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Original Article

Idiopathic Labyrinthitis: Symptoms, Clinical Characteristics, and Prognosis

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BACKGROUND: Labyrinthitis is an inner ear disorder of unknown incidence, characterized by sudden hearing loss and concurrent vertigo. Cohort studies of patients diagnosed with labyrinthitis are nonexistent. This study aims to describe the clinical characteristics and prognosis of patients diagnosed with idiopathic labyrinthitis.

METHODS: Patients with labyrinthitis in the absence of a clear viral, bacterial, or autoimmune pathogenesis were retrospectively identified from electronic patient files. Symptoms at presentation and results from vestibular testing were retrieved. The 9-item Vestibular Activity Avoidance Instrument, administered during follow-up interviews by telephone, was used to assess the presence of persistent balance problems and activity avoidance behavior.

RESULTS: Sixty-one patients with idiopathic labyrinthitis were included. All patients had vestibular weakness at presentation. After a median of 61 months of follow-up (interquartile range 81), 72.5% of patients still experienced balance problems. Subjective hearing recovery only occurred in 20% of cases.

CONCLUSION: Patients presenting in a tertiary dizziness clinic with idiopathic labyrinthitis have a poor prognosis for both hearing and balance function impairment. Prospective observational cohorts are required to establish objectifiable vestibular and audiological follow-up data.

KEYWORDS: Labyrinthitis, sudden sensorineural hearing loss, vestibulopathy, balance difficulty

INTRODUCTION

Labyrinthitis is an inner ear disorder that manifests itself with acute hearing loss and vertigo. The population incidence of labyrinthitis is unknown.^{1,2} In the past, suppurative labyrinthitis was a well-known complication of bacterial meningitis and otitis media, but since the global use of antibiotics, these have become rare entities.³⁻⁵ Nowadays in the absence of signs of meningitis or otitis, it is assumed that the most common cause of labyrinthitis is a viral infection, although the viral agent usually cannot be identified. In some, especially elderly patients, labyrinthitis might be caused by vascular disease, similarly to certain cases of sudden deafness and vestibular neuritis.⁶⁻⁸ Since a clear cause cannot be identified in the majority of patients, the term idiopathic labyrinthitis may be more suitable than viral labyrinthitis. Although the term acute idiopathic unilateral vestibulopathy in combination with sudden sensorineural hearing loss (SSNHL) may be more appropriate, in this article, we will continue the use of "idiopathic labyrinthitis" until the pathophysiology of acute vestibulopathy and SSNHL is clarified. Several empirical biomedical studies concerning labyrinthitis have been published,^{3,4,9} but cohort studies are nonexistent. This retrospective study was conducted to describe the demographic and clinical characteristics, comorbidity, and prognosis in terms of balance difficulty, subjective hearing improvement, and activity avoidance of patients diagnosed with idiopathic labyrinthitis.

MATERIAL AND METHODS

The study design is a retrospective cohort study that consists of 2 components, i.e., retrospectively gathered data regarding medical history, diagnostic tests and treatment from electronic patient files, and follow-up interviews to assess balance difficulty and

Table 1. Diagnostic Criteria for Idiopathic Labyrinthitis

Definite Acute Idiopathic Labyrinthitis	History of Acute Idiopathic Labyrinthitis
<p>A. Acute or subacute onset of sustained spinning or non-spinning vertigo (i.e., an acute vestibular syndrome) lasting for at least 24 hours.</p> <p>B. Spontaneous peripheral vestibular nystagmus, i.e., generally horizontal torsional, direction fixed, and enhanced by the removal of visual fixation.</p> <p>C. Unambiguous evidence of reduced vestibulo-ocular reflex function on the side opposite the direction of the fast phase of the spontaneous nystagmus, measured by video head impulse test or caloric testing.</p> <p>D. Unilateral sensorineural hearing loss of at least 30 dB over 3 consecutive frequencies occurring in a 72-hour window.</p> <p>E. Not better characterized by another disorder, such as physical exam evidence of acute otitis media or cholesteatoma, or imaging evidence of retrocochlear causes for acute hearing loss and vertigo, such as vestibular schwannoma.</p>	<p>A. History of acute or subacute onset of sustained spinning or non-spinning vertigo lasting at least 24 hours (i.e., an acute vestibular syndrome) and slowly decreasing in intensity over days.</p> <p>B. Evidence of unilaterally reduced vestibulo-ocular reflex function, measured with video head impulse test or caloric testing.</p> <p>C. Evidence of unilateral sensorineural hearing loss of at least 30 dB over 3 consecutive frequencies occurring in a 72-hour window.</p> <p>D. Not better characterized by another disorder, such as physical exam evidence of acute otitis media or cholesteatoma, or imaging evidence of retrocochlear causes for acute hearing loss and vertigo, such as vestibular schwannoma.</p>

