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H.I.N.T.S. to Diagnose Stroke in the Acute Vestibular Syndrome —Three-Step Bedside Oculomotor Exam More Sensitive than Early MRI DWI

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Abstract

Background and Purpose—Acute vestibular syndrome (AVS) is often due to vestibular neuritis but can result from vertebrobasilar strokes. Misdiagnosis of posterior fossa infarcts in emergency-care settings is frequent. Bedside oculomotor findings may reliably identify stroke in AVS, but prospective studies have been lacking.

Methods—Prospective, cross-sectional study at an academic hospital. Consecutive AVS patients (vertigo, nystagmus, nausea/vomiting, head-motion intolerance, unsteady gait) with ≥1 stroke risk factor underwent structured examination including horizontal head impulse test (h-HIT) of

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vestibulo-ocular-reflex function, observation of nystagmus in different gaze positions, and prism cross-cover test of ocular alignment. All underwent neuroimaging and admission (generally <72 hours after symptom onset). Strokes were diagnosed by MRI or CT. Peripheral lesions were diagnosed by normal MRI and clinical follow-up.

Results—101 high-risk AVS patients included 25 peripheral and 76 central lesions (69 ischemic strokes, 4 hemorrhages, 3 other). The presence of either normal h-HIT, direction-changing nystagmus in eccentric gaze, or skew deviation (vertical ocular misalignment) was 100% sensitive and 96% specific for stroke. Skew was present in 17% and associated with brainstem lesions (4% peripheral, 4% pure cerebellar, 30% brainstem involvement, χ^2 p=0.003). Skew correctly predicted lateral pontine stroke in 2 of 3 cases where an abnormal h-HIT erroneously suggested peripheral localization. Initial MRI DWI was falsely negative in 12% (all <48hrs after symptom onset).

Conclusions—Skew predicts brainstem involvement in AVS and can identify stroke when an abnormal h-HIT falsely suggests a peripheral lesion. A three-step bedside oculomotor exam (H.I.N.T.S.: Head-Impulse—Nystagmus—Test-of-Skew) appears more sensitive for stroke than early MRI in AVS.

Keywords

vertigo; diagnosis; cerebrovascular accident; neurologic examination; sensitivity and specificity

Acute vestibular syndrome (AVS) is characterized by the rapid onset (over seconds to hours) of vertigo, nausea/vomiting, and gait unsteadiness in association with head-motion intolerance and nystagmus, lasting days to weeks. Patients often have a self-limited, presumed-viral cause for their symptoms known as vestibular neuritis or labyrinthitis, classified together as *acute peripheral vestibulopathy* (APV). Of the 2.6 million emergency department visits for dizziness or vertigo annually in the US, APV is diagnosed in nearly 150,000.[1] However, some patients with AVS instead harbor dangerous brainstem or cerebellar strokes that mimic APV.[2–6] Small observational studies suggest perhaps 25% or more of acute vestibular syndrome presentations to the emergency department represent posterior-circulation infarctions.[3, 6] CT scans have low sensitivity (~16%) for acute infarction,[7] particularly in the posterior fossa,[8] and brain MRI is not always readily available. Studies also suggest that false negative MRI can occur with acute vertebrobasilar strokes.[6, 9, 10] Consequently, bedside predictors are essential to identify patients with acute *central* vestibulopathies.

While classical teaching suggests a focus on long-tract or frank cerebellar signs,[11, 12] fewer than half of AVS presentations have limb ataxia, dysarthria, or other obvious neurologic features.[6] Careful eye movement assessment may be the only bedside method to identify vertebrobasilar stroke in these patients.[8] The most consistent bedside predictor of pseudo-labyrinthine stroke in AVS appears to be the horizontal head impulse test (h-HIT) of vestibulo-ocular reflex (VOR) function[8] (Video 1 a/b). This test was first described in 1988 by Halmagyi and Curthoys as a bedside test for peripheral vestibular disease.[13] Some authors have suggested the h-HIT be used as a definitive test to distinguish APV from stroke in AVS patients.[4, 14] Recent studies provide evidence that a *normal* VOR by h-HIT strongly

indicates a central localization, but an *abnormal* VOR is a weaker predictor of a peripheral localization.[5, 6] The sign's diagnostic utility is diluted principally by the fact that some patients with abnormal h-HIT (implying APV) actually harbor lateral pontine strokes.[6]

