Journal of Neurology (2022) 269:294–306
https://doi.org/10.1007/s00415-021-10627-1

ORIGINAL COMMUNICATION

Capturing vertigo in the emergency room: three tools to double the rate of diagnosis

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Received: 17 January 2021 / Revised: 23 May 2021 / Accepted: 24 May 2021 / Published online: 16 August 2021

Abstract

Objective Many patients attending the emergency room (ER) with vertigo, leave without a diagnosis. We assessed whether the three tools could improve ER diagnosis of vertigo.

Methods A prospective observational study was undertaken on 539 patients presenting to ER with vertigo. We used three tools: a structured-history and examination, nystagmus video-oculography (VOG) in all patients, additional video head-impulse testing (vHIT) for acute-vestibular-syndrome (AVS).

Results In the intervention-group ($n=424$), case-history classified AVS in 34.9%, episodic spontaneous-vertigo (ESV 32.1%), and episodic positional-vertigo (EPV 22.6%). In AVS, we employed "Quantitative-HINTS plus" (Head-Impulse, Nystagmus and Test-of-Skew quantified by vHIT and VOG, audiometry) to identify vestibular-neuritis (VN) and stroke (41.2 and 31.1%). vHIT gain ≤ 0.72, catch-up saccade amplitude $> 1.4^{\circ}$, saccade-frequency $> 154\%$, and unidirectional horizontal-nystagmus, separated stroke from VN with 93.1% sensitivity and 88.5% specificity. In ESV, 66.2 and 14% were diagnosed with vestibular migraine and Meniere's Disease by using history and audiometry. Horizontal-nystagmus velocity was lower in migraine $0.4 \pm 1.6^{\circ}$/s than Meniere's $5.7 \pm 5.5^{\circ}$/s ($p < 0.01$). In EPV, benign positional vertigo (BPV) was identified in 82.3% using VOG. Paroxysmal positional-nystagmus lasting < 60 s separated BPV from non-BPV with 90% sensitivity and 100% specificity. In the control group of ER patients undergoing management-as-usual ($n=115$), diagnoses included BPV (38.3%) and non-specific vertigo (41.7%). Unblinded assessors reached a final diagnosis in 90.6 and 30.4% of the intervention and control groups. Blinded assessors provided with the data gathered from each group reached a diagnosis in 86.3 and 41.1%.

Conclusion Three tools: a structured-assessment, vHIT and VOG doubled the rate of diagnosis in the ER.

Keywords All cerebrovascular disease/stroke · Vertigo · Nystagmus · HINTS · Diagnostic test assessment

Introduction

Vertigo is a common, disabling and treatable symptom with a lifetime prevalence of up to 36% [1–3]. Dizziness presentations constitute 4% of total Emergency Room (ER) visits of which ~ 3% are potentially life-threatening posterior circulation strokes [4, 5]. Up to 55% of ER presentations receive no aetiological diagnosis and 20–35% an incorrect diagnosis [6–9]. Patients presenting to ER with vertigo have a subsequent seven to nine-fold increase in risk of an acute stroke compared with the general population [10, 11]. Those discharged from ER labelled with benign dizziness are at 50-fold increased risk of re-presenting with stroke in the next seven days relative to matched controls [11].

Vertigo presents as distinctive syndromes (acute, episodic or chronic vestibular syndromes) which can be identified

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with a focussed history. Acute vestibular syndrome (AVS) refers to an abrupt-onset of spontaneous, continuous vertigo, dizziness, or unsteadiness lasting a day or longer, accounting for ~ 20% of ER vertigo presentations [6]. AVS can be due to vestibular neuritis (VN), an innocuous and treatable disorder or a potentially life-threatening posterior circulation stroke (PCS). Acute transient vestibular syndrome (ATVS) is a single episode of transient dizziness and vertigo lasting < 1 day [12], associated with a high prevalence of stroke [13]. Episodic Vestibular Syndromes (EVS) represent multiple episodes of vertigo, lasting seconds to hours and rarely days. Vestibular migraine (VM) and Menière's disease (MD) are two common causes of episodic spontaneous vertigo (ESV) whereas benign positional vertigo is a common cause of episodic positional vertigo (EPV) produced by changes in head position with respect to gravity. Chronic vestibular syndromes (CVS) denote chronic dizziness or unsteadiness lasting months to years and may be accompanied by unilateral or bilateral vestibular system dysfunction.

Acute vertigo is usually accompanied by nystagmus, the spatiotemporal characteristics of which may point to its origin. Acute peripheral vestibular disorders like VN, for example, display ictal nystagmus which is horizontal-torsional, beats away from the affected ear and obeys Alexander's law, where nystagmus direction is maximal on looking in the direction of the fast phase [14]. PCS in contrast have diverse spontaneous nystagmus patterns influenced by the brainstem and cerebellar structures involved [15–19]. Patients with acute vertigo seldom present to specialty clinics while acutely dizzy. In contrast, the ER and general practice are two settings where nystagmus recorded from acutely vertiginous patients could facilitate an early diagnosis and treatment.

The video head-impulse test (vHIT) [20] is a non-invasive investigation that could be performed at the bedside. In AVS, "HINTS" (head-impulse, nystagmus and testing for skew) provides excellent separation of stroke from VN [21]. Although bedside head impulse testing is subjective and may not be used with confidence by emergency physicians, the vHIT, offers the opportunity of performing a quantitative test that yields an objective result in the ER.

In the present study, we sought to improve the rate of vertigo aetiological diagnosis in the emergency room using three tools: (1) a structured history to identify the vertigo syndrome, (2) nystagmus event-monitoring using VOG and (3) vHIT, to help identify the underlying cause. We hypothesised that this would lead to a higher rate of definitive diagnoses thereby facilitating early treatment and improved outcomes.

Methods

Participants: intervention group

This prospective cohort study was conducted within the Neurology and Emergency departments of Royal Prince Alfred Hospital, Sydney (January 2015–May 2019). Patients presenting to ER with acute vertigo were non-consecutively convenience recruited, during weekdays and typical working hours. Data collection were undertaken by two neuro-otologists with subspecialty training (MW, BN), one neuro-otology nurse consultant (NR) and one ER physician with subspecialty experience (KB). 424 patients were included in the intervention group. All underwent a structured history, VOG assessment of spontaneous, gaze-evoked and positional nystagmus (Supplementary Appendix 1 and Supplementary-video 1) and, in the case of AVS, audio-vestibular testing (vHIT and audiometry) within 24 h from the time of arrival ($n = 278$) or within a mean of 2.3 days (median one day) of initial presentation to the ER.