The definition of idiopathic labyrinthitis is divided in a definite idiopathic labyrinthitis and history of idiopathic labyrinthitis. This definition is derived from the Bárány society criteria for unilateral vestibulopathy/vestibular neuritis.¹⁰

activity avoidance by telephone. The study gained ethics approval from the institutional review board of Gelre Hospital Apeldoorn (LTC number 2021_36).

The cohort consisted of all patients diagnosed with idiopathic labyrinthitis between January 2006 and May 2022 at the outpatient tertiary dizziness clinic and the department of otorhinolaryngology.

Worldwide accepted diagnostic criteria for labyrinthitis do not exist. Therefore, we adopted the preliminary criteria for unilateral vestibulopathy/vestibular neuritis of the Bárány society,¹⁰ see Table 1. We included patients with either definite acute idiopathic labyrinthitis or a history of acute idiopathic labyrinthitis. Definitive acute labyrinthitis is characterized by acute onset vertigo, SSNHL, and the presence of either a spontaneous horizontal torsional nystagmus or objectified vestibular loss of function in the (sub)acute phase. A history of acute labyrinthitis is characterized by a past episode of acute onset vertigo, sensorineural hearing loss, and currently objectifiable vestibular loss of function. Patients with labyrinthitis secondary to a herpes zoster ear infection, meningitis, syphilis, human immunodeficiency virus, or an autoimmune disorder were excluded. Patients who developed a different form of dizziness or recurrent episodes of dizziness, resulting in a change of diagnosis, were reported and excluded from the analysis.

The vestibulo-ocular reflex (VOR) function was measured using a commercially available mono-ocular video oculography system (ICS

Impulse System, version 1.20 up to version 4.00, OTOsuite Vestibular software; Otometrics, Taastrup, Denmark). The VOR gain was defined as the ratio of the eye movement velocity to the head movement velocity. The video head impulse test (v-HIT) was considered abnormal if the VOR gain was below 0.6, preferably confirmed by the presence of corrective saccades.

Caloric testing was performed using a bithermal open-loop water irrigation system. Each ear was irrigated with a constant flow alternating between hot and cold water. The maximum slow peak velocity of nystagmus was evaluated after irrigation. We used Jongkees' equation to calculate canal paresis. Details of the technique used have been described in detail elsewhere.¹¹ The threshold for canal paresis was set at $\geq 22\%$.

Hearing thresholds were evaluated at 0.5, 1, 2, 4, and 8 kHz using standardized methods for pure tone threshold audiometry.¹² Following the American Academy of Otolaryngology-Head and Neck Surgery guideline, SSNHL was defined as >30 dB hearing loss on 3 consecutive frequencies occurring within a 72-hour window.¹³ In case no audiometry was available from before the onset of symptoms, the uninvolved ear was considered normal.

The primary study outcome was the number of patients with ongoing self-reported balance problems at follow-up. Ongoing balance problems and their associated fear-avoidance behavioral responses, the co-primary outcome, were assessed using the Dutch translation of the 9-item Vestibular Activity Avoidance Inventory (VAAI-9);¹⁴ see Table 2. This instrument evaluates limitations patients experience due to dizziness in job responsibilities, household chores, social events, physical activity, and exercises. The instrument also assesses the fear patients have about making dizziness worse, engaging in exercise, and going outside the home.¹⁵ These items are rated on a 7-point scale: strongly disagree, disagree, somewhat disagree, neutral, somewhat agree, agree, and completely agree, where 7 indicates completely agree.¹⁶ The total score ranges from 0 to 63. The VAAI-9 strongly correlates with activity limitations and participation restrictions and has shown moderate associations with anxiety and depression symptoms and quality of life among people with vestibular disorders.¹⁵ The VAAI-9 was administered during a follow-up interview by telephone in early 2022 in all participating patients. The questionnaire was

MAIN POINTS

- The authors advice to use the term idiopathic labyrinthitis in case of acute vertigo with vestibular function loss and sensorineural hearing loss of minimal 30dB on 3 consecutive frequencies, in the absence of a clear cause.
- Patients with idiopathic labyrinthitis have a poor prognosis, with subjective hearing recovery in only 20% of cases.
- Seventy and a half percent of patients have long-term balance difficulty after labyrinthitis.
- Vestibular testing should be considered in all cases of concurrent acute hearing loss and vertigo.

