Clinical Characteristics and Related Factors of Cerebral Infarction in Acute Vestibular Syndrome: A Postprint

Authors: Zhang Chunyue, Fang Liqun, Fang Liqun

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Abstract

Background: Acute cerebral infarction is a critical condition among acute vestibular syndromes. Patients with acute vestibular syndrome present with sudden onset and severe symptoms. CT demonstrates low sensitivity in diagnosing acute cerebral infarction, while MRI cannot be readily performed immediately, rendering the diagnosis of acute cerebral infarction manifesting as acute vestibular syndrome challenging. Therefore, it is imperative to investigate examination and evaluation methods applicable to patients with acute vestibular syndrome.

Objective: To analyze the risk factors associated with acute cerebral infarction in patients with acute vestibular syndrome, thereby providing reference for future diagnosis of acute cerebral infarction in this population and striving to secure the golden therapeutic window for patients with acute cerebral infarction.

Methods: A total of 102 patients with acute vestibular syndrome who presented to the Department of Neurology, Fourth Affiliated Hospital of Harbin Medical University between April 2021 and July 2022 were enrolled. Relevant clinical signs were recorded. MRI findings served as the gold standard for cerebral infarction diagnosis. Patients were divided into a cerebral infarction group (16 cases) and a non-cerebral infarction group (86 cases). Clinical characteristics were compared between the two groups. Univariate and multivariate Logistic regression analyses were employed to explore influencing factors associated with cerebral infarction. Receiver operating characteristic (ROC) curves were constructed to evaluate the predictive value of relevant influencing factors for cerebral infarction.

Results: Comparison of clinical data between the cerebral infarction and non-cerebral infarction groups revealed that smoking history, alcohol consumption

history, positive head impulse-nystagmus-skew deviation test (HINTS) proportion, and ABCD2 scores were significantly higher in the cerebral infarction group ($P<0.05$). Univariate Logistic regression analysis identified HINTS positivity, ABCD2 score, smoking history, alcohol consumption history, and hearing loss as influencing factors for cerebral infarction. Multivariate Logistic regression analysis demonstrated that HINTS positivity and ABCD2 score were influencing factors for cerebral infarction. The areas under the ROC curve (AUC) for multi-index combination, HINTS positivity, ABCD2 score, smoking history, alcohol consumption history, and hearing loss in predicting cerebral infarction were 0.949, 0.874, 0.734, 0.643, 0.649, and 0.604, respectively. The optimal cutoff values were 0.181, 0.293, 0.147, 0.23, 0.238, and 0.241, respectively.

Conclusion: The proportion of non-cerebral infarction is relatively high among patients with acute vestibular syndrome, with vestibular neuritis being the most common etiology. HINTS positivity and ABCD2 score are closely associated with the occurrence of cerebral infarction in acute vestibular syndrome.

Full Text

Introduction

Acute vestibular syndrome (AVS) refers to a constellation of clinical manifestations characterized by sudden onset of persistent vertigo, often accompanied by nausea, vomiting, nystagmus, and postural instability, with symptoms lasting for days or weeks. AVS can be categorized by lesion location into central and peripheral causes, among which cerebral infarction represents the most diagnostically challenging central pathology [**?**]. Current diagnostic modalities for AVS patients encompass imaging studies, vestibular function tests, general neurological examinations, and otolaryngologic and ophthalmologic assessments. Diffusion-weighted imaging (DWI) is recognized as the gold standard for diagnosing new cerebral infarction. However, diagnosing stroke in AVS patients remains a significant clinical challenge, as these patients typically present with cerebellar or brainstem lesions lacking classic neurological deficits. Approximately 20% of vertebrobasilar ischemia patients exhibit isolated vertigo. Since acute persistent dizziness often stems from posterior fossa lesions, imaging false-negative results are more likely to occur. Although MRI-DWI is superior to CT for detecting new cerebral infarction, MRI is frequently unavailable in emergency settings. The National Institutes of Health Stroke Scale (NIHSS) does not include vertigo among its items, and the Face-Arm-Speech-Time (FAST) test similarly omits vertigo or dizziness. It is estimated that up to 35% of AVS patients are misdiagnosed [**?**], with misdiagnosed cerebellar infarction patients facing higher mortality risk [**?**]. These patients are often misdiagnosed with peripheral vestibular disorders, consequently missing opportunities for reperfusion therapy and secondary prevention, which delays treatment and compromises prognosis. This has prompted clinicians to explore methods to improve diagnostic accuracy for cerebral infarction in AVS.

