CRITICALLY APPRAISED TOPIC

FOCUSED CLINICAL QUESTION

In a 70-year old male with acute vestibular syndrome (AVS), is a bedside exam or imaging better at determining the cause (central vs. peripheral)?

AUTHOR

Prepared by	Christie Clem	**Date**	November 24, 2015
Email address	cclem@med.unc.edu		

CLINICAL SCENARIO

During my acute clinical rotation, I saw multiple patients that had AVS and it was a more common presentation that I had expected. My clinical instructor has completed additional vestibular training and was often called to examine these patients on the same day they were admitted to the hospital. There were a few patients that the physicians diagnosed with peripheral vestibular impairment, but after doing a bedside exam my CI thought they had a central cause. Some physicians were willing to have an open discussion and others adamantly stated it was not a central cause because the MRI was negative.

AVS can be from a peripheral cause such as vestibular neuritis or labyrinthitis, or from a central cause such as posterior circulation stroke in the brainstem or cerebellum. AVS can begin in a matter of seconds; it consists vertigo, nausea/vomiting, and gait imbalance due to nystagmus or motion intolerance which lasts days up to weeks.[1] Some studies found that ≥25% of the patients with AVS that are seen in the emergency department have posterior circulation infarcts.[1,2]

SUMMARY OF SEARCH

[Best evidence appraised and key findings]

- Ten studies met the inclusion/exclusion criteria and were included in the review: one systematic review, four prospective cross-sectional studies, one ambispective cross-sectional study, one proof of concept study, and three retrospective chart reviews.
- Isolated acute vestibular syndrome (AVS) can be caused by a posterior circulation stroke and present without the more common general neurologic signs. These strokes can be caused by lacunar or nonlacunar mechanisms and have been identified in both younger and older adults.
- A multi-step bedside oculomotor exam such as HINTS (**H**ead **I**mpulse, **N**ystagmus, **T**est of **S**kew) or HINTS "plus" (the addition of finger rub for hearing) is more sensitive for stroke in patients with AVS than MRI performed within 48 hours. A negative early MRI should not be the deciding factor in ruling out stroke.
- The bedside oculomotor exam is reliable when performed by neuro-otology specialists and in clinicians that have received a few hours of training. Increased training and implementation of the bedside exam could increase the recognition of stroke in patients with isolated AVS and improve patient care.

CLINICAL BOTTOM LINE

Evidence suggests that a multi-part bedside oculomotor exam such as HINTS or HINTS "plus" is better at ruling out stroke in patients with isolated AVS as compared to MRI performed within 48 hours of symptom onset. Although, MRI does have better specificity for ruling in a stroke. Because of the rate of false negative early MRIs in patients with AVS, some evidence suggests waiting at least 48 hours before performing the first MRI to gain a more accurate result. The HINTS exam can be performed in a less than a few minutes, but does require some training to accurately interpret the results. Clinicians that had only a few hours of general neuro-otology training were able to reliably differentiate between a central and peripheral cause of AVS.

This critically appraised topic has been individually prepared as part of a course requirement and has been peer-reviewed by one other independent course instructor

The above information should fit onto the first page of your CAT

SEARCH STRATEGY

Terms used to guide the search strategy			
Patient/Client Group	**I**ntervention (or Assessment)	**C**omparison	**O**utcome(s)
Older adult* Elderly Geriatric Aging Acute vestibular syndrome Vestibular neuritis Vestibular labyrinthitis Dizzy* Vertigo Vestib*	Exam Test Screen Vestibular Nystagmus Head thrust Head impulse	Image* Magnetic resonance imaging Magnetic resonance angiogram x-ray Computerized axial tomography Radiology MRI CT	Diagnosis* Cause Etiology Central Peripheral Stoke Infarct Neuritis

Final search strategy:

Show your final search strategy from one of the databases you searched. In the table below, show how many results you got from your search from each database you searched.

For PubMed

1. older adult* OR elderly OR geriatric OR aging
2. acute vestibular syndrome OR vestibular neuritis OR vestibular labyrinthitis OR dizzy* OR vertigo OR vestib*
3. exam OR test OR screen
4. vestibular OR nystagmus OR head thrust OR head impulse
5. image* OR magnetic resonance imaging OR magnetic resonance angiogram OR x-ray OR computerized axial tomography OR radiology OR MRI OR CT
6. diagnosis* OR cause OR etiology
7. central OR peripheral OR stroke OR infarct OR neuritis
8. #1 AND #2 AND #3 AND #4 AND #5 AND #6 AND #7
9. #8 Filters: humans, English

Databases and Sites Searched	**Number of results**	**Limits applied, revised number of results (if applicable)**
PubMed	**105**	**90 – filter humans, English**
Cochrane Library	**14**	
CINAHL	**0** **126**	**#8 (search line)** **#2 AND #4 AND #6 AND #7 – filter English** **All of these titles/abstracts were reviewed for relevance**

INCLUSION and EXCLUSION CRITERIA

Inclusion Criteria
• English • Published before September 2015 • Included any type of imaging in determining diagnosis • Included any part of vestibular exam in determining diagnosis • Adults > 50 years old • Study design: prospective/cohort, cross-sectional, retrospective, or case-control
Exclusion Criteria
• Narrative reviews, abstracts, editorials • Studies with pediatric patients • Patients with moderate to severe cognitive impairments • Patients with acute traumatic injuries

RESULTS OF SEARCH

Summary of articles retrieved that met inclusion and exclusion criteria

For each article that meets your inclusion and exclusion criteria, score for methodological quality on an appropriate scale, categorize the level of evidence, and note the study design (e.g., RCT, systematic review, case study).

