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ORIGINAL ARTICLE

Validation of a comprehensive diagnostic algorithm for patients with acute vertigo and dizziness

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Abstract

Background and purpose: Vertigo and dizziness are common complaints in emergency departments and primary care, and pose major diagnostic challenges due to their various underlying etiologies. Most supportive diagnostic algorithms concentrate on either identifying cerebrovascular events (CVEs) or diagnosing specific vestibular disorders or are restricted to specific patient subgroups. The aim of the present study was to develop and validate a comprehenisve algorithm for identifying patients with CVE and classifying the most common vestibular disorders.

Methods: The study was conducted within the scope of the "PoiSe" project (**P**revention, **O**nline feedback, and **I**nterdisciplinary Therapy of Acute Vestibular **S**yndromes by **e**-health). A three-level algorithm was developed according to international guidelines and scientific evidence, addressing both the detection of CVEs and the classification of non-vascular vestibular disorders (unilateral vestibulopathy, benign paroxysmal positional vertigo, vestibular paroxysmia, Menière's disease, vestibular migraine, functional dizziness). The algorithm was validated in a prospectively collected dataset of 407 patients with acute vertigo and dizziness presenting to the Emergency Department at the Ludwig-Maximilian University of Munich.

Results: The algorithm assigned 287 of 407 patients to the correct diagnosis, corresponding to an overall accuracy of 71%. CVEs were identified with high sensitivity of 94%. The six most common vestibular disorders were classified with high specificity, above 95%. Random forest identified presence of a paresis, sensory loss, central ocular motor and vestibular signs (HINTS [head impulse test, nystagmus assessment, and test of skew deviation]), and older age as the most important variables indicating a cerebrovascular event.

Conclusions: The proposed diagnostic algorithm can correctly classify the most common vestibular disorders based on a comprehensive set of key questions and clinical examinations. It is easily applied, not limited to subgroups, and might therefore be transferred to broad clinical settings such as primary healthcare.

KEYWORDS
diagnostic algorithm, neuro-ophthalmology, stroke, vertigo, vestibular disorders

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INTRODUCTION

Acute vertigo and dizziness are common complaints in primary care and in emergency departments (EDs) [1–3]. Irrespective of the care setting, physicians face two major diagnostic challenges: (i) to identify patients with cerebrovascular events (CVEs) with a high sensitivity in order to initiate emergency management, and (ii) to assign patients to distinct vestibular disorders in order to allow appropriate targeted treatments or referral to specialized physicians.

Of all patients presenting to the ED with vertigo and dizziness 3%–13% are cases of cerebral stroke [4–7]. In EDs, strokes are missed in approximately 10% of cases, especially when patients present with mild or transient symptoms [8]. Furthermore, patients discharged from the ED with a suspected peripheral vestibular disorder have a higher risk of a subsequent CVE [9, 10]. Data on the prevalence of CVEs among patients with vertigo and dizziness in the primary healthcare sector are not available. However, there may be a considerable overlap of patient cohorts and characteristics across different care settings, given the high rate of self-referral or referral by primary care physicians to EDs [11]. Various attempts have been made to develop supporting diagnostic tools [12–15]. One clinical approach for detection of stroke in acute vestibular syndrome is the combination of head impulse test, nystagmus assessment, and test of skew deviation (HINTS) [14], or the evaluation of spontaneous versus positional nystagmus, nystagmus direction, head impulse test, and stance/gait (STANDING) [15, 16].

Besides the detection of a CVE, the correct classification of acute onset vertigo and dizziness into the most common vestibular syndromes (e.g., benign paroxysmal positional vertigo [BPPV], Menière's disease [MD], vestibular migraine [VM], unilateral vestibulopathy [UVP]) has a relevant clinical and economic impact because even "benign" peripheral vestibular disorders might have a