Another bedside predictor of central pathology in the acute vestibular syndrome is nystagmus which changes direction on eccentric gaze.[5] AVS should generally be associated with a characteristic, dominantly-horizontal nystagmus that beats only in one direction and increases in intensity when the patient looks in the direction of the nystagmus fast phase.[15, 16] Vertical or torsional nystagmus in this clinical context is a clear sign of central pathology, but most strokes presenting an AVS picture have nystagmus with a predominantly horizontal vector that mimics APV.[6] What sometimes distinguishes the nystagmus typical of central AVS from APV is a change in direction on eccentric gaze[6] (Video 2 a/b).

A third bedside predictor of central pathology is skew deviation. Skew deviation is vertical ocular misalignment that results from a right-left imbalance of vestibular tone (i.e., neural firing), particularly otolithic inputs, to the oculomotor system.[17] It often occurs as part of the pathologic ocular tilt reaction (OTR)—the subtle clinical triad of skew deviation, head tilt, and ocular counterroll.[17] Skew is generally detected by alternate cover testing (Video 3), with or without a quantifiable prismatic correction. Although reported in patients with diseases of the vestibular periphery,[18] skew (with or without complete OTR) has principally been identified as a central sign in those with posterior fossa pathology.[17] It is most commonly seen with brainstem strokes[17] and has been reported as a herald manifestation of basilar occlusion.[19] A recent retrospective case-control study comparing oculomotor features in those with vestibular neuritis (i.e., APV) to those with "vestibular pseudoneuritis" (mostly due to stroke) suggests skew deviation could be a specific sign of central disease in AVS patients.[5]

We sought to assess the diagnostic accuracy of skew deviation for identifying stroke in AVS, including any added value beyond h-HIT. We hypothesized that the presence of skew would be insensitive but specific for stroke and that it would add probative diagnostic information to h-HIT results alone. We further sought to assess the overall sensitivity and specificity of a three-step bedside oculomotor exam (Head-Impulse—Nystagmus—Test-of-Skew or "H.I.N.T.S.") for differentiating stroke from APV in AVS.

Materials and Methods

Data derive from an ongoing study of stroke in AVS patients over the past nine years. The study methods have been detailed previously in a report of h-HIT findings in 43 subjects[6] whose clinical data are also presented here in a larger series (101 subjects). Briefly, we present results of a prospective, cross-sectional study of patients presenting with AVS, focusing on those at high risk for stroke. This IRB-approved study was conducted at a single urban, academic hospital serving as a regional stroke referral center for 25 community hospitals. Patients with the core features of AVS (rapid onset of vertigo, nausea, vomiting, and unsteady gait, with or without nystagmus) were identified primarily from the hospital emergency department (ED). Additional patients were identified by review of stroke

admissions for cerebellar infarction. Included were patients with at least one stroke risk factor (smoking, hypertension, diabetes, hyperlipidemia, atrial fibrillation, eclampsia, hypercoagulable state, recent cervical trauma, or prior stroke or myocardial infarction). Excluded were subjects with a history of prior recurrent vertigo, with or without auditory symptoms.

For patients consenting to screening, the study neuro-ophthalmologist (JCK) conducted a neurologic and vestibular examination (including h-HIT, prism cross-cover test for ocular alignment, and observation of nystagmus in different gaze positions) according to a standard protocol.[6] A search for ocular counterroll by head-upright fundus photography to determine the presence of complete pathologic OTR was performed in patients with either head tilt or vertical misalignment (suspected skew) without internuclear ophthalmoplegia (INO). We defined severe truncal ataxia as the inability to sit upright unassisted without the use of arms to stabilize, and included patients where lethargy may have contributed to their inability to sit.