Participants: control group

For the control group, 364 consecutive patients presenting to the ER with vertigo or dizziness over a 6-month period overlapping with the intervention group were considered for study inclusion. The history, examination and final diagnoses of the control group were retrospectively obtained from electronic medical records, with local ethics committee approval. Exclusion criteria for the control group included: (1) patients first assessed in ER by neuro-otology staff, and (2) patients with a proven cardiac rhythm disturbance, orthostatic hypotension, or other non-vestibular cause such as anaemia or hypoglycaemia. Ultimately, 115 patients were recruited to the control group. The demographics of both groups are summarised in Supplementary Appendix 2.

Vestibular event monitoring

All patients in the active group underwent VOG in the ER, on the day of arrival, using custom-built portable monocular video-frenzel glasses (VestiTest Inc, Sydney Australia). Eye movements were recorded in the primary position, left and rightward gaze and in either Dix–Hallpike position. Videos were recorded in frames of 720 × 576 pixels at 30 fps and analysed using a custom written pupil-tracker using threshold-based ellipse fitting (developed and validated by AB) on a LabVIEW (National Instruments, Austin, Texas) platform [22]. Eye movements were analysed in horizontal and vertical planes, and nystagmus slow phase velocity (SPV) was measured in degrees per second (°/s) and plotted as a

function of time. For positional nystagmus, a second-order exponential curve was fitted to the data using iterative gradient descent. The onset, rise time, peak velocity, time taken for SPV to decay to half the peak velocity (T50), and nystagmus duration were then determined from this curve. When T50 was incalculable due to persistence of nystagmus, it was designated a value of 1000 after extrapolation of the curve.

Structured assessment

Patients in the active group underwent a devised structured clinical assessment selected by clinician experts GMH and MW (Supplementary Appendix 1). The assessment documented (1) whether it was a first-ever vertigo episode, (2) vertigo duration (seconds/minutes/hours/days or longer), (3) spontaneous or positional vertigo, (4) aural symptoms (tinnitus/fullness/hearing loss), (5) migraine symptoms: headache, visual aura, photo or phonophobia, (6) neurological symptoms e.g. diplopia, dysarthria, numbness, (7) vascular risk factors e.g. atrial fibrillation, hypertension, hyperlipidaemia, diabetes mellitus, smoking. Clinical examination included (1) the head-impulse test, (2) primary-position spontaneous, gaze-evoked, and positional nystagmus, (3) test of skew, (4) pursuit and saccades, (5) limb and gait examination for weakness or ataxia.

Quantitative vestibular testing

All patients with a history of AVS underwent vHIT and pure tone audiometry if hearing loss was reported. Patients with ESV underwent audiometry and event monitoring in ER; more detailed testing with vHIT, VEMP and caloric testing were undertaken outside ER on follow-up. Those with EPV did not undergo routine vestibular testing. Since our study focuses on early diagnosis of ER vertigo, to which VEMPs were non-contributory, we do not discuss VEMP data in the results.

Video head-impulse (vHIT)

High velocity (> 120°/s) and low (10°) amplitude (Anterior, Posterior, Horizontal) canal plane head movements administered by an examiner, with the participants fixating on a target 1–1.4 m away using the vHIT goggles (Otometrics, Denmark). Vestibulo-ocular reflex (VOR) gain (eye-velocity divided by head-velocity) was calculated using a custom LabVIEW programme. Impulses, reaching peak head-velocity of 150–250°/s for horizontal-canal and 120–200°/s for vertical-canals were analysed. The programme also enabled analysis of saccade properties through best-fit saccade matching using automated (in overt saccades i.e. occurring after the head impulse) and manual (in covert saccades i.e. occurring during the impulse) means. Saccade measurement methods are as documented in Calic et al. [23]. Saccade prevalence refers to the total number of saccades detected for all impulses delivered in the ipsilesional canal plane (inclusive of first and successive saccades) expressed as a percentage i.e. per 100 impulses.

An abnormal horizontal head impulse test on objective vHIT testing was defined as having two or more of the three following attributes: (1) decreased VOR gains (≤ 0.72), (2) increased catch-up saccade prevalence (> 154 per 100 impulses), (3) first saccade amplitude size (> 1.4°). These limits represented values falling outside the 95% reference range for healthy aged-matched controls [23, 24].

Audiogram

We tested hearing using conventional audiometry or a portable iPad-audiometer (Shoebox audiometry, Ottawa, Canada) [25]. Otoscopy was done to ensure the absence of occlusive cerumen. Three interaural-differences of 10 dB in adjacent low to mid-frequencies, two adjacent interaural-differences of $\geq$ 15 dB in the low to mid-frequencies, or one interaural difference of $\geq$ 20 dB at any frequency were deemed asymmetric [26].

Final diagnosis and neuroimaging protocol

Vestibular neuritis was diagnosed based upon (1) abnormal video head impulse, (2) peripheral spontaneous nystagmus obeying Alexander's law, (3) absent skew and (4) no reported hearing loss. If all four criteria were obeyed and there were no additional neurological examination deficits to suggest PCS, VN was diagnosed and an MRI brain was not generally organised.

Delayed MRI brain with diffusion weighted imaging (DWI) sequences was done between 48 and 168 h after symptom onset, unless contraindicated (e.g., permanent pacemaker/cochlear implant) in AVS patients not meeting VN diagnostic criteria.

In this "non-VN" group if delayed MRI (after 48 h) imaging was negative or if DWI imaging done before 48 h demonstrated acute PCS, neuroimaging was not repeated. Patients who had skew, but fulfilled all other criteria for VN, were diagnosed as VN if the delayed MRI were normal.

Definite PCS was diagnosed on demonstration of a posterior circulation diffusion defect. A small number of patients classified as "non-VN" received a final diagnosis of stroke despite the absence of MRI abnormalities due to the presence of central oculomotor findings; they are not included in the definite PCS group. EVS was classified as VM, MD or BPV as per Bárány Society Criteria [27–29] or as "other".

To compare diagnostic rate in the intervention and control group, history and examination templates (Supplementary Appendix 1) for each subject in the intervention and control

group were scored by four blinded expert clinicians (GMH, NR, SRW, MW), who were asked to classify all 539 patients as one of the following: AVS/VN, AVS/Non-VN, ATVS, EVS/VM, EVS/MD, EVS undifferentiated, BPV, non-BPV positional vertigo, CVS or unknown.

Those who fell into the unknown category were considered undiagnosed. If any of the other categories (based on vertigo syndrome or aetiological diagnosis) were selected by the blinded clinician, this constituted a diagnosis. The rates of patients with a diagnosis from the blinded clinicians in the intervention and control group were then assessed.

Analysis and statistical method

Statistics were performed using SPSS Statistics for Windows, Version 24.0 (Armonk, NY. The relationship between binary outcomes (normal or abnormal) for various test combinations were explored with cross-tabulations. Normally distributed data (vHIT gains and saccade properties) were compared using paired-t tests, and non-normally distributed data with Wilcoxon signed-rank tests. Significance was determined at the 5% level of significance, adjusted with the Bonferroni correction to control for family-wise error. Since nystagmus SPV data were not normally distributed, Mann–Whitney *U* Tests were used. Sensitivity and specificity were calculated using ROC curves and Youden's index for threshold selection. Logistic regression was used to calculate odds ratios in multivariate analysis.