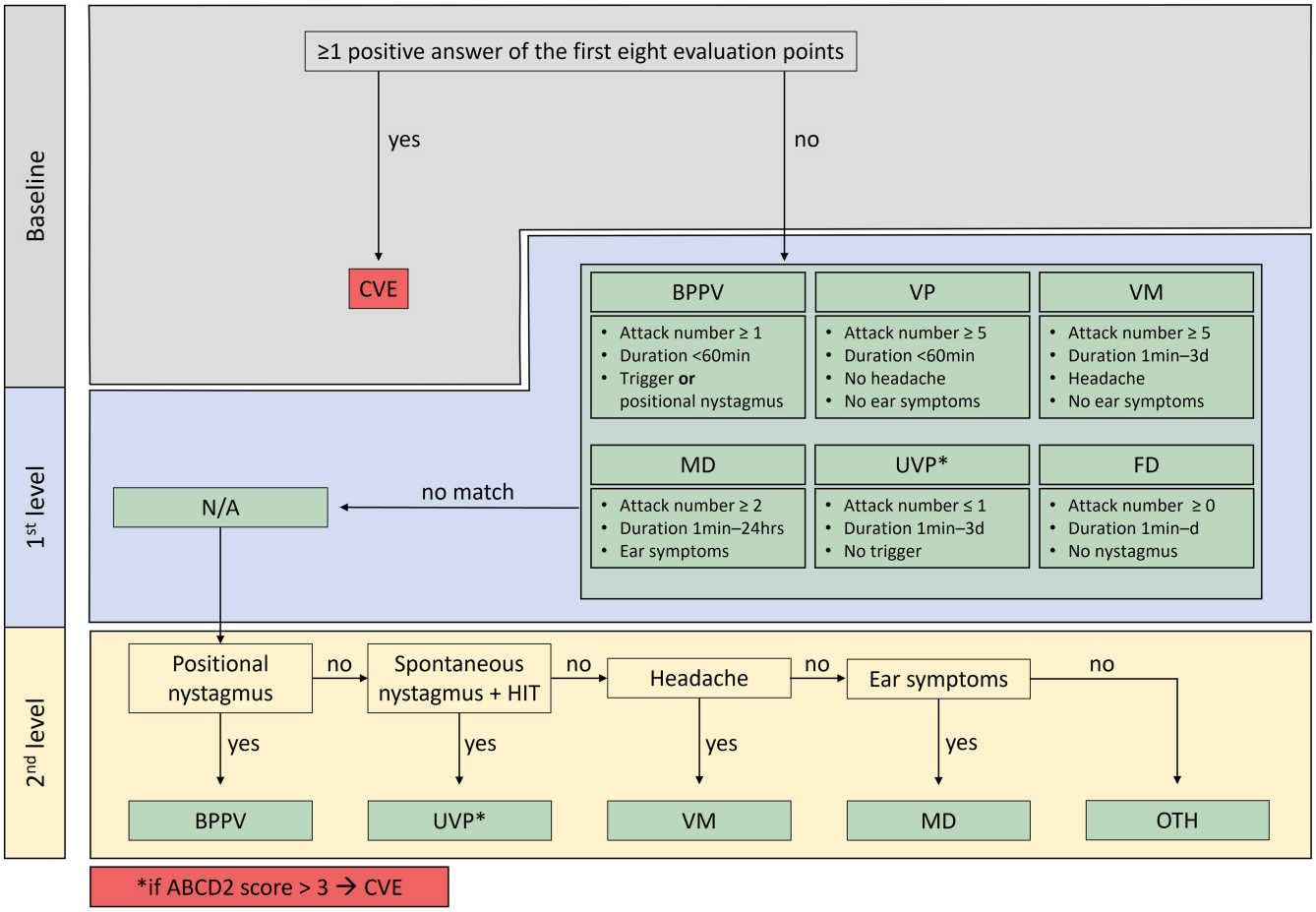

FIGURE 1 PoiSe diagnostic multi-step algorithm for patients with acute vertigo and dizziness. At baseline level, patients with a suspected cerebrovascular event (CVE) were detected based on 'red flags' from history taking and clinical examination. The remaining patients were categorized into six diagnostic groups of non-vascular vestibular disorders (BPPV, benign paroxysmal positional vertigo; FD, functional dizziness; MD, Menière's disease; VM, vestibular migraine; VP, vestibular paroxysmia; UVP, unilateral vestibulopathy), mostly using information on attack duration, frequency, triggers, and accompanying symptoms (first level). An attack number of 0 (zero) corresponded to a first and persistent vertigo/dizziness presentation. Patients not assigned to one of the defined diagnostic subgroups were passed on to the second level, which included a more advanced sequential evaluation of clinical nystagmus features, cardiovascular risk factors, and accompanying symptoms to allow for a "second-look" diagnosis. Patients with a suspected UVP and an ABCD2 score > 3 were classified as CVE, given their previously reported higher risk for stroke. If still none of the diagnostic categories was applicable, patients were classified as "others" (OTH). HIT, head impulse test [Colour figure can be viewed at wileyonlinelibrary.com]

considerable impact on daily life, for example, due to an increased risk of falls [17]. A correct diagnosis is often possible by careful history taking and a few clinical tests so that the most common vestibular disorders can be managed in primary care [18–20]. However, non-standardized diagnostic approaches frequently lead to misdiagnosis, subsequent insufficient management and disproportionately high and increasing healthcare utilization [21–24].