Author (Year)	Study quality score	Level of Evidence	Study design
Tarnutzer (2011)[3]	**Validity checklist from Jewell** **Moderate risk**	**4**	**Systematic review**
Chen (2010)[4]	**QUADAS-2** **10/11-low risk**	**1b**	**Prospective cross-sectional study**
Kattah et al (2009)[1]	**QUADAS-2** **10/11**	**1b**	**Prospective cross-sectional study**
Newman-Toker et al (2008)[2]	**QUADAS-2** **9/11**	**1b**	**Prospective cross-sectional study**
Sabre Tehrani et al (2014)[5]	**QUADAS-2** **10/11**	**2b**	**Ambispective cross-sectional study**
Newman-Toker et al (2013)[6]	**QUADAS-2** **8/11**	**1b**	**Prospective cross-sectional study**
Newman-Toker et al (2012)[7]	**QUADAS-2** **10/11**	**2b exploratory**	**Proof of concept**
Braun et al (2011)[8]	**QUADAS-2** **9/11**	**2b**	**Retrospective chart review**
Casani et al (2012)[9]	**QUADAS-2** **6/11**	**4**	**Retrospective chart review**
Morita et al (2011)[10]	**QUADAS-2** **7/11 – moderate risk**	**2b**	**Retrospective chart review**

(All 10 articles should appear in the reference list at the end)

BEST EVIDENCE

The following 3 studies were identified as the 'best' evidence and selected for critical appraisal. Reasons for selecting these studies were:

- Kattah et al (2009)[1]: This is a prospective cross-sectional study (level 1b), that assessed the overall sensitivity and specificity of HINTS, a 3 step oculomotor bedside exam (Head Impulse, Nystagmus, Test of Skew) for differential diagnosis between stroke and acute peripheral vestibulopathy in patients that had acute vestibular syndrome along with ≥1 stroke risk factor. A positive HINTS exam was 100% sensitive and 96% specific for acute stroke, while MRI taken <48 hours from symptom onset was falsely negative in 12% of the patients. This study had a larger sample size than any of the other studies and directly applies to the patient in my PICO question.
- Chen et al (2010)[4]: This is a prospective cross-sectional study (level 1b) that assessed the accuracy of using a 4 part oculomotor bedside exam to diagnose posterior circulation stroke from vestibular neuritis in patients with acute vestibular syndrome in a hospital. Finding 1 component of the 4-part exam was 100% sensitive and 90% specific for stroke. Computerized tomography and transcranial Doppler missed 40% of the strokes. This study was of particular interest because the oculomotor exam was performed by clinicians

with little neuro-otology training (3 hour video and 1 hour training), which I believe is similar to many clinicians (including myself as a future clinician).

- Saber Tehrani et al (2014)[5]: This is a ambispective cross sectional study (level 2b). It is ambispective because a retrospective chart analysis was done on subjects that were part of a prospective cross-sectional study. The charts of patients with acute vestibular syndrome that were caused by a small posterior circulation stroke (<10 mm) were analyzed. The diagnostic accuracy of the bedside exam HINTS Plus (head impulse, nystagmus, test of skew, hearing with finger rub) was compared to that of imaging. The study showed low risk of bias earning 10/11 points on the QUADAS-2 and specifically looked at the charts of patients that had an initial false-negative MRI for stroke.

SUMMARY OF BEST EVIDENCE

(1) Description and appraisal of HINTS to Diagnose Stroke in the Acute Vestibular Syndrome: Three-Step Bedside Oculomotor Examination More Sensitive Than Early MRI Diffusion-Weighted Imaging by Kattah, J., Talkad, A., Wang, D., Hseih, Y., and Newman-Toker, D. (2009)

Aim/Objective of the Study/Systematic Review:

The aim of this study was to determine the diagnostic accuracy of the HINTS exam, a bedside exam consisting of 3 oculomotor tests (**H**ead **I**mpulse, **N**ystagmus, **T**est of **S**kew), to identify the cause of acute vestibular syndrome (AVS) as either a stroke or acute peripheral vestibulopathy (APV).

Study Design

[e.g., systematic review, cohort, randomized controlled trial, qualitative study, grounded theory. Includes information about study characteristics such as blinding and allocation concealment. When were outcomes measured, if relevant]

Note: For systematic review, use headings 'search strategy', 'selection criteria', 'methods' etc. For qualitative studies, identify data collection/analyses methods.

- Prospective, cross-sectional study at one academic regional stroke center hospital in the United States
- Subjects were consecutive patients admitted with AVS with at least 1 risk factor for stroke over a 9-year period. Additional subjects were identified as having a cerebellar stroke at admission.
- Non-study physicians identified the potential subjects at admission and then contacted the study neuro-ophthalmologist for screening
- Neurological and vestibular exam was performed by a single neuro-ophthalmologist; neuro-ophthalmologist was blinded to neuroimaging results, but not to the patient's history, neurological exam, or vestibular exam
- Neuroimaging according to the hospital's stroke protocol was performed on all patients (usually after the clinical exam); no comment on who read the imaging results
- All subjects were admitted to the hospital and underwent daily observation and examination by the same neuro-ophthalmologist that performed the initial exam to identify neurologic or vestibular changes; subjects were seen in the outpatient setting 2 weeks after discharge to look for any improvements

Setting

[e.g., locations such as hospital, community; rural; metropolitan; country]

All subjects were patients admitted to one academic hospital in an urban setting in the United States.

This hospital was a stroke center for 25 smaller regional hospitals. Information was not provided about where the outpatient follow-up appointments took place.

Participants

[N, diagnosis, eligibility criteria, how recruited, type of sample (e.g., purposive, random), key demographics such as mean age, gender, duration of illness/disease, and if groups in an RCT were comparable at baseline on key demographic variables; number of dropouts if relevant, number available for follow-up]

Note: This is not a list of the inclusion and exclusion criteria. This is a description of the actual sample that participated in the study. You can find this descriptive information in the text and tables in the article.

- Subjects were consecutive patients with AVS (quick onset of vertigo, nausea, vomiting, and unsteady gait, with or without nystagmus) and at least 1 stroke risk factor (smoking, high blood pressure, diabetes, atrial fibrillation, hyperlipidemia, eclampsia, hypercoagulable state, recent neck trauma, or history of stroke or myocardial infarction) that were identified by an emergency department physician that was not involved in the study
- Additional subjects were consecutive patients with identified cerebellar stroke that presented with severe

truncal ataxia or gait instability, but did not have nystagmus, extremity weakness or ataxia, or other clear signs of a brainstem lesion
- 121 total subjects with AVS and stroke risk factors OR cerebellar stroke were screened by the single study neuro-ophthalmologist
- 101 of these subjects met additional inclusion criteria and agreed to participate; 92 were included by the clinical screen and 9 were included due to cerebellar stroke; all 101 patients were included in the final analysis
- 49 were admitted through the emergency department, 37 were transferred from other hospitals, 4 were inpatients that developed symptoms, and 1 was identified in an outpatient setting
- Population description: 65% men, mean age 62 years (range 26-92), 75% were examined within 24 hours of symptom presentation, 95% were examined within 26 hours of onset
- 76 of the subjects were diagnosed with a stroke; the ages ranged from 26-92 years, 6 of the subjects with a stroke were <40 years old and 9 were between 40-49 years
- 30% of the subjects with a stroke had 1 risk factor while 70% had ≥2 risk factors
- 97% of subjects had an MRI according to stroke protocol at admission; the 3 subjects that did not have an MRI had a CT that confirmed a cerebellar stroke; imaging happened within 6 hours of the clinical exam for 70% of subjects and within 72 hours for 92% of the total patients
- A second MRI was performed on 8 subjects that had an initially negative MRI due to the development of neurologic symptoms or a change in the HINTS exam during daily follow-up exams