Power calculation

Our pilot studies indicated the rate of a vertiginous patient leaving ER with a diagnosis was 17%. We sought a doubling of the rate of diagnosis. The proportion in the treatment group is assumed to be 0.17 under the null hypothesis and 0.34 under the alternative hypothesis. Equal sample sizes of 79 in each group achieve a power of 80% to detect a difference between the group proportions of 0.17. The proportion in the control group is 0.17 using a one-sided *Z* test with unpooled variance. The significance level, α, is 5%

Results

Intervention group

There were 424 patients in the intervention group. Their mean age was 60.3(± 16.9) and 54.1% were female. Presentations included acute vestibular syndrome in 34.9%, acute transient vestibular syndrome in 7.5%, episodic spontaneous vertigo 32.1% and episodic positional vertigo 22.6%. Only 2.9% presented with chronic vestibular syndrome (Fig. 1).

Acute vestibular syndrome

In this group of 148 patients, 61 (41.2%) were diagnosed with VN and 46 (31.1%) with stroke. Fifty-eight of the 61 VN patients met all three clinical HINTS criteria: positive bedside head-impulse test (HIT), unidirectional horizontal nystagmus and absent skew; 56 had quantitative HINTS indicative of VN. Three had a negative horizontal HIT, but positive HIT in the posterior canal plane, primary contraversive horizontal and/or downbeat nystagmus and a normal MRI and were diagnosed with inferior VN. Forty-six had a clinical diagnosis of stroke; 28 of these patients had diffusion defects on MRI and eight had CT evidence of acute ischemic infarction or haemorrhage; the remaining 10 were imaging negative and diagnosed based upon central oculomotor signs or cerebellar ataxia (Supplementary Appendix). In the 41 AVS patients that were not diagnosed with VN or PCS, the diagnoses included vestibular migraine ($n=15$), undefined central vertigo ($n=7$), Meniere's Disease ($n=3$), sudden sensorineural hearing loss and vertigo ($n=3$), demyelination ($n=2$), autoimmune inner ear disease ($n=2$), Ramsay-Hunt syndrome ($n=1$), suppurative labyrinthitis ($n=1$), trauma ($n=1$) iatrogenic vertigo post ossicular-chain reconstruction ($n=1$) and unknown ($n=5$). Isolated spontaneous vertigo constituted 72.3% of the entire AVS group.

Clinical HINTS helped separate PCS from VN with 88.9% sensitivity and 91.8% specificity (95% CI 0.83–0.98, 0.7–0.95). HINTS test results are summarised in Table 1. The various diagnoses and their frequencies in the AVS group are summarised in Supplementary Appendix 4.

Structured history in VN and PCS

Only two questions (any additional neurological symptoms and presence of vascular risk factors) of the structured history yielded significantly different responses in VN and PCS. On multivariate analysis, the odds of having a stroke were higher for those with > 1 vascular risk factor (OR 6.0 (95% CI 1.6–21.5, $p<0.01$)) or additional neurological symptoms (OR 41.7 (95% CI 4.7–368.8, $p<0.01$)) (Supplementary Appendix 5).

Ictal nystagmus in VN and PCS presenting with acute vestibular syndrome

For VN ($n=61$, assessed 1.1 ± 1.6 days since symptom onset) all subjects had primary position spontaneous nystagmus; 59 demonstrated unidirectional contraversive horizontal nystagmus (horizontal SPV 11.8 ± 6.3, 2.6–34.3°/s) (Supplementary-video 2). Two demonstrated torsional–downbeat nystagmus (Supplementary-video 3). For the 36 radiologically confirmed PCS patients presenting as AVS (assessed 1.3 ± 1.4 days since symptom onset), Primary position