Table 2. The 9-Item Vestibular Activity Avoidance Instrument (the right column displays the questionnaire each item is derived from)

Item	Text	Adapted from ^a
1	It is difficult for me to do strenuous homework or yard work because of my dizziness.	DHI
2	My participation in social activities, such as going out to dinner, going to the movies, dancing, or going to parties, is significantly restricted because of my dizziness.	DHI
3	My dizziness interferes with my job or household responsibilities.	DHI
4	I cannot do physical activities, which might make my dizziness worse.	FABQ
5	I can't do all the things normal people do because of my dizziness.	TSK
6	I am afraid that I might make myself dizzy or unsteady if I exercise.	TSK
7	I am afraid to leave my home without having someone go with me because of my dizziness.	DHI
8	I should not do my regular work with my present dizziness.	FABQ
9	My work makes my dizziness worse.	FABQ

^aTable derived from PhD thesis of P. Dunlap. DHI, dizziness handicap inventory; FABQ, Fear Avoidance Beliefs Questionnaire; TSK, Tampa scale of kinesiophobia.

administered, and the balance problems the patients experienced were identified by 2 researchers, FO and CC. Prior to the interview, patients were asked for verbal informed consent to participate in the study.

The secondary study outcome was an overview of demographic and clinical characteristics, the results of the diagnostic workup, including v-HIT and caloric testing, and the therapy given to patients presenting with idiopathic labyrinthitis. This information was gathered retrospectively from electronic patient files.

Statistical analysis was performed using the Statistical Package for Social Science Statistics software, version 25.0 (IBM SPSS Corp.; Armonk, NY, USA). Frequencies and percentages were calculated for sex, type of idiopathic labyrinthitis, type of diagnostic test performed, and results of the VAAI-9 instrument. In addition, means and SDs, or median and interquartile range (IQR) in the case of non-normally distributed data, were calculated for age, time span to presentation, the v-HIT gain, the vestibular asymmetry with caloric testing, and the mean VAAI score based on non-missing data. For analyzing the percentages of patients either with or without complaints, we reduced the 7-point VAAI-9 scale to a 3-point scale, where somewhat agree, agree, and strongly agree are merged into the category agree and somewhat disagree, disagree, and strongly disagree are merged into the category disagree.

RESULTS

Study Population

Ninety-six patients presented with simultaneous acute hearing loss and vertigo in the ~16-year study period, representing 0.39% of the

Table 3. Demographic and Clinical Characteristics of 61 Patients Diagnosed with Idiopathic Labyrinthitis.

	Percentage (%)
Age [mean (SD)]	59 (12)
Sex	
Male	44.3
Female	55.7
Time span to presentation (months) [median (IQR)]	8 (12)
Labyrinthitis criteria	
Definite acute labyrinthitis	4.9
History of acute labyrinthitis	95.1

IQR, interquartile range; N, number of non-missing cases.

entire population referred to our center. Thirty-five patients were excluded. Eleven of these patients had clinical signs of middle ear infection with the otoscopic examination. In 2 cases, a varicella-zoster infection was suspected because of an ipsilateral vesicular eruption. One patient had developed labyrinthitis secondary to meningitis. Two patients were excluded since they developed Menière’s disease over time. The remaining 21 excluded patients did not meet the diagnostic criteria for idiopathic labyrinthitis. Eight of these patients were suspected of labyrinthitis but did not have an objectified vestibular weakness. Table 3 shows the characteristics of the 61 patients who met the inclusion criteria.

All patients underwent pure-tone audiometry at presentation in the outpatient setting. The average sensorineural hearing loss in the affected ear was 58.1 dB (high Fletcher index, SD 25.1). Figure 1 displays the average hearing threshold in the affected versus the non-affected ear. The rate of initial oral or intratympanic corticosteroid therapy after SSNHL had occurred could not be reliably retrieved from the patient files since this was not documented in 25 cases.