Intervention Investigated

[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided]

All patients (prospective cohort study for diagnostic accuracy)

- Received neurologic and vestibular exam at admission to screen for participants; performed by a single neuro-ophthalmologist
    - Vestibular exam included: horizontal head impulse test (h-HIT), prism cross-over test for alignment of eyes, multiple gaze positions to identify nystagmus)
    - Standard protocol for bedside exam
        - Ability to balance trunk in sitting and standing; tandem gait it trunk balance was normal
        - Eye movements: look for spontaneous nystagmus in primary gaze position, ocular vergence tests, both horizontal and vertical saccadic movements and smooth pursuit tests, sustained eccentric gaze and gaze evoked nystagmus in different directions
        - Eye movements were again tested with Frenzel goggles, which took away the patient's ability to fix their gaze: looked for spontaneous nystagmus in primary and eccentric positions. Movements to induce nystagmus, such as head shaking, hyperventilation, vibration to the mastoid, and positional testing were performed if no spontaneous nystagmus was present
        - Horizontal head impulse test (h-HIT): the head started in the eccentric position (rotated to 1 side) and was moved back to a midline position; repeated multiple times
        - General neurologic exam
- Neuroimaging according to stroke protocol to diagnose stroke; typically performed on the day of the bedside exam – did not comment on who performed the imaging or interpreted the results
- Admitted to the hospital for daily neurologic exam to monitor for changes and progression of signs/symptoms; performed by the same neuro-ophthalmologist that did the initial screen
- The majority of patients diagnosed with APV, underwent caloric testing to confirm a peripheral cause at a follow-up appointment 2 weeks after discharge

Outcome Measures (Primary and Secondary)

[Give details of each measure, maximum possible score and range for each measure, administered by whom, where]

- All components of the clinical exam were performed by a single neuro-ophthalmologist at bedside
- Reference (gold) standard for diagnosing stroke- MRI with diffusion weighted imaging (DWI)
- Reference (gold) standard for acute peripheral vestibulopathy (APV) or peripheral acute vestibular syndrome (PAVS)– no acute brainstem or cerebellar stroke on MRI, no neurological findings on repeated daily neurological exam, and a characteristic APV course
    - 22 of the 25 patients diagnosed with APV had caloric testing to confirm a peripheral vestibular cause
- HINTS exam [Head Impulse, Nystagmus, Test of Skew) for subtle oculomotor signs
    - Benign: abnormal h-HIT AND direction-fixed horizontal nystagmus AND no skew deviation
    - Abnormal/positive: normal or variable h-HIT OR horizontal direction changing nystagmus OR the presence of a skew deviation
- Severe truncal imbalance/ataxia defined as inability to sit without upper extremity support (part of inclusion

criteria for patients with cerebellar stroke)

- h-HIT: assesses the vestibule-ocular reflex; examiner quickly moves the head from an eccentric position to a straight ahead position while the patient keeps the eyes fixed on the examiners nose throughout. The ability to keep the eyes fixed is a negative (normal) finding. A positive (abnormal) result would be a corrective saccade that is needed to reposition the eyes on the examiner's nose. An abnormal h-HIT when the head is rotated toward the side of the lesion is characteristic of a peripheral vestibular problem.
- Nystagmus: gaze evoked nystagmus is tested by having the patient look straight ahead (primary position) and to each side (right and left gaze) for several seconds while keeping the head in midline. Nystagmus is named by the direction of the fast beat (this is the corrective saccade). With peripheral vestibular damage nystagmus beats away from the side of the lesion.
- Test of Skew: skew deviation is tested by the alternate cover test (the examiner uses his hand to cover 1 of the patient's eyes and then moves the hand to cover the other). The examiner is looking at the vertical alignment of the eyes, which would be maintained by the right/left vestibular tone. A positive (abnormal) finding would be an eye that moves up/down to re-align during the test.

Main Findings

[Provide summary of mean scores/mean differences/treatment effect, 95% confidence intervals and p-values etc., where provided; you may calculate your own values if necessary/applicable]

- 76 of the 101 total subjects had a central lesion (69 ischemic stroke, 4 hemorrhagic stroke, 2 demyelinating conditions, 1 anticonvulsant toxicity) that caused the AVS
- 25 of the 101 total subjects had a peripheral lesion that caused the AVS;
    - 22 of the 25 subjects had the peripheral cause confirmed with caloric testing at a follow-up appointment
- Signs/symptoms for all subjects with a peripheral cause (PAVS) vs. a central cause (CAVS)
    - Acute hearing changes, headache, or neck pain: PAVS 12%, CAVS 41%; NLR 0.67, *
    - Neurological signs (sensory, motor, or cognitive changes): PAVS 0%, CAVS 51%; NLR 0.49, *
    - Major oculomotor signs (nystagmus that is vertical or torsional, paralysis): PAVS 0%, CAVS 32%; NLR 0.68, *
    - Subtle oculomotor signs, these test make up the HINTS exam: PAVS 4%, CAVS 100%; NLR 0.00 Large effect, *
        - Normal Horizontal Head Impulse Test (h-HIT): PAVS 0%, CAVS 93%; NLR 0.07 large effect, *
        - Direction changing horizontal nystagmus: PAVS 0%, CAVS 20%; NLR 0.80, *
        - Positive skew deviation or untestable (ie. Paralysis): PAVS 4%, CAVS 24%; NLR 0.78, *
    - Initial imaging with acute ischemic or hemorrhagic findings: PAVS 0%, 86%; NLR 0.14 moderate effect *
        - Negative likelihood ratio: the extent to which a normal (benign) HINTS decreases the odds of a stroke, 95% CI, * p= <0.05 difference in symptoms between PAVS and CAVS
- A positive (dangerous) HINTS exam was 100% sensitive and 96% specific for CAVS; PLR of 25 (95% CI, 3.66 – 170.59); NLR 0.00 (95% CI, 0.00 – 0.12)
    - HINTS was more sensitive than general neurologic exam, obvious oculomotor signs, and early MRI <48 hours from symptom onset
- A negative h-HIT was the strongest single predictor of stroke from the 3 parts of the HINTS exam; NLR 0.07
- Positive skew deviation identified strokes in 7 of the 8 subjects with that had a false negative on initial MRI
- 8 of the 69 subjects (12%) with an ischemic stroke had falsely negative MRI results on the initial early scan
    - follow-up MRI obtained 2-10 days later were positive for stroke
- Early MRI with DWI had a sensitivity of 88% (72% for lateral medullary and lateral pontine locations) and specificity of 100% for posterior circulation ischemic stroke; NLR 0.12 (moderate effect) for stroke with normal (benign) HINTS
- The sensitivity of bedside exam (HINTS) is more accurate than early MRI (<48 hours) for ischemic stroke

