Risk of Alzheimer Disease and Vascular Dementia in Patients With Peripheral Vestibular Disorders:

A Longitudinal Study of 140,726 Participants

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Abstract

Objective: The associations between peripheral vestibular disorders (PVDs)—specifically Meniere's disease, benign paroxysmal positional vertigo (BPPV), vestibular neuritis, and unspecified PVD—and dementia risk are unclear.

Methods: By using data from the Taiwan National Health Insurance Research Database, this study included 70,363 patients aged ≥45 years with PVD between 1998 and 2011. An age-matched control group of 70,363 individuals without PVD was also established. All the included participants were followed up from the time of enrollment until the end of 2013 to assess the risk of dementia-related conditions, including Alzheimer's disease (AD), vascular dementia, and unspecified dementia.

Results: Cox proportional hazards regression models, adjusted for demographic characteristics and psychiatric comorbidities, revealed that patients with PVD exhibited a significantly elevated risk of any form of dementia during the follow-up period (hazard ratio [HR] = 1.83, 95% CI, 1.69–1.97) compared with the control group. Notably, patients with BPPV exhibited the highest risk of AD (HR = 3.14, 95% CI, 2.35–4.19), followed by Meniere's disease (HR= 2.79, 95% CI, 2.17–3.59) and vestibular neuritis (HR = 2.66, 95% CI, 2.11–3.35).

Conclusions: PVDs are a risk factor for dementia, regardless of psychiatric comorbidities. Further research is warranted to elucidate the pathophysiological mechanisms underlying the association between PVDs and dementia.

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Vestibular disorders are a common but often underestimated category of sensory deficits that affect the inner ear and central nervous system, which play a vital role in maintaining balance and spatial orientation. These disorders can lead to debilitating symptoms, such as vertigo, dizziness, imbalance, and visual disturbances, that significantly affect patients' daily functioning.[1] Vestibular disorders are typically categorized into central and peripheral types, with peripheral vestibular disorders (PVDs) being more prevalent. PVDs typically involve the inner ear or the vestibular nerve, both of which are essential for maintaining balance and spatial orientation.[2,3] Epidemiological studies have indicated that PVDs affect a substantial portion of the population, with an average annual incidence rate of 1.49% in Taiwan, which closely aligns with the prevalence rate of 1.6% reported in Germany.[4,5] PVD subtypes such as Meniere's disease (MD), benign paroxysmal positional vertigo (BPPV), and vestibular neuritis (VN) significantly contribute to the health care burden associated with these disorders.[6]

Recent research has indicated that PVDs have substantial implications for cognitive function. Specifically, vestibular disorders are associated with impairments in spatial memory, attention, and visuospatial cognition, which may be attributable to the degeneration of cortical vestibular networks and disrupted neurogenesis in the hippocampus.[7] This decline in cognitive function is particularly pronounced in older adults, with studies linking vestibular dysfunction to an increased risk of conditions involving cognitive decline and dementia, particularly Alzheimer's disease (AD).[8] Recent studies have also indicated that older adults with vestibular dysfunction exhibit significant

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Clinical Points

- Evidence has shown an association between peripheral vestibular dysfunction and subsequent cognitive decline.
- This study reported that peripheral vestibular disorders (PVDs) increased the subsequent dementia risk, including Alzheimer's disease and vascular dementia.
- The association between PVDs and dementia was independent of dementia-related comorbidities such as depression and diabetes.

cognitive impairments, particularly in terms of immediate memory and visuospatial abilities.[8] Additionally, individuals with mild cognitive impairment and AD have been demonstrated to exhibit notable vestibular and balance deficits, suggesting that vestibular assessment could aid in the early diagnosis of cognitive decline.[9]

Dementia is a critical public health concern, with its prevalence projected to drastically increase by 2050, thereby posing substantial challenges to global health care systems.[10] Although conventional risk factors such as hypertension, obesity, and smoking have been extensively documented, emerging evidence suggests that sensory deficits, including vestibular dysfunction, may play a considerable role in the risk of cognitive decline and dementia.[11] Several studies have underscored the strong association between vestibular loss and dementia, particularly in cases of bilateral vestibulopathy.[7,12] Moreover, large-scale epidemiological studies have corroborated this association.[13,14] Individuals with reduced vestibular function often exhibit poor performance on tasks that require spatial cognition and navigation, as the vestibular system provides crucial information to the brain regarding head orientation and movement.[15]