While most diagnostic algorithms concentrate on either identifying CVEs or diagnosing specific non-vascular vestibular disorders, there are few validated diagnostic approaches addressing both. Therefore, the present study suggests and validates a practical and comprehensive algorithm based on established key questions and clinical examinations to identify stroke and to increase the diagnostic accuracy and classification of the most common non-vascular vestibular disorders at first clinical examination.

METHODS

Development of the diagnostic algorithm

A group of three experts (F.F., A.Z., D.H.) developed a clinical algorithm for diagnosing vestibular and balance disorders in patients presenting with acute onset of vertigo and dizziness according to national and international guidelines [25] and current scientific evidence [26]. The algorithm comprises questions on the patient's medical history and easy-to-perform clinical examinations. Because the algorithm is intended for future clinical use in the primary healthcare sector in the context of the prospective **"PoiSe"** project (**P**revention, **O**nline Feedback, and **I**nterdisciplinary Therapy of Acute Vestibular **S**yndromes by **e**-health) [27], no instrument-based diagnostic procedures were considered.

A three-level process was developed, whereby the baseline level was intended to identify most patients with central CVEs underlying acute vertigo and dizziness and the first and second levels to classify common non-vascular vestibular syndromes (Figure 1). All patients were analysed through all levels. At baseline level, patients were identified as high risk for CVEs, if at least one of eight symptoms or clinical signs (i.e., paresis/sensory deficits, limb ataxia, aphasia/speaking difficulty, double vision/visual loss, new headache, central HINTS sign, central nystagmus pattern, inability to walk) was present. A central HINTS sign was defined as present if one or more of the following clinical signs were detected: normal head impulse test, direction-changing nystagmus, and/or skew deviation in presence of a spontaneous nystagmus [14]. Limb ataxia was defined in patients' history as a coordination deficit of one or more limbs, and in the neurological examination as a pathological finger-to-nose or heel-to-shin test. Truncal ataxia was included in the evaluation of walking ability. Details of the baseline assessment are found in Table 1.

Patients who did not fulfil one of the above eight criteria for being at high risk of a CVE were further evaluated and categorized into groups of distinct vestibular disorders. To this end, information on four additional features (i.e., number and duration of attacks, vertigo-specific triggers, accompanying symptoms, nystagmus indicative of peripheral vestibular disorders) were assessed (first and second algorithm levels [Table 1]). The number of attacks was classified as 0, ≥1, ≥2 or ≥5. Zero ("0") was used if vertigo and dizziness occurred for the first time. All other features could be answered with "yes" or "no". A positive trigger was considered if vertigo and dizziness was caused by change of head position, standing up, or specific situations (e.g., in a crowded bus). Accompanying ear symptoms included fluctuating hearing, tinnitus, or aural fullness. Accompanying headache had to be of known quality.

Based on this assessment, patients were classified into one of the following six diagnostic groups: CVE; acute unilateral vestibulopathy (UVP); BPPV; vestibular paroxysmia (VP); MD; VM; and functional dizziness (FD). Patients, who were not assigned to one of these groups at the first or second level of the algorithm, were classified as "others" (OTH). If patients were categorized into the UVP group and had a cardiovascular ABCD2 (**a**ge, **b**lood pressure, **c**linical features, **d**uration, **d**iabetes) risk score above 3, they were categorized as having CVE for safety reasons, based on previous literature [28]. Figure 1 gives an overview of the diagnostic algorithm.

Validation of the PoiSe algorithm

Study cohort and data acquisition

We validated the PoiSe algorithm using data from the prospective EMVERT trial (EMergency VERTigo) [29]. All patients presenting with acute onset of vertigo, dizziness, postural or gait instability, or double vision at the ED of the University Hospital of Ludwig-Maximilian University of Munich (*Ludwig-Maximilians-Universität München* [LMU]) between 2016 and 2019 were eligible for inclusion in the study. Symptoms had to be present for at least 10 min within the last 24 h. We used the dataset from this trial cohort for two reasons: first, because we hypothesized that this setting would yield a representative sample of patients presenting with acute vertigo and dizziness (>60% self-referral), and second, because this prospectively raised dataset included a standardized multimodal diagnostic workup, which allows for precise post hoc diagnostic validation by experts. All patients from the EMVERT trial who were included underwent a standardized assessment as follows:

(i) Clinical history taking (including duration, quality of symptoms, accompanying symptoms, triggers, previous history of vertigo and dizziness, cardiovascular risk factors, comorbidities, medications).
(ii) Clinical vestibular, neuro-otological and neuro-ophthalmological examination (including head impulse test, test for spontaneous nystagmus, provocation nystagmus, positional nystagmus, skew deviation, smooth pursuit, saccades, gaze-holding, fixation suppression of the vestibulo-ocular reflex, hearing)
(iii) Neurological status (including motor, sensory, coordination, cranial nerve, higher cognitive function assessment)