Original Authors' Conclusions

[Paraphrase as required. If providing a direct quote, add page number]

A positive or abnormal HINTS exam (normal or variable h-HIT OR horizontal direction changing nystagmus OR the presence of a skew deviation) in a patient with AVS has a higher sensitivity for stroke than MRI with DWI done within 48 hours of symptom onset (100% vs. 88%). Therefore, HINTS is the better tool to rule out stroke in patients with AVS. The abnormal findings for HINTS can be remembered by the INFARCT acronym: **I**mpulse **N**ormal, **F**ast-phase **A**lternating, **R**efixation on **C**over **T**est. [(p. 3507)] If AVS is caused by a peripheral lesion, one would expect to see direction fixed nystagmus that beats away from the side of the lesion and a positive h-HIT when the head is rotated toward the side of the lesion. Of the 3 parts of the HINTS exam, a normal h-HIT was the most common indicator for stroke. The sensitivity of h-HIT alone in this study was 89% which is almost identical to early MRI. Skew deviation is able to identify many of the posterior circulation strokes that are

missed by early MRI and a positive h-HIT test that would point incorrectly point toward a peripheral cause of AVS.

Critical Appraisal

Validity

[Identify the strengths and limitations of the study, including potential sources of bias. Comment on the overall methodological quality (including the score) as you determined from your assessment of the article. Comment on anything you believe was missing in the paper.]

- QUADAS-2 Score: 10/11. Patient selection: consecutive sample: yes; case-controlled design avoided: yes; avoided inappropriate exclusions: yes; could patient selection have introduced bias: low risk; Index test: index test results interpreted without knowledge of reference standard results: yes; pre-specified threshold: yes; could interpretation of index test introduce bias: low; Reference standard: reference standard likely to correctly classify condition: yes; reference standard results interpreted with knowledge of index test: yes; could interpretation of reference standard introduce bias: low; Flow and timing: appropriate interval between index and reference: yes; all patients get reference standard: no; all patients included in analysis: yes; could patient flow have introduced bias: low; Concerns regarding applicability: concern that patients don't match review question: low; concern index test differed from review question: low; concern that target condition didn't match review question: low.
- The neuro-ophthalmologist was blinded to the reference standard results (imaging), but not blinded to the patient history and initial clinical exam (general neurological or obvious oculomotor) when performing the HINTS exam
- Not all subjects with an initially negative MRI results had a follow-up MRI. Only subjects that had a change in neurologic signs/symptoms or a newly abnormal HINTS exam at a daily follow-up exam received a second MRI. Some subjects that were diagnosed with peripheral AVS could have actually had a central lesion
- The subject sample is not generalizable to the entire population because all subjects had to have at least 1 stroke risk factor to be included in the study
- The HINTS exam was performed by a trained neuro-ophthalmologist; not all clinicians may be adequately trained in these techniques

Interpretation of Results

[This is YOUR interpretation of the results taking into consideration the strengths and limitations as you discussed above. Please comment on clinical significance of effect size / study findings. Describe in your own words what the results mean.]

This study found that a positive (dangerous) HINTS exam is better at ruling out a stroke in patients with acute vestibular than an MRI with DWI done within 48 hours of symptom onset. This is important because patients with AVS caused by a stroke can present with no other neurological symptoms. Being able to perform the HINTS exam in less than 2 minutes can allow for better identification, monitoring, treatment, and education for the patients. The 3 parts of the HINTS exam are easy to perform, but the interpreting the results of the tests could be difficult for some clinicians. In this study all of the bedside exams were performed by a single trained neuro-ophthalmologist. Interpretation of the tests might not have been as accurate or consistent if performed by multiple, less trained clinicians.

76 of the 101 total subjects in this study had a central lesion with 69 being an ischemic stroke. These numbers lead me to think that the majority of patients with AVS have central cause, but this could be because all of the subjects included in the study had to have at least 1 stroke risk factor. If patients with AVS, but without stroke risk factors were included the incidence of AVS caused by central lesion would probably decline and the sensitivity and specificity of the HINTS exam might show different results. Because neuroimaging is expensive cost could be a limiting factor in including additional patients in similar studies.

Overall, the study was well conducted. The 100% sensitivity and 96% specificity of a positive or abnormal HINTS exam to identify a central cause of AVS is clinically meaningful. Patients would benefit if clinicians, both PTs and physicians, learned this bedside exam and implemented it into their practice.

(2) Description and appraisal of Small strokes causing severe vertigo: Frequency of false-negative MRIs and nonlacunar mechanisms by Saber Tehrani, A., Kattah, J., Mantokoudis, G., et al. (2014)

Aim/Objective of the Study/Systematic Review:

The aim of this study was to describe the characteristics of small strokes that cause acute vestibular syndrome (AVS) from patients that were previously identified during a prospective cross-sectional study.

Study Design

[e.g., systematic review, cohort, randomized controlled trial, qualitative study, grounded theory. Includes information about study characteristics such as blinding and allocation concealment. When were outcomes measured, if relevant]

Note: For systematic review, use headings 'search strategy', 'selection criteria', 'methods' etc. For qualitative studies, identify data collection/analyses methods.

- Ambispective, cross-sectional study at one academic regional stroke center hospital in the United States
  - A retrospective analysis of subjects in a prospective cross-sectional study
- Prospective study to identify cause of AVS as central or peripheral
  - Subjects were consecutive patients admitted with AVS with at least 1 risk factor for stroke over a 12-year period. Additional subjects were identified as having a cerebellar stroke at admission.
  - Non-study physicians identified the potential subjects at admission and then contacted the study neuro-ophthalmologist for screening
  - Neurological and vestibular exam was performed by a single neuro-ophthalmologist; neuro-ophthalmologist was blinded to neuroimaging results, but not to the patient's history, neurological exam, or vestibular exam
  - Neuroimaging according to the hospital's stroke protocol was performed on all patients (usually after the clinical exam); no comment on who read the imaging results
  - All subjects were admitted to the hospital and underwent daily observation and examination by the same neuro-ophthalmologist that performed the initial exam to identify neurologic or vestibular changes
- Retrospective analysis
  - The charts and imaging results of all subjects with AVS in the prospective study were reviewed to determine the size of the stroke lesion; no comment on who reviewed the charts
  - The anatomical location of the stokes were confirmed by 2 posterior fossa neuroimaging experts and 2 otoneurologists

Setting

[e.g., locations such as hospital, community; rural; metropolitan; country]

All subjects were patients admitted to one academic hospital in an urban setting in the United States. This hospital was a stroke center for 25 smaller regional hospitals.