Age-related declines in vestibular function are closely associated with impairments in spatial cognition, particularly in tasks such as mental rotation, spatial memory, and navigation.[13] Vestibular impairment is considerably more pronounced in individuals with AD than in individuals without AD. The loss of vestibular function, particularly when coupled with AD, exacerbates cognitive deficits, with spatial cognition being particularly affected. These findings indicate that vestibular dysfunction may contribute to a specific "spatial" subtype of AD,[16] thereby reinforcing the connection between vestibular dysfunction and cognitive decline.

Although the association between vestibular dysfunction and cognitive impairment has been established, the associations between PVD subtypes and specific types of dementia remain less investigated and unclear. A Korean study involving 496 elderly people with MD revealed a significantly higher likelihood of subsequent AD (hazard ratio [HR]: 1.69, 95% confidence interval [CI], 1.20–2.37) and vascular dementia (1.99, 1.10–3.57) in the MD group compared with the control group.[17] Lo et al[18] and Kim et al[19] indicated an association between BPPV and all-cause dementia but did not further elucidate its associations with dementia subtypes. A retrospective study involving 989 patients with any dementia and 2,967 controls without dementia reported that patients with any dementia exhibited an elevated risk of pre-existing VN (odds ratio: 2.44, 95% CI, 1.36–4.37) compared with those without dementia.[20] Again, this study did not clarify associations between VN and dementia subtypes.[20]

The present study used data from the Taiwan National Health Insurance Research Database (NHIRD) to conduct a large-scale longitudinal analysis involving 140,726 participants. The primary objectives of the study were to determine whether PVDs increase the risk of dementia and to identify which PVD subtypes are most closely associated with specific types of dementia, namely, AD, vascular dementia, and unspecified dementia. By employing a large, well-defined cohort and a longitudinal design, this study provided robust evidence that can inform future research and clinical practices aimed at mitigating dementia risk among patients with PVD.

METHODS

Data Source

The National Health Research Institute audits and releases the Taiwan NHIRD for scientific and study reasons upon the official application of a particular research and data analysis proposal. The present research analysis was conducted using data from the Longitudinal Health Insurance Database of NHIRD, which includes all medical records from 1996 to 2013. Dates of clinical visits, diagnoses, interventions, and prescriptions were all included in this dataset for 3,000,000 insured people who were chosen at random from the larger Taiwanese population (~28,000,000). The diagnostic codes used were based on the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*). The NHIRD has been extensively used in many epidemiologic studies in Taiwan.[21–24] The protocol for this study was approved by the institutional review board of Taipei Veterans General Hospital, and informed consent was waived since the investigation used de-identified data and had no contact with human individuals.

Inclusion Criteria for Patients With PVD and Control Group

Based on previous longitudinal follow-up studies investigating an association between midlife (mean age: ~45 years) risk factors and subsequent dementia,[25,26]

only adults aged ≥45 years who were diagnosed with any PVD by board-certified otorhinolaryngologists at least twice between 1998 and 2011 and had no prior history of any dementia were included as a PVD group. PVD includes MD (*ICD-9-CM* code: 386.0), BPPV (*ICD-9-CM* code: 386.11), VN (*ICD-9-CM* code: 386.12), and unspecified PVD (*ICD-9-CM* codes: 386.10, 386.19, and 386.9).[27] The first time of a PVD diagnosis was defined as the time of enrollment. For exact matching, the PVD group was paired with controls who had neither a history of any PVD nor any dementia prior to the enrollment at a 1:1 ratio. Matching was based on age (±1 year), enrollment time, dementia-related medical and mental comorbidities, income level (categorized as levels 1–3 per month: ≤19,100 NTD (New Taiwanese Dollars), 19,001–42,000 NTD, and ≥42,001 NTD), and urbanization level of residence (categorized as levels 1–5, ranging from most to least urbanized).[28] 1 United States Dollar is 32.94 NTD. Dementia-related comorbidities included hypertension, dyslipidemia, diabetes mellitus, cerebrovascular diseases, traumatic brain injury, major depressive disorder, substance use disorder, and alcohol use disorder. Additionally, Charlson Comorbidity Index (CCI) and all-cause clinical visits were provided for the PVD and the matched-control cohorts. CCI consisting of 22 physical conditions was also assessed to determine the systemic health conditions of all enrolled subjects.[29]

