%)	1 (17%)	11 (100%)	12 (70%)	
Cranial nerve pathologies	50 (43%)	24 (45%)	21 (47%)	45 (46%)	0	5 (45%)	5 (29%)	0.21
Ocular palsy	17 (15%)	10 (19%)	7 (16%)	17 (17%)	0	0	0	0.06
Facial palsy	28 (24%)	12 (23%)	11 (24%)	23 (23%)	0	5 (45%)	5 (29%)	0.60
Accommodation reflex pathology	9 (8%)	7 (13%)	2 (4%)	9 (9%)	0	0	0	0.19
Impaired pursuit	10 (9%)	5 (9%)	4 (9%)	9 (9%)	1 (17%)	0	1 (6%)	0.66
Dysarthria	34 (30%)	22 (42%)	10 (22%)	32 (33%)	0	2 (18%)	2 (12%)	0.08
Dysesthesia	19 (17%)	12 (23%)	3 (7%)	15 (15%)	0	4 (36%)	4 (24%)	0.40
Limb paresis	18 (16%)	7 (13%)	8 (18%)	15 (15%)	0	3 (27%)	3 (18%)	0.81
Finger–nose dysmetria	30 (26%)	22 (42%)	6 (13%)	28 (29%)	0	2 (18%)	2 (12%)	0.15
Limb ataxia	36 (31%)	23 (43%)	9 (2%)	32 (33%)	1 (17%)	3 (27%)	4 (24%)	0.45

Abbreviations: NA, not available; NIHSS, National Institutes of Health Stroke Scale.

[a]Patients with concomitant anterior and posterior stroke were not included in this table.

[b]Only magnetic resonance-positive strokes.

[c]Comparing anterior and posterior circulation strokes.

[d]HINTS acronym signifies Head Impulse Test, Nystagmus and Test of Skew. A "central HINTS" was recorded if either a gaze-evoked or direction-changing nystagmus, and/or a skew deviation and/or an absence of corrective saccades on the head impulse test could be detected. The head impulse test was not taken into consideration if the patient did not have SN. A "peripheral HINTS" was recorded if there was no gaze-evoked direction-changing nystagmus, no skew deviation, and an abnormal head impulse test in patients showing SN.

(e.g., diabetes, hypothyroidism) (Table S2). Table S3 shows the most common therapeutic agents given, with antihypertensive medication predominating.

DISCUSSION

In this cross-sectional study, we found a stroke prevalence of 13% in patients with acute onset of vestibular symptoms visiting the ED. Half of these stroke patients presented with AVS; however, a small proportion (<5%) had EVS, and the remaining 45% had AVS without nystagmus or AIS. Approximately half of all the stroke patients included reported vertigo as the chief complaint, even those with an anterior circulation stroke. Almost half of the patients had no SN, and only one third of them reported having no focal weaknesses at admission and were thus at risk of being misdiagnosed. One third of dizzy patients with an anterior circulation stroke initially had an undiagnosed concomitant posterior circulation stroke.

Stroke prevalence and vestibular syndromes

The reported stroke prevalence (13%) in this cohort of patients with dizziness was higher than that reported in the current literature (~4%) [19, 20]. Our previous retrospective study reported a similar stroke prevalence of 12.5% of all patients with vestibular symptoms,

TABLE 5 Distribution of clinical signs comparing patients with and without spontaneous nystagmus.

Clinical signs	Stroke without spontaneous nystagmus, $n = 61$	Stroke with spontaneous nystagmus, $n = 61$	p [χ^2]
NIHSS = 0	20 (33%)	10 (16%)	0.036
NIHSS = 1–4	26 (43%)	31 (51%)	0.36
NIHSS > 4	15 (25%)	13 (21%)	0.67
Pathologic cranial nerves	27 (44%)	24 (39%)	0.58
Facial palsy	15 (26%)	13 (21%)	0.52
Ocular palsy	8 (13%)	10 (16%)	0.61
Pathologic accommodation reflex	4 (7%)	7 (11%)	0.34
Dysarthria	14 (23%)	21 (34%)	0.16
Limb ataxia	12 (20%)	24 (39%)	0.02
Pathologic motor system	11 (18%)	7 (11%)	0.31
Pathologic smooth pursuit	5 (8%)	6 (10%)	0.75
Pathologic finger-to-nose test	8 (13%)	22 (36%)	0.003
Pathologic sensory system	7 (11%)	12 (20%)	0.21