Participants

[N, diagnosis, eligibility criteria, how recruited, type of sample (e.g., purposive, random), key demographics such as mean age, gender, duration of illness/disease, and if groups in an RCT were comparable at baseline on key demographic variables; number of dropouts if relevant, number available for follow-up]

Note: This is not a list of the inclusion and exclusion criteria. This is a description of the actual sample that participated in the study. You can find this descriptive information in the text and tables in the article.

- Subjects were consecutive patients with AVS (quick onset of vertigo, nausea, vomiting, and unsteady gait, with or without nystagmus) and at least 1 stroke risk factor (smoking, high blood pressure, diabetes, atrial fibrillation, hyperlipidemia, eclampsia, hypercoagulable state, recent neck trauma, or history of stroke or myocardial infarction) that were identified by an emergency department physician that was not involved in the study
- Additional subjects were consecutive patients with identified cerebellar stroke that presented with severe truncal ataxia or gait instability, but did not have nystagmus, extremity weakness or ataxia, or other clear signs of a brainstem lesion
- 190 total subjects presented with AVS and stroke risk factors; 105 of these presentations were caused by stroke
- The charts/imaging results for all 105 of the subjects with AVS caused by stroke were reviewed
- 15 of the 105 (14%) subjects had a small lesion; small lesion defined as ≤ 10 mm
- Population description of the 14% with a small lesion: mean age 65.4 years, median age 64, age range 41-85; 33% female, 67% male, 80% Caucasian, 20% African American

- Time between symptom onset and MRI: lesions ≤ 10 mm – Median 12 hours, interquartile range 6-48 hours; >10 mm – Median 12 hours, interquartile range 4-24 hours
- 97% of patients had MRI with diffusion-weighted imaging (DWI); the 3% that did not have an MRI had a large stroke confirmed by CT and were too unstable to undergo MRI

Intervention Investigated

[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided]

All patients (initially from a prospective cohort study for diagnostic accuracy; retrospective analysis)

- Prospective cross-sectional study
    - Received neurologic and vestibular exam at admission to screen for participants; performed by a single neuro-ophthalmologist
        - Vestibular exam included: horizontal head impulse test (h-HIT), prism cross-over test for alignment of eyes, multiple gaze positions to identify nystagmus)
        - Standard protocol for bedside exam: balance, eye movements, general neurologic exam
    - Neuroimaging according to stroke protocol to diagnose stroke; typically performed on the day of the bedside exam – did not comment on who performed the imaging or interpreted the results
    - Admitted to the hospital for daily neurologic exam to monitor for changes and progression of signs/symptoms; performed by the same neuro-ophthalmologist that did the initial screen
- Retrospective imaging/chart analysis
    - MRI-DWI results for all subjects with AVS caused by stroke were analyzed
        - The size and anatomic location of the stroke was confirmed
    - The frequency of the small lesions was determined
    - Results of the bedside exam were compared to MRI-DWI results

Outcome Measures (Primary and Secondary)

[Give details of each measure, maximum possible score and range for each measure, administered by whom, where]

- Stroke confirmed by MRI-DWI: visible lesion and no evidence of another etiology
- No stroke: no visible lesion on MRI-DWI, no neurologic signs during initial or follow-up bedside exams
- Stroke size
    - Small lesions ≤10 mm axial diameter
    - Large lesions >10 mm axial diameter

Main Findings

[Provide summary of mean scores/mean differences/treatment effect, 95% confidence intervals and p-values etc., where provided; you may calculate your own values if necessary/applicable]

- 15 of the 105 (14%) subjects with a stroke had a small lesion
- The most commonly involved vestibular structure was the inferior cerebellar peduncle (73%)
- The most commonly location for the lesion was the lateral medulla (60%)
    - Two-thirds of these subjects presented with isolated AVS initially
- Only 27% of the subjects with small lesions presented with non-oculomotor (general neurologic) signs at admission
- The bedside HINTS "plus" exam (**H**ead **I**mpulse, **N**ystagmus, **T**est of **S**kew plus finger rub hearing) had better sensitivity than MRI-DWI done within 48 hours of onset when identifying small strokes in subjects with AVS. (HINTS plus 100%, early MRI 47%, n=7/15; p<0.001); in subjects with isolated AVS (sensitivity: HINTS plus 100%, early MRI 36%, n=4/11, p<0.001)
- False-negative MRIs happened between 6 and 48 hours after vestibular symptoms began
- MRI-DWI sensitivity decreased with small lesions; small 47%, large 92%
- The bedside HINTS "plus" sensitivity did not vary with lesion size; small 100%, large 99%
- The h-HIT test incorrectly identified 2 subjects with pontine strokes as having a peripheral cause, but other aspects of the HINTS "plus" exam indicated a central cause
- Nonlacunar mechanisms including vertebral artery dissection, vertebral artery occlusion, and atrial fibrillation were responsible for 7 of the 15 (47%) of the small strokes

Original Authors' Conclusions

[Paraphrase as required. If providing a direct quote, add page number]

Small strokes that cause AVS can happen anywhere in the brainstem, but more often than not occur in the lateral medulla and directly affect the inferior cerebellar peduncle. Approximately 75% of the subjects with small lesions had isolated AVS without general neurologic signs of stroke. The bedside HINTS "plus" exam was

better at identifying small strokes than early MRI (done within 48 hours of onset). An early negative MRI is not sensitive enough to detect small strokes that cause AVS and should not be used alone to rule out a central cause of the AVS.

Critical Appraisal

Validity

[Identify the strengths and limitations of the study, including potential sources of bias. Comment on the overall methodological quality (including the score) as you determined from your assessment of the article. Comment on anything you believe was missing in the paper.]