TABLE 1 Three-level assessment in the PoiSe algorithm for identifying patients with a high cerebrovascular risk and classifying the most common non-vascular vestibular disorders

Baseline assessment	First- and second-level assessment
Does the patient present with… 1. a history or clinical presence of a **paresis or sensory deficits** of the face or extremities? 2. a history or clinical presence of **ataxia** of the extremities? 3. a history or clinical presence of **speaking difficulties**? 4. a **visual impairment** (double vision or acute vision loss)? 5. a **new headache** of unknown quality? 6. at least one central **HINTS** sign? 7. a **central nystagmus pattern** (e.g., simultaneous presence of a spontaneous and positional nystagmus)? 8. a lost ability to **walk**?	How many **vertigo/dizziness attacks** did the patients experience (zero "0" represents the first manifestation of a persistent vertigo/dizziness sensation)? If ≥1: how long did the attacks last? Is vertigo/dizziness triggered? Does the patient present with one of the following **accompanying symptoms**? • Headache • Ear symptoms Is there a **nystagmus** with one of the following characteristics? • Spontaneous nystagmus with a contralateral pathological head-impulse test (HIT) • Positional nystagmus indicative of posterior canal benign paroxysmal positional vertigo

(iv) Instrument-based assessment of vestibular, ocular motor and postural functions (by video-oculography, mobile posturography, testing of subjective visual vertical)

(v) Scales and scores (including Dizziness Handicap Inventory [30], modified Rankin scale [31], ABCD2 [28])

(vi) Magnetic resonance imaging (MRI) including magnetic resonance angiography within 7 days of symptom onset

(vii) Clinical follow-up for central neurological signs within 7 days of symptom onset.

Diagnostic classification of the study cohort

Patients were classified according to the current guidelines of the American Stroke Organization and European Stroke Organization and the Bárány Society [25] into the following diagnosis groups: ischemic stroke (STR; indicated by a diffusion restriction on MRI or a persistent distinct central clinical sign such as central positional nystagmus or intranuclear ophthalmoplegia), UVP [32], BPPV [33], VP [34], MD [35], VM [36], and FD [37]. Patients with transient vertigo or dizziness and no clear indication for one of the above-named distinct vestibular disorders were classified as acute transient vestibular syndrome (ATVS) as suggested previously [38]. To further characterize patients with ATVS, we subclassified four diagnostic entities: (i) transient ischemic attack (TIA), as indicated by an acute onset of symptoms, and the presence of transient central clinical signs accompanying vertigo and dizziness such as hemiparesis; (ii) "migraine-like" disorders in patients with evidence of migraine in previous history, or in the follow-up examination 7 days after symptom onset, and/or a current headache fulfilling migraine criteria, but no cardiovascular risk profile; (iii) "miscellaneous," comprising different diagnoses such as hypertensive crisis or horizontal canal BPPV; (iv) "unclassified," including patients with symptom constellations that were not characteristic for any distinct clinical entity. Patients with none of the above-named entities were categorized as unknown/OTH, and included also rare central disorders such as multiple sclerosis, tumors, or encephalitis. Patients in the ATVS group who had a diffusion restriction on MRI indicative of cerebral stroke were included in the STR group.

Statistical analysis

For data description, mean and standard deviation (SD) values for continuous variables are reported, as well as absolute and relative frequencies for categorical variables. Group comparisons were based on a chi-squared test for categorical variables and ANOVA for continuous variables. To evaluate the quality of the algorithm, we used the agreed expert diagnoses as the outcome variable (expert standard). This outcome is a multinomial distributed variable with the following different categories: UVP, BPPV, VP, MD, VM, FD, OTH, STR and ATVS. The CVE group in the PoiSe diagnostic algorithm was compared to a merged group of STR and ATVS patients, because ATVS patients may have a markedly increased stroke risk [38].

Overall accuracy of the algorithm was defined as the percentage of exact agreement of the diagnosis suggested by the algorithm and the expert standard. The quality of the PoiSe algorithm was described separately for each outcome category using sensitivity, specificity, positive predictive value, and negative predictive value. As these measures are only defined for binary and not for multinomial outcomes, we applied separate binary classification problems using a "one-versus-all" approach as proposed before [39].