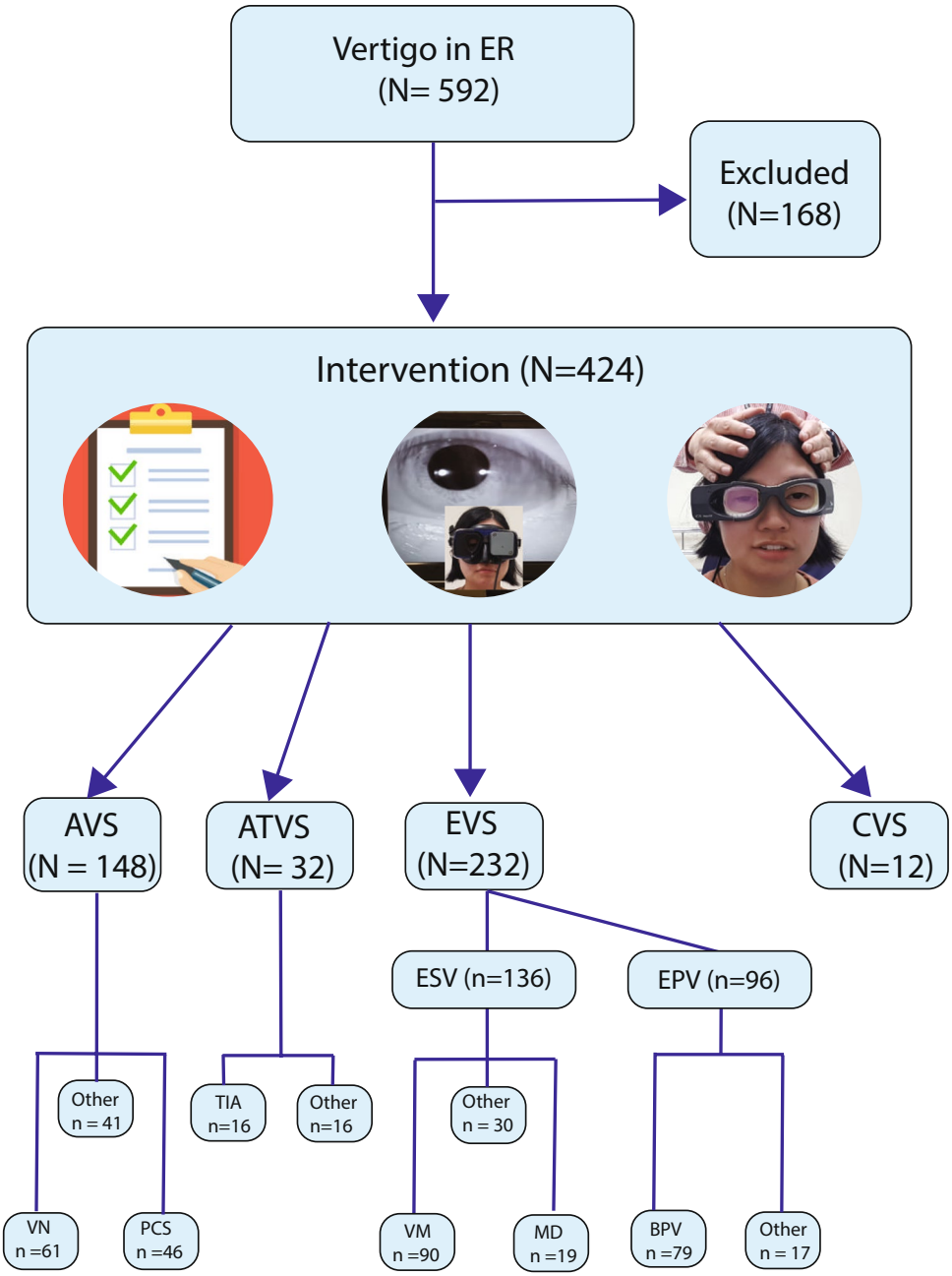

Fig. 1 Patient flowchart. Flowchart of patients recruited and included in study. 424 patients received the three interventions of a structured history and examination, video-oculography and video head impulse testing when appropriate. *ATVS* acute transient vestibular syndrome, *AVS* acute vestibular syndrome, *BPV* benign positional vertigo, *CVS* chronic vestibular syndrome, *EPV* episodic positional vertigo, *ESV* episodic spontaneous vertigo, *ER* emergency room, *EVS* episodic vestibular syndrome, *MD* Meniere's disease, *PCS* posterior circulation stroke, *TIA* transient ischemic attack, *VM* vestibular migraine, *VN* vestibular neuritis

Table 1 Clinical and quantitative HINTS profile of AVS patients

AVS ($n=148$)	Clinical HINTS		Quantitative HINTS	
	VN ($n=61$)	Radiological PCS ($n=36$)	VN ($n=61$)	Radiological PCS ($n=29$[a])
Head-impulse positive	58 (95.1%)	7 (19.4%)	56 (91.8%)	5 (17.2%)
Peripheral nystagmus	58 (95.1%)	9 (25%)	59 (96.7%)	7 (24.1%)
Absent skew	60 (98.3%)	25 (69.4%)	60 (98.3%)	19 (65.5%)

[a]Of the 36 radiological PCS, only 29 could have vHIT, and therefore, quantitative HINTS as seven patients had contraindications to vHIT e.g. neck pain/dissection

horizontal nystagmus (mean SPV 2.8 ± 3.0°/s) was observed in 15 patients for whom 10 had typical peripheral horizontal unidirectional nystagmus (Supplementary-videos 4, 5, 6). The remaining 21 had one or more nystagmus findings that did not fit with VN e.g. gaze evoked or vertical/torsional nystagmus (Table 2). Horizontal nystagmus SPV was significantly faster for VN than PCS ($p < 0.01$). In patients seen within 24 h of arrival, primary-position horizontal nystagmus (without visual fixation) with an SPV ≥ 5.27°/s separated VN from stroke with a sensitivity and specificity of 94.4% and 62.5% (95% CI 0.84–0.99, 0.41–0.8).

Video head impulse testing in VN and PCS

vHIT gain

51 of 61 subjects diagnosed with VN and 12 of 36 subjects diagnosed with PCS had abnormal horizontal canal (HC) gains. vHITs were not done on seven of 36 radiologically confirmed PCS patients due to contraindications (e.g. neck pain/dissection). Mean ipsilesional vHIT gains in VN and PCS were 0.45(± 0.26) and 0.9(± 0.25). The ipsilesional HC VOR gain was significantly lower for VN than PCS ($p < 0.01$). A HC VOR gain ≤ 0.84 separated VN from PCS with a sensitivity and specificity of 95.1 and 68.9% (95% CI 0.85–0.99, 0.49–0.84). vHIT characteristics are summarised in Table 3.

Refixation-saccades

In VN, mean first refixation-saccade amplitude was 4.8 ± 2.5°, significantly greater than in PCS (1.7 ± 1.1°, $p < 0.01$). Saccade prevalence was higher in VN (208.6 ± 60.0%) than PCS (94.2 ± 65.1%) per 100 impulses ($p < 0.01$). (Fig. 2) There were three VN patients with refixation saccades predominantly outside the 600 ms captured sweep.

Table 2 Nystagmus characteristics of stroke and vestibular neuritis

Nystagmus and oculomotor characteristics	PCS ($n = 46$)	PICA ($n = 14$)	AICA ($n = 3$)	SCA ($n = 3$)	Pontine perforator ($n = 4$)	Basilar or multiple ($n = 6$)	PCA ($n = 3$)	Pontine bleed ($n = 3$)	Vestibular neuritis ($n = 61$)
Ictal spontaneous nystagmus	32 (70%)	7	3	1	2	4	2	3	61 (100%)
Horizontal nystagmus	22 (69%)	4	3	1	0	4	1	2	59 (96.7%)
Vertical nystagmus	8 (25%)	3	0	0	1	0	1	1	0 (0%)
Torsional nystagmus	2 (6%)	0	0	0	1	0	0	0	2 (3.3%)
No nystagmus	14 (30%)	7	0	2	2	2	1	0	0 (0%)
Gaze evoked nystagmus	17 (37%)	5	1	2	1	3	0	1	0 (0%)

AICA anterior inferior cerebellar artery, *PCA* posterior cerebellar artery, *PCS* posterior circulation stroke, *PICA* posterior inferior cerebellar artery, *SCA* superior cerebellar artery

Table 3 vHIT characteristics of VN and stroke

All AVS ($n = 148$)	VN ($n = 61$)	Stroke[a] ($n = 46$)
Number receiving vHIT (%)	61 (100%)	39 (84.8%)
Ipsilesional horizontal vHIT VOR gain ± SD	0.45 ± 0.26	0.89 ± 0.28
Mean 1st saccade amplitude ± SD	4.76 ± 2.45	1.70 ± 1.13
Mean saccade prevalence ± SD	208.65 ± 59.97	94.2 ± 65.07
Abnormal HC VOR gain < 0.73 (%)	51 (83.6%)	4 (10.2%)
Abnormal first saccade amplitude > 1.4° (%)	58 (95.1%)	19 (48.7%)
Abnormal saccade prevalence > 154% (%)	51 (83.6%)	7 (17.9%)
Contralesional horizontal vHIT VOR gain ± SD	0.90 ± 0.16	0.95 ± 0.18
Ipsilesional anterior canal vHIT VOR gain ± SD	0.45 ± 0.24	0.67 ± 0.23
Ipsilesional posterior canal vHIT VOR gain ± SD	0.69 ± 0.2	0.62 ± 0.22
Contralesional anterior canal vHIT VOR gain ± SD	0.82 ± 0.19	0.69 ± 0.24
Contralesional posterior canal vHIT VOR gain ± SD	0.68 ± 0.16	0.61 ± 0.18