- From the prospective cross-sectional study (Kattah, 2009)[1]
  - QUADAS-2 Score: 10/11. Patient selection: consecutive sample: yes; case-controlled design avoided: yes; avoided inappropriate exclusions: yes; could patient selection have introduced bias: low risk; Index test: index test results interpreted without knowledge of reference standard results: yes; pre-specified threshold: yes; could interpretation of index test introduce bias: low; Reference standard: reference standard likely to correctly classify condition: yes; reference standard results interpreted with knowledge of index test: yes; could interpretation of reference standard introduce bias: low; Flow and timing: appropriate interval between index and reference: yes; all patients get reference standard: no; all patients included in analysis: yes; could patient flow have introduced bias: low; Concerns regarding applicability: concern that patients don't match review question: low; concern index test differed from review question: low; concern that target condition didn't match review question: low.
  - The neuro-ophthalmologist was blinded to the reference standard results (imaging), but not blinded to the patient history and initial clinical exam (general neurological or obvious oculomotor) when performing the HINTS exam which could have introduced researcher bias
  - Not all subjects with an initially negative MRI results had a follow-up MRI. Only subjects that had a change in neurologic signs/symptoms or a newly abnormal HINTS exam at a daily follow-up exam received a second MRI. Some subjects that were diagnosed with peripheral AVS could have actually had a central lesion
  - The subject sample is not generalizable to the entire population because all subjects had to have at least 1 stroke risk factor to be included in the study
  - The HINTS exam was performed by a trained neuro-ophthalmologist; not all clinicians may be adequately trained in these techniques
- From the retrospective analysis
  - The ≤10 mm size to categorize a small lesion was selected to make sure there was a clear cut-off to identify lesions as small, but the number was somewhat random. Examiners wanted a size that was small enough to be able to identify specific anatomic structure affected instead of a larger region and small enough to be considered clinically unimportant (thought to have a lacunar mechanism)
  - Did not state if the charts/imaging results were reviewed independently and blinded to the other's interpretation

Interpretation of Results

[This is YOUR interpretation of the results taking into consideration the strengths and limitations as you discussed above. Please comment on clinical significance of effect size / study findings. Describe in your own words what the results mean.]

This study found that the bedside HINTS "plus" exam is more sensitive to small strokes than MRI that is performed within 48 hours of symptom onset. The HINTS alone was also more sensitive, but adding the finger rub test to assess for hearing loss identified a patient with a central cause that would have been missed otherwise. The HINTS "plus" can be performed in a short amount of time, but the clinician should be trained in proper technique and in how to correctly interpret the results. Almost 75% of the subjects with small strokes presented with AVS and no general neurologic stroke signs. Being able to administer and interpret the HINTS "plus" might be the only way to identify patients with a stroke that would otherwise be missed.

It is also important to realize that almost half of the small strokes were caused by nonlacunar mechanisms. Nonlacunar or cortical lesions are caused by problems with the larger vessels while lacunar strokes are lesions that are caused by blockage of the small vessels that go to the deep portions of the brain. Typically nonlacunar strokes have a greater risk of death or recurrence, so realizing nonlacunar strokes can present as AVS is important for the overall management of the patient. Because vertebral artery dissections can occur in younger adults that typically are not thought of as patients that are at-risk for stroke, performing HINTS "plus" on anyone with AVS is key for proper identification.

(3) Description and appraisal of Diagnostic Accuracy of Acute Vestibular syndrome at the Bedside in a Stroke Unit by Chen, L., Lee, W., Chambers, R., Dewey, HM. (2010)

Aim/Objective of the Study/Systematic Review:

The purpose of this study is to demonstrate that strokes are reliably differentiated from vestibular neuritis (VN) in the hospital stroke unit even though the clinician has little experience in neuro-otology.

Study Design

[e.g., systematic review, cohort, randomized controlled trial, qualitative study, grounded theory. Includes information about study characteristics such as blinding and allocation concealment. When were outcomes measured, if relevant]

Note: For systematic review, use headings 'search strategy', 'selection criteria', 'methods' etc. For qualitative studies, identify data collection/analyses methods.

- Prospective, cross-sectional study in the stroke unit at one tertiary hospital in the Australia
- Patients were referred to the study investigators if the Emergency Department identified them as having acute isolated vertigo with an unclear etiology, vascular/stroke risk factors, and an inability to be discharged safely due symptoms.
- One of two trained examiners performed the bedside exam on all subjects
    - Neuro-otology training consisted of a 3-hour video lecture and 1-hour small group session
- All subjects had an imaging according to the hospital's stroke protocol (CT, MRI-DWI, MR angiogram, and transcranial Doppler (TCD))
- CT results were available to examiners at the time of the referral and before the bedside vestibular exam
- Examiners were blinded to the results of the MRI until after the bedside vestibular exam

Setting

[e.g., locations such as hospital, community; rural; metropolitan; country]

All subjects were patients admitted to one tertiary hospital in Australia. The hospital stroke unit has approximately 700 admissions per year.

Participants

[N, diagnosis, eligibility criteria, how recruited, type of sample (e.g., purposive, random), key demographics such as mean age, gender, duration of illness/disease, and if groups in an RCT were comparable at baseline on key demographic variables; number of dropouts if relevant, number available for follow-up]

Note: This is not a list of the inclusion and exclusion criteria. This is a description of the actual sample that participated in the study. You can find this descriptive information in the text and tables in the article.

- Subjects were patients identified in the ED who were then admitted to the hospital stoke unit. Subjects had to have acute vertigo, unknown diagnosis, the presence of at least one vascular risk factor (smoking, hypertension, diabetes, dyslipidemia, atrial fibrillation, or trauma to the neck), and be unsafe for discharge due to symptoms.
- 36 subjects were referred to study investigators for possible inclusion over the 1 year period
- 24 were included in the study; 12 were excluded after clinical exam (due to vestibular migraine, BPPV, Horner's syndrome, lower cranial nerve palsy, bedside evidence of stroke)
- Population description of 24 subjects: 63% men, mean age 64 years (range 42-83)
- All subjects had a bedside exam within 72 hours of symptom onset; 17 (71%) were examined within 24 hours of onset
- Subjects were divided into 2 groups according to symptoms: vestibular only and cochleovestibular
    - Vestibular only (n=20); 10 diagnosed with stroke, 10 diagnosed with VN
    - Cochleovestibular (n=4)
- 40% of the subjects with a stroke had 1 vascular risk factor, 60% had ≥ 2 risk factors
- 30% of the subjects with VN had 1 vascular risk factor, 70% had ≥ 2 risk factors
- This was the first episode of vertigo in 100% of the subjects with VN; 20% of the subjects with a stroke had at least 1 previous episode of vertigo that lasted 10-20 minutes
- 50% of the subjects with stroke and 50% of the subjects with VN had gait disturbance

Intervention Investigated

[Provide details of methods, who provided treatment, when and where, how many hours of treatment provided]