Identification of Dementia

During the follow-up period (from enrollment to December 31, 2013, or death), board-certified psychiatrists or neurologists recorded the diagnosis of dementia (*ICD-9-CM* codes: 290.0, 290.1, 290.2, 290.3, 290.4, 294.1, 294.2, 331.0, 331.1, 331.2, 331.82) at least twice. The first date of dementia diagnosis was defined as the time of outcome. AD was classified using the *ICD-9-CM* code 331.0 or by the *ICD-9-CM* codes for dementia (*ICD-9-CM* codes: 290.0, 290.1, 290.2, 290.3, 290.4, 294.1, 294.2) in conjunction with the use of dementia medications. Reimbursable therapies for dementia (ie, cholinesterase inhibitors) were only approved, in accordance with the NHI regulations, following extensive laboratory and imaging examinations aimed at ruling out other potential causes of cognitive decline, such as thyroid dysfunction, vitamin B_{12} deficiency, or cerebrovascular events. When there was evidence of cerebrovascular lesions, medications for AD were not approved. Vascular dementia was defined by the specific *ICD-9-CM* code of 290.4. We classified other types of dementia as unspecified dementia in our study because the *ICD-9-CM* codes 290.0, 290.1, 290.2, 290.3, 290.4, 294.1, and 294.2 alone do not clearly define the definite dementia pathology without concurrent medication prescription for AD, reflecting Taiwanese clinical practice. This unspecified dementia classification includes a diagnosis of AD with evidence of any cerebrovascular lesion in our study. For this reason, the diagnostic validity of AD as the sole reason for neurocognitive degeneration is high.

Statistical Analysis

For between-group comparisons, the F test was used for continuous variables and Pearson χ^2 test for nominal variables. Cox regression analyses with adjustment of demographic characteristics (age, sex, income, and residence), comorbidities, CCI scores, and all-cause clinical visits were performed to assess the dementia (any dementia, AD, vascular dementia, or unspecified dementia) risks between the PVD and control groups. A log-minus-log plot reported that the Cox regression analyses did not violate the Cox assumption for proportional hazards. Furthermore, we also assessed the dementia risk stratified by PVD subtypes. Given the insidious onset of dementia, 2 types of sensitivity analyses were performed to validate the results by minimizing underdiagnosis of occult dementia at the time of PVD diagnosis. In the "exclusion of observation period" model, the first 3 or 5 years of observation after the PVD diagnosis were excluded, eliminating all cases of dementia diagnosed within these first years following the PVD diagnosis. In the "exclusion of enrollment period" model, only patients diagnosed with PVD prior to the dates December 31, 2007, or December 31, 2009, were included in the analyses; patients with PVD diagnosed after these time points were selectively excluded. Finally, analyses using competing risk-regression model were also performed with death as a competing risk. Statistical significance was set at 2-tailed $P \leq .05$. Data are presented as the mean (standard deviation [SD]). Data processing and statistical analyses were performed with SAS (version 9.1, SAS Institute, Cary, NC).

Data Availability Statement

The NHIRD was released and audited by the Department of Health and Bureau of the NHI Program for the purpose of scientific research (https://www.apre.mohw.gov.tw/). NHIRD can be obtained through the formal application that is regulated by Department of Health and Bureau of the NHI Program.

RESULTS

The study included a total of 70,363 patients with PVD, comprising 27,259 males and 43,104 females, with a mean age of 58.45 years (SD: 11.49). Of these, 11,656 patients were diagnosed with MD, 9,115 with BPPV, 18,095 with VN, and 28,501 with unspecified PVD. Patients in the PVD group had significantly higher CCI scores and higher all-cause clinical visits compared to the control group (Table 1).

Table 1.

