ABSTRACT

Objectives: We aimed to investigate the diagnostic accuracy of Caloric Testing and video Head Impulse Testing (vHIT) in differentiating between vestibular neuritis and strokes in acute dizziness.

Design: Prospective cross-sectional study.

Setting: Emergency department of a tertiary referral center.

Participants: 1677 adult patients were screened between 2015 and 2020 for AVS, of which 152 met the inclusion criteria. Inclusion criteria consisted of a state of continuous dizziness, associated with nausea or vomiting, head-motion intolerance, new gait or balance disturbance and nystagmus. Patients were excluded if symptoms lasted <24 hours or if the index ED visit was >72 hours after symptom onset. Eighty-five patients completed testing of which 58 were vestibular neuritis and 27 strokes.

Main outcome measures: All patients underwent calorics and vHIT followed by a delayed MRI (gold standard for vestibular stroke confirmation).

Results: The sensitivity/specificity for detecting stroke (caloric asymmetry cut-off of 30.9%) was 75% and 86.8% respectively (Negative likelihood ratio (NLR) 0.29) compared to 91.7% and 88.7% for vHIT (NLR 0.094). Best VOR gain cut-off was 0.685. Twenty-five percent of vestibular strokes were misclassified by calorics, 8% by vHIT.

Conclusions: Caloric testing demonstrated lower accuracy than vHIT in discriminating stroke from vestibular neuritis in acute dizziness. Asymmetric caloric responses can also occur with vestibular strokes and might put the patient at risk for misdiagnosis. We therefore recommend replacing calorics with vHIT in the acute setting. Caloric testing has still its place as a diagnostic tool in an outpatient setting.

Key words: Caloric Testing, Head-Impulse Test, Neuritis, Acute Stroke, Vertigo, Dizziness.

Key Messages Box

- Asymmetrical caloric testing in acute dizziness is falsely reassuring with 1 out of every 4 strokes being potentially misdiagnosed as neuritis.
- The video head impulse test (vHIT) is superior to caloric testing in terms of accuracy for the exclusion of vestibular stroke.
- vHIT is non-invasive as well as time- and cost-efficient compared to calorics.
- We therefore recommend to abandon caloric testing in current practice and replace it with vHIT.

INTRODUCTION

Since its discovery in 1907 by Robert Bárány (1), who received the Nobel prize in 1916 (2), Caloric Testing has been widely accepted as a Gold Standard for detecting a vestibular hypofunction in patients with dizziness. However, the accuracy of calorics in discriminating vestibular strokes from vestibular neuritis in patients with acute dizziness is not known. One study reported a false negative rate of up to 22% of vestibular strokes (3). Between 5 - 25% of isolated dizziness end up with a final diagnosis of posterior fossa infarction (3-5) with a reported initial misdiagnosis rate of up to 28% (6). This is because central vestibular disorders mimic in many cases peripheral disease (7). Caloric testing is very uncomfortable, consumes vast emergency department (ED) resources and is potentially less accurate due to great inter-subject and test- retest variability (8). In view of all these disadvantages, any solution to replace calorics and to increase diagnostic accuracy is crucial. Currently, the most accurate triage test in detecting vestibular strokes is the Head Impulse Test (HIT) (3). Disconcordant eye and head movements (pathologic VOR) indicate a peripheral vestibular deficit, such as vestibular neuritis. An intact VOR (concordant eye/head movements) is indicative of vestibular stroke. With the advent of digital technologies such as eye- and head-tracking by Video-Oculography (VOG) (9), it has been possible to offer non-invasive, time- and cost-efficient diagnostic techniques in the ED. Although many studies have investigated the correlation between caloric testing and vHIT, none have focused on acute vestibular disorders (10, 11). In our study, we aim to investigate the diagnostic accuracy of Caloric Testing when compared to vHIT in differentiating between vestibular neuritis and strokes in acute dizziness.