All patients underwent neuroimaging, generally after bedside evaluation. If neuroimaging was performed prior to the study evaluation, the examiner was masked to these results at the time of clinical assessment. All patients (including suspected APV patients) were admitted for observation and underwent serial daily examinations for evolution of clinical findings. The reference standard for a stroke diagnosis was confirmation of acute stroke by neuroimaging, generally MRI with DWI on the day of the index visit. The reference standard for a diagnosis of APV was absence of acute stroke in the brainstem or cerebellum by MRI with DWI, lack of neurologic signs on serial exam, and a characteristic clinical course. Most also underwent confirmatory caloric testing of vestibular function.

For predictive accuracy of skew deviation, we compared proportions with skew deviation in peripheral versus central cases, and offer results stratified by h-HIT findings. Based upon prior literature suggesting that three subtle oculomotor signs (normal h-HIT, direction-changing nystagmus, and skew deviation) might be, in aggregate, the best predictor of stroke in AVS,[8] we analyzed these three signs together. A priori, we defined the H.I.N.T.S. exam as either *benign* (abnormal h-HIT *plus* direction-fixed horizontal nystagmus *plus* absent skew) or *dangerous* (normal/untestable h-HIT *or* direction-changing horizontal nystagmus present/untestable *or* skew deviation present/untestable) and compared this test battery's sensitivity, specificity, and likelihood ratios for the presence of stroke relative to other neurologic findings and early MRI with DWI. We calculate both *positive* likelihood ratios (the extent to which dangerous H.I.N.T.S. increase the odds of stroke or "rule in" the disease) and *negative* likelihood ratios (the extent to which benign H.I.N.T.S. decrease the odds of stroke or "rule out" the disease). Fisher's exact and Pearson's chi-squared were used for comparison of proportions with SAS 9.1 (SAS Institute Inc., Cary, NC). Likelihood ratios and confidence intervals were calculated with MedCalc 9.6 (MedCalc Software, Mariakerke, Belgium). All p-values were two-sided, with $p<0.05$ considered significant.

Results

We screened 121 AVS patients and excluded 19 for a history of recurrent vertigo or dizziness (7 Menière syndrome, 5 vestibular migraine, 4 idiopathic recurrent vertigo, and 3 other disorders). One eligible subject refused enrollment. Of 101 patients reported here, 92 were identified by primary clinical screening, and 9 through review of admitted cerebellar infarcts. Fifty-nine presented initially to the ED, 4 were inpatients at symptom onset, 1 presented as an outpatient, and 37 were transferred to the neurology ward from other institutions (mostly from affiliate hospital EDs admitted directly to the stroke service).

The study population was 65% men with a mean age of 62 years (standard deviation 13 years, range 26–92). The age range for stroke patients was 26–92 with 15 patients under age 50, including 6 under age 40. In 30%, only 1 stroke-risk factor was present; the others had at least 2 risk factors. Most were examined within 24 hours of symptom onset (75%). In 5 patients, the precise time of exam relative to symptom onset was unclear, because the precise time of symptom onset was unknown. Among the remaining 96 patients, the mean time to first examination was 26 hours (range 1 hour to 9 days).

Most patients (97%) underwent stroke-protocol MRI at the time of admission. One patient underwent CT followed by open MRI at another facility because of claustrophobia, and 3 underwent CT but no MRI (one was claustrophobic, one died prior to obtaining MRI, and one required ventriculo-peritoneal shunt placement and was too ill for MRI). All 3 who did not have MRI had unequivocal cerebellar stroke by CT. Initial imaging occurred within 6 hours of study examination in most (70%). Among the 96 patients in whom time of symptom onset was known, imaging occurred within 72 hours of symptom onset in 97%; two patients were imaged at 4 days and one at 9 days after AVS onset. Eight with initial negative MRI underwent repeat MRI for unexplained signs (on initial or follow-up examination) suggesting brainstem localization. No patients suffered complications from diagnostic testing, other than one claustrophobic reaction.