Abbreviation: NIHSS, National Institutes of Health Stroke Scale.

including those with dizziness as an accompanying symptom [1]. Stroke prevalence was probably skewed due to the wider inclusion criteria, a potential referral bias (tertiary care stroke center), and a higher proportion of patients receiving a safety MRI (60%–80%) compared to that reported in the literature (2.3%) [21]. Moreover, we cannot exclude a possible selection bias, as not all screened patients underwent an MRI.

Half of the dizzy patients with a stroke had AVS, characterized by a state of continuous dizziness and/or vertigo lasting >24 h, which also corresponds to what is reported in the literature [7, 22]. Episodes of vertigo or recurrent vertigo, however, may occur a few days before stroke admission [6].

Can anterior circulation strokes cause vertigo?

The strokes provoking vestibular symptoms mostly occurred in the posterior circulation. In 80% of patients, strokes were purely localized in the posterior circulation, involving the vertebral, basilar, posterior inferior cerebellar, anterior inferior cerebellar, superior cerebellar, and posterior cerebral arteries. This can be explained by the anatomical location of the vestibular pathways in the posterior fossa and the brainstem. Vertigo (sensation of self-motion), however, also occurred in patients with anterior circulation strokes (47%, Table 2), which is potentially an underestimate, as reported in a previous study [9, 23] and unfortunately not mentioned in the definition of "vascular vertigo and dizziness" of the classification of vestibular disorders of the Bárány society [24]. Lesions in the PIVC, for example, are well known to induce vertigo [23], but this occurs only rarely and transiently [25]. In our study, 14% of all MR-positive strokes were purely localized in the anterior circulation.

Is the presence of nystagmus a hallmark of acute vestibular syndrome?

Half of the stroke patients included exhibited an acute state of continuous vestibular symptoms but no detectable SN. Current definitions of vestibular syndrome consider the presence of nystagmus as a necessary "biomarker" [16, 26]. This is plausible, as current diagnostic approaches such as the bedside HINTS examination [27] show the greatest sensitivity and specificity when nystagmus is present. AIS seems to be a new and specific diagnostic category, and further investigation is required to clarify the use and significance of the HINTS triad for this type of patients [28]. Caution is necessary, especially when performing and interpreting a head impulse test in patients without SN, as a "normal" result (no catch-up saccades) might lead to false-positive results regarding a central pathology. The low prevalence of SN in our study is in line with recent studies [29, 30], but might be accentuated due to prospective but nonstandardized eye examinations by nonexperts outside office hours (~20% of all dizzy patients screened).

Nystagmus was described in six of 17 patients who had an anterior circulation stroke, but is not a typical sign. A secondary review revealed that one of these six patients had concomitant strokes in the posterior circulation, which were only detected in a delayed (48–72 h) MRI. Three other patients were thought to have had an MR-negative stroke in the posterior circulation, with two of them presenting with grade 3 horizontal SN. One was initially diagnosed with a vestibular migraine and also presented with grade 3 SN. No concomitant pathology was diagnosed in the others. It is known that >50% of small strokes (<1 cm) are not detectable in early MRI-DWI [31]. In addition, a supratentorial stroke might hide another stroke or other underlying cause. Vestibular symptoms might also arise from other simultaneously occurring pathologies

like migraine or vestibular neuritis. We conclude that in anterior stroke patients with vestibular symptoms and nystagmus, one should look for secondary stroke locations in early and delayed MRI-DWI.

How to detect strokes with no focal neurological signs?

In patients with AVS, central vestibular disorders can often mimic peripheral diseases and more than 50% lack any focal neurological signs [3].

Any solution to improve diagnostic accuracy in these patients is crucial. The current scales (e.g., the NIHSS) are not very sensitive in detecting posterior circulation strokes, which leads to delayed treatment and potentially worse outcomes [32, 33]. An expanded version of the NIHSS (e-NIHSS) was designed to improve sensitivity for posterior circulation strokes [34]; however, this was not routinely used in the current study.