All patients

- Received bedside vestibular exam by one of two trained examiners – exam performed within 12 hours of referral to the study examiners
    - 4 part ocular motor exam: horizontal head impulse test (hHIT), nystagmus, skew deviation, and vertical smooth pursuit
- Daily neurologic exam looking for general signs of stroke in addition to the 4 part ocular motor exam
- Neuroimaging according to hospital stroke protocol (CT, MRI-DWI, and MRA) and TCD

Outcome Measures (Primary and Secondary)

[Give details of each measure, maximum possible score and range for each measure, administered by whom, where]

- Reference (gold) standard for diagnosing stroke – positive MRI-DWI
- Reference (gold) standard for diagnosing VN – negative MRI-DWI and no neurologic signs of stroke on daily exam until discharge
- Transcranial Doppler – performed by sonographers and reported by stroke neurologist with neurosonology expertise
- 4 part oculomotor exam (horizontal head impulse test (hHIT), nystagmus, skew deviation, and vertical smooth pursuit) – performed by one of two trained examiners
    - Benign: abnormal/positive hHIT AND unilateral/direction fixed nystagmus, AND no skew deviation, and normal vertical smooth pursuit
        - Positive hHIT: presence of clear catch-up saccade
    - Abnormal/positive for stroke: normal or variable hHIT OR "central" nystagmus OR skew deviation OR abnormal vertical smooth pursuit.
        - Central nystagmus = direction changing, gave-evoked, purely vertical or purely torsional
- Ability to stand unassisted – if able to stand from a lying position without the assistance from another person

Main Findings

[Provide summary of mean scores/mean differences/treatment effect, 95% confidence intervals and p-values etc., where provided; you may calculate your own values if necessary/applicable]

- TCD was normal in all subjects with VN, but missed 70% of the strokes
- MRA was normal in all subjects with VN, but missed 40% of the strokes
- TCD correctly identified all of the subjects with basilar artery or multiple artery stenosis
- MRA found vascular stenosis in 3 subjects that was not identified with TCD
- A positive test result on at least 1 of the 4 ocular motor test resulted in 100% sensitivity and 90% specificity for stroke
    - Central nystagmus 56% sensitivity, 100 specificity
    - Negative hHIT: 80% sensitivity, 90% specificity
    - Skew deviation and head tilt: 50% sensitivity, 90% specificity
    - Skew deviation only: 30% sensitivity, 90% specificity
    - Vertical smooth pursuit: 70% sensitivity, 90% specificity
- All subjects with VN had unidirectional nystagmus and a clear positive hHIT
- The 4 subjects in the cochleovestibular group presented with vertigo and unilateral hearing loss; all had normal MRI-DWI, but 3 had abnormal vertical smooth pursuit and 1 had skew deviation; all 4 suggestive of labyrinthine infarct that did not progress to an anterior inferior cerebellar artery (AICA) infarct

Original Authors' Conclusions

[Paraphrase as required. If providing a direct quote, add page number]

The authors' concluded that using the 4-part ocular motor exam (hHIT, nystagmus, skew deviation, and vertical smooth pursuit) in their hospital stroke unit is a reliable way to differentiate AVS caused by stroke from AVS caused by VN. Both examiners were able to accurately administer and interpret the test results with a very limited about of training in neuro-otology. A positive finding on at least one of the four tests had a 100% sensitivity and 90% specificity for stroke identification. MRA and TCD were accurate in identifying vascular stenosis, but both missed more strokes that the bedside exam and MRI. Subjects in this study that presented with hearing loss and abnormal vertical smooth pursuits or skew deviation had a normal MRI-DWI. These

patients could have had a labyrinthine infarct that did not progress to an anterior inferior cerebellar artery infarct that would have shown up on MRI.

Critical Appraisal

Validity

[Identify the strengths and limitations of the study, including potential sources of bias. Comment on the overall methodological quality (including the score) as you determined from your assessment of the article. Comment on anything you believe was missing in the paper.]

- QUADAS-2 Score: 10/11. Patient selection: consecutive sample: no; case-controlled design avoided: yes; avoided inappropriate exclusions: yes; could patient selection have introduced bias: low risk; Index test: index test results interpreted without knowledge of reference standard results: yes; pre-specified threshold: yes; could interpretation of index test introduce bias: low; Reference standard: reference standard likely to correctly classify condition: yes; reference standard results interpreted with knowledge of index test: yes; could interpretation of reference standard introduce bias: low; Flow and timing: appropriate interval between index and reference: yes; all patients get reference standard: yes; all patients included in analysis: yes; could patient flow have introduced bias: low; Concerns regarding applicability: concern that patients don't match review question: low; concern index test differed from review question: low; concern that target condition didn't match review question: low.
- The trained examiners were blinded to the MRI results at the time of the ocular motor exam, but not blinded to the CT results or the clinical history and presentation of each subject
- All of the subjects had at least 1 vascular risk factor, so this sample may not be generalizable to the general population
- Both examiners received a 3-hour video lecture and a1-hour small group training on neuro-otology including the hHIT. Even thought this is a short amount of training, it is more than some clinicians have received and may not be generalizable to clinicians without any specific training

Interpretation of Results

[This is YOUR interpretation of the results taking into consideration the strengths and limitations as you discussed above. Please comment on clinical significance of effect size / study findings. Describe in your own words what the results mean.]

This study found that a 4-part ocular motor bedside exam is reliable in differentiating between central and peripheral causes of AVS in patients with at least 1 risk factor for stroke. The two examiners did not specialize in neuro-otology, but instead completed a total of four hours of video and small group instruction. This is clinically meaningful, and it supports the idea that non-specialists can be effectively trained in a relatively short amount of time. Because posterior circulation strokes can present as isolated AVS without general neurologic signs, increasing the number of clinicians that are able to recognize when to administer and how to correctly interpret an ocular motor exam will decrease the number of patients with strokes that are misdiagnosed.

EVIDENCE SYNTHESIS AND IMPLICATIONS

Implications for Practice

The evidence reviewed in this paper supports the use of a bedside oculomotor exam in the differential diagnosis between central and peripheral causes of AVS. Posterior circulatory strokes can present as peripheral vestibular disorders causing AVS. More than half of the individuals with AVS caused by a stroke do not have general neurologic signs,[3,6] so the stroke must be identified in another way. Correctly identifying individuals with AVS caused by a stroke is necessary because these individuals are at-risk for additional strokes, complications related to the initial stroke, and death.[3] Both lacunar and nonlacunar mechanisms can be the cause of the stroke.[5] Nonlacuanar mechanisms relate the larger vessels of the brain and can include vertebral artery dissection and vertebral artery occlusion. Younger and middle aged adults are not typically considered to be at-risk for stroke, but vertebral artery dissections have been identified as a cause for AVS in these patients.[1,3,5] No matter the age of the patient, a detailed history, multi-step bedside oculomotor exam, and general neurologic exam should be performed on all patients presenting with AVS. Stroke risk factors, recurrent episodes of dizziness in the preceding weeks or months, auditory symptoms, headache, neck pain or recent trauma all increase the likelihood that a stroke is the cause of the AVS.