DESIGN, SETTING AND PARTICIPANTS

We conducted a prospective cross-sectional study (convenience sample), between February 2015 and May 2020, of all cases presenting with acute dizziness at the ED in a tertiary referral center. 1677 patients were screened for Acute Vestibular Syndrome (AVS), of which 152 met the inclusion criteria and were enrolled. Inclusion criteria consisted of a state of continuous dizziness, associated with nausea or vomiting, head-motion intolerance, new gait or balance disturbance and nystagmus. Patients were excluded if they were younger than 18 years, if symptoms lasted <24 hours or if the index ED visit was >72 hours after symptom onset. Figure 1S (Appendix) shows a flow diagram with all screened patients, inclusions and exclusions of dizzy patients. All enrolled patients underwent when feasible a thorough physical examination, Caloric Testing and vHIT testing. All patients received an MRI either at the index visit or a second, delayed MRI if there was no acute MRI indicated based on clinical grounds or if the first MRI was non-diagnostic. The delayed MRI served as a reference standard for stroke detection. Enrolled patients were clinically re-evaluated between day 3 and day 10, at day 30 and day 90. All images were reviewed by a certified second blinded neuroradiologist, discrepancies were resolved by consensus and inter-rater concordance reported. Figure 1 shows the two investigated tests, the required equipement, stimulation modalities and recording setup.

We performed caloric tests irrigating sequencially both ears with warm (44°C) and cold (30°C) water for 30s and a total water volume of 250 ml (Vario Otopront device) in patients lying 30° supine (Figure 2S, supplementum, panel A). Intervals between irrigations were 5 minutes long, starting first with warm irrigation on the right ear. Convection flows of inner ear fluid (particularly in the horizontal semicircular canal) produced horizontal nystagmus, which were recorded in darkness (blocked visual fixation) with a calibrated VOG device (EyeSeeCam, Munich). The Cut-off for pathologic Caloric responses was 20% asymmetry (12), which was calculated using Jongkee's formula (13) after correcting for spontaneous nystagmus.

In contrast, vHIT was performed by fast passive horizontal head movements (high frequency, 10-20° head excursion in 100-300msec corresponding to a 1000-6000°/sec^2 acceleration) in room light during visual target fixation at >1m distance. We recorded head and eye movement velocity with a head mounted infrared highspeed camera (EyeSeeCam, Munich) connected to a laptop by USB (Figure 2S, Panel B). VOR gain values were derived from eye velocity divided by head velocity at 60ms after HIT onset (14). vHIT exams were classified as abnormal based on VOR gains (Gain <0.79 based on own laboratory normative values) and the presence of corrective saccades. Additionally we collected information on age, gender, duration of symptoms, and other associated relevant otological or neurological symptoms.

Statistics

Cohen's Kappa was calculated for the assessment of inter-rater agreement between two experienced neuroradiologist. Descriptive statistics were reported using SPSS statistical software (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). We used a binary logistic regression to evaluate stroke predictors derived from caloric and vHIT exams in 65 patients who underwent both test modalities. We calculated a receiver characteristics curve (ROC) with its corresponding sensitivity, specificity, accuracy and negative likelihood ratio with its impact on post-test probability for each test. Best cut-off points based on Youden's J. We followed the STARD guidelines for reporting the diagnostic accuracy. Our estimated sample size was 52 with an estimated marginal error of 0.1 (95% CI, 80% power) and a diagnostic accuracy (AUC) of 0.90 for vHIT. The two ROC curves were compared using the method of DeLong et al (15).

