

Vascular Vertigo and Dizziness: Diagnostic Criteria

*Consensus document of the Committee for the Classification of Vestibular Disorders
of the Bárány Society*

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Abstract

This paper presents diagnostic criteria for vascular vertigo and dizziness as formulated by the Committee for the Classification of Vestibular Disorders of the Bárány Society. The classification includes vertigo/dizziness due to stroke or transient ischemic attack as well as isolated labyrinthine infarction/hemorrhage, and vertebral artery compression and subclavian steal syndromes. Vertigo and dizziness are among the most common symptoms of posterior circulation strokes. Vascular vertigo/dizziness may be acute and prolonged (≥ 24 hours) or transient (minutes to < 24 hours). This diagnosis should be considered in patients who present with acute vestibular symptoms and additional central neurological symptoms and signs, central HINTS signs (normal head-impulse test, direction-changing gaze-evoked nystagmus, or skew deviation), particularly in the presence of vascular risk factors. Isolated labyrinthine infarction does not have a confirmatory test, but should be considered in individuals at increased vascular risk and can be presumed in cases of acute unilateral vestibular loss (most often with, but rarely without hearing loss) if accompanied or followed within 30 days by ischemic stroke in the anterior inferior cerebellar artery territory. For diagnosis of vertebral artery compression and subclavian steal syndromes, typical symptoms and signs in combination with imaging or sonographic documentation of vascular compromise are required.

Key words: Vertigo, Dizziness, Imbalance, Infarction, Stroke, Brainstem, Cerebellum

1. Introduction

The Bárány Society representing the international community of basic scientists, otolaryngologists and neurologists committed to vestibular research mandated a Classification Committee for an International Classification of Vestibular Disorders (ICVD) [12].

Vertigo/dizziness is one of the most common symptoms of posterior circulation stroke [31, 55, 109]. Its onset is typically acute and may be prolonged (≥ 24 hours, acute prolonged vertigo/dizziness) or transient (< 24 hours, acute transient vertigo/dizziness) [112, 133]. Transient vertigo/dizziness may recur in episodes (recurrent spontaneous vertigo/dizziness). An isolated positional vestibular syndrome (or recurrent positional vertigo/dizziness) due to vascular vertigo/dizziness is rare. Vertigo/dizziness in cerebrovascular disorders is usually accompanied by other neurological symptoms and signs [51, 76, 97, 156]. Recent advances in clinical neuro-otology/neuro-ophthalmology and neuroimaging have led to a consensus that strokes involving the brainstem or cerebellum can also present with isolated vertigo or imbalance [109]. Finally, acute transient vertigo/dizziness is also one of the most common manifestations of vertebrobasilar ischemia and is occasionally isolated [22, 56, 57, 85].

It is important to differentiate isolated vertigo of a vascular cause from non-vascular disorders (e.g., acute unilateral vestibulopathy (AUVP)/vestibular neuritis) involving the labyrinth or vestibular nerve since therapeutic strategies and prognosis differ in these two conditions [112]. Misdiagnosis of acute stroke may result in loss of effective treatment opportunities, which may increase morbidity and mortality, while over-diagnosis of vascular vertigo would lead to unnecessary costly work-ups and medication [32, 151-153]. Depending on the underlying etiology, more aggressive treatments including thrombolysis or endovascular intervention as well as transient dual antiplatelet therapy or anticoagulation may be indicated to treat a stroke and prevent recurrences of stroke in vascular vertigo [41, 42, 124]. Finally,

from a scientific point of view, detailed evaluation of patients with infarctions restricted to specific vestibular structures also allows a better understanding of the function of each vestibular structure and definition of various ischemic vestibular syndromes [94, 95].

To develop the diagnostic criteria for vascular vertigo and dizziness, creation of the subcommittee was initiated by the Members of the Classification Committee of the Bárány Society (CCBS) for the International Classification of Vestibular Disorders (ICVD) in Uppsala, 2012. They selected a chairperson (JSK) to choose subcommittee members representing different subspecialties from three different continents. Diagnostic criteria were developed through discussions among the subcommittee members. Draft criteria were presented to the CCBS in November 2020 and then modified based on comments. A revised draft became available for comments by the Bárány Society membership in July 2021.

2. Diagnosis of vascular vertigo/dizziness

Depending on the presentation, vascular vertigo/dizziness can be divided into acute prolonged (acute central vestibular syndrome) and episodic spontaneous vertigo/dizziness. Acute transient vertigo/dizziness may be termed when the patients with AVS are evaluated within 24 hours from symptom onset, or the patients present with a previous episode(s) of transient vertigo/dizziness of less than 24 hours [154].

2.1. Diagnostic criteria for acute prolonged vascular vertigo/dizziness

2.1.1. Acute prolonged vascular vertigo/dizziness

Criteria A-C should be fulfilled to make the diagnosis of acute prolonged vascular vertigo/dizziness.

A) Acute onset of vertigo, dizziness, or unsteadiness lasting for 24 hours or more¹⁾

B) Imaging evidence of ischemia or hemorrhage in the brain or inner ear, which corresponds to the symptoms, signs and findings²⁾

C) Not better accounted for by another disease or disorder

2.1.2. Probable acute prolonged vascular vertigo/dizziness

Criteria A-C should be fulfilled to make the diagnosis of probable acute prolonged vascular vertigo/dizziness.

A) Acute onset of dizziness, vertigo, or unsteadiness lasting for 24 hours or more¹⁾

B) At least one of the following:

1. Focal central neurological symptoms and signs, or severe postural instability³⁾

2. At least one component of central HINTS (normal head impulse test, direction-changing/gaze-evoked nystagmus, and skew deviation)⁴⁾

3. Other central ocular motor abnormalities (e.g., central nystagmus, impaired saccades or saccadic smooth pursuit)⁵⁾

4. Increased risk for vascular events (e.g., ABCD² score of 4 or more, or atrial fibrillation)⁶⁾

C) Not better accounted for by another disease or disorder

2.1.3. Notes

1) Acute prolonged vestibular syndrome consists of continuous vertigo/dizziness, imbalance, oscillopsia, vegetative symptoms (nausea/vomiting) and/or head motion intolerance lasting more than 24 hours [66, 165]. It has been estimated that 10-25% of patients with AVS may have a dangerous underlying central cause such as a stroke [77, 165].