In contrast to standard regression methods, a classification tree does not indicate which variables were most important for the diagnostic decision. To estimate variable importance, we applied random forest classification [40], which yields estimates of variable importance values [41–43]. We obtained the importance for each variable using the Gini-impurity criterion [44], that is, the mean decrease in the node impurity measured by the Gini index

by splits on a certain variable. Variable importance was reported for each sign and symptom for baseline assessment only and for all assessment levels.

Statistical significance was set at a two-tailed 5% level. R 3.6.1 was used for all analyses [45]. The variable importance was assessed with the "RandomForestExplainer" package in R [46].

Ethical standards

The authors confirm that all methods were performed according to National Institutes of Health guidelines and in adherence with the Declaration of Helsinki. The study protocol was approved by the Data Protection Officer and the Ethics Committee of the Medical Faculty of the LMU. Written informed consent was obtained from all participants included in the study. The PoiSe project is registered in the international clinical trials registry platform of the World Health Organization and the German Clinical Trial Registration under www.drks.de and http://www.who.int/clinical-trials-registry-platform with the ID DRKS00024146. The EMVERT trial is registered with the universal trial number U1111-1172-8719.

RESULTS

Study cohort characteristics

The dataset used for validation of the PoiSe diagnostic algorithm included 407 patients (46% female) with a mean (SD) age of 60.9 (16.9) years. The most frequent expert-validated diagnosis was ATVS (28%), followed by UVP (17.7%), stroke (15.7%), MD (8.6%), VM (8.4%) and BPPV (7.4%). In ATVS, TIA was the most frequent diagnostic subgroup (8.6%; Table 2). Comparison of features from baseline assessment indicated significant differences for stroke/ATVS versus all other diagnoses except for presence of spontaneous nystagmus (for details, see Table 3). Patients at high risk of a CVE were older (mean [SD] age: stroke 66 [13] years, ATVS 66 [SD] 15 years, vs. non-stroke/non-ATVS 57 [17] years; $p < 0.0001$), had a lower number of previous vertigo attacks ($p < 0.0001$), less frequently had specific triggers ($p = 0.0008$), and less often had headache ($p = 0.007$) or ear symptoms ($p = 0.0003$) accompanying vertigo and dizziness (additional data are listed in Table S1 in the Supplement).

Validation of diagnostic algorithm

The PoiSe algorithm correctly classified 287 of the 407 patients (71%). It showed a high sensitivity for CVE (93.8%) and a high specificity of between 95.2% and 99.2% for all other diagnostic groups (BPPV, VP, MD, VM, UVP, FD, OTH) in a one-versus-all comparison. The positive predictive value ranged between 65% and 76% for all diagnoses, except for FD (25%) and VP (33%), where only a low number of patients were included (eight and two, respectively; Table 2). The negative predictive value was between 91.2% and 100% for the different diagnoses (Table 4).

TABLE 2 Distribution of the final diagnoses made by the clinical experts in the validation dataset

Diagnosis	*N*	Percentage
Acute transient vestibular syndrome	114	28.0
Transient ischemic attack	35	8.6
Migraine-like	17	4.2
Miscellaneous	31	7.6
Unspecified	31	7.6
Unilateral vestibulopathy	72	17.7
Cerebral stroke	64	15.7
Menière's disease	35	8.6
Vestibular migraine	34	8.4
Benign paroxysmal positional vertigo	30	7.4
Functional dizziness	8	2.0
Vestibular paroxysmia	2	0.5
Others	48	11.8

Abbreviations: ATVS, acute transient vestibular syndrome; HINTS, head impulse test, nystagmus, test of skew.

Importance of diagnostic assessment features

The most important variables and assessment features for the detection of patients with a high risk of CVE at the baseline level of the PoiSe algorithm were loss of motor or sensory function, followed by presence of a central HINTS sign (especially skew deviation), double vision/visual loss, limb ataxia, and inability to walk. Furthermore, speaking difficulties (aphasia/dysarthria) and new headache of unknown quality ranked among the most important features for CVE detection. When considering all assessment levels of the PoiSe algorithm as well as demographic data, there was a broad overlap for the most important features. In this setting, age and the number of previous vertigo/dizziness attacks were the most important factors for the detection of a CVE, followed by motor/sensory loss, central HINTS (especially negative HIT), and an ABCD2 score above 3 (Table 5).