In 36 patients (59.0%), a v-HIT was done; in 54 patients (88.5%), caloric testing was performed; and 29 patients (47.5%) received both diagnostic tests. All patients showed loss of vestibular function; 12

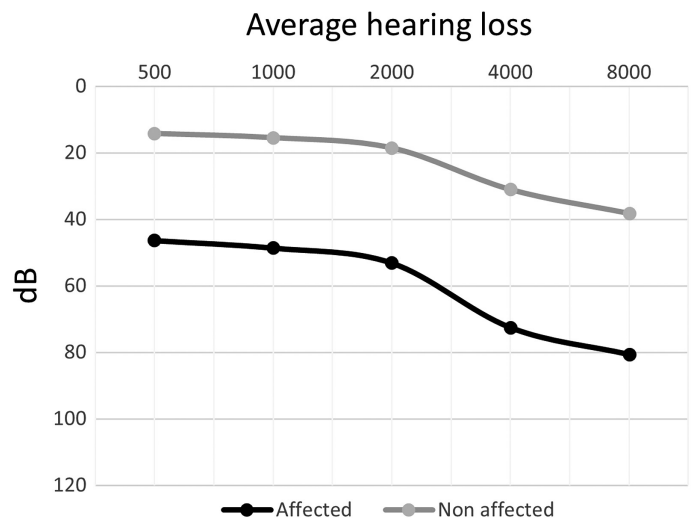


Figure 1. Average PTA results of the affected and non-affected ear in 61 patients with idiopathic labyrinthitis. dB: decibel; PTA, pure-tone audiometry.

patients (19.6%) had a VOR-gain below 0.6 with either covert, overt, or both types of saccades, and 53 patients (86.9%) had a unilateral weakness with caloric testing. The average unilateral vestibular weakness measured by caloric testing was 54.0% (SD 20), and the average VOR gain using v-HIT was 0.465 (SD 0.08). One patient had bilateral vestibulopathy, measured with caloric testing. In 1 patient, the v-HIT demonstrated no abnormal gain, but overt saccades were seen on both sides.

Forty-one patients (67.2%) received a referral for vestibular rehabilitation after presentation at the dizziness clinic or had previously undergone vestibular rehab in primary care clinics. If the referred patients had eventually received vestibular rehabilitation, and if so, the details of the exact vestibular rehab protocols received could not be retrieved.

Follow-up

Follow-up information was obtained from 40 patients (65.6%) after a median duration of 61 months (IQR 32-113). Three patients had died; in 9 patients, the contact information was not up to date; 3 patients did not give informed consent; and the remainder could not be reached despite multiple attempts. Seven patients (17.5%) experienced some or complete hearing recovery, while 32 patients (80%) noticed no hearing improvement. Twenty-nine patients (72.5%) still experienced balance problems.

Figure 2 shows the results for the different questions from the VAAI-9. The mean VAAI score was 20.4 (SD 12.9). Forty-two and a half percent of the follow-up patients had trouble performing heavy tasks in and around the house; 45% experienced difficulty in social activities due to balance problems or vertigo; and 40% experienced difficulty in