2) Even though the gold standard for acute stroke is mostly based on the findings of neuroimaging, initial MRIs including DWI are false negative in 12-50% of the stroke patients within the first 48 hours [21, 75, 77, 153]. This has two implications: First, if the initial MRI is

normal, serial radiological evaluation is required to identify an acute lesion in these patients. Second, it increases the importance of a systematic clinical examination, which has a higher sensitivity during the acute phase than imaging. Further, since the internal auditory artery (IAA), usually a branch of the AICA, supplies the inner ear [127], vertigo and hearing loss can also be due to labyrinthine or very rarely eighth cranial nerve infarction [38, 83, 92]. As isolated labyrinthine damage may precede ponto-cerebellar involvement in AICA infarction, audio-vestibular loss may serve as an opportunity to prevent the progression to a more widespread infarction involving the posterior circulation, mainly in the AICA territory [90, 105].

A really rare entity is labyrinthine hemorrhage. It may occur spontaneously, but more frequently in association with head trauma or bleeding disorders [99, 175]. It shares with labyrinthine infarction the frequent association of vertigo and hearing loss but without brainstem involvement [175]. In labyrinthine hemorrhage, the vertigo is often severe and hearing loss is profound or total with a poor prognosis [175]. Labyrinthine hemorrhage may be identified by a hyperintense signal in the labyrinth on T1 or FLAIR MRIs, although this signal can also be inflammatory [175].

3) Severe postural instability is defined when the patients cannot maintain the upright sitting or standing posture (even with the feet apart) without a support [109].

4) In a study of 101 patients (69 ischemic strokes, 4 hemorrhages, and 28 non-strokes), a refined bedside examination protocol that incorporates HINTS performed by a clinical expert showed an up to 100% (69/69 with ischemic strokes, 95% CI = 95 - 100%) sensitivity and 96% (24/25 with acute peripheral vestibulopathy, 95% CI = 80 - 100%) specificity, giving a positive likelihood ratio of 25 (95% CI = 3.66 - 170.59) and a negative likelihood ratio of 0.00 (95% CI = 0.00 - 0.11), compared with delayed MRI in identifying ischemic strokes in patients with acute prolonged vertigo of more than 24 hours and one vascular risk factor, whereas initial DWIs were normal in 12% (8/69 ischemic strokes) [75]. Another report on 20 patients with

acute pure vestibular syndrome (10 with strokes and 10 with vestibular neuritis) also found diagnostic utility of the signs including normal horizontal HITs, SD, abnormal vertical smooth pursuit, and central type nystagmus at the bedside [19]. Since a mild degree of SD may go unnoticed during bedside examination and gaze-evoked nystagmus (GEN) may be absent in cerebellar strokes [109], bedside HIT may be the best tool for differentiating isolated vertigo due to cerebellar strokes from AUVP/vestibular neuritis. Indeed, of the three bedside signs of ‘HINTS’, the horizontal HIT had the greatest combined sensitivity (0.85, 95% CI =0.79-0.91) and specificity (0.95, 95% CI=0.90-1.00) for central causes [165]. Since pathological HITs and SD can be seen in either peripheral or central lesions, these tests are complementary in diagnosing central vestibular disorders [39, 75, 101]. Another study from a single academic center used a prospective design and a stroke outcome determinant of clinical and research study MRIs (either positive for infarction <24 hours from onset or negative for infarction and performed >24 hours from onset) as the gold standard [77]. The study found infarction on MRI in 10.7% (29 of 272; 95% CI = 7.3 - 15.0%) of patients [77]. Clinical parameters independently associated with infarction on MRI were as follows: vascular risk factors [ABCD² score; odds ratio (OR) = 1.74; 95% CI = 1.20 – 2.51), any other CNS features (OR = 2.54; 95% CI = 1.06 – 6.08), and central HINTS findings (OR = 2.82; 95% CI = 0.96 – 8.30). No stroke cases were in the model’s low-risk probability category (0/86, 0%), whereas 9 were in the moderate-risk category (9/94, 9.6%) and 20 were in the high-risk category (20/92, 21.7%) [77].

5) The HINTS may not be sufficiently robust to detect an AICA infarction since the HIT is mostly pathological in this disorder [69]. Patients with AICA territory infarction may develop isolated vertigo with negative HINTS (pathological HITs in the absence of GEN and skew deviation), mimicking unilateral peripheral vestibulopathy [108]. Since the AICA supplies the inner ear, the signs of an AUVP may overshadow the central signs and HINTS may be negative in AICA territory infarctions [36]. Indeed, about 5% of patients with AICA

territory ischemic strokes presented acute prolonged vertigo and canal paresis without hearing loss, mimicking acute peripheral vestibular syndrome [108]. Another study also showed negative HINTS in 5 of 17 patients (29.4%) with AICA infarction [69]. In those cases, addition of horizontal head shaking and hearing test with finger rub (HINTS plus) may aid in detecting a central lesion [69, 153].

6) By adopting the ABCD² score (age, blood pressure, clinical features, duration, and presence of diabetes), the future risk of stroke may be predicted in patients with *transient vertigo* [71]. In a previous study, only 1.0% (5/502) of dizzy patients with an ABCD² score of 3 or less had a stroke compared with 8.1% (25/369) in the patients with a score of 4 or more. Notably, 27% (7/26) of the patients with a score of 6 or 7 suffered from strokes [132]. Thus, the ABCD² score may predict cerebrovascular attacks in patients with vertigo [178]. A prospective study of emergency department dizziness presentations from a single center found that the ABCD² score as a continuous variable was an independent predictor of acute infarct on MRI (OR = 1.74, 95% CI = 1.20 – 2.51) adjusting for findings on the general neurologic and oculomotor examination [77].