Previous studies have demonstrated that the Head-Impulse–Nystagmus–Test-of-Skew (HINTS) examination and ABCD2 score perform excellently in distinguishing stroke among AVS patients, with multiple studies indicating that HINTS outperforms ABCD2 [**?**]. Additionally, research has identified hearing loss, smoking, and alcohol consumption as risk factors for stroke [**?**], though further investigation is needed to confirm and evaluate these risk factors. This study collected AVS patients from a vertigo clinic, comprehensively recorded clinical data, performed neurological examinations, HINTS testing, and vestibular assessments, and used imaging findings as the diagnostic standard to analyze the clinical characteristics and risk factors for acute cerebral infarction in AVS.

1.1 Study Subjects

Referencing the International Classification of Vestibular Disorders (ICVD) established by the Bárány Society in 2006, we enrolled 102 AVS patients who presented to the Department of Neurology at the Fourth Affiliated Hospital of Harbin Medical University between April 2021 and July 2022.

1.1.1 Inclusion Criteria

(1) Meeting AVS diagnostic criteria: first episode of vertigo, dizziness, or balance disturbance lasting >24 hours; (2) Age $ $18 years.

1.1.2 Exclusion Criteria

(1) Refusal to provide informed consent; (2) Inability to complete imaging, HINTS, or electronystagmography examinations; (3) Presence of new neurological deficits (dysarthria, hemiplegia, limb weakness, etc.); (4) New intracerebral hemorrhage or intracranial mass compression; (5) Impaired consciousness or advanced age ($ $80 years); (6) Ocular diseases severely affecting electronystagmography results.

1.2 Methods

1.2.1 Clinical Data Collection For patients meeting AVS diagnostic criteria, detailed history was obtained, including age, sex, vertigo-related symptoms (presence of nausea/vomiting, gait instability, rotational vertigo, new hearing loss), cerebrovascular risk factors (history of cerebrovascular disease, coronary artery disease, smoking, alcohol consumption, hyperlipidemia), and previous vertigo history. ABCD2 scores and Dizziness Handicap Inventory (DHI) scores were also completed. The ABCD2 scale, developed by Rothwell et al. at Oxford University in 2005, is a scoring system based on patient age, blood pressure, clinical features, and symptom duration (total score 7 points, including age, blood pressure, clinical signs, symptom duration, and diabetes), which has been validated for predicting stroke risk within 7 days after transient ischemic attack (TIA) [**?**]. The DHI comprises 25 questions yielding a total index and three

sub-indices (DHI-P, DHI-F, DHI-E), with the total index ranging from 0-100 to assess overall subjective severity of vertigo symptoms [**?**].

1.2.2 Bedside Examination Within 24 hours of admission, specialized vertigo physicians and vestibular technicians performed neurological and bedside vestibular examinations, including bedside nystagmus observation, horizontal head impulse test, head shaking test, crude hearing assessment, Romberg test, and Fukuda stepping test.

1.2.3 Vestibular Function Assessment

(1) Video head impulse test: Performed using the Eye SeeCam video head impulse device from Danish Interacoustics. Professional vestibular technicians conducted the examination. Procedure: In a dark room, patients sat upright wearing video head impulse goggles, maintaining fixation on a straight-ahead target. The examiner held the patient' s head bilaterally, first performing horizontal head impulse tests with the head flexed 30° forward, then making sudden, small-amplitude, rapid random head rotations left and right. After horizontal testing, patients turned their head 45° left to fixate on a left-anterior target for sagittal plane head impulses to assess right anterior and left posterior semicircular canal VOR pathways. Similarly, with the head turned 45° right, left anterior and right posterior canal VOR pathways were examined. Each direction was tested 15 times, with $ $8 overt saccades recorded as positive and <8 as negative. (2) Videonystagmography (VNG): Using the VO425 VNG analyzer from Danish Interacoustics, operated by specialized technicians. The examination included eight components: positioning tests, spontaneous nystagmus, gaze test, saccade test, smooth pursuit, optokinetic test, positional tests (Roll Test, Hallpike Test), and caloric testing. Patients exhibiting central nystagmus (gaze-evoked nystagmus, vertical nystagmus in any position, torsional nystagmus) were recorded as nystagmus-positive. Presence of any one of three findings—normal video head impulse, central nystagmus, or skew deviation—was recorded as HINTS-positive.