A multi-step bedside oculomotor exam, HINTS or HINTS "plus", has been found to have a high sensitivity and specificity in patients with AVS for differentiation between a central and peripheral cause.[1,5] When all components of the HINTS exam are performed, this bedside exam is better at ruling out a stroke than MRI-DWI that is performed within the first 48 hours of symptom onset. Early MRI has been shown to miss AVS causing

strokes in the posterior fossa one out of five times.[3] Because early MRI has a 20% false negative rate in patients with AVS,[3] a negative imaging result should not be the deciding factor to rule out a stroke. The HINTS exam (**H**ead **I**mpulse, **N**ystagmus, **T**est of **S**kew) or HINTS "plus" (addition of the finger rub test for hearing) can be performed in less than two to three minutes with a 100% sensitivity and 96% specificity for a central cause of AVS.[1] If the components of the exam are used individually, the horizontal head impulse test (hHIT) is the most accurate at identifying stroke. The sensitivity of the hHIT alone is almost identical to that of early MRI.[1,3] The abnormal findings for HINTS can be remembered by the INFARCT acronym: **I**mpulse **N**ormal, **F**ast-phase **A**lternating, **R**efixation on **C**over **T**est. [(1p. 3507)] If AVS is caused by a peripheral lesion, one would expect to see direction fixed nystagmus that beats away from the side of the lesion and a positive h-HIT when the head is rotated toward the side of the lesion.

The majority of the studies reviewed for this paper used a trained neuro-ophthalmologist or other neuro-otology specialist to perform the bedside oculomotor exam. Even though the HINTS exam can be performed in less than a few minutes and the tests are simple to administer, the proper interpretation of the results is vital. A study found that the HINTS "plus" was reliable when used in a hospital Stoke Unit by clinicians that had received four hours of general neuro-otology training,[4] but no evidence was found on the accuracy of clinicians that had not received specific training. Overall, posterior stroke identification in individuals with AVS can improve if more clinicians are educated in how to administer and interpret the HINTS exam. Understanding that an abnormal HINTS has higher sensitivity than early MRI can alter patient management and improve patient care.

Implications for Future Research

The studies reviewed for this paper included subjects that presented with AVS and at least one stroke risk factor.[1,4,5] Some stated funding was the reason for only including subjects with stroke risk factors, because they were unable to justify the cost of performing MRIs on individuals that were not at increased risk of stroke. Approximately 70% of the subjects with AVS in the study by Kattah[1] had an ischemic stroke, but this rate could be inflated when compared to the general population because all of the subjects had risk factors for stroke. It is also probable that patients with isolated AVS and no stroke risk factors are incorrectly diagnosed with peripheral AVS in the Emergency Department and discharged. Future research should include patients without stroke risk factors to determine if the diagnostic accuracy of HINTS is as strong in these patients as in those with stroke risk factors.

Research investigating the ability of physical therapists to effectively and accurately perform the HINTS exam should also be conducted. Current studies have used trained specialists, but it is not a realistic option to have neuro-ophthalmologist at all emergency departments and other locations where patients seek help for acute vestibular syndrome. Research identifying the amount of training and the best way to educate clinicians (physical therapists, physicians, and any other providers that evaluate patients with AVS) will help determine the usefulness of the HINTS exam.[1,3]

Notes

- *This section synthesizes your appraisal of your articles; you may mention other related research that you have read or that supports your interpretation and discussion of this evidence. Please be sure to address the quality of the evidence available to guide clinical practice related to your PICO question. Discuss the implications for clinical practice and research.*
- *Students may wish/need to discuss implications with clinicians or peers for suggestions*
- *This section should be ¾-1 page*
- *Be sure to address both implications for clinical practice and future research (separately)*

REFERENCES

[List all references cited in the CAT]

1. Kattah JC, Talkad A V, Wang DZ, Hsieh Y-H, 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. doi:10.1161/STROKEAHA.109.551234.

2. Newman-Toker DE, Kattah JC, Alvernia JE, Wang DZ. Normal head impulse test differentiates acute cerebellar strokes from vestibular neuritis. *Neurology*. 2008;70(24 Pt 2):2378-2385. doi:10.1212/01.wnl.0000314685.01433.0d.

3. Tarnutzer A a., Berkowitz AL, Robinson K a., 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):571-592. doi:10.1503/cmaj.100174.

4. Chen L, Lee W, Chambers BR, Dewey HM. Diagnostic accuracy of acute vestibular syndrome at the bedside in a stroke unit. *J Neurol*. 2011;258(5):855-861. doi:10.1007/s00415-010-5853-4.

5. 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. doi:10.1212/WNL.0000000000000573.

6. Newman-Toker DE, Kerber KA, Hsieh Y-H, et al. HINTS outperforms ABCD2 to screen for stroke in acute continuous vertigo and dizziness. *Acad Emerg Med*. 2013;20(10):986-996. doi:10.1111/acem.12223.

7. Newman-Toker DE, Saber Tehrani AS, Mantokoudis G, et al. Quantitative video-oculography to help diagnose stroke in acute vertigo and dizziness: toward an ECG for the eyes. *Stroke*. 2013;44(4):1158-1161. doi:10.1161/STROKEAHA.111.000033.

8. Braun EM, Tomazic PV, Ropposch T, Nemetz U, Lackner A, Walch C. Misdiagnosis of acute peripheral vestibulopathy in central nervous ischemic infarction. *Otol Neurotol*. 2011;32(9):1518-1521. doi:10.1097/MAO.0b013e318238ff9a.

9. Casani a. P, Dallan I, Cerchiai N, Lenzi R, Cosottini M, Sellari-Franceschini S. Cerebellar Infarctions Mimicking Acute Peripheral Vertigo: How to Avoid Misdiagnosis? *Otolaryngol -- Head Neck Surg*. 2013;148(3):475-481. doi:10.1177/0194599812472614.

10. Morita S, Suzuki M, Iizuka K. False-negative diffusion-weighted MRI in acute cerebellar stroke. *Auris Nasus Larynx*. 2011;38(5):577-582. doi:10.1016/j.anl.2011.01.017.