[a]All 46 strokes were included including DWI negative strokes, in the cases that were DWI negative, the ipsilesional side was determined by the clinical features or lateralised to the side with the lower VOR gain

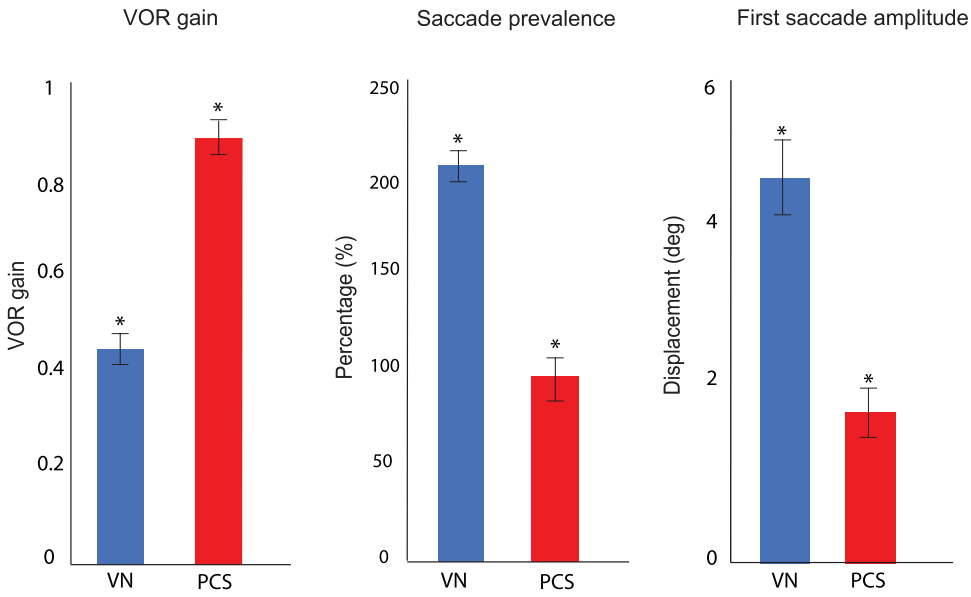

Fig. 2 Horizontal canal vHIT metrics in AVS. In patients with vestibular neuritis, as compared to posterior circulation stroke, the mean ipsilesional VOR gain is significantly lower and mean saccade prevalence and first saccade prevalence is significantly larger, as indicated by the asterisks ($p < 0.01$). *PCS* posterior circulation stroke, *VN* vestibular neuritis

Utility of abnormal HC VHIT alone

Based on pilot studies on subjects with VN, we used three criteria to define an abnormal vHIT: vHIT gain < 0.73, first saccade amplitude > 1.4°, saccade prevalence > 154%. When impulses satisfying two of these three criteria were considered abnormal, the vHIT alone separated stroke from VN with 89.7% sensitivity and 91.8% specificity (95% CI 0.72–0.97, 0.81–0.97).

Quantitative HINTS

We examined the diagnostic utility of three parameters which included (1) abnormal vHIT (having at least two of the three above-described gain or saccades abnormalities), (2) presence of peripheral nystagmus on VOG and (3) absence of skew. If all three parameters were met, the patient was labelled as peripheral HINTS. Absence of spontaneous nystagmus (in a vertiginous patient), pure vertical or torsional nystagmus and/or gaze-evoked nystagmus on VOG was defined as consistent with central vertigo. Quantitative HINTS testing separated stroke from VN with a sensitivity and specificity of 93.1 and 88.5% (95% CI 0.76–0.99, 0.77–0.95).

Four patients with PCS had "peripheral" HINTS plus examinations but three had abnormalities on more detailed oculomotor examination (such as broken smooth pursuit or dysmetric saccades) and one had limb weakness which indicated PCS. One PCS patient had peripheral HINTS but had sudden sensorineural hearing loss (Fig. 3). Five patients that failed HINTS plus (due to skew, negative initial bedside HIT which became positive on day 2, negative horizontal HIT in inferior VN) had a final diagnosis of VN. Skew deviation can be seen in peripheral vestibulopathy and can be large in magnitude [30, 31].

Vestibular migraine presenting with AVS

VM constituted 10.7% of AVS presentations. All had delayed MRI (> 48 h from ictus) to exclude PCS. 93% of patients had "central" HINTS plus assessments. One patient had left-beating nystagmus and rightward positive bedside head-impulse but normal VOR gain and no refixation-saccades on vHIT. 40% of patients had central positional nystagmus ictally and 90% of patients had a history of pre-existing migraine. The remaining 10% had migraine headaches after their presentation. Four patients with a diagnosis of probable VM later returned with one or two spontaneous episodes of vertigo without migraine headaches and were diagnosed as undifferentiated central vertigo.

Episodic spontaneous vertigo

In this group ($n = 136$), a diagnosis was reached in ER on 70.6%: the final diagnoses were VM in 66.2% ($n = 90$), MD in 14.0%, miscellaneous diagnoses in 4.4%; the diagnosis was uncertain in 15.4%. Miscellaneous other diagnoses reached ($n = 6$) included autoimmune inner ear disease, vertebrobasilar insufficiency, cholesteatoma and vestibular paroxysmia.

Structured history in ESV

Using multivariate analysis, the odds of having VM were significantly higher for those with any migraine [OR 39.7