DISCUSSION

We present a valid diagnostic algorithm for patients with acute vertigo and dizziness that is based on a concise assessment including medical history and clinical features and that aims both to identify CVEs and to classify the most common distinct non-vascular vestibular disorders. The algorithm was developed in accordance with international guidelines and validated clinical tests, such as HINTS. Overall, the algorithm assigned 71% of the patients

TABLE 3 Baseline assessment features in expert-validated diagnostic subgroups

Variable	Labels	All	Stroke	ATVS	Non stroke/ ATVS	*p* value
Sample size	-	407	64	114	229	
Demographics						
Age, years (SD)	-	60.88 (16.86)	66.19 (13.34)	65.71 (15.32)	56.99 (17.49)	<0.0001
Sex, *n* (%)	Female	189 (46)	19 (30)	57 (50)	113 (49)	0.0659
	Male	218 (54)	45 (70)	57 (50)	116 (51)	
Baseline assessment features, *n* (%)						
Motor/sensory loss	Yes	42 (10)	16 (29)	24 (20)	2 (1)	<0.0001
	No	365 (90)	40 (71)	98 (80)	227 (99)	
Limb ataxia	Yes	39 (10)	9 (16)	25 (20)	5 (2)	<0.0001
	No	368 (90)	47 (84)	97 (80)	224 (98)	
Aphasia/dysarthria	Yes	22 (5)	12 (19)	7 (6)	3 (1)	<0.0001
	No	385 (95)	52 (81)	107 (94)	226 (99)	
Double vision/Visual loss	Yes	70 (17)	26 (41)	25 (22)	19 (8)	<0.0001
	No	337 (83)	38 (59)	89 (78)	210 (92)	
New headache of unknown quality	Yes	26 (6)	4 (6)	15 (13)	7 (3)	0.0033
	No	381 (94)	60 (94)	99 (87)	222 (97)	
Central HINTS feature	Yes	85 (21)	22 (34)	41 (36)	22 (10)	<0.0001
	No	322 (79)	42 (66)	73 (64)	207 (90)	
Spontaneous and positional nystagmus	Yes	12 (3)	8 (13)	0 (0)	4 (2)	0.0645
	No	395(97)	56 (87)	114 (100)	252 (98)	
Inability to walk	Yes	33 (8)	13 (20)	13 (11)	7 (3)	<0.0001
	No	374 (92)	51 (80)	101 (89)	222 (97)	

Abbreviations: ATVS, acute transient vestibular syndrome; HINTS, head impulse test, nystagmus, test of skew.

to the correct diagnosis. Most importantly, the algorithm correctly identified approximately 94% of patients presenting with a CVE. Non-vascular vestibular diagnoses were identified with a high specificity (>95% for all diagnoses). The most important assessment features of the algorithm for identifying a possible CVE (stroke and ATVS including TIAs) were presence of a paresis or sensory loss, a central HINTS sign, double vision/visual loss, and presence of limb ataxia. Furthermore, older age, number of vertigo attacks, and ABCD2 score above 3 were important factors for the differentiation of CVE patients versus non-vascular vestibular disorders.

Detection of a CVE

The classification of the underlying etiology in patients who present with vertigo and dizziness has a high clinical, therapeutic, and socioeconomic impact [8, 9, 21, 47]. The etiology with the most imminent importance for further therapeutic actions, namely, cerebral stroke or TIA, must be excluded before other diagnoses can be considered. Therefore, correct diagnosis of a CVE in patients with vertigo and dizziness has been the focus of research, leading to the development of distinct clinical index tests, such as HINTS [14], PCI score (posterior circulation ischemia score) [48], and CATCH2 [49], and diagnostic algorithms, such as STANDING, [15, 16] and TiTrATE [13]. In most of these tests, accuracy has been found to be good. However, many of these approaches mainly apply to specific subgroups of patients such as patients with posterior circulation ischemia in the PCI score, or HINTS for acute vestibular syndrome (with spontaneous nystagmus).

In the detection of a possible CVE (including TIAs), the PoiSe algorithm showed a high sensitivity (94%) and a decent specificity (70%). The structure of this diagnostic algorithm was tuned toward a sensitive identification of patients with a high risk of a CVE at the cost of a lower specificity. For example, patients with UVP and an ABCD2 score above 3 were assigned to the CVE group even in absence of central features. This led to the correct identification of 11 CVEs in the UVP group. Although, recently, some studies have found a low reliability of the ABCD2 score in identifying patients with a CVE [50–52], it has been suggested that it might be useful when used in combination with other clinical signs [53] This is also supported by data from the present study, since the sensitivity for the detection of a CVE decreased (87.6 vs. 93.8%) when the ABCD2 criterion was excluded. Overall, we feel that the approach used in the PoiSe diagnostic algorithm adequately considers the existing evidence of a high stroke risk in specific subgroups of patients with vertigo and

