Prospective Clinical Research Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
48(12) 1–9

DOI: 10.1177/0300060520973093
journals.sagepub.com/home/imr
SAGE

Risk factors for residual dizziness in patients successfully treated for unilateral benign posterior semicircular canal paroxysmal positional vertigo

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Abstract

Objective: The risk factors for residual dizziness (RD) after successful treatment of benign paroxysmal positional vertigo (BPPV) are poorly characterized. We determined the risk factors for RD in patients with benign unilateral posterior semicircular canal paroxysmal positional vertigo (pc-BPPV) after successful treatment.

Methods: We conducted a prospective study of patients diagnosed with unilateral pc-BPPV between March 2015 and January 2017. Bone mineral density (BMD) was measured by dual-energy X-ray bone mineral densitometry. Participants underwent bithermal caloric testing (C-test) using videonystagmography and a canalith repositioning procedure (CRP). The occurrence of RD was the primary outcome. The participants underwent follow-up 1 week, 1 month, and 1 year after successful CRP, consisting of outpatient visits, questionnaires, and telephone interviews.

Results: We assessed 115 participants with unilateral pc-BPPV (31 men and 84 women) who were 53.2 ± 8.8 years old. RD occurred in 60 (52.2%) participants. The participants who experienced RD were older, had vertigo for longer before treatment, and were more likely to show a positive C-test and significant BMD loss.

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Conclusions: We found that a significant reduction in BMD (T-score < -1 standard deviation), a positive C-test, and older age are independently associated with RD in patients with pc-BPPV after successful CRP.

Keywords
Benign paroxysmal positional vertigo, dizziness, semicircular canal, bone mineral density, osteoporosis, canalith repositioning procedure, bithermal caloric test

Date received: 10 August 2020; accepted: 21 October 2020

Introduction

Benign paroxysmal positional vertigo (BPPV), the most commonly diagnosed peripheral vestibular disorder, is categorized as either idiopathic BPPV (iBPPV) or secondary BPPV, and has a lifetime prevalence of 2.4%.[1–3] The peak onset of the disorder is at 50 to 60 years of age, and women are more often affected than men.[1,3] BPPV is the ultimate diagnosis in 17% to 42% of patients who have symptoms of vertigo, which makes it the most common cause of vertigo.[1,2] The posterior semicircular canal is the most frequently affected site (80% to 90%), followed by the horizontal (5% to 30%) and anterior (1% to 2%) canals.[1,3,4]

The canalith repositioning procedure (CRP) is widely used to manage BPPV, and a dramatic beneficial effect can be obtained in the majority of patients with BPPV using this tecnique.[1,2,5,6] Nevertheless, residual dizziness (RD) affects 38% to 61% of BPPV patients, despite successful treatment.[6,7] RD is defined as nonpositional, persistent imbalance, dizziness, or a feeling of floating.[1] The exact etiology of RD remains to be defined, but proposed mechanisms include: i) persistence of debris in the canal, which is insufficient to trigger cupular deflection, with subsequent nystagmus; ii) incomplete central adaptation following CRP; and iii) undetected accompanying vestibular or utricular dysfunction occurring alongside BPPV.[7,8]

It is unclear whether there is an association between canal paralysis (CP) and RD, although there is evidence that suggests an association between CP and BPPV recurrence.[8] In addition, osteopenia and osteoporosis are risk factors for the occurrence and recurrence of BPPV.[9–12] However, whether osteoporosis is a risk factor for RD in patients with BPPV remains to be determined. The presence of debris might reduce the caloric response on the affected side, but the results of previous studies have suggested that the influence of otoliths on the results of the bithermal caloric test (C-test) in patients with BPPV in the horizontal canal is controversial.[13–15]

The aim of the present study was to identify the clinical risk factors for RD in patients with benign unilateral posterior semicircular canal paroxysmal positional vertigo (pc-BPPV) after successful treatment.

Materials and methods

Study design and participants

We performed a prospective study of consecutive patients who had been diagnosed with unilateral pc-BPPV in the Department of Otorhinolaryngology-Head

and Neck Surgery of our hospital between March 2015 and January 2017. The study was reviewed and approved by the institutional ethics review board of the Sir Run Run Shaw Hospital, an affiliate of the Zhejiang Medical College Hospital (Name: BPPV, number: 20141203-1), and was conducted in compliance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all the participants.

The inclusion criteria were: 1) >18 years of age; 2) a diagnosis of unilateral pc-BPPV; 3) agreement to undergo bone mineral density (BMD) measurement and the C-test before CRP (Epley maneuver). The exclusion criteria were: 1) concurrent inner ear disease, trauma, or cranial tumor, e.g. Meniere's disease or acoustic tumor; 2) contraindications for videonystagmography (VNG), including tympanic membrane perforation and severe systemic disease; 3) medical therapy with drugs that might affect the VNG results, such as vestibular inhibitors; 4) a history of long-term steroid therapy; 5) a history of endocrine or vertebral diseases or fracture; 6) recent vertigo other than that caused by BPPV; and 7) nervous system disease that could cause dizziness. Patients that were unsuccessfully treated were also excluded from the study.