1.2.4 Imaging Examination Using Philips 3.0T Achieva MRI system with dedicated 8-channel head coil. All patients initially underwent CT in the emergency department, followed by MRI, MRA, and DWI within 48 hours of admission. Patients with suspected cervical vascular stenosis after excluding peripheral vestibular and stroke lesions underwent cervical CTA. Patients highly suspected of central lesions with initial negative DWI received repeat brain DWI within 72 hours.

Statistical Analysis

The Shapiro-Wilk test assessed normality of continuous variables. Normally distributed data were expressed as mean ± standard deviation, with intergroup

comparisons using independent samples t-test. Non-normally distributed data were presented as median (P25, P75), with comparisons using Wilcoxon rank-sum test. Categorical data were expressed as frequency (percentage) and compared using ^{2} test. Univariate and multivariate logistic regression analyses explored factors influencing cerebral infarction. Receiver operating characteristic (ROC) curves evaluated the predictive value of influencing factors. Two-tailed tests were used with $P<0.05$ considered statistically significant.

Results

2.1 Comparison of Clinical Data Between Cerebral Infarction and Non-Cerebral Infarction Groups

This study enrolled 102 patients, including 16 with cerebral infarction (15.7%) and 86 without (84.3%). Infarction locations included cerebellum, pons, medulla, brachium pontis, and occipital lobe, with multiple patients having more than one new infarct lesion. The non-cerebral infarction group comprised 36 cases of vestibular neuritis (VN), 4 labyrinthitis, 2 Ramsay Hunt syndrome (RHS), 21 episodic vestibular syndrome, and 23 cases of undetermined etiology.

Comparison of clinical data revealed no statistically significant differences between groups in sex ratio, age, cerebrovascular disease history, coronary artery disease history, hyperlipidemia, new hearing loss, rotational vertigo, nausea/vomiting, or previous vertigo history ($P>0.05$). However, the cerebral infarction group showed significantly higher rates of HINTS positivity, ABCD2 scores, smoking history, and alcohol consumption history compared to the non-cerebral infarction group ($P<0.05$) .

2.2 Analysis of Influencing Factors for Cerebral Infarction in AVS

To identify clinical factors associated with cerebral infarction in AVS patients, DWI positivity served as the gold standard for diagnosing new cerebral infarction. Using new cerebral infarction (yes=1, no=0) as the dependent variable and patient sex (male=1, female=0), age (actual value), hearing loss (yes=1, no=0), history of cerebral infarction (yes=1, no=0), coronary artery disease (yes=1, no=0), smoking history (yes=1, no=0), alcohol consumption history (yes=1, no=0), hyperlipidemia (yes=1, no=0), rotational vertigo (yes=1, no=0), nausea/vomiting (yes=1, no=0), previous vertigo history (yes=1, no=0), ABCD2 score (actual value), and HINTS positivity (yes=1, no=0) as independent variables, univariate logistic regression analysis identified HINTS positivity, ABCD2 score, smoking history, alcohol consumption history, and hearing loss as influencing factors . Multivariate logistic regression incorporating statistically significant factors from univariate analysis revealed HINTS positivity and ABCD2 score as independent influencing factors for cerebral infarction .

2.3 Predictive Value of Influencing Factors for Cerebral Infarction in AVS

HINTS positivity, ABCD2 score, smoking, and alcohol consumption were combined in a multivariate logistic model to generate a composite indicator for predicting cerebral infarction. ROC curve analysis demonstrated that the areas under the curve (AUC) for the composite indicator, HINTS positivity, ABCD2 score, smoking history, and alcohol consumption history in predicting cerebral infarction in AVS were 0.949 [95%CI (0.910, 0.989)], 0.874 [95%CI (0.783, 0.964)], 0.734 [95%CI (0.600, 0.868)], 0.643 [95%CI (0.512, 0.774)], and 0.649 [95%CI (0.518, 0.780)], respectively. The optimal cutoff values were 0.181, 0.293, 0.147, 0.23, and 0.238, respectively [Figure 1: see original paper].