2.2. Diagnostic criteria for transient vascular vertigo/dizziness and vascular vertigo/dizziness in evolution

2.2.1. Transient vascular vertigo/dizziness or vascular vertigo/dizziness in evolution

Criteria A-C should be fulfilled to make the diagnosis of acute transient vascular vertigo/dizziness.

- A) Acute spontaneous vertigo, dizziness, or unsteadiness lasting less than 24 hours¹⁾
- B) Imaging evidence of ischemia or hemorrhage in the appropriate brain regions²⁾
- D) Not better accounted for by another disease or disorder

2.2.2. Probable transient vascular vertigo/dizziness or vascular vertigo/dizziness in evolution

Criteria A-C should be fulfilled to make the diagnosis of probable acute transient vascular vertigo/dizziness.

A) Acute spontaneous vertigo, dizziness, or unsteadiness lasting less than 24 hours¹⁾

B) At least one of the followings during the attacks

1. Focal central neurological symptoms and signs, or severe postural instability
2. At least one component of central HINTS (normal head impulse tests, direction-changing/gaze-evoked nystagmus, and skew deviation)³⁾
3. Other central ocular motor abnormalities (e.g., central nystagmus, impaired saccades or saccadic smooth pursuit)
4. New onset of moderate to severe cranio-cervical pain⁴⁾
5. Increased risk for vascular events (e.g. ABCD² score of 4 or more, or atrial fibrillation)
6. Significant (>50%) narrowing of an artery of the vertebrobasilar system⁵⁾

C) Not better accounted for by another disease or disorder⁶⁾

2.2.3. Notes

1) Many patients develop acute transient vertigo/dizziness or imbalance lasting less than a day, which may be termed acute transient vestibular syndrome (ATVS) [22], even though the National Institute of Neurological Disorders and Stroke (NINDS) III Classification and the European Stroke Organization (ESO) Executive Committee and the ESO Writing Committee do not embrace isolated vertigo as a symptom of TIA involving the vertebrobasilar territory (VB-TIA) [53]. The use of the previous terminology “vertebrobasilar insufficiency” is not recommended [18]. ATVS frequently occurs in VB-TIA [57, 147]. Indeed, isolated episodic

vertigo was the only manifestation in 21% (6/29) of patients with a presumptive diagnosis of VB-TIA [56], and 62% (29/42) of the patients with vertigo due to VB-TIA and 29% (12/42) of patients with vertebrobasilar infarction had a history of isolated episodic vertigo [57]. Furthermore, recent studies reported that preceding transient isolated brainstem symptoms are common in patients with a completed stroke in the vertebrobasilar territory [147]. The episodic vertigo is typically spontaneous in onset and lasts for minutes in VB-TIA [57, 66]. Despite detailed neuro-otologic examination and neuroimaging studies including MRIs with DWI and perfusion imaging, underlying etiologies remained unknown in more than half of the patients with ATVS [22]. It may be attributed to rapid resolution of some peripheral vestibular disorders such as BPPV or Meniere's disease during their first attack. Transient brainstem hypoperfusion may be another possibility since perfusion imaging has limitations in detecting a small perfusion defect restricted to the brainstem.

2) DWI provides evidence of acute infarction in one third (27/87, 31%) of the patients with TIA and in 23% (13/56) of the patients with a clinical diagnosis of a transient neurological attack (TNA) [173]. A recent study also found stroke in 27% [23/86, cerebral infarction in 15% (13/86) and cerebellar hypoperfusion in 12% (10/86)] of the patients presenting ATVS [22].

3) Whereas application of HINTS has greatly enhanced the diagnosis of stroke in acute prolonged vascular vertigo, the diagnostic utility of HINTS/HINTS plus examination and MRIs was limited in ATVS. HINTS plus could not be applied to the majority of patients with ATVS since the vestibular symptoms or signs had already resolved by the time of evaluation in about 73% (63/86) of the patients [22].

4) Even though headache is a common symptom, moderate to severe craniocervical pain is very rare in peripheral vestibular disorders. Thus, when patients experience new onset of moderate to severe craniocervical pain along with acute vestibular symptoms, vascular dissection or posterior circulation strokes including hemorrhages should be suspected,

especially when migraine or vestibular migraine is unlikely. Indeed, associated craniocervical pain was a clue for strokes with an OR of 15.2 (95% CI = 2.5 - 93.8, multivariate logistic regression analysis) in a study of 86 patients who were diagnosed with ATVS [22].

5) In a previous study on ATVS [22], eight of the 10 patients with unilateral cerebellar hypoperfusion only on perfusion images without an infarction on DWI showed a focal stenosis or hypoplasia of the corresponding VA. The results of multivariate logistic regression analysis showed that VA stenosis or hypoplasia (OR = 7.0, 95% CI = 1.7 - 29.4) is a risk factor for strokes in patients with acute transient vestibular syndrome [22]. Besides atherosclerotic stenosis or occlusion, hypoplasia of the VA may be a predisposing factor for posterior circulation stroke especially when vascular risk factors coexist [2, 73].

6) A vascular origin is a serious concern in patients with new onset episodic vertigo/dizziness and vascular risk factors. If, however, episodes have been occurring for many months or years, other diagnoses such as vestibular migraine or Menière's disease are more likely [133]. In conclusion, currently we still do not have an accurate tool for the diagnosis of vascular vertigo presenting with transient vertigo.

2.3. Diagnostic criteria for vertebral artery compression syndrome (VACS)

2.3.1. Vertebral artery compression syndrome (VACS)

Criteria A-D should be fulfilled to make the diagnosis of VACS.