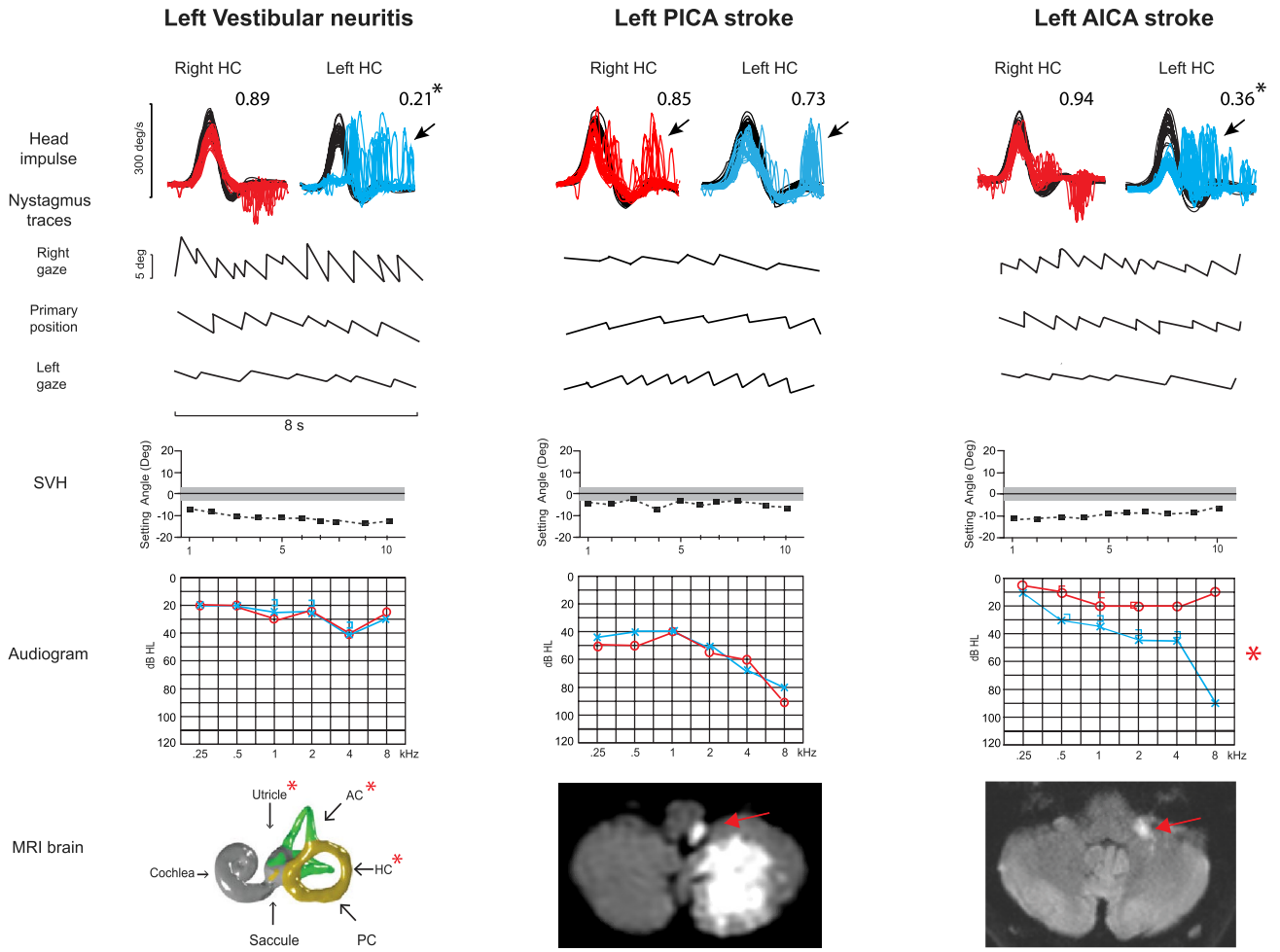

Fig. 3 Vestibular test comparison between VN and PCS. Three patients with left vestibular neuritis (VN), left posterior-inferior cerebellar artery (PICA) stroke and left anterior-inferior cerebellar artery (AICA) stroke and their respective vestibular testing features. All patients had a positive clinical head impulse test to the left (black arrows), only the cases of VN and AICA stroke showed decreased vestibulo-ocular (VOR) gain on the video head impulse (black asterisks). The AICA stroke mimics VN with peripheral appearing nystagmus, an ipsilesional deviation on the subjective visual horizontal but there is ipsilesional asymmetric hearing loss on audiometry with the AICA stroke (large red asterisk) whereas hearing is spared in VN. The PICA stroke shows central gaze evoked (bi-directional) nystagmus i.e. right beating nystagmus on right gaze and left beating nystagmus on left gaze. The subjective visual horizontal is a static psycho-visual-perceptive test that correlates with degree and direction of ocular torsion. *AICA* anterior inferior cerebellar artery, *HC* horizontal canal, *PICA* posterior inferior cerebellar artery, *SVH* subjective visual horizontal, *VN* vestibular neuritis. For audiometry, red circles = right ear values and blue crosses are left ear values

(95% CI 3.2–490.8, $p < 0.01$)] compared to MD, whilst the odds of having MD were higher in the presence of any unilateral audiological symptoms [OR 140.3 (95% CI 9.8–2015.6, $p < 0.01$)] (Supplementary Appendix 5).

Ictal nystagmus in ESV

In the VM group ($n = 90$); 8.9% of patients had spontaneous nystagmus. 38.9% had only positional nystagmus on Dix–Hallpike testing. 52.2% had no nystagmus. Primary position spontaneous nystagmus was horizontal in $n = 7$ ($0.4 \pm 1.5^{\circ}$/s) and torsional downbeat in one patient. Positional nystagmus patterns included: persistent downbeat (30.2%) (Supplementary-video 7), apogeotropic horizontal (11.6%), geotropic horizontal (9.3%), persistent unidirectional horizontal (16.3%), persistent upbeat (2.4%), persistent horizontal and vertical nystagmus in opposite lateral-lying positions (30.2%). In 19 patients diagnosed with MD (Supplementary-video 8); we demonstrated spontaneous ictal horizontal nystagmus in 13 subjects (SPV of $5.7 \pm 5.5^{\circ}$/s). Mean nystagmus SPV for MD was significantly faster than VM ($0.4 \pm 1.6^{\circ}$/s) ($p < 0.01$). Pure tone averages across three frequencies (0.5, 1, 2 kHz) in the worse hearing ear were 57.4 and 15.5 dB in MD and VM. Asymmetrical audiometric thresholds separated MD

and VM with a sensitivity and specificity of 88.2% and 85.2% (95% CI 0.62–0.98, 0.73–0.93).

Episodic positional vertigo

In this sub-group ($n=96$), 50 were diagnosed with BPV [posterior canal (PC) canalithiasis (70%), HC canalithiasis (18%), HC cupulolithiasis (8%) and multi-canal BPV (4%)] based upon VOG in ER; thirteen were diagnosed with probable BPV based upon a history of recurrent positional vertigo lasting seconds in the absence of positional nystagmus. Fifteen patients returned for follow-up with paroxysmal positional nystagmus consistent with BPV (Supplementary-videos 9 and 10). Nine had non-paroxysmal positional nystagmus, of whom six were diagnosed with probable VM (Fig. 4 and Supplementary-video 7). Other diagnoses included hyper-viscosity state with positional vertigo ($n=1$) and positional dizziness of unknown origin ($n=7$).