Demographic Data and Incidence of Dementia Among Patients With PVD and Control Group

	Patients with PVD (n = 70,363)	Controls (n = 70,363)	*P* value
Age at enrollment, mean (SD), y	58.45 (11.49)	58.44 (11.50)	.841
Sex, n (%)			>.999
Male	27,259 (38.7)	27,259 (38.7)	
Female	43,104 (61.3)	43,104 (61.3)	
PVD diagnosis, n (%)			
Meniere's disease	11,656 (16.6)		
BPPV	9,115 (13.0)		
Vestibular neuritis	18,095 (25.7)		
Unspecified PVD	28,501 (40.5)		
Dementia-related comorbidities, n (%)			
Cerebrovascular diseases	17,312 (24.6)	17,312 (24.6)	>.999
Traumatic brain injury	3,326 (4.7)	3,326 (4.7)	>.999
Hypertension	37,172 (52.8)	37,172 (52.8)	>.999
Dyslipidemia	25,301 (36.0)	25,301 (36.0)	>.999
Diabetes mellitus	16,960 (24.1)	16,960 (24.1)	>.999
Depressive disorder	6,204 (8.8)	6,204 (8.8)	>.999
Alcohol use disorder	1881 (2.7)	1881 (2.7)	>.999
Substance use disorder	1,486 (2.1)	1,486 (2.1)	>.999
CCI score, mean (SD)	2.99 (2.34)	2.40 (2.22)	<.001
Level of urbanization, n (%)			>.999
1 (most urbanized)	9,280 (13.2)	9,280 (13.2)	
2	16,903 (24.0)	16,903 (24.0)	
3	5,398 (7.7)	5,398 (7.7)	
4	6,553 (9.3)	6,553 (9.3)	
5 (most rural)	32,229 (45.8)	32,229 (45.8)	
Income-related insured amount, n (%)[a]			>.999
≤19,100 NTD/mo	30,811 (43.8)	30,811 (43.8)	
19,001–42,000 NTD/mo	33,157 (47.1)	33,157 (47.1)	
>42,000 NTD/mo	6,395 (9.1)	6,395 (9.1)	
Incidence of any dementia, n (%)	2,932 (4.2)	956 (1.4)	<.001
Age at diagnosis of any dementia, mean (SD), y	76.52 (9.08)	77.94 (9.26)	<.001
Duration between enrollment and dementia, mean (SD), y	6.20 (3.37)	8.22 (3.52)	<.001
Dementia type, n (%)			
Alzheimer disease	655 (0.9)	144 (0.2)	<.001
Vascular dementia	442 (0.6)	175 (0.2)	<.001
Unspecified	1835 (2.6)	637 (0.9)	<.001
All-cause clinical visits (times per year), mean (SD)	22.28 (15.91)	14.26 (12.67)	<.001

[a]32.94 NTD = 1 USD.
Abbreviations: BPPV = benign paroxysmal positional vertigo, CCI = Charlson Comorbidity Index, NTD = new Taiwan dollar, PVD = peripheral vestibular disorder.

The incidence of dementia among patients with PVD was 4.2% (2,932 out of 70,363), significantly higher than in the control group, where the incidence was 1.4% (956 out of 70,363; $P < .001$) (Table 1). The average age at dementia diagnosis in the PVD group was 76.52 years (SD: 9.08), slightly younger than the control group, which had an average diagnosis age of 77.94 years (SD: 9.26) ($P < .001$). The mean duration from enrollment to dementia diagnosis was also shorter in the PVD group, averaging 6.20 years (SD: 3.37), compared to 8.22 years (SD: 3.52) in the control group ($P < .001$) (Table 1).

Regarding the specific types of dementia, Table 1 shows that 0.9% of patients with PVD developed AD (655 out of 70,363), 0.6% developed vascular dementia (422 out of 70,363), and 2.6% had an unspecified dementia diagnosis (1,835 out of 70,363). The HR for developing dementia was 1.83 (95% CI, 1.69–1.97) in the PVD group, indicating a significantly higher risk compared to the control group (Table 2).