A) Vertigo with or without tinnitus provoked by a sustained eccentric neck position, especially in an upright body position¹⁾

B) Presence of nystagmus with the symptoms during an attack²⁾

C) Either 1) or 2) during the provoking head motion³⁾

1) Documentation of VA compression using a dynamic angiography

2) Demonstration of decreased blood flow in the posterior circulation using transcranial Doppler

D) Not better accounted for by another disease or disorder⁴⁾

2.3.2. Previously used terms

Bow hunter's syndrome, rotational VA syndrome, rotational VA compression syndrome, rotational VA occlusion syndrome

2.3.3. Notes

1) Episodic vertigo, nystagmus and syncope may rarely occur due to mechanical compression of the VA induced by horizontal or diagonal neck rotation, tilt or extension [102, 170, 188]. Tinnitus develops several seconds after the onset of vertigo and nystagmus, which suggests that the vestibule is more sensitive to ischemia than the cochlea [30, 163]. Those are the neck movements which lead to the vascular compression, and not the head motion as such.

2) Oculographic analyses of nystagmus reveal various patterns of nystagmus during the attacks of VA compression syndrome [34, 125, 163]: the initial nystagmus is mostly downbeat, with the horizontal and torsional components beating either towards the compressed VA side, indicating a transient excitation of the labyrinth [163], or directed away [34]. Some patients show spontaneous reversal of the nystagmus and no or markedly diminished responses on immediate retrial of neck rotation (habituation) [34].

3) Patients with VACS usually have one hypoplastic or stenotic VA, or the VA terminating as PICA, and the contralateral dominant VA that is compressed or occluded at the atlantoaxial junction during head rotation to the contralateral side [30, 34, 138]. VACS is confirmed when angiography documents compression of the VA during the attacks of vertigo induced by neck motion [30], but may also be diagnosed by demonstrating neck rotation-

induced decrease of the blood flow in the posterior circulation using transcranial Doppler [155]. There is no evidence that contractions or spasms of the neck muscles could lead to VA compression.

4) VACS should be differentiated from other disorders that may give rise to vertigo/dizziness by head motion, which include BPPV [176], posterior fossa tumors and inflammation, cysts in the cerebello-pontine angle [5], multiple sclerosis, vestibular paroxysmia [162], and Chiari malformation [48].

2. 4. Diagnostic criteria for vertigo/dizziness due to subclavian steal syndrome

2.4.1. Vertigo/dizziness due to subclavian steal syndrome

Criteria A-D should be fulfilled to make the diagnosis of vertigo/dizziness due to subclavian steal syndrome.

- A) Acute or episodic dizziness, vertigo, or unsteadiness¹⁾
- B) Imaging documentation of a proximal stenosis or occlusion of the subclavian artery²⁾
- C) Demonstration of retrograde (reversed) blood flow in the VA³⁾
- D) Not better accounted for by another disease or disorder⁴⁾

2.4.2. Notes

1) In subclavian steal syndrome, either acute or episodic vestibular syndrome may occur from decreased perfusion in the posterior circulation due to an occlusion or stenosis of the subclavian artery proximal to the origin of the VA and resultant reversal of the blood flow in the VA [50, 149]. The symptoms of vertebrobasilar ischemia are typically induced or aggravated during exercise of the arms; rarely they may occur spontaneously [171].

2) Subclavian steal syndrome occurs three times more often on the left side, and atherosclerosis is the most common cause of subclavian artery stenosis [171].

3) The retrograde blood flow in the VA may be demonstrated with conventional angiography, duplex ultrasound or transcranial doppler [98, 148, 149].

4) The differential diagnoses for subclavian steal syndrome include all those for acute and episodic vestibular syndrome [59, 118, 133].

Comments

3. Lesion sites responsible for isolated vascular vertigo

In a study performed in the ED of a tertiary referral hospital, 47 (13.4%) of 351 patients with acute and isolated vestibular or ocular motor symptoms of unclear etiology showed acute unilateral stroke on MRIs [190]. Volumetric analyses showed that medial cerebellar strokes are associated with vertigo, lateral cerebellar strokes with dizziness, and pontomesencephalic strokes with double vision [190]. In contrast, cerebral cortical lesions were rare and presented with milder symptoms of shorter duration [190].

3.1. Brainstem

In brainstem lesions, vertigo/dizziness is commonly associated with other neurological symptoms and signs, but some patients with isolated vestibular syndrome showed a small lesion restricted to the vestibular nuclei or root entry zone of the eighth cranial nerve in the pontomedullary junction [52, 168], dorsolateral medulla [88, 116, 169], pontine or midbrain tegmentum [47, 186, 190], and cerebellar peduncles [9, 23, 114, 153],

Patients with an infarction involving the caudal lateral medulla may present with isolated imbalance, probably due to interruption of the lateral vestibulospinal or dorsal spinocerebellar tracts. In a study of 105 patients with AVS and at least one stroke risk factor

from a single academic medical center, approximately 15% (15/105) of the patients with a stroke had isolated AVS from a small (≤ 10 mm) infarction, and 11 of them (11/15, 73%) showed a lesion involving the inferior cerebellar peduncle, mostly in the lateral medulla (9/11, 82%) [153]. Interestingly, only one patient showed isolated small infarction in the cerebellum [153], which is known as one of the most common sites causing AVS when involved [21, 109]. The inferior cerebellar peduncle carries various input and output fibers to and from the cerebellum, which are mainly concerned with integrating the proprioceptive sensory inputs with the vestibular function such as balance. Proprioceptive information from the body is carried to the cerebellum via the posterior spinocerebellar tract in the inferior cerebellar peduncle. The vestibulocerebellum also receives mossy fiber inputs from the vestibular nuclei and nerve, and projects efferent fibers to the vestibular nuclei via the inferior cerebellar peduncle. Thus, an infarction involving the inferior cerebellar peduncle may result in imbalance with vertigo and nystagmus [23]. Since the medial vestibular nucleus is more vulnerable to ischemia than other structures in the brainstem or cerebellum according to a recent animal study [110], ischemia of the dorsolateral medulla where the vestibular nuclei are located may be a mechanism of isolated vascular vertigo. Indeed, several studies described isolated vertigo from infarctions restricted to the vestibular nuclei [88]. Rarely, cerebral hemispheric infarctions involving the vestibular cortices can cause isolated vertigo with spontaneous nystagmus and SVV tilt [1, 13, 177].