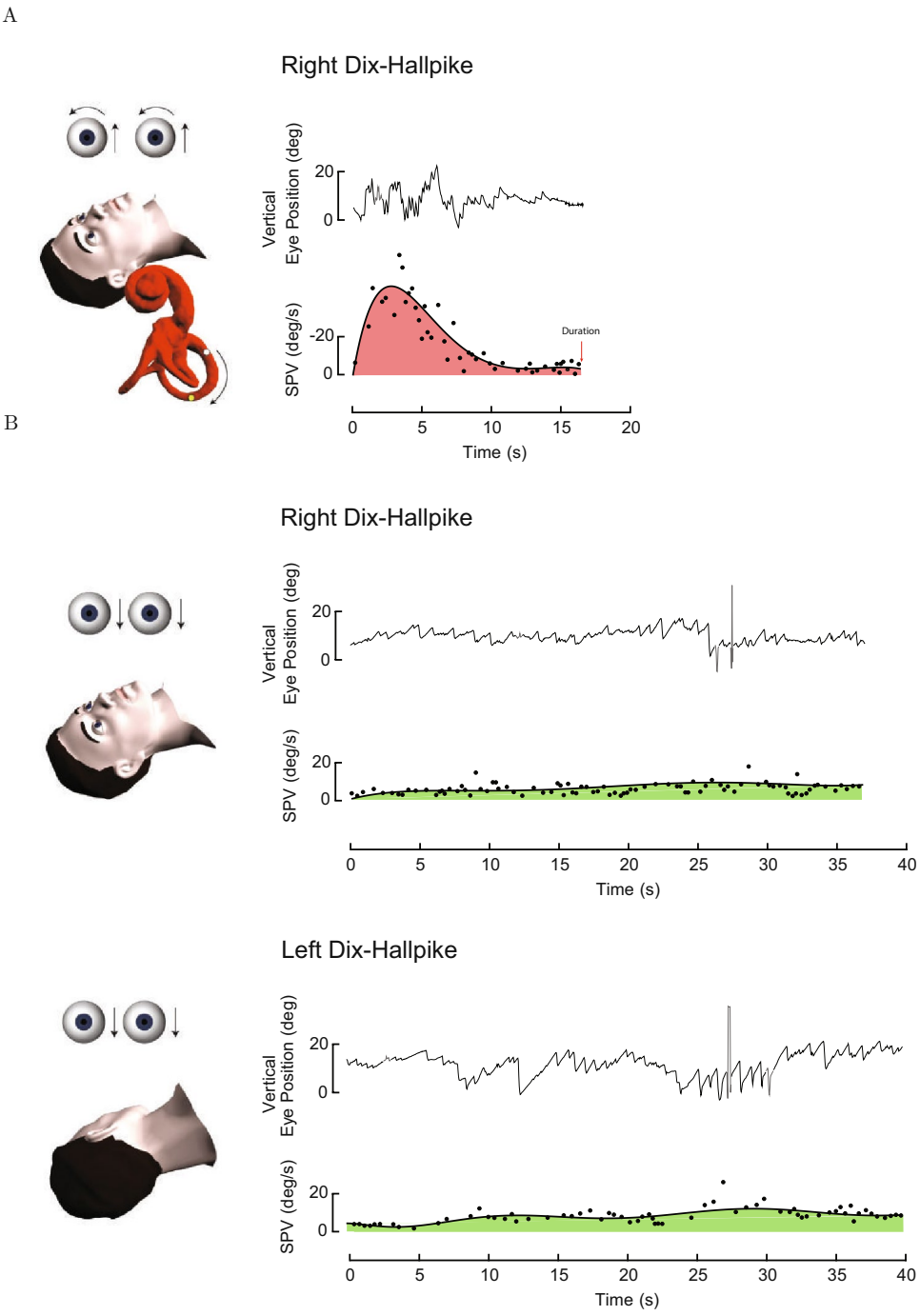

Fig. 4 Posterior canal BPV versus non-paroxysmal positional nystagmus. **a** The patient has right-sided posterior canal BPV with a paroxysm of up-beating rightward torsional nystagmus in the right Dix–Hallpike test. A typical crescendo-decrescendo waveform of velocity–time is displayed in red. **b** A patient with central positional nystagmus due to vestibular migraine has persistent downbeat nystagmus in both Dix–Hallpike positions. The velocity–time curves in green are flatter depict a persistent nystagmus that did not cease while the head remained in the Hallpike position. *SPV* slow phase velocity

Structured assessment in EPV

On multivariate analysis, no questions on structured history significantly distinguished BPV from non-BPV.

Ictal nystagmus in EPV

Mean peak-SPV with the affected ear down was 43.5 ± 33.8°/s and 69.1 ± 51.9°/s for PC and HC BPV. The time taken for halving of peak-SPV (T50) for PC and HC BPV were 14.4 and 13.8 s. Mean duration of nystagmus for PC and HC BPV were 32.4 ± 35.4 and 45.5 ± 42.2 s. For non-BPV positional vertigo, mean peak SPV, T50 and paroxysm duration were 24.5 ± 15.4°/s, 46.8 and 361.1 ± 437.5 s. Positional nystagmus duration under 60 s distinguished BPV from central positional nystagmus with a sensitivity of 90% and specificity of 100% (95% CI 0.75–0.97,0.56–1). VOG characteristics of EPV are summarised in Supplementary Appendix 6.

Comparison between Intervention and Treatment as Usual

There were 115 patients in the ER control group. Their demographics and vertigo characteristics are summarised in Supplementary Appendix 2. The ER diagnoses were BPV (38.3%), "Vertigo" (27.8%), "Peripheral Vertigo" (11.3%), VN (5.2%), MD (2.6%), mal de debarquement (0.9%) and no diagnosis (13.9%). Only 40.9% of diagnosed BPV had a corroborative history of positional vertigo or a positive Dix–Hallpike Test. Only 50% of diagnosed VN had an abnormal head-impulse documented. When unblinded clinicians perused the notes, the prevalence of a diagnosis concordant with the history and examination was 30.4% and 90.3% for the control and intervention groups. The "undiagnosed" subset included those classified as "vertigo", "peripheral vertigo", BPV without Hallpike testing and VN without a history of spontaneous vertigo, spontaneous nystagmus or a positive head-impulse test. The history and examination extracted from all patients was used to generate a single de-identified history and examination sheet (Supplementary Appendix 1) and provided to four blinded clinicians (GMH, NR, SRDW, MW). Video nystagmus findings were incorporated qualitatively (e.g. paroxysmal up-beating torsional nystagmus, positive head impulse). Clinicians were asked to place each patient in one of the following categories: AVS-VN, AVS Non-VN, ATVS, EVS VM, EVS MD, EVS undifferentiated, BPV, non-BPV positional vertigo, CVS or unknown. The mean rate of categorical diagnosis by blinded examiners was 41.1% and 86.3% in the control and intervention groups.

Discussion

In this study, we sought to improve the rate of "capture" of acute vertigo in ER. A structured history and video-eye examination was used on all patients; in the context of AVS, audiometry and vHIT were used to perform an objective and verifiable HINTS examination. A twofold increase in the diagnostic rates of acutely vertiginous patients was secured. Our findings indicate that a structured history and quantitative testing can improve the number of vertiginous patients leaving ER with a correct diagnosis.