When stratified by PVD subtype, the HRs for dementia were 1.73 (95% CI, 1.54–1.94) for MD, 1.97 (95% CI, 1.73–2.25) for BPPV, 1.86 (95% CI, 1.69–2.06) for VN, and 2.00 (95% CI, 1.82–2.20) for unspecified PVD (Table 2). The risk of developing specific types of dementia—AD, vascular dementia, and unspecified dementia—was significantly all higher in patients with PVD compared to the control group. Specifically, the HR for AD was 2.59 (95% CI, 2.15–3.12); for vascular

Table 2.
Risk of Developing Dementia Among Patients With PVD and Controls[a]

	Alzheimer disease			Vascular dementia			Unspecified dementia			Total		
	n (%)	HR (95% CI)[b]	HR (95% CI)[c]	n (%)	HR (95% CI)[b]	HR (95% CI)[c]	n (%)	HR (95% CI)[b]	HR (95% CI)[c]	n (%)	HR (95% CI)[b]	HR (95% CI)[c]
Control group	144 (0.2)	1 (ref)		175 (0.2)	1 (ref)		637 (0.9)	1 (ref)		956 (1.4)	1 (ref)	
Patients with PVD	655 (0.9)	**2.59 (2.15–3.12)**	**2.46 (2.04–2.98)**	442 (0.6)	**1.49 (1.24–1.79)**	**1.38 (1.45–1.67)**	1835 (2.6)	**1.75 (1.59–1.92)**	**1.69 (1.53–1.86)**	2,932 (4.2)	**1.83 (1.69–1.97)**	**1.83 (1.69–1.97)**
Meniere's disease	136 (1.2)	**2.79 (2.17–3.59)**	**2.54 (1.95–3.30)**	175 (0.2)	1.17 (0.87–1.58)	1.00 (0.73–1.37)	637 (0.9)	**1.63 (1.42–1.88)**	**1.51 (1.31–1.75)**	531 (4.6)	**1.73 (1.54–1.94)**	**1.73 (1.54–1.93)**
BPPV	86 (0.9)	**3.14 (2.35–4.19)**	**2.86 (3.13–3.86)**	50 (0.5)	**1.44 (1.03–2.00)**	1.24 (0.88–1.75)	215 (2.4)	**1.87 (1.58–2.20)**	**1.69 (1.43–2.00)**	351 (3.9)	**1.97 (1.73–2.25)**	**1.97 (1.73–2.25)**
Vestibular neuritis	181 (1.0)	**2.66 (2.11–3.35)**	**2.45 (1.93–3.11)**	130 (0.7)	**1.55 (1.22–1.98)**	**1.38 (1.08–1.77)**	514 (2.8)	**1.77 (1.53–2.00)**	**1.66 (1.46–1.88)**	825 (4.6)	**1.86 (1.69–2.06)**	**1.86 (1.68–2.05)**
Unspecified PVD	225 (0.8)	**2.57 (2.06–3.21)**	**2.35 (1.87–2.95)**	177 (0.6)	**1.83 (1.46–2.28)**	**1.65 (1.31–2.07)**	658 (2.3)	**1.91 (1.70–2.15)**	**1.80 (1.60–2.03)**	1,060 (3.7)	**2.00 (1.82–2.20)**	**2.00 (1.82–2.20)**

[a]Adjusted by demographic characteristics, medical and mental comorbidities, CCI score, and all-cause clinical visits. **Bold type** indicates statistical significance.
[b]Death as a censor.
[c]Death as a competing risk.
Abbreviations: BPPV = benign paroxysmal positional vertigo, HR = hazard ratio, PVD = peripheral vestibular disorder.

dementia, it was 1.49 (95% CI, 1.24–1.79); and for unspecified dementia, it was 1.75 (95% CI, 1.59–1.92) (Table 2). When further analyzed by the PVD subtype, the highest HR for AD was observed in patients with BPPV (HR: 3.14, 95% CI, 2.35–4.19). For vascular dementia, the highest HR was found in patients with unspecified PVD (HR: 1.83, 95% CI, 1.46–2.28), and for unspecified dementia, the highest risk was also in patients with unspecified PVD (HR: 1.91, 95% CI, 1.70–2.15).