Discussion

This study demonstrated that the cerebral infarction group in AVS had higher rates of HINTS positivity, ABCD2 scores, smoking history, and alcohol consumption history compared to the non-cerebral infarction group. Multivariate regression analysis identified HINTS positivity and ABCD2 score as independent risk factors for cerebral infarction in AVS. Furthermore, a multi-factor combined assessment model showed the best predictive performance for new stroke in AVS patients, with HINTS demonstrating excellent sensitivity and specificity.

Vertigo patients constitute a large population in neurology outpatient clinics, most with neurological etiologies. Cerebrovascular disease is the primary cause of central vertigo. While most stroke patients with vertigo symptoms present with limb weakness, speech disturbances, and other neurological deficits, stroke can be easily misdiagnosed as benign peripheral vestibular disease when central neurological signs are absent or manifest as isolated vertigo. Previous studies reported that only 0.7% (9/1297) of patients presenting with isolated vertigo (not limited to AVS) were diagnosed with stroke at initial evaluation [**?**]. However, follow-up studies of emergency department patients diagnosed with dizziness found a 0.3% stroke rate within 90 days, suggesting that initial dizziness likely represented missed stroke or TIA warning symptoms [**?**].

Numerous studies have examined vertigo and stroke, but this study differs in several aspects. First, we selected AVS patients rather than general dizziness patients. At the population level, the proportion of dizziness meeting AVS criteria is unknown, though a single-center study found that approximately 10% (373/3296) of screened dizziness patients had AVS features [**?**]. Compared with previous studies, AVS patients show higher stroke incidence than general dizziness patients [**?**, **?**], which motivated our focus on AVS to better identify central lesions among numerous dizziness patients. Our study' s stroke proportion of 15.7% exceeds that of previous studies using vertigo patients as enrollment criteria. Second, our AVS diagnostic criteria followed the latest ICVD requirements, excluding vestibular migraine, benign paroxysmal positional vertigo, Ménière' s

disease, and vestibular paroxysmia, thereby narrowing the inclusion scope and enhancing precision. Third, we restricted enrollment to patients without new, obvious neurological deficits, as dysarthria and limb weakness already strongly suggest neurological impairment. Additionally, our nystagmus examinations utilized video electronystagmography and video head impulse devices, substantially improving observation accuracy.

Previous research indicates that AVS etiology is predominantly peripheral vestibular disease, most commonly vestibular neuritis, with central disease representing a smaller proportion. In our study, non-cerebral infarction patients accounted for 74% of cases, exceeding cerebral infarction patients. Among those with identified etiologies, VN was most common, with fewer cases of RHS and labyrinthitis, consistent with previous studies. Sixteen patients in our study remained etiologically undefined after excluding central and common peripheral vestibular disorders, warranting further investigation. Central diseases are mostly ischemic stroke, typically located in the cerebellum (PICA>AICA), medulla, or pons, with rare involvement of other regions such as thalamus or parietal lobe [**?**]. Our 16 cerebral infarction patients (15.7%) had infarcts involving cerebellum, pons, medulla, brachium pontis, and occipital lobe, with four patients having multiple new infarct lesions, most commonly in the cerebellum.

Central nervous system structures associated with vertigo include the cerebellar flocculonodular lobe, vestibular nuclei, and the intracranial entry point of the eighth cranial nerve. These structures are not more sensitive to ischemia than peripheral structures; therefore, when damaged, patients typically present with vertigo accompanied by other neurological deficits such as ataxia or limb weakness. In rare cases, small infarcts limited to the cerebellar flocculus, dorsal insular cortex, or small brainstem lesions may cause isolated vertigo. However, large cerebellar infarcts can also occur without limb weakness or ataxia, likely due to compensation by surrounding structures. The eighth nerve entry point is richly vascularized and rarely causes isolated vertigo from infarction, though demyelination-induced isolated vertigo has been reported [**?**]. Our study included one patient with medullary infarction presenting solely with vertigo and initial negative DWI, likely related to small lesion size and compensation by surrounding structures. The vestibular nuclei are more sensitive to ischemia than the former structures, making isolated vertigo from vestibular nuclear infarction not uncommon and similar in presentation to acute unilateral vestibulopathy (AUV), including unilateral canal paresis, horizontal nystagmus, and decreased VOR. Such patients are more easily misdiagnosed [**?**]. Similarly, anterior inferior cerebellar artery (AICA) territory infarcts are easily misdiagnosed as AICA supplies the peripheral vestibular nerve, causing AUV resembling VN. A large retrospective AVS study found that 18.7% of ischemic stroke patients had vertebral artery dissection [**?**]. In our study, seven patients had moderate-to-severe vertebral artery stenosis, dysplasia, or basilar artery stenosis identified on cervical CTA after excluding stroke and peripheral vestibular disease; these were temporarily classified as central AVS. While CT and DWI serve as gold stan-

dards for stroke diagnosis, they are not applicable for such vascular stenosis cases.