However, since previous reports on isolated vestibular syndrome of vascular cause are mostly limited to anecdotal case reports, small case series from a single center, and specific subtypes of posterior circulation ischemia, the overall frequency and the structures involved remain to be determined in strokes presenting with isolated vestibular syndrome.

3.2. Cerebellum

The frequency of acute isolated vascular vertigo and the structures involved were analyzed in 132 prospectively recruited consecutive patients with posterior circulation infarctions in a referral Stroke Center [21]. This study found that approximately 26% (34/132) of patients with posterior circulation infarction present with isolated vestibular syndrome: cerebellar infarction (67.6%) was most frequent, mostly in the territory of medial PICA. These results are consistent with those of previous and recent studies that showed a high frequency of medial PICA infarction in patients presenting with acute isolated vascular vertigo, and frequent isolated vertigo in medial PICA infarction [109, 190]. Indeed, dysmetria, a major sign of cerebellar dysfunction, may be minimal or absent in cerebellar infarctions involving the territory of medial PICA, especially when the infarction is not large. In the cerebellum, the nodulus and ventral uvula may cause isolated vestibular syndrome when damaged [107, 129]. A study of eight patients from a single center also showed that isolated nodular infarction mostly presents with isolated vertigo and imbalance without other neurological deficits, mimicking acute peripheral vestibulopathy [129]. The flocculus and paraflocculus may be another neural structures leading to isolated vestibular syndrome [113, 144, 183]. They participate in the control of smooth tracking, gaze-holding, and eye movements induced by vestibular stimulation, and experimental lesions cause GEN, downbeat nystagmus, post-saccadic drift, and impaired smooth pursuit and cancellation of the VOR [189]. However, since the flocculus is supplied by a branch from the AICA, which also supplies the dorsolateral pons and inner ear, an infarct involving the flocculus usually accompanies other brainstem signs or hearing loss [4]. Studies have also suggested the inferior cerebellum as a lesion site responsible for isolated vascular vertigo. In AVS due to stroke, the lesions are mostly found in the cerebellum, usually in the territory of PICA [109]. In a previous retrospective study of 240 patients with a cerebellar infarction in a single center, isolated vestibular syndrome mimicking vestibular neuritis was found in 10% (25/240) of patients [109]. A patient with multiple vascular risk factors and

isolated recurrent vertigo lasting several seconds to minutes showed a severe focal stenosis (80%) of PICA along with impaired perfusion in the caudal cerebellum [81]. Another patient also developed VACS due to compression of the VA terminating as PICA [138]. Since the circulation through the basilar artery from the contralateral VA remained intact during the attack, the vertigo was ascribed to transient ischemia of the inferior cerebellum or lateral medulla [138]. Even a patient with recurrent asystole due to sick sinus syndrome [25] or the patients with severe orthostatic hypotension [24] showed downbeat nystagmus during the vertigo attacks, which suggests that the inferior cerebellum is vulnerable to hypoperfusion.

3.3. Inner ear

Even though infarction or ischemia restricted to the central vestibular structures is more common in isolated vascular vertigo/dizziness, the inner ear is also a strong candidate due to its requirement for high-energy metabolism and absence of collateral circulation [92, 139]. The labyrinth and its individual components appear to be vulnerable to ischemia because the IAA is an end artery with minimal collaterals from the otic capsule [127], leading most often to a severe peripheral vestibular deficit and loss of hearing (see above). By contrast, the vestibulocochlear nerve is felt to be less vulnerable to ischemia based on the arterial system of the internal auditory canal [127]. However, it is nearly impossible to document isolated labyrinthine infarction, labyrinthine component infarction, or vestibulocochlear nerve infarction without a pathologic study [38, 92, 119].

4. Epidemiology of vascular vertigo/dizziness

Approximately 20% of ischemic events are known to involve the neural structures supplied by the posterior (vertebrobasilar) circulation, and vertigo/dizziness is one of the most common

symptoms of vertebrobasilar diseases [147, 156]. Recent large database prospective studies also reported dizziness as a presenting symptom in 47-75% of patients with posterior circulation stroke [3, 158]. In the USA, dizziness and vertigo account for 3.3% to 4.4% of visits to emergency departments (ED) [134], and stroke is responsible for 3-4% of these presentations [76, 77, 134]. Furthermore, those patients hospitalized with isolated vertigo have a 3 times (95% CI, 2.20-4.11; $p < 0.001$; absolute risk, 6.1% vertigo group vs 1.9% comparison group) higher risk for stroke than a comparison group of patients hospitalized for appendectomy during the 4-year follow-up [104]. Nearly all of the excess risk for stroke occurred in vertigo patients with vascular risk factors. In particular, those patients with three or more risk factors had a 5.51-fold higher risk for stroke (95% CI, 3.10-9.79; $p < 0.001$) than those without risk factors [104]. Nearly all of the excess risk for stroke occurred in vertigo patients with vascular risk factors. Overall, patients with vertigo/dizziness show a 2-fold (95% CI, 1.35-2.96, $p < 0.001$) higher risk of stroke or cardiovascular events than a non-dizziness comparison group during a follow-up of 3 years after adjusting for confounding and risk factors [103]. Thus, even if we accept that a (proven) cerebrovascular cause is rare in isolated vertigo in unselected samples and risk of future stroke is low, the future risk of stroke is considerably relatively higher in those with vertigo/dizziness than in those with non-dizziness visits [6], especially when several vascular risk factors are present. Furthermore, there has been an accumulation of evidence indicating that posterior circulation ischemia can present with isolated vertigo without other focal signs [21, 109].

Vertebrobasilar ischemia is also a serious concern when patients present with acute transient vertigo [51, 56, 57]. It typically occurs abruptly, and usually lasts several minutes to hours [22, 51]. In one study of 84 patients with vertigo due to vertebrobasilar ischemia, 62% had at least one isolated episode of vertigo, and 19% developed vertigo as the initial symptom [57]. In another study, 21% of the 29 patients with transient ischemia within the vertebrobasilar

circulation reported episodic vertigo as the only symptom for at least 4 weeks [56]. In a study, 22% of posterior circulation stroke patients reported subtle transient neurological symptoms in the 90 days preceding their stroke, most frequently vertigo [147]. Patients with infarction in the territory of the anterior inferior cerebellar artery (AICA) can also experience isolated recurrent vertigo, fluctuating hearing loss, and/or tinnitus (similar to Menière's disease) as the initial symptoms 1-10 days prior to the infarction [11, 106, 120]. Thus, to prevent future strokes, it is crucial to identify those patients presenting with vertiginous episodes as a symptom of a transient ischemic attack (TIA)[85, 172].