TABLE 4 Diagnostic accuracy of the PoiSe algorithm

			Expert diagnosis								Sensitivity, %	Specificity, %	PPV, %	NPV, %
		n	STR/ATVS	UVP	MD	VM	BPPV	FD	VP	OTH				
PoiSe algorithm diagnosis	CVE	235	**167**	14	16	15	5	2	0	16	93.8	70.3	71.1	93.6
	UVP	67	2	**51**	1	4	1	1	0	7	70.8	95.2	76.1	93.8
	MD	21	1	0	**17**	0	1	0	0	2	48.6	98.9	81	95.3
	VM	23	1	3	1	**15**	0	0	0	3	44.1	97.9	65.2	95.1
	BPPV	32	4	1	0	0	**23**	1	0	3	76.7	97.6	71.9	98.1
	FD	4	1	0	0	0	0	**1**	0	2	12.5	99.2	25	98.3
	VP	6	0	3	0	0	0	0	**2**	1	100	99	33.3	100
	OTH	19	2	0	0	0	0	3	0	**14**	29.2	98.6	73.7	91.2

Abbreviations: ATVS, acute transient vestibular syndrome; BPPV, benign paroxysmal positional vertigo; CVE, cardiovascular event; FD, functional dizziness; MD, Menière's disease; NPV, negative predictive value; OTH, others; PPV, positive predictive value; STR, stroke; VM, vestibular migraine; VP, vestibular paroxysmia; UVP, unilateral vestibulopathy. BOLD: correctly assigned diagnoses by the algorithm
Bold represents the correctly assigned diagnoses by the algorithm.

TABLE 5 Feature importance for the identification of a cerebrovascular event derived from either baseline assessment or all level assessment of the PoiSe algorithm

Baseline assessment	Gini decrease	All level assessment	Gini decrease
Motor/sensory loss	18.564	Age	22.782
Central HINTS	15.179	Number of attacks	13.948
Double vision/visual loss	9.725	Motor/Sensory loss	13.264
Limb ataxia	9.273	HIT	13.153
Skew deviation	7.889	HINTS	11.979
Inability to walk	4.913	ABCD2 score	11.853
Aphasia/dysarthria	4.303	Double vision/Visual loss	8.171
New headache	3.351	Spontaneous nystagmus	6.717

Abbreviation: HINTS, head impulse test, nystagmus assessment, and test of skew deviation; HIT, head impulse test.

dizziness [7, 10, 28] and addresses the concerns of physicians not to miss a CVE [6]. The most frequent false-positive CVE diagnosis in our study originated from the UVP, MD and VM subgroups. This is in line with previous studies where approximately 10% of UVP cases were initially misdiagnosed as stroke, followed by MD and VM [24].

As indicated by the feature importance analysis of the PoiSe algorithm, the most important factors for diagnosing a possible CVE were classic signs of stroke, such as paresis, sensory deficits, double vision, visual loss, and limb ataxia, but also a positive HINTS sign, which is known to be highly sensitive and specific for the detection of cerebral stroke in acute vestibular syndrome [14]. Furthermore, older age was an important factor for predicting CVE in patients with vertigo and dizziness, which is consistent with data from the ABCD2 score [28].

Distinguishing non-vascular vestibular disorders

Distinguishing the most common non-vascular vestibular disorders poses a great challenge and there are only limited data available to increase the diagnostic accuracy in non-vascular vestibular disorders by means of index tests or algorithms. This might be attributable to the wide spectrum of differential diagnoses for vestibular disorders among different medical specialities [54, 55]. However, a correct classification of vestibular disorders has a direct impact on further diagnostic and therapeutic procedures, especially in the primary care setting [23]. The PoiSe algorithm, similarly to the TiTrATE approach [13], combines different aspects of agreed classification criteria, existing algorithms, and expert opinion to classify the six most common non-vascular vestibular disorders, after exclusion of a CVE. Previously reported approaches for distinguishing among the most common vestibular disorders are the proposed five key questions by Brandt et al. [56] and the TiTrATE algorithm by Newman-Toker

et al. [13], which however were never validated in a prospective clinical study. Other approaches based on different machine-learning methods use a great amount of input data, but also have not been prospectively validated in patient care [20, 57]. Only one study that used a computer-based decision-making algorithm to classify patients with vertigo and dizziness was validated in a tertiary referral outpatient setting and showed a high specificity (>80%) and a sensitivity between 40% and 81% [58].