In our study, 36 patients (30%) without focal neurological signs had a central HINTS and five (4%) patients had a HINTS examination with peripheral vestibular features. Previous studies have shown that the unfiltered application of HINTS to all dizzy patients, including those without nystagmus, will decrease its sensitivity and specificity [27, 28, 35–37].

In dizzy patients without nystagmus, the BE-FAST (balance, eyes, face, arm, speech, time) algorithm showed a higher accuracy in detecting stroke compared to the FAST (face, arm, speech, time) algorithm [38]. Our data support this finding, as a nonnegligible number of patients had facial palsy, dysarthria, and limb ataxia (Table 4). In addition, we suggest that a more precise examination of oculomotor function (saccades, smooth pursuit, optokinetic nystagmus) could detect the only clinical signs leading to the suspected diagnosis, as demonstrated in recent literature [39].

In patients who exhibit only vestibular symptoms without any other neurological signs, the use of risk stratification rules, specifically the ABCD2 score, which has a stroke sensitivity of 61% [37], may be applicable [40]. Furthermore, the use of video-oculography may assist ED physicians in the diagnostic process [41].

Strengths and limitations

This study aimed to determine stroke prevalence in patients with AVS and non-AVS symptoms by prospectively screening a large number of dizzy patients in the ED. However, it has several limitations. Retrospective data review and variability in the skill level and experience of the examiner might have introduced biases and an underestimation of stroke prevalence. Variability in MRI protocols and the small number of HINTS examinations performed and fully documented probably affected accuracy. Exclusion of patients with subtle signs might have skewed results toward those with more pronounced symptoms.

Clinical implications

The HINTS examination is an easy and sensitive clinical bedside test to differentiate central from peripheral vestibular disorder in the acute phase after symptom onset. However, a large proportion of patients do not have nystagmus, and thus the test's accuracy remains unknown. We recommend the use of video-Frenzel goggles or video-oculography devices to increase the sensitivity of nystagmus assessment. Acute strokes produce rather low-intensity nystagmus with slow phase velocities ranging from 1 to 13°/s, which can be reliably detected by video-oculography [3]. In patients with no vestibular syndrome or no detectable nystagmus, further assessments with the e-NIHSS and BE-FAST including specific oculomotor examination (e.g., smooth pursuit, saccades, head-shaking nystagmus) can be helpful. The patient's history and vascular risk factors assessed with the ABCD2 score [37] should also be taken into consideration in patients with atypical clinical symptoms and signs.

Patients with anterior circulation strokes and nystagmus should be reassessed to check for an undiscovered concomitant posterior circulation stroke. In addition to a second, delayed MRI, we recommend a more intensive effort to look for a proximal cardioembolic cause such as atrial fibrillation and to evaluate the need for more invasive tools such as implantable recording devices.

CONCLUSIONS

A stroke was identified in 13% of ED patients presenting with acute vestibular symptoms. In 5%, it was EVS. Most strokes were in the posterior circulation territory; vertigo occurred with similar frequency in anterior and posterior circulation stroke, and absence of nystagmus was common in both.

FUNDING INFORMATION

Eyeseetec company loaned the video-oculography goggles. This study was supported by the Swiss National Science Foundation #320030_173081.

CONFLICT OF INTEREST STATEMENT

None of the investigators has any financial interests, activities, relationships, or affiliations that represent a relevant financial conflict of interest with respect to the conduct or analysis of this study.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Franca Wagner https://orcid.org/0000-0001-7502-4814
Georgios Mantokoudis https://orcid.org/0000-0003-2268-7811