5. Evaluation of vascular vertigo/dizziness

When acute vertigo/dizziness accompanies other neurological symptoms and signs, diagnosis of central, most often vascular vertigo is straightforward in most cases even without documentation of a stroke with neuroimaging. Even though introduction of diffusion-weighted MRI (DWI) has greatly enhanced detection of infarctions in patients with vascular vertigo/dizziness especially due to compromised posterior circulation or atrial fibrillation, bedside neuro-otologic evaluation by experts has been more sensitive than acute MRI including DWI in detecting acute small infarction on a delayed MRI as the cause of spontaneous vertigo lasting more than 24 hours, especially during the first 48 hours [21, 75, 136, 153].

Thus, vascular vertigo should be strongly suspected in patients with acute vestibular syndrome (AVS) and vascular risk factors even though confirmation of a stroke is mostly based on the findings of the neurotological examination and imaging of the brain and cerebral vasculature [179]. Vascular causes should also be suspected in non-positional episodic vestibular syndrome (EVS), especially when the dizzy spells last only minutes in patients with risk factors for stroke [57]. Brain imaging assists in determining the involved territories and

stroke etiology. Finally, ischemic strokes account for about 80% of all strokes [43] and most posterior circulation stroke are of embolic origin [16].

5.1. Clinical evaluation

Despite the marked progress in laboratory medicine and neuroimaging, systematic history taking and bedside identification of central vestibular, ocular motor and other neurological symptoms and signs provide the foundation for accurate diagnosis of vestibular disorders [44, 68, 77, 174]. Patients with vascular vertigo/dizziness invariably present with sudden onset of these symptoms, either transient or persistent [57]. Patients often have vascular risk factors or atrial fibrillation and, in most cases, in association with other neurological symptoms and signs. History may disclose preceding attacks of dizziness/vertigo suggestive of transient vertebrobasilar ischemia [51, 57]. Patients with vertigo/dizziness should have bedside evaluation for ocular misalignment including skew deviation (SD) as a component of the ocular tilt reaction (OTR), spontaneous and gaze-evoked nystagmus, head impulse test (HIT), and posture and balance function [39, 46, 68]. Positional testing and examination of head-shaking nystagmus, saccades and smooth pursuit may provide additional support in discriminating a central from a peripheral lesion location [28, 39, 69].

Ocular tilt reaction (OTR) and tilt of the subjective visual vertical (SVV). The OTR refers to the triad of head tilt, SD, and ocular torsion [14, 62, 182]. The OTR and SVV tilt may be attributed to unilateral lesions involving the graviceptive pathways from the otolithic organs and semicircular canals [14, 54, 62]. SD indicates vertical misalignment of the eyes in the absence of an extraocular muscle palsy or strabismus. The presence of SD or other ocular misalignment should be determined with the cover and in particular the alternating cover test. In OTR, the head tilt and ocular torsion occur toward the lower eye. Even though SD may be

observed in peripheral vestibular disorders, it has been included as a part of an ocular motor assessment to discriminate central from peripheral causes of AVS [39, 75]. However, since SD is found in only about one third of patients with acute unilateral brainstem infarctions, it is not very sensitive (31%, n=111) [14], but quite specific since it was not observed in any of the 43 patients with vestibular neuritis in one study [39]. However, another study reported that 14% (7/50) of patients with vestibular neuritis had SD [82]. Pathological SVV tilts (94%, n=111) and ocular torsion (83%, n=111) are the most sensitive signs of vestibular imbalance in the roll plane in patients with acute unilateral brainstem infarction [14], but they do not discriminate between a peripheral and central lesion [191]. SVV can be easily measured in the emergency department (ED) by the bucket test [191]. In patients with vertigo/dizziness and ocular motor palsy, a pathological SVV deviation in the non-paretic eye may aid in differentiation of central from peripheral lesions [100]. The measurement of ocular torsion requires fundus photography or a scanning laser ophthalmoscope [14, 62, 191].

Spontaneous, gaze-evoked, head-shaking and positional nystagmus

Spontaneous nystagmus. Patients with AUVP/vestibular neuritis show spontaneous horizontal-torsional nystagmus that beats away from the lesion side [46]. The nystagmus is unidirectional and maximal when looking in the direction of the fast phases of nystagmus (Alexander's law). In contrast, pure downbeat, upbeat, or torsional nystagmus is well recognized in central vestibular lesions [117]. Marked suppression by visual fixation has been considered a hallmark of peripheral nystagmus [63]. The effects of visual fixation on spontaneous nystagmus are variable in central lesions [65, 123]. Failure of fixation suppression is observed in about 50% of patients with cerebellar infarctions, especially when the nodulus and flocculus are affected [86]. Thus, proper observation of nystagmus requires the use of Frenzel's goggles or M glasses [161]. Fixation may even evoke nystagmus or augment

spontaneous nystagmus in central lesions [29, 164].

Gaze-evoked nystagmus (GEN). Integrity of the central neural network is evaluated by inducing eccentric gaze [117]. Direction-changing GEN or gaze-holding nystagmus in the horizontal or vertical plane is generally considered a sign of impaired neural integration from lesions involving the brainstem and cerebellum [46]. However, with a peripheral lesion, a reversal of the nystagmus direction can occur with gaze in the opposite direction to the spontaneous slow phase on close inspection in the dark based on the theory of a leaky neural integrator induced by the acute peripheral vestibular asymmetry [78, 150] .