Of 101 high-risk AVS patients, 25 had APV and 76 had a central lesion. Peripheral lesions were confirmed by caloric testing in 22 patients (19 with canal paresis, usually severe; 3 with only directional preponderance); two patients could not complete testing due to discomfort and one refused. Central lesions included 69 ischemic strokes, 4 hemorrhages (1 dentate nucleus, 3 pontine [2 with pontine cavernoma]), 2 demyelinating disease (1 presumed midbrain lesion, 1 medullary lesion), and 1 anticonvulsant toxicity (carbamazepine). Two patients did not have a demonstrable structural lesion on MRI that corresponded with the acute clinical syndrome (1 patient with seesaw nystagmus and a presumed midbrain lesion who had demyelinating lesions elsewhere in the brain and the patient with anticonvulsant toxicity). Key clinical features suggesting a central localization (n=76) are presented in Table 1. These features are stratified by stroke location for ischemic lesions (n=69) in Table 2.

Acute auditory symptoms were infrequent but associated with strokes in the AICA territory and presumed secondary to labyrinthine infarction, cochlear nucleus involvement, or both. Craniocervical pain was more common among patients with central than peripheral lesions

(38% vs. 12%, p=0.02). All patients were unsteady (i.e., broad-based gait or difficulty with tandem walking), but severe truncal ataxia (inability to sit without the use of arms or assistance) was seen only among those with central lesions (34% vs. 0%, p<0.001). As expected, lateral medullary (n=7), lateral pontine (n=5), and inferior cerebellar strokes (n=12) frequently mimicked APV (absent general neurologic or obvious oculomotor signs) while medial brainstem cerebrovascular events did not (45% vs. 5%, p=0.001). Another 36% of these lateral brainstem and cerebellar events (including one dentate hemorrhage) had severe truncal ataxia as their only obvious sign. Not surprisingly, medially-located brainstem strokes and hemorrhages were associated with oculomotor paralysis while lateral brainstem and cerebellar cerebrovascular events were not (80% vs. 0%, p<0.001).

Skew deviation (mean 9.9 prism-diopters, range 3–20) was present in 17% of our 101 subjects (case descriptions in online supplement) and untestable in 4% with central lesions due to seesaw nystagmus or oculomotor paralysis. Despite the large vertical ocular deviations, only three patients complained of symptomatic diplopia at presentation, and two of these had co-morbid INO; several patients became aware of their diplopia during the cross cover test or developed symptomatic diplopia days or weeks after presentation as their oscillopsia abated. Skew was evident in 4% (n=1/25) with APV, 4% (n=1/24) with pure cerebellar lesions, and 30% (n=15/50) with demonstrated structural brainstem involvement (χ^2 p=0.003). A complete OTR was found in 6 subjects, all with brainstem strokes (2 lateral medullary, 2 lateral pontine, 2 interstitial nucleus of Cajal). Results of cross-cover testing for skew deviation, stratified by h-HIT result, are compared to final diagnosis based on neuroimaging and clinical follow-up in Table 3. The majority (59%) of skews were associated with lateral medullary or lateral pontine strokes. Finding a skew correctly predicted the presence of a central lesion in 2 of 3 cases of lateral pontine stroke where a positive h-HIT incorrectly suggested benign APV and 7 of 8 cases with false negative initial MRI. Taking skew together with h-HIT and direction-changing nystagmus as a three-step bedside exam battery, a dangerous H.I.N.T.S. result was 100% sensitive and 96% specific for the presence of a central lesion, giving a positive likelihood ratio of 25 (95%CI 3.66–170.59) and a negative likelihood ratio of 0.00 (95%CI 0.00–0.11). Compared to traditional findings thought to indicate brainstem or cerebellar involvement in AVS, the H.I.N.T.S. battery was more sensitive than general neurologic signs (100% vs. 51%), obvious oculomotor signs (100% vs. 32%), or both of these taken together (100% vs. 67%) (all p<0.001).