A diagnosis of pc-BPPV was made in accordance with the diagnostic guidelines of the International Classification of Vestibular Disorders, published in 2015.[16] The diagnostic criteria included rotatory vertigo (lasting <30 s and evoked by head movements), and the Dix–Hallpike maneuver (pc-BPPV; brief latency [1–5 s], limited duration [<30 s], torsional nystagmus toward the downward-facing ear, reversal of nystagmus upon sitting, and fatigability of the response).

Procedure

Before CRP, neurological and neurotological examinations were performed in all the participants. BMD was measured using dual-energy X-ray bone mineral densitometry.

The C-test was performed by VNG, using the following sequence:[17] irrigation of the right ear with air at 24°C, irrigation of the left ear with air at 24°C, irrigation of the right ear with air at 50°C, and irrigation of the left ear with air at 50°C. The participants were asked to perform mental arithmetic during the nystagmus recordings.

BMD, the preferred criterion for the diagnosis of osteoporosis, was measured using dual-energy X-ray absorptiometry (GE Lunar Prodigy Scanner, GE Lunar Corporation, Madison, WI, USA) for the proximal femur and posteroanterior lumbar vertebrae (L1 to L4). Dual-energy X-ray absorptiometry measures the quantity of mineral per unit area or volume of the bone image. The results are provided as a T-score, which is derived by comparing the measured BMD with a normative database of results from 30-year-old women. The BMD values recorded were the lowest T-scores for the vertebrae and femur. The T-scores were classified as normal (≥ -1 SD), osteopenia (-1 to -2.5 SD), or osteoporosis (≤ -2.5 SD).[18]

All the participants were treated using the CRP (Epley maneuver), which was performed as described previously.[19] Thirty minutes after the CRP, the Dix–Hallpike test was performed to evaluate the efficacy of treatment.[20] The CRP was considered to be successful if the Dix–Hallpike test was negative. However, if the Dix–Hallpike test was positive, the CRP was performed again, but on no more than three occasions. One week later, the participants were re-evaluated. When positional nystagmus and vertigo were absent, the treatment was regarded as successful, but if the Dix–Hallpike test was positive, the CRP was performed again, as described for the first treatment cycle.

Data collection and definitions

The general characteristics of the participants were recorded before the first CRP, including age, sex, C-test results, BMD results, and comorbidities. Bilateral semicircular canal hypofunction was considered when the slow-phase velocity produced by cold or hot air stimulation was $<6°/s$. Unilateral semicircular canal hypofunction was defined by a CP value $>25\%$. A C-test was considered to be positive (+) in the presence of unilateral or bilateral semicircular canal hypofunction. T-scores <-1 SD were considered to indicate abnormal BMD.

Outcome and follow-up

The outcome was the occurrence of RD, which was defined as non-positional, persistent imbalance, dizziness, or a feeling of floating that occurred after successful treatment.

Once successful treatment of a participant was confirmed, the occurrence of persistent and nonpositional dizziness was subsequently recorded. The successfully treated participants were then allocated to two groups. The non-RD group comprised participants who did not report any dizziness, whereas the RD group comprised those who reported persistent and nonpositional dizziness or a feeling of floating. The participants underwent follow-up examination on at least three occasions: 1 week, 1 month, and 1 year after successful CRP. This follow-up comprised outpatient visits, questionnaire completion, and telephone interviews.

Statistical analysis

The data were analyzed using SPSS 20.0 (IBM Inc., Armonk, NY, USA). Continuous data are presented as mean ± SD and were analyzed using Student's *t*-test. Categorical variables are presented as numbers and percentages, and were analyzed using the chi-square or Fisher's exact test. Logistic regression analysis was performed to determine the factors that significantly contribute to RD. Spearman's correlation coefficient was determined to analyze the relationship between T-score and CP value. Two-sided P-values <0.05 were considered to indicate statistical significance.

Results

Characteristics of the participants

In total, 125 participants (39 men and 86 women) were enrolled in the study; of these, 123 were defined as having been successfully treated by 1 week after the first CRP, and two were defined as having been successfully treated by 1 week after the second CRP. Ten participants were excluded because of missing data during the follow-up period. Thus, data from 115 participants (31 men and 84 women) were analyzed.

The mean age of the participants was 53.2 ± 6.8 years (range, 32 to 84 years). Hypertension was present in 29 (25.2%) participants, diabetes mellitus was present in 11 (8.8%), and four (3.2%) participants had both diabetes and hypertension. The pc-BPPV course of paroxysmal vertigo events prior to treatment was 1 to 90 days. Of the 115 participants with pc-BPPV, 67 (58.3%) did not experience recurrence and 48 did (41.7%, 48/115). RD occurred in 60 (52.2%, 60/115) participants. The duration of RD was 3 to 28 days (3 to 7 days in 39 participants and 7 to 28 days in 21 participants). A positive C-test and abnormal BMD were present in 52.2% (60/115) and 56.5% (65/115) of the participants, respectively.