The survival analysis showed that patients with PVD had a lower probability of remaining dementia-free over time compared to the control group, a trend that persisted throughout the study period (Figure 1). Sensitivity analyses confirmed the robustness of these findings, with the HRs remaining significantly elevated even after excluding dementia cases diagnosed within the first 3 or 5 years post-PVD diagnosis. Specifically, the HRs were 1.74 (95% CI, 1.60–1.88) for the 3-year exclusion and 1.61 (95% CI, 1.47–1.76) for the 5-year exclusion. Similarly, in the "exclusion of enrollment period" model, the HRs for dementia development were 1.88 (95% CI, 1.73–2.03) for patients diagnosed before December 31, 2009, and 1.94 (95% CI, 1.78–2.11) for those diagnosed before December 31, 2007, respectively (Table 3). Finally, the competing risk for mortality showed consistent findings (Tables 2 and 3).

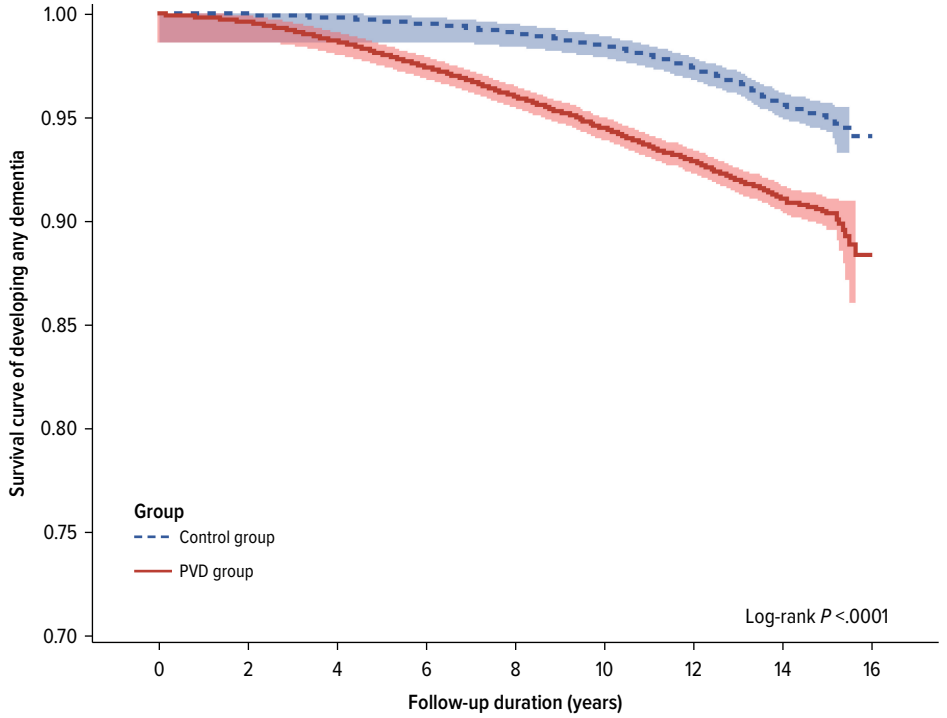
DISCUSSION

This study investigated the association between PVDs and the risk of dementia in a large, well-defined Taiwanese cohort. The findings revealed a significantly elevated risk of dementia among patients with PVD compared with matched controls, supporting the hypothesis that PVDs are not solely associated with vestibular symptoms but also constitute a potential risk factor for cognitive decline. These results are consistent with existing clinical research that has reported that patients with vertigo and vestibular disorders frequently experience symptoms such as memory loss, commonly referred to as "brain fog," along with mental confusion and difficulties in concentration and cognitive performance.[30,31]

The hazard ratios identified in this study indicate that patients with various PVD subtypes, including MD, BPPV, and VN, exhibit an increased risk of different forms of dementia, including AD, vascular dementia, and unspecified dementia. Notably, the highest HR for AD was observed in patients with BPPV, suggesting a particularly strong association between this subtype and neurodegenerative processes underlying dementia. The strong association between unspecified PVD and both vascular and unspecified dementia further underscores the complex relationship between vestibular dysfunction and cognitive health.

Figure 1.

Survival Curve of Developing Any Dementia Among Patients With PVD and Control Group



Control group	70363	69829	57321	44626	32945	21290	12169	4239	0
PVD group	70363	69792	57008	44015	32171	20518	11629	4010	0

Abbreviation: PVD = peripheral vestibular disorder.

Table 3.