Neuroimaging by MRI with DWI was falsely negative in 8 ischemic stroke patients (5 lateral medullary, 1 lateral ponto-medullary, and 2 middle cerebellar peduncle infarctions). Negative scans were obtained 8–48 hours after symptom onset, including 4 that were negative at 24 hours or beyond. Follow-up MRI an average of 3 days later (range 2 to 10 days) revealed the strokes. The sensitivity of early MRI with DWI for lateral medullary or pontine infarction was lower than that of the bedside exam (72% vs. 100%, p=0.004) with comparable specificity (100% vs. 96%, p=1.0). MRA, performed in 33 of 69 with ischemic stroke, revealed unilateral vertebral or PICA occlusion in 15, bilateral vertebral stenosis in 3, and was normal in 15. Four were diagnosed radiographically with vertebral artery dissection, all young (ages 26, 35, 42, 52).

Imaging evidence of mass effect was seen in the initial scan in nine patients, and in follow-up scan in one patient, all with cerebellar involvement. Among these 10 of 23 patients with cerebellar infarction, 3 were lethargic, but 7 had isolated, severe truncal ataxia without other obvious neurologic signs at or near the time of imaging showing mass effect. In the majority of APV patients (92%), MRI revealed non-specific areas of periventricular high signal intensity on T2 or FLAIR imaging but normal DWI compatible with chronic gliosis, presumed secondary to ischemic leukoencephalopathy in this population with one or more stroke risk factors.

Discussion

Our study demonstrates that skew deviation in AVS is strongly linked to the presence of brainstem lesions, most often ischemic strokes in the lateral medulla or pons. This study also proves that finding one of three dangerous, subtle oculomotor signs (normal h-HIT *or* horizontal nystagmus that changes direction in eccentric gaze *or* skew deviation) is more sensitive than the combined presence of all other traditional neurologic signs for identifying stroke as a cause of AVS. The dangerous signs can be remembered using the acronym I.N.F.A.R.C.T. (Impulse Normal, Fast-phase Alternating, Refixation on Cover Test). Perhaps most importantly, we have shown that a benign H.I.N.T.S. exam result at the bedside “rules out” stroke better than a negative MRI with DWI in the first 24–48 hours after symptom onset, with acceptable specificity (96%).

The association between skew deviation and brainstem stroke is not surprising. Although cases of primary-position skew have been reported with peripheral vestibular disease and alternating skew deviation in lateral gaze is seen in some patients with bilateral cerebellopathy, lesions causing skew and the pathologic OTR have most often been found in the brainstem.[17] Our prospective findings build on prior retrospective work suggesting a strong link between subtle oculomotor signs and stroke in patients with central AVS mimicking APV.[4, 5] Although a normal h-HIT remains the single best bedside predictor of stroke[6] and its test properties are comparable to those of early MRI DWI, roughly one in ten strokes will still be missed if other findings are not considered. We have identified two other subtle findings that should improve bedside detection of stroke without substantial loss of specificity.

Although physicians have become increasingly reliant on MRI DWI for acute stroke diagnosis, our study presents further evidence that care should be taken not to use DWI alone to rule out stroke in AVS in the first 24–48 hours after symptom onset. In our series, the sensitivity of DWI was 88% overall and 72% for lateral medullary and lateral pontine infarctions, with these localizations very frequent among vertebrobasilar strokes mimicking APV closely. These estimates echo results from two prior studies of early DWI that reported on 206 vertebrobasilar strokes and found 77% sensitivity within 24 hours of symptom onset.[9, 10]

Frontline misdiagnosis of posterior circulation strokes presenting with dizziness appears common, occurring in perhaps 35% of cases.[20] The high rate of misdiagnosis may not be surprising given that 58% of patients in our series either had no obvious signs or had only

isolated, severe truncal ataxia. Inappropriate reliance on CT to exclude stroke likely exacerbates the problem.[21, 22] The consequences of such misdiagnoses can be profound, with one small series of missed cerebellar infarctions indicating adverse outcomes in 40%.[21] Misdiagnosis may be more likely in younger patients who are not generally considered to be at risk for stroke.[21] Vertebral artery dissections, the leading identifiable cause of posterior circulation stroke among young adults,[23] can present with an APV mimic.[24] We found 15 of our stroke patients were under age 50, and 3 of these were due to dissections.