Head-shaking nystagmus (HSN) and positional nystagmus. Both may give additional information. HSN may be ipsi- or contralesional according to the location and extent of central lesions [33, 67, 69]. However, vigorous HSN ($> 50^{\circ}/s$) or HSN with cross-coupling (mostly downbeat after horizontal head shaking) should be considered a central sign [185]. Vigorous horizontal HSN is typically observed in patients with lateral medullary infarction [33]. HSN with cross-coupling has been reported in strokes involving the cerebellum or brainstem [27, 67, 69, 84, 89], and has been explained by enhanced responses of the anterior canal pathway due to cerebellar dysfunction [27].

Positional maneuvers can evoke nystagmus or modulate the spontaneous nystagmus in central as well as peripheral vestibular disorders. Central positional vertigo and nystagmus may be paroxysmal (<1 minute in duration) or persistent [11, 15, 26, 28]. Since the paroxysmal and persistent forms of central positional nystagmus may mimic the positional nystagmus from benign paroxysmal positional vertigo (BPPV) [15, 93], a central lesion should be suspected in patients with positional nystagmus when atypical for BPPV, mimicking multi-canal BPPV, or refractory to repeated treatment maneuvers [93, 131]. However, vascular causes are very rare in pure positional vertigo/dizziness, and there have been no convincing cases of a central lesion causing a typical nystagmus pattern of posterior canal BPPV: upward/torsional nystagmus with

a transient crescendo-decrescendo pattern, elicited on the Dix-Hallpike/diagnostic Sémont maneuver to the affected side. Geotropic or apogeotropic central positional nystagmus can also be differentiated from BPPV involving the horizontal semicircular canal by the temporal profile of the positional nystagmus, associated central symptoms and signs, and no response to repeated canalith repositioning maneuvers [26, 28, 35]

Head-impulse test (HIT)

The bedside HIT is a useful tool for differentiating central vascular vertigo from disorders of the peripheral vestibular structures involving the inner ear [39, 75, 135], but it has a low sensitivity and specificity to diagnose a vestibular deficit [187]. Therefore, whenever possible the video-HIT should be applied (see below). Pathological HITs with corrective catch-up saccades due to a reduced gain of the vestibulo-ocular reflex (VOR) are generally considered as localizing to the peripheral vestibular structures, particularly the vestibular nerve or labyrinth [61]. In contrast, a bilaterally normal HIT indicates that the peripheral vestibular function is intact, and therefore is suggestive of a central lesion in patients with AVS [75]. Indeed, bedside HITs were normal in 24 patients with isolated vertigo from cerebellar infarction involving the medial posterior inferior cerebellar artery (PICA) territory [109]. However, the HIT may also be pathological in patients with cerebellar or brainstem strokes (3/34, 9%) [135]. Recent studies documented pathological HITs in patients with lesions involving the central vestibular structures such as the root entry zone of the vestibular nerve, vestibular nucleus [88], flocculus [144], and nucleus prepositus hypoglossi (NPH) [96]. In unilateral lesions involving the flocculus or NPH, pathological HITs may be more prominent when the head is turned to the intact side. Bedside HITs were also positive during contralesional head rotation in about 20% of patients with posterior inferior cerebellar or superior cerebellar artery territory infarction (4 of 20) [20]. Thus, while normal HITs are a strong indicator of central vestibular dysfunction in

patients with AVS, pathological HITs do not necessarily indicate a peripheral lesion. Furthermore, bedside HITs may be normal (false negative), especially when the vestibular deficits are partial, e.g., in Menière's disease with a low-frequency deficit only or during an attack of Menière's disease, or when the corrective saccades occur during the head impulse (covert saccades) [39, 115, 128, 180]. It should also be noted that up to 12% of patients with acute unilateral vestibular loss/vestibular neuritis may have an isolated inferior divisional involvement and thus show normal HITs for the horizontal semicircular canals [7, 91, 111].

In these respects, the video-HIT can provide objective measurements of VOR gains and document isolated vertical canal involvements during HITs [8, 121]. Relative to quantitative testing with a magnetic scleral search coil technique, the sensitivity of clinical HITs for identifying vestibular hypofunction at the bedside ranges widely between 35% and 71% depending on the test technique and the extent of vestibular loss [10, 157, 187]. More importantly, examiner skill plays an important role in detecting an abnormal result [72], raising questions about whether inexperienced examiners should use the clinical HIT to make high-stakes triage decisions about stroke in acute dizziness in the ED [40, 142]. Eye and head movements can now be recorded at the bedside using light-weight portable video goggles with an integrated high-speed infrared camera [8, 121]. These VOG goggles, also referred as the video-HIT (see below), assist physicians to correctly perform a standardized HIT and facilitate interpretation of the test results [130]. It was demonstrated that portable VOG can be used in the ED in real time to help differentiate brain infarction from acute unilateral peripheral vestibular loss/vestibular neuritis in patients with AVS [122, 137].

Central ocular motor signs

Saccades. Abnormal saccades may be a feature of central lesions. Slow saccades in association with or without limited ocular motor ranges (gaze palsy) indicate a brainstem lesion in the

midbrain affecting the rostral interstitial nucleus of the medial longitudinal fascicle for vertical saccades and the paramedian pontine reticular formation for horizontal saccades (ipsiversive) [117]. Hypermetric saccades suggest lesions involving the cerebellum (fastigial nucleus) or lateral medulla, and hypometric saccades imply lesions involving the dorsal ocular motor vermis [117].

Smooth pursuit. Impaired smooth pursuit is also considered a central sign, and is considered a hallmark of subacute and chronic cerebellar disorders such as immune-mediated and neurodegenerative disorders. However, smooth pursuit is typically less relevant in identifying acute vascular vertigo and should be interpreted with caution since it could be affected by various factors including an underlying spontaneous nystagmus, age, drugs and mental status.

Posture and gait

Patients with vascular vertigo should have evaluation of balance while standing and gait. Severe postural instability or instability out of proportion to the vertigo is a predictor of a central lesion [58, 109, 174, 184].