Sensitivity Analyses of Developing Any Dementia Among Patients With PVD and Controls[a]

		Exclusion of observation period		Exclusion of enrollment period	
	Total HR (95% CI)	>3 years HR (95% CI)	>5 years HR (95% CI)	Enrollment year ≤2009 HR (95% CI)	Enrollment year ≤2007 HR (95% CI)
PVD					
Presence[b]	**1.83 (1.69–1.97)**	**1.74 (1.60–1.88)**	**1.61 (1.47–1.76)**	**1.88 (1.73–2.03)**	**1.94 (1.78–2.11)**
Presence[c]	**1.83 (1.69–1.97)**	**1.80 (1.60–2.03)**	**1.57 (1.44–1.72)**	**1.88 (1.73–2.03)**	**1.94 (1.78–2.11)**
Absence	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)

[a]Adjusted by demographic characteristics, medical and mental comorbidities, CCI score, and all-cause clinical visits. **Bold type** indicates statistical significance.
[b]Death as a censor.
[c]Death as a competing risk.
Abbreviations: HR = hazard ratio, PVD = peripheral vestibular disorder.

This study focused on the varying effects of various PVD subtypes on the risk of dementia forms, particularly AD. The findings revealed a significant association between BPPV and AD, consistent with recent research on the cognitive effects of vestibular disorders. BPPV, characterized by brief episodes of vertigo caused by otolith displacement within the semicircular canals, may contribute to cognitive decline through recurrent disruptions in spatial orientation and balance. These frequent episodes can exert cumulative stress on the brain's vestibular and cognitive processing centers, particularly in regions involved in spatial memory and navigation, such as the hippocampus.[32] Research has indicated that BPPV may serve as an early marker of broader neurodegenerative processes within the nervous system, potentially linking it to an increased risk of dementia.[33] This connection is particularly compelling considering that the vestibular system, the

phylogenetically oldest sensory system, may begin to deteriorate as an early marker of dementia.[34] Furthermore, the anxiety and fear associated with sudden vertigo episodes may exacerbate cognitive decline by impairing attention and concentration over time.[35] Bhattacharyya et al[35] investigated cognitive impairment in 107 patients with BPPV and MD, using a questionnaire-based approach in their investigation. They reported lower cognitive scores in patients with BPPV and MD compared with controls, corroborating the present findings. However, the present study expands on this by using a substantially larger sample size and a more comprehensive analysis, thereby offering deeper insights into the associations between specific PVD subtypes and dementia risk, including AD.

Rizk et al[36] reported a minimal effect of BPPV on cognitive function, as measured using the Cognitive Failures Questionnaire. In their cross-sectional study of 186 patients at a tertiary vestibular clinic, the Cognitive Failures Questionnaire scores of those with BPPV were comparable to those of older adult controls, suggesting that intermittent and brief episodes of BPPV may not lead to long-term cognitive dysfunction in all cases. This contrasts with our findings and highlights the potential variability in cognitive outcomes associated with BPPV. Such variability may be influenced by factors such as the frequency and severity of vertigo episodes as well as individual susceptibility to cognitive decline. These discrepancies highlight the need for further research to elucidate the specific conditions under which BPPV might contribute to cognitive impairment.

MD, characterized by episodic vertigo, fluctuating hearing loss, and tinnitus, may affect cognition through mechanisms involving both the vestibular and auditory systems. The chronic and unpredictable nature of MD often results in significant psychological stress, compounded by persistent vertigo and hearing impairment. This stress can activate the hypothalamus–pituitary–adrenal axis, leading to elevated cortisol levels, which have been associated with hippocampal atrophy.[37] Furthermore, reductions in hippocampal volume observed in patients with MD may be another key factor contributing to the cognitive deficits associated with this disorder.[38,39] Although the present study revealed that other PVD subtypes, such as BPPV, were associated with higher risks for dementia, MD was significantly associated with cognitive decline. These findings underscore the need for further investigation into the specific mechanisms by which MD affects brain health.

The findings of the present study are consistent with those of studies that have established a clear link between vestibular dysfunction and cognitive impairment. A study demonstrated that vestibular disorders can lead to substantial cognitive deficits, particularly in spatial memory and navigation, due to the degeneration of cortical vestibular networks and impaired neurogenesis in the hippocampus.[40] Vestibular dysfunction may contribute to degeneration in regions of the cortical vestibular network, negatively affecting synaptic plasticity and neurogenesis in the hippocampus. This disruption can lead to neuronal atrophy and cell death, ultimately resulting in impairments in memory and visuospatial functions.