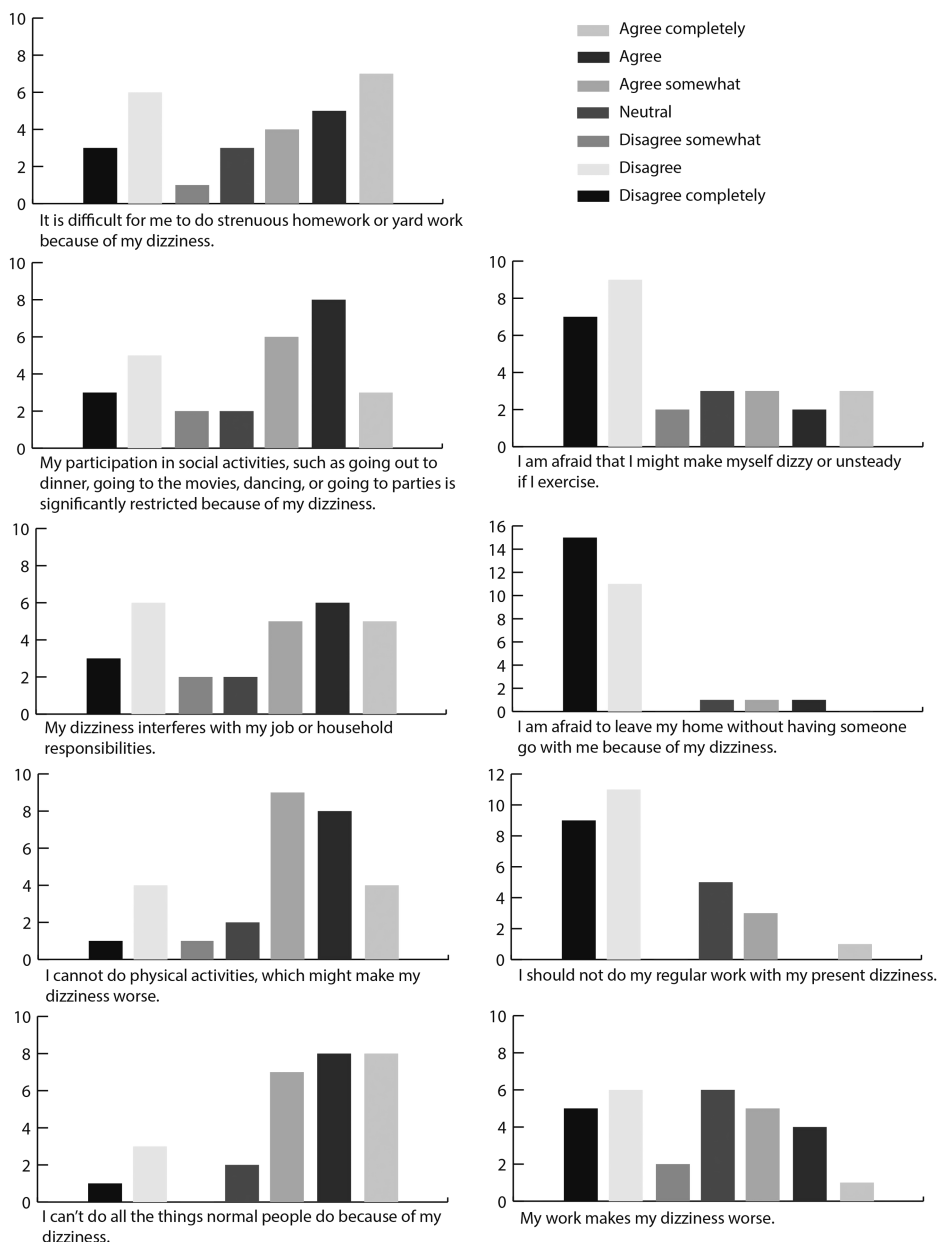


Figure 2. Results of the VAAI-9 instrument in 40 patients after a median of 61 months of disease. For each item on the x-axis, the number of patients in each category of the 7-point VAAI-9 scale is displayed on the y-axis. VAAI-9: 9-item Vestibular Activity Avoidance Instrument.

work or household. Fifty-seven and a half percent of patients could not perform activities they knew would provoke their dizziness, and 62.5% could not perform all daily tasks they did before experiencing labyrinthitis; this percentage increased to 77% when the patients who did not report any complaints of dizziness at follow-up ($n = 11$) were removed from the calculation.

Almost all patients reported having adjusted to their symptoms. At follow-up, 5% of patients were afraid to some degree of leaving the house unaccompanied, and 20% of patients were afraid of performing specific movements that might provoke dizziness. Finally, 5 out of 34 patients (17.4%) of working age were not allowed to perform their current job due to their vertigo complaints, and in 32.5% of working patients, their work aggravated their dizziness complaints. Nine patients had to change jobs or reduce their workload as a consequence of their dizziness complaints.

DISCUSSION

This study aimed to describe the clinical and demographic characteristics, comorbidity, and prognosis in terms of balance difficulties and associated fear-avoidance behavioral responses in patients diagnosed with idiopathic labyrinthitis. To date, little is known about the characteristics and clinical course of this disorder since cohort studies are nonexistent.

We retrospectively evaluated 61 patients diagnosed with idiopathic labyrinthitis in our tertiary dizziness clinic in the last 16 years. This comprised only a small proportion of the entire population presenting at our clinic during this period. All patients included in the cohort had vestibular function loss at initial presentation. They presented at our dizziness clinic a median of 8 months after disease onset (IQR 12 months). After a median follow-up of 61 months (i.e., ~5 years), 72.5% of patients still experienced balance problems. Of these patients, 77% had not returned to their daily life activities due to these problems.