The PoiSe algorithm was able to diagnose the six most common non-vascular vestibular disorders (BPPV, FV, VM, MD, UVP, VP, accounting for approximately 66% of all vestibular diagnoses) [59], with an accuracy of approximately 70%, a high specificity (>95%), and a variable sensitivity of 13%–100%. Therefore, its accuracy, sensitivity and specificity were similar to those in two previous studies using computer-based decision-making systems [58, 60]. The diagnostic approach of the PoiSe algorithm, however, greatly differs from these studies, as the previously reported decision-making systems consider a large number of clinical findings, medical history, and instrument-based diagnostic procedures to make the diagnosis. In contrast, the PoiSe algorithm only uses a concise set of clinical features without the need for specialized examinations, which considerably simplifies the diagnostic approach and makes it applicable in different care settings. The EMBalance decision support system [61] is, to our knowledge, the only approach that has been validated in primary care [60]. Interestingly, the diagnostic accuracy in the primary care setting was smaller (54%) [60] than initially expected (59%–90%) [61]. Due to the simple diagnostic approach, the PoiSe algorithm might lead to better results when used by non-experts, for example, in primary care; however, this will have to be evaluated in the future [27] because the algorithm partially depends on experience in testing and interpretation of distinct clinical signs such as the head impulse test or nystagmus characteristics.

Limitations

The following limitations of the present study need to be acknowledged: Validation of the PoiSe algorithm was carried out in an ED patient cohort recruited via the EMVERT study, which may imply a selection bias. For instance, patients with a clinically definite BPPV on initial routine assessment were not included in the study cohort based on the EMVERT protocol [29]. Furthermore, general practitioners or emergency ambulances referred patients to the ED more often if a central etiology was suspected. This referral and inclusion practice may explain the relatively high number of patients with a possible CVE and the low number of patients with VM, MD, and BPPV. Accordingly, in the group of all patients screened for inclusion in the EMVERT study, BPPV was the most frequent etiology. Thus, the reported diagnostic performance of the PoiSe algorithm currently applies to the clinical spectrum of vertigo and dizziness patients in an ED study cohort only and cannot be transferred one-to-one to different care settings (e.g., primary care) without further validation. The low sensitivity (13%) for FV and the high sensitivity (100%) for VP can only be interpreted with utmost caution because of the limited number of patients with these diagnoses included in the dataset. A further limitation of any diagnostic algorithm, which is partially based on clinical signs (such as the head impulse test, or nystagmus assessment), is that the examination and interpretation relies on the experience and continuous skills training of the clinician.

CONCLUSION

We present a diagnostic algorithm that uses information from medical history and results from easy-to-perform clinical examinations in patients with acute vertigo and dizziness not only to detect patients with a higher risk of a CVE (e.g., stroke and ATVS including TIAs), but also to differentiate among the most common non-vascular/peripheral etiologies. In comparison to existing diagnostic approaches, the PoiSe algorithm has considerable advantages. Because it uses a small number of evaluation points, it is easy to apply in everyday practice and is therefore potentially transferable to different clinical settings (e.g., primary care). The PoiSe algorithm is not restricted to specific subgroups of patients (such as those with acute vestibular syndrome) but is applicable to all patients presenting with acute vertigo and dizziness. It shows a high sensitivity for detection of a CVE and a high specificity in the differentiation of acute non-vascular/peripheral vestibular disorders.

Correctly classifying patients with vertigo and dizziness at first presentation might have a direct impact on diagnostic and therapeutic proceedings, as well as on healthcare utilization and economics. Future research should focus on the transferability of the algorithm to other settings, especially primary care, and the possible impact on the long-term clinical outcome and health economics [27].

AUTHOR CONTRIBUTIONS

Filipp Filippopulos: Conceptualization (lead); data curation (equal); formal analysis (equal); methodology (equal); project administration (lead); resources (lead); supervision (lead); writing – original draft (lead); writing – review and editing (equal). **Ralf Strobl:** Data curation (equal); formal analysis (equal); methodology (equal); validation (equal); writing – review and editing (equal). **Bozidar Belanovic:** Data curation (equal); investigation (equal); writing – review and editing (equal). **Konstanze Dunker:** Data curation (equal); investigation (equal); writing – review and editing (equal). **Eva Grill:** Conceptualization (supporting); formal analysis (equal); methodology (equal); validation (equal); writing – review and editing (equal). **Thomas Brandt:** Conceptualization (supporting); formal analysis (supporting); methodology (equal); supervision (supporting); writing – review and editing (equal). **Andreas Zwergal:** Conceptualization (equal); data curation (lead); formal analysis (equal); investigation (supporting); methodology (equal); supervision (supporting); validation (equal); writing – original draft (equal); writing – review and

editing (equal). **Doreen Huppert:** Conceptualization (equal); data curation (lead); funding acquisition (equal); investigation (equal); supervision (lead); validation (equal); writing – original draft (equal); writing – review and editing (equal).

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

The data supporting the conclusions of this article will be made available by the authors upon reasonable request to the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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