RESULTS

We screened 1677 patients with AVS of which 152 patients were enrolled aged between 20 and 91 (mean 55.67y). Out of 152 patients, 58 were diagnosed with vestibular neuritis (mean age 54y +/- 15.7) while the remaining 27 patients were vestibular strokes (mean age 62.1y +/- 15.9y). Vascular territories included the PICA (17), SCA (3), AICA (2), basilar artery (3), vertebral artery (2), anterior (1) and middle cerebral artery (4). There was an excellent inter-rater agreement regarding masked MRI assessment (94%, $\kappa = 0.78$). None of the patients with a normal caloric response had an abnormal vHIT (Table 1). Patients with an abnormal vHIT, however, systematically showed a pathologic caloric response as well. Table 1 shows the number of concordant or disconcordant exams comparing vHIT with calorics. Every increase of 0.1 VOR gain increased significantly the stroke risk (OR 2.832, 95% CI 1.5-5.2, $P<0.001$, Table 2). A decreased asymmetry of 1% steps, however, decreased slightly the stroke risk (OR 0.926, 95% CI 0.88-0.97, $P=0.001$, Table 2). Figure 2 shows the receiver operating characteristic (ROC) curves for vHIT (AUC= 0.93, 95% CI 0.84-1.00, $P<0.001$) and calorics (AUC=0.86, 95% CI 0.74-0.99, $P<0.001$) with curves going to the left upper corner. There was no statistical difference between the two ROC curves ($P=0.22$) and thus, there was no inferiority regarding vHIT.

The overall sensitivity in discriminating strokes with caloric testing was 75% with a specificity of 86.8% (Table 3). The accuracy of caloric testing was 84.6% using a cut-off of 30.9% asymmetry. The accuracy of vHIT in detecting stroke was 89.3% with a sensitivity of 91.7% and specificity of 88.7% using a cut-off of 0.685 VOR gain. Table 3 shows alternative cut-off values and their corresponding sensitivity/specificity. The negative likelihood ratio for ruling-out stroke was 0.288 for calorics and 0.094 for vHIT (Table 3). Table 4 shows the pre-test and post-test probabilities of stroke assuming pre-test probabilities based on risk stratification rules. Table 4 illustrates the impact of the negative likelihood ratio (NLR) on stroke probability. Stroke probability decreased by 9-53% points after a vHIT exam and by 6.9-28.6%points after calorics depending on the assumed pretest probability.

DISCUSSION

Every forth vestibular stroke would have been missed based on a caloric test in acute dizziness. A pathological caloric test puts a dizzy patient at risk being misclassified as a vestibular neuritis. Considering currently accepted test cut-off values for caloric response asymmetry, even every 2nd to 3rd patient would have been misdiagnosed. On the contrary, a vHIT test yields a significantly higher sensitivity and specificity for vestibular stroke detection. An increased gain value was significantly associated with stroke. A pathological vHIT result with low gain was, however, systematically associated with a pathological Caloric Test result. Thus, we never observed a normal caloric test when vHIT was abnormal.

Is caloric testing accurate for discrimination between peripheral and central dizziness?

Admittedly, for calorics, we observed a decent decrease of stroke risk for every 1% of increase in asymmetry which was not described in the literature before. The cut-off value, however, to rule-in stroke was higher (31% asymmetry) compared to the test cut-off used in laboratories (20-25%) for the detection of vestibular deficits (12). We demonstrated, that central lesions can cause pathologic caloric responses in every 4th patient, which is in line with current literature (3) (supplemental material). Thus, a pathologic caloric response is not a hallmark for a peripheral lesion but rather documents a deficit of vestibular pathways at any neuronal level in the low frequency range.

vHIT is more sensitive for vestibular stroke detection

Each incremental increase in VOR gain in vHIT resulted, however, in a significant incremental increase in stroke risk. Our test cut-off of 0.685 gain confirmed previously reported test thresholds for stroke discrimination with vHIT (16). Even clinically performed HITs (which assess VOR function qualitatively by simple eye observation looking for corrective saccades) yield a high sensitivitiy of stroke detection in acute dizziness, provided that it is performed by experts. However, a quantitive method, such as vHIT, would allow for more reliable and more examiner independent results. A recent study from our group showed, that even non-experts and novices were able to perform valid HITs using a video recording system (17). Thus, a point-of care examination with vHIT in the ED has the potential of a widespread use, providing an accurate, cost-efficient and non-invasive method for stroke detection in acute dizzy patients.