After experiencing acute vestibular loss of function, vertigo generally lasts only a few hours up to days, while balance difficulties and oscillopsia may persist for a much longer period of time.¹⁷ This persisting imbalance is thought to slowly disappear after several weeks due to central compensation with the restoration of spontaneous activity in the affected vestibular nucleus, explaining the good prognosis that has been ascribed to labyrinthitis by other authors.^{1,2,17,18} However, the findings of our study contradict this statement. After a median of 61 months after disease onset, 72.5% of patients still experienced balance problems. The mean score on the VAAI questionnaire at follow-up was 20.4 (SD 12.9), which is lower than the mean score of 28 (SD 12) found by Vereeck et al in a subset of 43 patients with dizziness of variable origin and considerably higher than the average 2.4 (SD 5.9) point score in healthy volunteers.¹⁴ It is important to note that Vereeck also included patients with recurrent vertigo, central vestibular disorders, and functional disorders.¹⁴ Especially patients with functional disorders and central vestibular disorders had high VAAI values, which might be explained by the association of functional disorders with anxiety and the chronic nature of central vestibular disorders.¹⁹ The relatively high VAAI scores in our cohort indicate poor improvement in balance and consequent limitations in terms of associated fear-avoidance behavioral responses for patients with labyrinthitis in the course of time.

In cases of unilateral vestibulopathy due to vestibular neuritis, complete caloric recovery after 12 months has been reported in 44.4%-70.2% of cases, regardless of corticosteroid use.²⁰ In our study, only 8 out of all 96 screened patients were primarily excluded because they did not have objectified vestibulopathy but otherwise matched the criteria for labyrinthitis. This resulted in 61 out of 69 (89%) patients suspected of idiopathic labyrinthitis having objectified vestibulopathy after a median of 8 months after the onset of vertigo. Vestibular neuritis might therefore have a better vestibular recovery than labyrinthitis. This statement should be considered with care. Up to now, there is insufficient knowledge of the ratio of concurrent sudden deafness and vestibulopathy in primary care compared to hospitals and specialized centers. Very few studies have focused on the vestibular recovery in patients with ISSNHL and concurrent vestibulopathy, let alone discuss the influence of glucocorticoids on this vestibular recovery. Hao et al²¹ have published a study protocol in 2020 to analyze the short- and long-term vestibular prognosis after ISSNHL with concurrent vertigo, while adjusting for glucocorticoid treatment strategies. This study might clarify the vestibular prognosis after concurrent vestibulopathy and sudden hearing loss.

In this study, subjective hearing recovery was found in only 20% of follow-up patients, with complete recovery in only 3 out of 40 patients. Several case-control studies demonstrated a poor prognosis of hearing recovery in patients with SSNHL and concomitant vestibulopathy compared to patients without vestibular complaints.²²⁻²⁵ Yu et al²⁶ summarized these results in a meta-analysis on the prognosis of hearing loss in patients experiencing SSNHL with and without vertigo. Vertigo was a prognostic factor for worse hearing recovery, implying a possible different pathophysiology in patients experiencing combined sudden deafness and vertigo versus sudden deafness alone.^{24,27} However, patients with concurrent vertigo who received intratympanic corticosteroids did not demonstrate a poorer hearing recovery than controls.

Since labyrinthitis, i.e., concurrent SSNHL and vestibulopathy, appears to have a smaller chance of hearing recovery than sudden deafness and a smaller chance of vestibular recovery than vestibular neuritis, we recommend using criteria to distinguish these 3 entities clearly. In this study, we used a set of criteria, for which we adapted the proposed criteria for unilateral vestibulopathy/vestibular neuritis from the Bárány Society and combined these with the guidelines for SSNHL.^{10,13} We believe this can be used as a framework for creating universally accepted diagnostic criteria for labyrinthitis.