Previous studies have demonstrated that specialist neurology or neuro-otology involvement in ER improves the diagnostic accuracy of vertigo by 26–60% [32–34]. In previous studies, clinical assessment protocols reduced unnecessary investigations and hospitalisation and improved the outcomes of patients presenting with vertigo [35]. Reported specialist diagnosis rates in emergency neuro-otology settings ranged from 44 to 93%. [13, 36–38]. Ictal nystagmus characteristics were also reported to help identify the aetiology of vertigo in ER [39, 40].

Clinical and quantitative HINTS

Clinical *HINTS* helped separate PCS from VN with 88.9% sensitivity and 91.8% specificity and remains a powerful diagnostic tool but required a skilled examiner. When quantitative HINTS assessment was done using vHIT and video-oculography we achieved comparable sensitivity and specificity of 93.1 and 88.5%. We propose that it is feasible for VOG, vHIT and a hearing test to be used by trained ER physicians separate stroke from VN. The portable, accessible and easy-to-use nature of VOG and vHIT makes it suitable for use in ER as a tool. In the present study, one researcher was an ER physician, who undertook structured history and VOG assessments. We expect that ER physicians could undertake training in eliciting a structured history and using custom-written electronic questionnaire, conducting VOG using equipment with automated analysis. Performing the vHIT, currently undertaken by diverse healthcare professionals in our institution (physicians, nurses, audiologists, physical therapists), is within the capability of a trained ER physician. Automated software analysis plays an important role in the delivery of quantitative results.

Our study used both vHIT gain and refixation-saccade metrics (amplitude and prevalence) to separate VN from PCS. Our observations replicate those of earlier search coil and vHIT studies that like us, demonstrated higher refixation-saccade prevalence, amplitude, peak velocity, duration, and a briefer latency in VN compared with stroke [23, 41].

VM presenting as AVS

Vestibular migraine accounted for ~ 10% of AVS in this study. These patients were investigated and treated as stroke and their diagnoses only became apparent on follow up. This finding suggests that VM presenting as AVS may be a common yet under recognised entity in ER where the diagnosis can only be made after subsequent neuroimaging and follow up. Larger case series with follow up data are needed, to optimise investigation and treatment of this subgroup.

Vertigo without nystagmus

Despite the availability of video event-monitoring in ER, 30% of patients presenting with vertigo demonstrated no ictal nystagmus. Most importantly, 35% of symptomatic stroke patients demonstrated no spontaneous nystagmus, indicating that in stroke, central nystagmus, peripheral nystagmus, or no nystagmus are possible findings. Although previous authors indicated that HINTS testing should not be administered in patients without spontaneous nystagmus [42], we propose that absence of nystagmus, without visual fixation, in the patient with AVS is a valuable "central" sign.

Although an earlier study conducted by our group demonstrated high ictal nystagmus SPV for MD and a high prevalence of ictal nystagmus in VM [22], the present study recorded lower values overall and no ictal nystagmus in the majority of VM. This may represent the delay from symptom onset to arrival in the ER and delays in video assessment. Thus, home-based event monitoring for nystagmus has a higher diagnostic yield in the context of recurrent spontaneous vertigo. It may also be worth recording nystagmus at the time of triage in ER.

Study limitations

Patients were not randomly allocated to our intervention. Prolonged vertigo is likely to have triggered emergency physicians to alert neuro-otology services urgently, which may account for the higher prevalence of AVS in our intervention group when compared with earlier studies [6, 21, 43]. Furthermore, this was a single-centre study which may affect the generalisability of our results. There was a high rate of diffusion weighted imaging (DWI) negative AVS presentations (22%) diagnosed and treated as strokes based on a central oculomotor examination, cranial nerve signs or ataxia (Supplementary Appendix 3). In these ten patients, already diagnosed as PCS, repeat neuroimaging was not undertaken. In DWI negative strokes, neuroimaging was not repeated unless the original MRI was done 48 h before symptom onset. False negative MRI rates in previous studies (12–18%) approach these proportions [13, 21, 44]. Some stroke patients were unable to proceed with the full battery due to safety considerations (e.g. vHIT excluded in suspected dissection).

Our study lacked a gold standard definition of VN which should have included a negative DWI MRI after 48 h in addition to history and examination. We have incorporated HINTS features in our diagnostic criteria for VN. This is problematic when seeking to define the sensitivity and specificity of clinical HINTS in the separation of stroke and VN. Ample validation of bedside HINTS exists in the literature and was not the focus of this manuscript [44–46].

The prevalence of a definitive diagnosis in the intervention group was also increased due to the ability to follow up the patients compared to the ER control group. Our diagnostic rates by the blinded clinicians which included only the information obtained on initial presentation offers a better comparison of the yield of our intervention. Poor documentation of history and physical examination may have resulted in a less complete assessment in the control group which may have artificially lowered the diagnostic rates in the ER group.

Although the vHIT yielded promising results when seeking to separate VN and PCS, some VN patients' vHITs (and bedside HITs) were negative when assessed on day one and demonstrated low gain and refixation saccades one or more days later. We also found that vHIT may appear falsely negative due to delayed catch up saccades that occur after 600 ms, given that the demonstrated eye velocity trace terminates at 600 ms. The present study was undertaken in ER, yet administering the clinical assessment, event monitoring and vestibular tests were undertaken by a neuro-otology fellow, nurse, or a trained emergency physician. Future feasibility studies are needed where all observations are conducted by frontline physicians themselves within ER.

Conclusion

The use of a structured history to separate vestibular syndromes, a structured examination inclusive of vestibular event monitoring and vHIT increases the rate of diagnosis of vertigo in the ER. We propose the use of these three tools to provide quantitative assessment of vertigo in the Emergency Room by emergency physicians.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00415-021-10627-1.

Funding This research was funded by the Garnett Passe and Rodney Williams Memorial Foundation and the National Health and Medical Research Council of Australia.

Data availability Data not published within the article will be available in a public repository and anonymized data will be shared by request from any qualified investigator.

Declarations

Conflicts of interest B. Nham, N. Reid, K. Bein and A.P. Bradshaw have no disclosures relevant to this manuscript. L.A. McGarvie is an unpaid consultant for Otometrics. E.C. Argaet, A.S. Young and S.R. Watson have no disclosures relevant to this manuscript. G.M. Halmagyi is an unpaid consultant for Otometrics. D.A. Black and M.S. Welgampola have no disclosures relevant to this manuscript.

Ethics approval This study received local ethics committee approval for the use of human participants (Protocol X13-0425 and HREC/13/RPAH/591) and written informed consent was obtained from all participants in accordance with the Helsinki Declaration of 1964.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent to publish The authors affirm that human research participants provided informed consent for publication of the images in the figures and videos of this manuscript.

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