REFERENCES

1. Goeldlin M, Gaschen J, Kammer C, et al. Frequency, aetiology, and impact of vestibular symptoms in the emergency department: a neglected red flag. *J Neurol*. 2019;266(12):3076-3086.
2. Kim Y, Faysel M, Balucani C, Yu D, Gilles N, Levine SR. Ischemic stroke predictors in patients presenting with dizziness, imbalance, and vertigo. *J Stroke Cerebrovasc Dis*. 2018;27(12):3419-3424.
3. Mantokoudis G, Wyss T, Zamaro E, et al. Stroke prediction based on the spontaneous nystagmus suppression test in dizzy patients: a diagnostic accuracy study. *Neurology*. 2021;97(1):e42-e51.
4. Kuruvilla A, Bhattacharya P, Rajamani K, Chaturvedi S. Factors associated with misdiagnosis of acute stroke in young adults. *J Stroke Cerebrovasc Dis*. 2011;20(6):523-527.
5. Grewal K, Austin PC, Kapral MK, Lu H, Atzema CL. Missed strokes using computed tomography imaging in patients with vertigo: population-based cohort study. *Stroke*. 2015;46(1):108-113.
6. Newman-Toker DE, Moy E, Valente E, Coffey R, Hines AL. Missed diagnosis of stroke in the emergency department: a cross-sectional analysis of a large population-based sample. *Diagnosis (Berl)*. 2014;1(2):155-166.
7. Akhtar N, Kamran SI, Deleu D, et al. Ischaemic posterior circulation stroke in State of Qatar. *Eur J Neurol*. 2009;16(9):1004-1009.
8. Searls DE, Pazdera L, Korbel E, Vysata O, Caplan LR. Symptoms and signs of posterior circulation ischemia in the new England medical center posterior circulation registry. *Arch Neurol*. 2012;69(3):346-351.
9. Zhou Y, Lee S-H, Mantokoudis G, et al. Vertigo and dizziness in anterior circulation cerebrovascular disease: a systematic review (P3.092). *Neurology*. 2014;82(10 Supplement):P3.092.
10. Guldin WO, Grüsser OJ. Is there a vestibular cortex? *Trends Neurosci*. 1998;21(6):254-259.
11. Eguchi S, Hirose G, Miaki M. Vestibular symptoms in acute hemispheric strokes. *J Neurol*. 2019;266(8):1852-1858.
12. Brandt T, Bötzel K, Yousry T, Dieterich M, Schulze S. Rotational vertigo in embolic stroke of the vestibular and auditory cortices. *Neurology*. 1995;45(1):42-44.
13. Mantokoudis G, Korda A, Zee DS, et al. Bruns' nystagmus revisited: a sign of stroke in patients with the acute vestibular syndrome. *Eur J Neurol*. 2021;28(9):2971-2979.
14. Morrison M, Korda A, Zamaro E, et al. Paradigm shift in acute dizziness: is caloric testing obsolete? *J Neurol*. 2022;269(2):853-860.
15. Korda A, Zamaro E, Wagner F, et al. Acute vestibular syndrome: is skew deviation a central sign? *J Neurol*. 2021;269:1396-1403.
16. Bisdorff A. Vestibular symptoms and history taking. *Handb Clin Neurol*. 2016;137:83-90.
17. Comolli L, Korda A, Zamaro E, et al. Vestibular syndromes, diagnosis and diagnostic errors in patients with dizziness presenting to the emergency department: a cross-sectional study. *BMJ Open*. 2023;13(3):e064057.
18. Bisdorff A, Von Brevern M, Lempert T, Newman-Toker DE. Classification of vestibular symptoms: towards an international classification of vestibular disorders. *J Vestib Res*. 2009;19(1–2):1-13.
19. Newman-Toker DE, Hsieh YH, Camargo CA Jr, Pelletier AJ, Butchy GT, Edlow JA. Spectrum of dizziness visits to US emergency departments: cross-sectional analysis from a nationally representative sample. *Mayo Clin Proc*. 2008;83(7):765-775.
20. Kerber KA, Meurer WJ, West BT, Fendrick AM. Dizziness presentations in U.S. emergency departments, 1995–2004. *Acad Emerg Med*. 2008;15(8):744-750.
21. Saber Tehrani AS, Coughlan D, Hsieh YH, et al. Rising annual costs of dizziness presentations to U.S. emergency departments. *Acad Emerg Med*. 2013;20(7):689-696.
22. Sparaco M, Ciolli L, Zini A. Posterior circulation ischaemic stroke-a review part I: anatomy, aetiology and clinical presentations. *Neurol Sci*. 2019;40(10):1995-2006.