In line with our findings, other studies have highlighted a strong association between vestibular disorders and cognitive decline, with conditions such as bilateral vestibulopathy being particularly associated with an increased risk of all forms of dementia, including AD.[14,41] For instance, individuals with bilateral vestibulopathy have been demonstrated to exhibit a substantially higher risk of AD due to the disruption of connections between the vestibular system and the hippocampus.[7] The vestibular system is directly connected to key areas responsible for higher cognitive functions, such as the prefrontal cortex, insula, and hippocampus.[7] Older adults with vestibular dysfunction often exhibit substantial impairments in immediate memory and visuospatial cognition, both of which are crucial for daily functioning.[8] Potential interventions for mitigating these cognitive deficits include virtual reality–based vestibular rehabilitation techniques and caloric stimulation.[8] Additionally, research has indicated that individuals with mild cognitive impairment and AD exhibit notable vestibular and balance deficits, suggesting that vestibular assessments may play a valuable role in early screening for cognitive decline.[9] For example, patients with AD have been reported to exhibit delayed latency in the p13 component of cervical vestibular-evoked myogenic potentials, which is correlated with poorer clinical balance scores. This finding underscores the role of vestibular dysfunction as a pivotal marker of cognitive decline. Scores in assessments such as the Timed Up and Go test, Performance-Oriented Mobility Assessment—Balance, and Functional Gait Assessment have been demonstrated to progressively worsen along the Alzheimer's continuum.[9] The findings of the present study emphasize the profound effect of vestibular dysfunction on dementia risk and the importance of early intervention, which may help reduce this risk of cognitive decline associated with vestibular disorders.

This study advanced the current body of knowledge by involving a large Taiwanese population and employing a longitudinal design, allowing for a more robust assessment of the temporal relationship between PVDs and dementia. Cultural and regional factors, such as lifestyle, health care resources, and genetic background, should be considered, which may influence the association between PVDs and dementia, potentially affecting the generalizability of these findings to other

populations. The longitudinal design of this study is particularly crucial because it addressed the limitations of previous cross-sectional studies that were unable to establish causality. Moreover, the large sample size and the use of comprehensive, well-validated diagnostic codes increase the generalizability of the findings.

Our study highlighted the importance of considering PVD subtypes in the assessment of dementia risk. The distinct risk profiles observed across various PVD subtypes suggest that the pathophysiological mechanisms underlying the relationship between vestibular dysfunction and dementia may vary depending on the specific PVD subtype. Additionally, exploring genetic and molecular mechanisms could further elucidate the contribution of vestibular dysfunction to cognitive decline, offering a more comprehensive understanding of the disease process. This underscores the need for further research to elucidate these mechanisms and to explore potential preventive strategies tailored to each PVD subtype.

Although this study offers valuable insights into the association between PVDs and dementia, several limitations must be acknowledged. First, the observational nature of this study limited the establishment of a definitive causal relationship between PVDs and dementia. The causal association between PVDs and dementia cannot be inferred based on our study. Second, despite adjustment of several potential confounders, the possibility of residual confounding from unmeasured variables such as environmental factors and lifestyle could not be completely ruled out. Third, due to the lack of information on the severity of both PVDs and dementia in the database, disease severity could not be considered in the analysis, which may have influenced the assessment of the association between PVDs and dementia. Fourth, the NHIRD only recorded individuals who sought medical consultation and treatment, potentially underestimating the rates of PVDs and dementia. However, all PVD and dementia diagnoses were given by board-certified specialists, ensuring the diagnostic validity. Finally, although population-based retrospective cohort studies provide valuable insights, they do not allow the direct investigation of the mechanisms underlying the relationship between PVDs and dementia.

In conclusion, this study provided compelling evidence that PVDs are associated with an increased risk of dementia, with varying risk profiles observed across different PVD subtypes. These findings underscore the importance of early recognition and management of vestibular disorders as a potential strategy for mitigating the risk of cognitive decline. Future research should prioritize the investigation of the underlying mechanisms linking PVDs to dementia and developing targeted interventions aimed at reducing this risk.

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