5.2. Laboratory tests

Examination of the vestibular, ocular motor and auditory systems. Likewise in vHIT, video-oculography may aid in documenting and characterizing spontaneous and evoked nystagmus, and other ocular motor function including saccades and smooth pursuit. Caloric tests are mostly normal and are of limited value in assessing the horizontal VOR in central vestibular disorders. Ocular and cervical vestibular evoked myogenic potentials (o/cVEMPs) have been applied to evaluate the function of the otolithic pathways in central as well as peripheral vestibular disorders [140]. In patients with isolated vestibular nucleus infarction, o/cVEMPs were diminished or absent during stimulation of the ipsilesional ear [88]. Above the vestibular

nucleus level, oVEMPs are impaired in lesions involving the medial longitudinal fasciculus [87, 141]. In unilateral cerebellar infarction, o/cVEMPs are frequently impaired (14/27, 51.9%) [37]. Thus, abnormalities of VEMP are not helpful in differentiating peripheral from central vestibular disorders [49].

Ocular torsion can be measured with fundus photos [62]. Patients may have quantitative evaluation of the SVV, for instance using the Bucket Test or more specialized equipment; a deviation of SVV is found in more than 90% (48/51) of patients with unilateral vestibular lesions [82], but it does not discriminate between a peripheral and central lesion [191].

In patients with acute auditory symptoms, pure tone and speech audiometry can aid in documenting hearing loss, in particular if an AICA-infarction is suspected [108].

Blood tests

In general, routine laboratory studies including complete blood counts, electrolytes, and thyroid function tests have a very low yield in diagnosing a cause of dizziness. In a meta-analysis, only 26 of 4,538 patients (0.6%) had laboratory abnormalities that could explain their dizziness [64]. The ischemic stroke guidelines also recommend a limited number of hematologic, coagulation, and biochemistry tests during the initial emergency evaluation, and only the assessment of blood glucose must precede the initiation of intravenous recombinant tissue plasminogen activator [70]. If giant cell arteritis is a concern, then inflammatory makers should be checked. The diagnostic values of serum biomarkers in differentiating central from peripheral causes remains to be elucidated [79, 160].

Cardiovascular work-up

Extra- and transcranial Doppler/duplex sonography, ECG monitoring, and echocardiography

are of course also recommended in patients with acute ischemic stroke [70].

5.3. Imaging

Neuroimaging studies are essential in the evaluation of stroke. CT has a limited value in detecting acute posterior circulation infarction, and is only recommended to detect hemorrhages [17, 45]. Introduction of DWI has greatly enhanced detection of infarctions in patients with isolated vascular vertigo. However, even DWI may miss up to one in five strokes occurring in the posterior fossa when performed during the first 24–48 hours, though this may relate in part to the MRI protocol of slice thickness and gaps [21, 75]. False negative initial MRIs (6–48 hours) were more common with small (≤ 10 mm) strokes than larger ones (53% vs 7.8%, $p < 0.001$) [153]. Furthermore, current imaging technique cannot detect isolated labyrinthine infarction that may progress to involve the portions of the brainstem and cerebellum supplied by the AICA [38, 90]. Thus, serial evaluation should be considered in patients with suspected vascular vertigo when the initial DWIs are normal [21, 75].

It is still challenging to visualize an image correlate of acute isolated vascular vertigo when MRIs including DWI do not show any evidence of acute infarction. Repetition of DWI may be useful. Since perfusion CT or MRI can detect hypoperfusion and potentially reversible injury to the brain, it may aid in detection of isolated vascular vertigo especially when MRIs including DWIs are normal [81, 166]. Perfusion imaging has mostly been applied to assess the risks or benefits of stroke intervention or to predict the outcome of the infarctions [166]. However, perfusion imaging does not readily detect small perfusion reduction in the brainstem, and thus the diagnostic yield of perfusion imaging still needs to be validated in isolated vascular vertigo [126].

Imaging of the cerebral vasculature using CT/CT-angiography or MRI/MR-angiography can be considered in patients with suspected vascular vertigo; however the

evidence base for vascular interventions in the posterior circulation is substantially less than that for interventions in the anterior circulation [112]. Unilateral cerebellar hypoperfusion is mostly caused by stenosis or occlusion of the ipsilesional vertebral artery (VA) or proximal PICA. In one study, approximately 80% (8/10) of patients with cerebellar hypoperfusion on perfusion CT or MRI showed a luminal irregularity or hypoplasia of the corresponding VA [22]. VA hypoplasia may be a risk factor for posterior circulation ischemia, especially when other vascular risk factors coexist [74, 145]. A study using perfusion CT revealed that VA hypoplasia can lead to a relative regional hypoperfusion in the territory of PICA [167]. In patients with vertigo/dizziness of unknown etiology, the prevalence of VA hypoplasia is higher than that in the control group [143]. Indeed, unilateral hypoplastic VA may rarely cause recurrent isolated vertigo and subsequent cerebellar infarction [2]. In patients with cerebellar hypoperfusion on perfusion CT or MRI in the presence of normal VA on the corresponding side, focal atherosclerosis or dissection of the PICA should be suspected, which may require conventional digital subtraction angiography for documentation [81, 146].

It is noteworthy that, if current imaging cannot detect isolated labyrinthine infarction, observation of a hypersignal in the labyrinth on pre-enhanced T1 or FLAIR MRIs is in keeping with the rare diagnosis of labyrinthine hemorrhage [80, 159, 181].

Finally, vascular imaging of the neck can be used to diagnose VA dissection, in particular in the setting of neck pain or trauma [60].

6. Conclusion

First, history taking about the characteristics of vestibular symptoms, associated central symptoms, and vascular risk factors should be the first step in diagnosing vascular vertigo/dizziness despite the marked progress in neuroimaging and laboratory medicine,

Second, a systematic examination focused on central vestibular and ocular motor signs, especially HINTS, is more accurate than EARLY imaging in diagnosing vascular vertigo/dizziness based on LATE imaging. Third, the video HIT and recording of eye movements may help to increase the diagnostic accuracy. Fourth, identifying the underlying etiology of vascular vertigo/dizziness is essential for appropriate treatments, including acute treatments and secondary prevention of further stroke.

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