Although the bedside techniques in the H.I.N.T.S. exam are not widely known among emergency physicians, internists, or even general neurologists, non-neuro-otologists can accurately interpret subtle oculomotor findings of this type,[25] suggesting that training in the use of these techniques may be possible. The three components of the H.I.N.T.S. (h-HIT of VOR function; observation for nystagmus in primary, right, and left gaze; alternate cover test for skew deviation) can be tested in approximately 1 minute at the bedside, while a more thorough, traditional neurologic exam generally takes 5–10 minutes or more. An acute MRI brain with DWI takes at least 5–10 minutes of scan time plus a wait time of several hours to several days and typically costs more than $1000. In an era where efficiency and cost containment are at a premium, this bedside method may offer a quick, inexpensive alternative to current practice. While additional confirmatory studies in a broader range of acute vestibular patients are needed, our data suggest that in time-pressured, frontline healthcare settings this approach could potentially supplant complete neurologic examination and neuroimaging without loss of diagnostic accuracy.

We identified several possible limitations to our study findings. Threats to internal validity include a partially-unmasked examiner and selective MRI follow-up scans. As described previously,[6] the study examiner (JCK), though masked to the results of imaging, was not masked to the patient's clinical history, general neurologic exam, or obvious oculomotor findings when testing for subtler eye signs. Observer bias in the interpretation of subtle eye findings could have artificially inflated the sensitivity of these signs, but this seems unlikely for the 33% of cases where obvious neurologic findings were absent. MRI follow-up scans were obtained in only selected cases based on evolution of new neurologic signs or atypical subtle oculomotor signs. This selective re-testing could have led to some misclassification of strokes as APV, increasing the apparent sensitivity of the H.I.N.T.S. battery. However, all of these APV patients were followed and evolved no neurologic deficits acutely nor suffered strokes in clinical follow-up.

Threats to external validity include generalizability of examination technique and sampling from a high-risk subpopulation. Since patients were evaluated by a single examiner, it is unknown whether clinical findings could have been replicated by other examiners. The growing literature on these subtle eye signs from multiple investigators suggests reproducibility, at least among subspecialists in the field.[4–6] We restricted our enrollment to high-risk AVS patients with no history of prior recurrent vertigo and at least one stroke risk factor. We chose this approach because funds were not available to image all low-risk patients in whom MRI could not be justified clinically. This selection led to a highly-enriched cerebrovascular cohort (76% central, 73% cerebrovascular, 69% ischemic stroke) and APV patients who might be atypical (92% with leukoariosis). It is possible that a

broader spectrum of APV patients could have disclosed more with negative h-HIT results (including those with isolated inferior vestibular neuritis[26]) or the other two subtle signs, reducing the specificity of the "dangerous" H.I.N.T.S. result. However, a previous study of unselected AVS patients suggests otherwise, estimating a 92% specificity when subtle eye signs were considered in a statistical prediction model.[5]

Summary

As has been shown previously, we found that lateral medullary, lateral pontine, and inferior cerebellar infarctions mimic APV very closely, and great caution must be exercised to avoid missing these posterior circulation strokes in AVS patients. One in five strokes causing AVS affects a patient under age 50 and one in ten a patient under age 40. Typical neurologic signs are absent in roughly half, and more than half of those with mass effect from large cerebellar infarctions have only severe truncal ataxia without other obvious neurologic or oculomotor signs. Initial MRIs are falsely negative in 12% and can prove misleading out to 48 hours after symptom onset.

Skew deviation is an insensitive marker of central pathology but fairly specific predictor of brainstem involvement among AVS patients. The presence of skew may help identify stroke when a positive h-HIT falsely suggests a peripheral lesion. Screening AVS patients for one of three dangerous oculomotor signs (normal h-HIT, direction-changing nystagmus, skew deviation) appears to be more sensitive than MRI with DWI in detecting acute stroke in the first 24–48 hours after symptom onset. These "H.I.N.T.S. to I.N.F.A.R.C.T." could help reduce frontline misdiagnosis of patients with stroke in AVS and should be studied head-to-head for their comparative cost-effectiveness against neuroimaging by MRI DWI.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Authors' contributions

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1. conceptualized and designed study, conducted primary data collection and analyses
2. authored data tables, critically reviewed and edited manuscript
3. approved final

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1. helped with data acquisition
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David Wang

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Yu Hsiang Hsieh

1. conducted statistical analyses
2. critically reviewed and edited manuscript
3. approved final

David Newman-Toker

1. helped conceptualize data analysis plan, oversaw data analysis
2. authored primary manuscript draft and all major revisions
3. approved final

Responsibility for Manuscript

The corresponding author (David Newman-Toker) had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. The corresponding author also had final responsibility for the decision to submit for publication.