Although clinicians have increased awareness of isolated vertigo diagnosis and have access to advanced imaging equipment, stroke presenting solely as isolated vertigo remains frequently misdiagnosed [**?**]. Given CT' s low sensitivity, its role in identifying acute ischemic stroke is limited, particularly in the posterior circulation [**?**]. Even MRI-DWI misses approximately 15-20% of acute posterior circulation infarctions within 24-48 hours of symptom onset. One study found that misdiagnosis rates are higher (approximately 50%) for small infarcts (<10 mm diameter) [**?**]. Among our 16 cerebral infarction patients, three had initial false-negative DWI results but positive HINTS, with one also having new hearing loss. Repeat DWI confirmed new infarcts in these three patients (medulla, medulla plus pons, and right cerebellar hemisphere plus left occipital lobe). The false-negative results in the first two cases likely resulted from small lesion volume and location in posterior circulation structures where DWI is prone to false negatives compared with other regions. This underscores the importance of multi-factor comprehensive assessment in AVS patients, particularly when multiple factors suggest cerebral infarction despite negative DWI, making repeat DWI essential.

Despite HINTS' high diagnostic value in vertigo patients, cerebrovascular risk factor assessment remains indispensable. Our study observed two false-negative HINTS cases (2/77) and eleven false-positive cases (11/25). Therefore, for AVS patients with high cerebrovascular risk factors but negative HINTS, we should not readily exclude cerebral infarction before imaging confirmation. A population-based retrospective study indicated that dizziness patients visiting emergency departments have seven times higher stroke risk than the general population, particularly when they have stroke risk factors such as atrial fibrillation and diabetes [**?**]. Our risk factor analysis ultimately identified smoking and alcohol consumption as showing good predictive value in the model, followed by new hearing loss. New hearing loss showed less robust performance than in previous studies [**?**], possibly because earlier studies often combined hearing loss with HINTS results. Age difference between groups was not significant in our study. As an important cerebrovascular risk factor, age performed poorly in our model, likely related to the younger age trend in stroke patients and higher incidence of vestibular dysfunction in elderly individuals, with more older men experiencing peripheral acute persistent dizziness.

Previous studies on ABCD2 in vertigo patients often used a cutoff of 4 to stratify high-risk versus low-risk groups, with high-risk groups showing higher stroke incidence [**?**, **?**]. However, new speech disturbance and limb weakness in the ABCD2 scoring system already strongly suggest neurological impairment and were excluded from our study. Therefore, our ABCD2 scores ranged from 0-3 points, yet still demonstrated significant differences between cerebral infarction and non-cerebral infarction groups, showing excellent predictive value in the model.

This study has several limitations. First, the relatively small sample size and exclusion of intracerebral hemorrhage patients may have resulted in incomplete statistical findings and bias. Second, although imaging served as the gold standard with repeat DWI in some patients, the possibility of false-negative imaging results in peripheral AVS patients and peripheral vestibular dysfunction in central AVS patients cannot be entirely eliminated. Third, the large proportion of undetermined etiology in peripheral AVS patients indicates room for improvement in AVS disease classification and diagnostic skills.

Conclusion

AVS patients are predominantly affected by peripheral vestibular disease, most commonly vestibular neuritis. HINTS positivity and ABCD2 score are independent risk factors for cerebral infarction in AVS. Multi-factor combined assessment provides the best predictive performance for cerebral infarction, with HINTS showing optimal single-factor predictive capability.

Author Contributions: Zhang Chunyue conceptualized the study, enrolled patients, performed bedside examinations, data entry, and manuscript writing. Fang Liqun contributed to study design refinement, data analysis, critical revision, and final approval.

Conflict of Interest: The authors declare no conflict of interest.

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