

Critical Appraisal Worksheet – Diagnosis
Eastern Virginia Medical School EM Journal Club

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Article: (Kattah) HINTS to Diagnose Stroke in the Acute Vestibular Syndrome
Three-Step Bedside Oculomotor Examination More Sensitive Than Early
MRI Diffusion-Weighted Imaging

Study Objectives:

1. Assess the diagnostic accuracy of skew deviation for identifying stroke in AVS, including any added value beyond h-HIT.
2. Assess the overall sensitivity and specificity of a 3-step bedside oculomotor examination (Head-Impulse-Nystagmus-Test-of-Skew [HINTS]) for differentiating stroke from APV in AVS.

Methodology:

A prospective, cross-sectional study of patients presenting with AVS focusing on the high risk for stroke. This IRB- approved study was conducted at a single urban, academic hospital (University of Illinois College of Medicine at Peoria) serving as a regional stroke referral center for 25 community hospitals.

We screened 121 patients with AVS and excluded 19 for a history of recurrent vertigo or dizziness. 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 emergency department, 4 were inpatients at symptom onset, one presented as an outpatient, and 37 were transferred to the neurology ward from other institutions (mostly from affiliate hospital emergency departments admitted directly to the stroke service).

For patients consenting to screening, the study neuro-ophthalmologist (J.C.K.) conducted a neurological 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.

All patients underwent neuroimaging, generally after bedside evaluation. If neuroimaging was performed before the study evaluation, the examiner was masked to these results at the time of clinical assessment. For predictive accuracy of skew deviation, they compared proportions with skew deviation in peripheral versus central cases and offer results stratified by h-HIT findings.

A priori, we defined the HINTS examination 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 neurological findings and early MRI with DWI.

We calculate both positive likelihood ratios (the extent to which dangerous HINTS increase the odds of stroke or "rule in" the disease) and negative likelihood ratios (the extent to which benign HINTS decrease the odds of stroke or "rule out" the disease).

Inclusion Criteria: 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 ED. Additionally

patients were identified by review of stroke admissions for cerebellar infarct. Included were patients with at least 1 stroke risk factor (smoking, HTN, DM, HLD, Afib, eclampsia, hypercoagulable state, recent cervical trauma, or prior stroke or MI).

Exclusion Criteria:

Patients with a history of recurrent vertigo with or without auditory symptoms.

Are the Results Valid?*	
<i>Questions</i>	<i>Comments</i>
A. Did clinicians face diagnostic uncertainty?	Yes, Diagnostic uncertainty regarding which patients with AVS had central vs. peripheral vertigo. Based upon overall patient population this was a higher risk group of patients.
B. Was there a blind comparison with an independent gold standard applied similarly to the treatment group and the control group? (Confirmation bias)	All patients underwent neuroimaging, generally after bedside evaluation. In cases when imaging occurred first, the examiner was blinded to the imaging results. All patients (including patients with suspected APV) 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 diffusion-weighted imaging (DWI) on the day of the index visit. 3 patients who underwent CT had definitive signs of cerebellar stroke.
C. Did the results of the test being evaluated influence the decision to perform the reference standard? (Ascertainment Bias)	No, ALL patients underwent imaging so the “gold standard” was applied to all patients. The HINTS exam results did not determine or influence decision to image.
What are the Results?*	
<i>Questions</i>	<i>Comments</i>
A. What reported likelihood ratios were associated with the range of possible test results?	<ol style="list-style-type: none"> 1. 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. 2. Taking skew together with h-HIT and direction-changing nystagmus as a 3-step bedside examination battery, a dangerous HINTS 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 to 170.59) and a negative likelihood ratio of 0.00 (95% CI, 0.00 to 0.11). 3. Compared with traditional findings thought to indicate brainstem or cerebellar involvement in AVS, the HINTS battery was more sensitive than general neurological signs (100% versus 51%), obvious oculomotor signs (100% versus 32%), or both of these taken together (100% versus

67%; all $P < 0.001$;

How Can the Results Apply to Patient Care?*

<i>Questions</i>	<i>Comments</i>
A. Will the reproducibility of the test result and its interpretation be satisfactory in my clinical setting?	Hard to say. This study had a neuroophthalmologist (J.C.K.) that conducted a neurological and vestibular exam. Because patients were evaluated by a single examiner, it is unknown whether clinical findings could have been replicated by other examiners. No use of inter-rater reliability was used. The growing literature on these subtle eye signs from multiple investigators suggests reproducibility, at least among subspecialists in the field. Observer bias in the interpretation of subtle eye findings could have artificially inflated the sensitivity of these signs.
B. Are the results applicable to patients in my clinical setting?	Yes. This study restricted their enrollment to high-risk patients with AVS with no history of prior recurrent vertigo and at least one stroke risk factor which we see everyday in our clinical settings. Effective application and interpretation of the HINTS exam could reduce unnecessary testing as well as help identify higher risk patients.
C. Will the results change my management strategy?	Simple bedside HINTS exam can be used to better evaluate and stratify patients of high-risk for central causes, but will not replace an MRI with DWI. Further studies regarding utility and training needed for accurate interpretation by EM physicians or others is warranted.
D. Will patients be better off as a result of the test?	Patient's with HINTS examine suggestive of central cause, but negative initial MRI, could benefit by raising the index of suspicion in those with a false negative initial MRI. May also improve unnecessary diagnostic testing.

Limitations:

Several possible limitations:

Threats to internal validity include a partially unmasked examiner and selective MRI follow-up scans. As described previously, the study examiner (J.C.K.), although masked to the results of imaging, was not masked to the patient's clinical history, general neurological examination, 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 in which obvious neurological findings were absent. MRI follow-up scans were obtained in only selected cases based on evolution of new neurological signs or atypical subtle oculomotor signs. This selective retesting could have led to some misclassification of strokes as APV, increasing the apparent sensitivity of the HINTS battery. However, all of these patients with APV were followed and evolved no neurological deficits acutely nor had strokes in clinical follow-up.

Threats to external validity include generalizability of examination technique and sampling from a high-risk sub- population. Because 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. Pretty high-risk patient population with a majority diagnosed with a central etiology.

Your Clinical Bottom Line:

HINTS examine is a simple and easy addition to clinical bedside evaluation in patients presenting with AVS with at least 1 risk factor for stroke.

Must remember interpretation:

Benign HINTS examination (**must have ALL 3 present**):

1. abnormal h-HIT
2. direction-fixed horizontal nystagmus
3. absent skew

Dangerous HINTS examination (**If any one of the 3 present**):

1. normal/untestable h-HIT
2. direction- changing horizontal nystagmus present/untestable
3. skew deviation present/untestable

Remember MRI with DWI is not 100% even when obtained up to 48 hours after symptom onset.