Role of Medical Writer or Editor

No medical writer or editor was involved in the creation of this manuscript.

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All persons who have made substantial contributions to the work but who are not authors

None.

IRB Approval

This study was approved by the Institutional Review Board of The University of Illinois College of Medicine at Peoria.

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Table 1

Key clinical features in patients with peripheral versus central AVS

Symptoms, Signs, and Imaging at Presentation	PAVS n=25	CAVS n=76	NLR Central (95%CI)
Associated symptoms	12%	41%	0.67 (0.53–0.85)*
• acute auditory symptoms	0%†	3%	0.97 (0.94–1.01)
• headache or neck pain	12%	38%	0.70 (0.56–0.88)*
General neurologic signs (including truncal ataxia)	0%	51%	0.49 (0.39–0.61)*
• facial palsy	0%	1%	0.99 (0.96–1.01)
• hemisensory loss	0%	3%	0.97 (0.94–1.01)
• crossed sensory loss	0%	3%	0.97 (0.94–1.01)
• dysphagia/dysarthria	0%	3%	0.97 (0.94–1.01)
• limb ataxia	0%	5%	0.95 (0.90–1.00)
• mental status abnormality (lethargy)	0%	7%	0.93 (0.88–0.99)
• hemiparesis (including UMN facial weakness)	0%	11%	0.89 (0.83–0.97)
• severe truncal instability (cannot sit unassisted)	0%	34%	0.66 (0.56–0.77)*
Obvious oculomotor signs	0%	32%	0.68 (0.59–0.80)*
• dominantly vertical or torsional nystagmus	0%	12%	0.88 (0.81–0.96)
• oculomotor paralysis (3–4–6, INO, gaze palsy)	0%	21%	0.79 (0.70–0.89)*
Subtle oculomotor signs	4%	100%	0.00 (0.00–0.11)*
• direction-changing horizontal nystagmus	0%	20%	0.80 (0.72–0.90)*
• skew deviation present or untestable	4%‡	25%§	0.78 (0.67–0.91)*
• h-HIT normal or untestable	0%	93%//	0.07 (0.03–0.15)*
Initial imaging abnormal#	92%	97%	0.33 (0.05–2.22)
• acute infarct or hemorrhage +/− chronic lesions	0%	86%	0.14 (0.08–0.25)*
• other acute pathology +/− chronic lesions	0%	1%	0.99 (0.96–1.01)
• only chronic lesions (leukoariosis)#	92%	11%	11.2 (2.95–42.35)*

AVS – acute vestibular syndrome; CAVS – central AVS; INO – internuclear ophthalmoplegia; NLR – negative likelihood ratio; PAVS – peripheral AVS

*p<0.05 for difference of proportion present in PAVS versus CAVS

†Patients with recurrent peripheral audio-vestibular disease were excluded from the study, therefore the absence of auditory symptoms in PAVS may not represent an unbiased estimate.

‡Two patients with peripheral lesions developed skew deviation more than a week after symptom onset. These patients did not have skew at initial examination and are not counted here.

§Includes 3 patients with untestable skew deviation due to obvious oculomotor pathology.

//Includes 4 patients with untestable h-HIT due to lethargy or obvious oculomotor pathology.

#All subjects were required to have at least one stroke risk factor, so it is not surprising that imaging would often show evidence of leukoariosis even in those with peripheral diagnoses.