In some patients, the symptoms due to vestibular loss recover completely, while others keep experiencing problems that are not entirely understood. Antiemetics or benzodiazepine use could influence the vertigo symptoms since there is some evidence suggesting that VOR function decreases after the intake of sedatives.²⁸⁻³⁰ Unfortunately, in our cohort, the use of antiemetics and sedatives was not explicitly mentioned in patient files and could, therefore, not be analyzed. As mentioned previously, glucocorticosteroids might influence both hearing and balance recovery. Unfortunately, we could not reliably retrieve whether patients had received oral corticosteroids within 14 days after SSNHL occurred, as is recommended in the Dutch treatment guideline.³¹ There were missing data in 41% of cases. Since only 25 patients had follow-up data, we could not perform a statistical analysis including corticosteroid therapy as a prognostic factor.

Dysfunctional vestibular perception, fear of falling or becoming dizzy when resuming daily tasks, and consequent activity avoidance might be other factors that contribute to disability following vestibulopathy caused by labyrinthitis or otherwise.^{16,32} Dunlap et al have investigated this fear-avoidance behavioral response in patients with vestibular disorders since there is a well-studied association between psychiatric symptoms and vestibular disorders, indicating shared neural networks that link anxiety, fear, and dizziness.³³ They objectified that stronger fear-avoidance responses at presentation were associated with more reported disability after 3 months of follow-up.³³ After a long follow-up with a median of 61 months, 5% of patients in the present cohort were afraid of leaving the house unaccompanied, and 20% of patients were worried about performing specific movements as they believed this would provoke their vertigo. These relatively low percentages are likely caused by the follow-up of almost 5 years. After several years, people stated they had modified their lifestyle to match their complaints, and most importantly, patients were not afraid anymore that another episode of vertigo might occur. In contrast, Dunlap et al only followed patients for up to 3 months,¹⁶ so this acceptance and adaptation had not yet occurred, presumably.

Most patients in our cohort had received vestibular rehabilitation, which may have improved their functional outcomes. In the literature, there is moderate-to-strong evidence to support the use of vestibular rehabilitation in patients with unilateral and bilateral vestibulopathy to reduce symptoms and improve vestibular recovery.^{34,35} Unfortunately, there is no standardized protocol for vestibular rehabilitation in cases of unilateral or bilateral vestibulopathy,³⁴ which complicates comparing different rehab protocols and evaluating their influence on vestibular recovery and activity avoidance.

Several limitations of the current study should be pointed out. First and most importantly, patients that are referred to a tertiary center are likely to have more severe symptoms, a longer duration of disease, or a worse recovery than the average patient experiencing labyrinthitis who does not require a hospital visit. Also, patients referred to our tertiary dizziness clinic are not seen in an acute setting. In these cases, the diagnosis is based on a persistent, objectified loss of vestibular function. This may have resulted in selection bias because patients whose vestibular function had been sufficiently restored before their visit to our center were not included. Second, in the absence of baseline outcome measurements, we could not compare the limitations in activity and fear-avoidance behavioral responses between disease onset and follow-up. Finally, we did not perform pure-tone audiometry or vestibular testing at follow-up and could thus not assess the differences in hearing thresholds at presentation and follow-up, nor could we relate this to the participants' self-reported subjective hearing recovery.

Regardless of the limitations of this study, we found that a significant number of patients with idiopathic labyrinthitis have a poor prognosis for both hearing and balance function. When comparing our observations to the literature, their prognosis appears to be worse than in sudden deafness or vestibulopathy alone.

In conclusion, patients presenting with idiopathic labyrinthitis in a specialized dizziness clinic have a poor prognosis, with subjective hearing recovery in only 20% of cases and persistent balance difficulties. After a median follow-up of 5 years, 72.5% of patients diagnosed

with idiopathic labyrinthitis still complained of balance problems or instability. Of these patients, 77% could not resume their normal daily activities. Prospective cohort studies are necessary to objectify persistent balance difficulty and relate this to vestibular recovery, hearing recovery, activity avoidance, and therapy strategies.

Ethics Committee Approval: This study was approved by the Institutional Review Board of Gelre Hospital Apeldoorn (Approval No: 2021_36, Date: December 24,2021).

Informed Consent: Verbal informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – R.L., T.B., F.O.; Design – F.O, R.L., T.B.; Supervision – R.L., T.B., T.S.; Resources – F.O., C.C.; Materials – F.O., C.C.; Data Collection and/or Processing – F.O., C.C.; Analysis and/or Interpretation – F.O., T.S.; Literature Search – F.O.; Writing – F.O.; Critical Review – R.L., T.B., T.S.

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