Can the caloric test be replaced by the vHIT in the acute setting?

vHIT demonstrated a better accuracy with a higher sensitivity/specificity in the detection of vestibular strokes. The rate of missed patients (false negative result) having a serious cause of dizziness was significantly lower with vHIT. The false positive rate, however, was the same for both tests. In previous cross-sectional studies, vHIT (performed within 24hours) was found to be even more sensitive for stroke detection than MRI (18) (16). There are no publications comparing the accuracy of vHIT versus calorics in detecting vestibular strokes in patients with an acute vestibular syndrome. Both exams have been extensively compared regarding the detection of vestibular deficits in subacute or chronic stages (10, 11), however, such deficits might originate from peripheral or central causes. Rather than seeking to initially detect a benign vestibular deficit, emergency physicians and general practictioners should prioritise the exclusion first and foremost of any dangereous cause of acute dizziness. Benign causes of dizziness could be further assessed and treated as a second line in an outpatient, sub-acute setting. We therefore suggest a paradigm shift towards vHIT testing in patients with acute dizziness and to abandon calorics in the acute setting.

When to perform calorics

There are differences reported in the literature regarding the detection of vestibular deficits (10, 11). Comparing vHITs to calorics is like comparing apples to pears (19); Calorics represent the measurement of low frequency stimulation of horizontal semicircular canals only whereas vHITs concentrate of high frequencies and test all 6 canals in all spatial planes. It is therefore not surprising to find a dissociation of the two.

Other articles did compare the clinical HIT (before the advent of video-oculography) with calorics (20). These articles support the idea that there is a low correlation between both exams, the vHIT having a very low sensitivity for the detection of canal paresis (10, 11), unless this canal paresis exceeds ~40% caloric asymmetry (21). vHIT sensitivity in detecting acute vestibular deficits is higher (63%) and lower in chronic dizziness (33%)(22) with an overall reported sensitivity ranging from 41% to 86% (23). Caloric tests, however, are more sensitive to diagnose Menière's disease (24) but measure only one single semicircular canal function and might miss an incomplete neuritis (inferior neuritis) (25).

Because the range calorics measure differ from vHIT (low frequency vs high frequency), it should not completely be excluded altogether. Rather it should be seen as a complementary exam of vestibular function. Thus patients presenting with AVS, a normal delayed MRI (3-10 days after symptom onset) and a normal vHIT, would be good candidates for further investigations by Calorics. If this is the case, one could argue for the redundancy of caloric testing in the acute setting and argue for its relegation to a later phase of non-acute testing, in order to extend investigations. However, there is no need to perform calorics if vHIT is abnormal, since we never observed a dissociation of the two tests when vHIT was abnormal.

Strenght and Limitations

Our paper is the first large study offering a direct comparison of Caloric Testing and vHIT in acute vestibular syndrome, however, our results are not generalizable to all dizzy patients. Careful vHIT interpretation is advised in patients with other pathologies such as e.g Menière's Disease, vestibulare Schwannoma (23), vestibular migraine or BPPV, which can cause episodic dizziness and with the risk of finding an asymptomatic patient at the examination time point. Best sensitivity of vHIT is yielded in patients with continuous dizziness and spontaneous nystagmus, serving as an objective clinical sign of dizziness and underlying the severity of the vestibular imbalance. We had a larger number of vHIT results versus caloric results; this could be due to a refusal by highly symptomatic patients to undergo caloric investigation. This could potentially lead to a selection bias in that highly symptomatic patients where inadvertendly excluded from the study.

Clinical implication

Our study results have an immediate impact in current clinical practice suggesting a paradigm shift from calorics towards a modern vHIT exam. Caloric testing has a variety of limitations: 1) Only one semicircular canal (horizontal) is stimulated per ear while the remaining 4 canals remain unassessed, 2) the stimulus is non-physiological stimulating at low frequencies only (<0.003Hz) and non-reciprocal (stimulus from the contralateral ear missing), 3) it is very disagreeable for patients, inducing vertigo lasting up to several minutes, 4) there is a large inter-subject variability due to ear anatomy resulting in a variable application of thermal energy, 5) it needs a special and stationary irrigation device to maintain a constant water temperature with a purified water supply, 6) has to be performed in total darkness (adapted room) with Frenzel or video Frenzel goggles in order to remove visual fixation and finally, 7) it is costly consuming both, vast human and time resources. We therefore suggest to replace calorics with a more convenient and simple vHIT in AVS patients in view of its non-inferiority.