23. Yeo SS, Jang SH, Kwon JW. Central vestibular disorder due to ischemic injury on the parieto-insular vestibular cortex in patients with middle cerebral artery territory infarction: observational study. *Medicine (Baltimore)*. 2017;96(51):e9349.
24. Kim JS, Newman-Toker DE, Kerber KA, et al. Vascular vertigo and dizziness: diagnostic criteria. *J Vestib Res*. 2022;32(3):205-222.
25. Dieterich M, Brandt T. Why acute unilateral vestibular cortex lesions mostly manifest without vertigo. *Neurology*. 2015;84(16):1680-1684.
26. Tarnutzer AA, Berkowitz AL, Robinson KA, Hsieh YH, Newman-Toker DE. Does my dizzy patient have a stroke? A systematic review of bedside diagnosis in acute vestibular syndrome. *CMAJ*. 2011;183(9):E571-E592.
27. Kattah JC, Talkad AV, Wang DZ, Hsieh YH, Newman-Toker DE. HINTS to diagnose stroke in the acute vestibular syndrome: three-step bedside oculomotor examination more sensitive than early MRI diffusion-weighted imaging. *Stroke*. 2009;40(11):3504-3510.
28. Kattah JC. Use of HINTS in the acute vestibular syndrome. An overview. *Stroke Vasc Neurol*. 2018;3(4):190-196.
29. Machner B, Choi JH, Trillenberg P, Heide W, Helmchen C. Risk of acute brain lesions in dizzy patients presenting to the emergency room: who needs imaging and who does not? *J Neurol*. 2020;267(Suppl 1):126-135.
30. Zwergal A, Möhwald K, Salazar López E, et al. A prospective analysis of lesion-symptom relationships in acute vestibular and ocular motor stroke. *Front Neurol*. 2020;11:822.
31. Saber Tehrani AS, Kattah JC, Mantokoudis G, et al. Small strokes causing severe vertigo: frequency of false-negative MRIs and nonlacunar mechanisms. *Neurology*. 2014;83(2):169-173.
32. Schneck MJ. Current stroke scales may Be partly responsible for worse outcomes in posterior circulation stroke. *Stroke*. 2018;49(11):2565-2566.
33. Sommer P, Posekany A, Serles W, et al. Is functional outcome different in posterior and anterior circulation stroke? *Stroke*. 2018;49(11):2728-2732.
34. Olivato S, Nizzoli S, Cavazzuti M, Casoni F, Nichelli PF, Zini A. E-NIHSS: an expanded National Institutes of Health stroke scale weighted for anterior and posterior circulation strokes. *J Stroke Cerebrovasc Dis*. 2016;25(12):2953-2957.
35. Dmitriew C, Regis A, Bodunde O, et al. Diagnostic accuracy of the HINTS exam in an emergency department: a retrospective chart review. *Acad Emerg Med*. 2021;28(4):387-393.
36. Ohle R, Montpellier RA, Marchadier V, et al. Can emergency physicians accurately rule out a central cause of vertigo using the HINTS examination? A systematic review and meta-analysis. *Acad Emerg Med*. 2020;27(9):887-896.
37. Newman-Toker DE, Kerber KA, Hsieh YH, et al. HINTS outperforms ABCD2 to screen for stroke in acute continuous vertigo and dizziness. *Acad Emerg Med*. 2013;20(10):986-996.
38. Aroor S, Singh R, Goldstein LB. BE-FAST (balance, eyes, face, arm, speech, time): reducing the proportion of strokes missed using the FAST mnemonic. *Stroke*. 2017;48(2):479-481.
39. Kudo Y, Takahashi K, Sugawara E, et al. Bedside video-oculographic evaluation of eye movements in acute supratentorial stroke patients: a potential biomarker for hemispatial neglect. *J Neurol Sci*. 2021;425:117442.

40. Navi BB, Kamel H, Shah MP, et al. Application of the ABCD2 score to identify cerebrovascular causes of dizziness in the emergency department. *Stroke*. 2012;43(6):1484-1489.
41. Mantokoudis G, Otero-Millan J, Gold DR. Current concepts in acute vestibular syndrome and video-oculography. *Curr Opin Neurol*. 2022;35(1):75-83.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Nikles F, Kerkeni H, Zamaro E, et al. Do monosymptomatic stroke patients with dizziness present a vestibular syndrome without nystagmus? An underestimated entity. *Eur J Neurol*. 2023;00:1-10. doi:10.1111/ene.16066