Table 2

Key clinical features in central AVS caused by ischemic stroke, by lesion location

Symptoms and Signs at Initial Presentation	LM +/− C (n)	LP or MCP +/− C (n)	MP or MM (n)	MB (n)	CO (N+) (n)	CO (N−) (n)	TOTAL (n)
Associated symptoms	5	2	0	1	6	14	**28**
• acute auditory symptoms	0	2	0	0	0	0	**2**
• headache or neck pain	5	0	0	1	6	14	**26**
General neurologic signs	10	7	2	3	2	9	**33**
• limb ataxia	0	0	0	1	0	0	**1**
• crossed sensory loss	2	0	0	0	0	0	**2**
• dysphagia/dysarthria	2	0	0	0	0	0	**2**
• mental status abnormality (lethargy)	0	0	0	0	0	3	**3**
• hemiparesis (including UMN facial weakness)	0	3	1	1	0	0	**5**
• severe truncal instability (cannot sit unassisted)	6	4	1	1	2	9	**23**
Oculomotor signs	17	12	11	6	8	15	**69**
• dominantly vertical or torsional nystagmus	3	1	1	1	0	0	**6**
• oculomotor paralysis (3-4-6, INO, gaze palsy)	0	0	9	5	0	0	**14**
• direction-changing horizontal nystagmus	7	4	0	0	1	3	**15**
• skew deviation present	6	4	2	3*	0	1	**16***
• h-HIT normal	17	8	11	5*	8	13*	**62***
TOTAL Ischemic Strokes	**17**	**12**	**11**	**6**	**8**	**15**	**69**

C cerebellum; CO cerebellum only; INO – internuclear ophthalmoplegia; LM lateral medulla; LP lateral pons; MCP middle cerebellar peduncle; MM medial medulla; MP medial pons; MB midbrain; (N+) nodulus involved; (N−) nodulus not involved

* does not count untestable cases (2 h-HIT, 2 skew; see Table 3)

Table 3

Skew deviation relative to neuroimaging in AVS, stratified by h-HIT results

	No stroke by final imaging (n)	Stroke by final imaging (n)	Other CNS Diagnosis
Skew Deviation absent	24	51	6
normal h-HIT	*0*	*47*	*4*
abnormal (untestable) h-HIT	*24 (0)*	*3 (1*[*]*)*	*0 (2*[†]*)*
Skew Deviation present	1	16	0
normal h-HIT	*0*	*14*	*0*
abnormal (untestable) h-HIT	*1 (0)*	*2 (0)*	*0 (0)*
Skew Deviation untestable	0	2[†]	1[†]
normal h-HIT	*0*	*1*	*1*
abnormal (untestable) h-HIT	*0 (0)*	*0 (1*[†]*)*	*0 (0)*
TOTAL	25	69	7

[*] untestable due to lethargy

[†] untestable due to oculomotor pathology (gaze palsy, bilateral 3rd palsy, seesaw nystagmus)

Table 4

Bedside signs and initial MRI with DWI test properties for ischemic stroke in AVS

	Sensitivity (n=69)	Specificity (n=25)	NLR Stroke (95%CI)
General neurologic signs*	19%	100%	0.81 (0.72–0.91)
Obvious oculomotor signs	28%	100%	0.72 (0.63–0.84)
Severe truncal ataxia	33%	100%	0.67 (0.56–0.79)
Any obvious signs	64%†	100%	0.36 (0.27–0.50)
Initial MRI with DWI	88%‡	100%	0.12 (0.06–0.22)
Dangerous bedside H.I.N.T.S.	100%	96%	0.00 (0.00–0.12)

APV – acute peripheral vestibulopathy; DWI – diffusion weighted imaging; NLR – negative likelihood ratio; H.I.N.T.S. – Head-Impulse-Nystagmus-Test-of-Skew

*excluding severe truncal ataxia

†of 25 ischemic strokes without obvious signs, 12 were pure cerebellar, 7 were lateral medullary, 5 were lateral pontine or middle peduncle, and 1 was a medial brainstem infarct

‡false negative initial MRI with DWI occurred in 5 patients with lateral medullary infarctions, 1 with lateral ponto-medullary infarction, and 2 with middle cerebellar peduncle infarction