Conclusions

Caloric testing proved to be less accurate than vHIT in discriminating stroke from vestibular neuritis in acute dizziness. Contrary to classic teaching, asymmetric caloric responses can also occur with vestibular strokes and might put the patient at risk for misdiagnosis. We therefore recommend to abandon caloric testing in current practice. vHIT could serve as a replacement test in the acute setting. Caloric testing has still its place as a diagnostic tool in an outpatient setting.

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Tables

Table 1. Concordance vHIT versus Calorics

Vestibular function		Video Head Impulse Test (vHIT)			Total
		Normal	Hypo-function right	Hypo-function left	
Bithermal Caloric Test (calorics)	Normal	5	0	0	5
	Hypofunction right	5	20	0	25
	Hypofunction left	5	0	25	30
	Bilateral Hypofunction	2	0	0	2
Total		17	20	25	62

Table 2. Stroke risk estimation for vHIT and Caloric asymmetry

	Increment Steps	Regression Coefficient	Standard Error	Wald	df	P Value	Odd's Ratio	95% Confidence Interval	
								Lower	Upper
vHIT gain	0.1	1.041	0.308	11.387	1	0.001	2.832	1.547	5.183
Caloric Asymmetry	1%	-0.077	0.024	10.446	1	0.001	0.926	0.883	0.970

Table 3. Sensitivity and Specificity for vHIT and calorics

	vHIT(Gain)		Calorics (% Asymmetry)	
Test Cut-off	>0.685	>0.805	<25.3%	<30.9%
AUC (95% CI)	0.926 (0.833-0.976)		0.863 (0.755 to 0.936)	
Sensitivity	91.7%	41.7%	58.3%	75%
Specificity	88.7%	96.2%	96.2%	86.8%
Negative test	48	58	56	49
Positive test	17	7	9	16
True positives	11	5	7	9
False positives	6	2	2	7
True negatives	47	51	51	46
False negatives	1	7	5	3
Likelihood Ratio Pos. Test	8.097	11.042	15.458	5.679
Likelihood Ratio Neg. Test	0.094	0.606	0.433	0.288
Accuracy	89.3	86.2	89.2	84.6

Table 4. Pre-test and post-test probabilities of stroke using calorics or vHIT to 'rule out' stroke

	Post-Test Probability of Stroke	
Test	Calorics (rule out stroke)	vHIT (rule out stroke)
Test cut-off	30.9% asymmetry	0.685 gain
Pre-Test Probability of Stroke (based on risk stratification rules)	Sn 75%, Sp 86.8% NLR 0.29	SN 91.7%, Sp 88.7% NLR 0.094
10% (low)	3.1%	1.0%
25% (average)	8.8%	3.0%
50% (high)	22.4%	8.6%
75% (very high)	46.4%	22.0%

Sn=Sensitivity, SP=Specificity, NLR=negative likelihood ratio

Figure Legends

Figure 1. Technical setup for the caloric exam compared to the Video-Head Impulse test

Diagram comparing the technical setup for the caloric exam with that of the vHIT; calorics are performed in the dark on a patient in a supine position and head rest positioned at 30° from horizontal. The outer ear canal on each side is irrigated sequentially for 30 seconds (at 30° C cold and 44° C warm water) and the resulting eye movements recorded for a duration of 3 minutes using VOG-goggles. The whole procedures takes up to 30 minutes including waiting intervals of 5 minutes between irrigations. The vHIT is performed in a normal lit room on a upright sitting patient. The head is moved rapidely from side to side (20 times in an impulse-like motion) and eye movements are recorded using adapted vHIT-goggles. When done correctly, the vHIT takes under 5 minutes.

Figure 2. ROC curves

ROC curve demonstrating a higher sensitivity and specificity for vHIT for the detection of stroke compared to calorics. Black circles indicate the optimal test discrimination cut-off for each test. The dotted line illustrates a likelihood ratio of 1 with an area under the curve (AUC) at 0.5 indicating an unhelpful test.