Univariate and multivariate analyses of the risk factors for RD

Among the 115 pc-BPPV participants, there were 55 without RD and 60 with RD. As shown in Table 1, compared with the non-RD group, the participants with RD were older (58.7 ± 7.8 *vs.* 46.3 ± 6.3 years, $P < 0.001$), had a longer duration of pc-BPPV prior to treatment (14.7 ± 3.8 *vs.* 8.2 ± 2.0, $P = 0.001$), were more likely to show a positive C-test (68.3% *vs.* 34.5%, $P < 0.001$), and were more likely to show significant BMD loss (71.7% *vs.* 40.0%, $P < 0.001$).

Multivariate analysis (Table 2) showed that older age (odds ratio [OR] = 1.04, 95% confidence interval [CI]: 1.00–1.08, $P = 0.037$), a positive C-test (OR = 1.36, 95% CI: 1.03–1.72, $P = 0.031$), and significant BMD loss (OR = 1.74, 95% CI: 1.17–2.53, $P = 0.005$) were independently associated with RD after CRP.

Discussion

Studies that have evaluated the risk factors for RD after the successful treatment of BPPV have yielded conflicting results.[8–15,21] Therefore, in the present study, we aimed to identify the clinical risk factors for RD in patients with unilateral pc-BPPV that developed after successful treatment. The results suggest that the prevalence of RD after CRP

Table 1. Comparisons of the risk factors and recurrence during the follow-up period between the RD and No-RD groups, performed using univariate analysis.

	All participants (n = 115)	No-RD group (n = 55)	RD group (n = 60)	*P*
Female	84 (73.0%)	41 (74.5%)	43 (71.7%)	0.728
Age (years), mean ± SD	53.2 ± 6.8	46.3 ± 6.3	58.7 ± 7.8	<0.001
Duration of vertigo before treatment (days)	12.1 ± 2.7	8.2 ± 2.0	14.7 ± 3.8	0.001
Underlying disease				0.372
Yes	36 (31.3%)	15 (27.3%)	21 (35%)	
No	79 (68.7%)	40 (72.7%)	39 (65%)	
C-test (+)	60 (52.2%)	19 (34.5%)	41 (68.3%)	<0.001
Abnormal BMD	65 (56.5%)	22 (40.0%)	43 (71.7%)	<0.001
Recurrence				0.263
Yes	48 (41.7%)	20 (36.4%)	28 (46.7%)	
No	67 (58.3%)	35 (63.6%)	32 (53.3%)	

RD: residual dizziness; SD: standard deviation; CRP: canalith-repositioning procedure; C-test: bithermal caloric test; BMD: bone mineral density.

Table 2. Multivariate logistic regression analysis of the risk factors for RD.

Risk factor	OR	95% CI	*P*
Age	1.038	1.004–1.077	0.037
C-test (+)	1.363	1.029–1.717	0.031
Abnormal BMD	1.743	1.165–2.529	0.005
Duration of vertigo before treatment (days)	0.725	0.169–1.317	0.539

RD: residual dizziness; OR: odds ratio; CI: confidence interval; C-test: bithermal caloric test; BMD: bone mineral density.

is high (52.2%). In addition, a significant reduction in BMD (T-scores <-1 SD), a positive C-test, and older age were found to be independently associated with RD in patients in whom pc-BPPV developed after successful CRP.

RD is defined as persistent dizziness that occurs in patients with BPPV after successful CRP who do not show paroxysmal vertigonystagmus during a positioning test. The symptoms of RD are often difficult to describe, but usually consist of subjective imbalance, unsteadiness, and lightheadedness. Several theories have been proposed to explain the occurrence of residual symptoms after the successful treatment of pc-BPPV. These hypotheses mainly involve the persistence of debris in the canal that is sufficient to induce RD but insufficient to provoke noticeable positional nystagmus, utricular dysfunction, coexisting vestibular disease, and incomplete central adaptation.[7,22–28] Previous studies have also suggested that RD is associated with mental health and autonomic function.[6,7,29] Although theoretically valid, these explanations have not been supported by definitive data. Therefore, even if RD is clinically observable, the reason why it develops after successful CRP remains to be determined.

Kitahara *et al.*[17] showed that periods of persistent vertigo/dizziness are significantly longer in patients with hBPPVcu, a positive C-test, endolymphatic hydrops, and a bone alkaline phosphatase concentration of $\geq$20.0 mg/L than in those with negative findings. This suggests that hBPPVcu, canal paresis, endolymphatic hydrops, and osteoporosis might render the disease refractory to treatment.[17] In their study, most of the patients (40/66) had hBPPV. In contrast, only individuals with unilateral pc-BPPV were analyzed in the present study. Interestingly, similar results were obtained, except with regard to the influence of age. As shown above, 60 (60/115, 52.2%) participants experienced RD after successful CRP treatment. Univariate analyses showed no associations of RD with sex or comorbidities, but there were significant differences in age, the duration of vertigo prior to treatment, the proportion of positive C-tests, and the loss of BMD between the two groups. Logistic regression analysis indicated that a positive C-test, the loss of BMD, and age are risk factors for RD in patients with unilateral pc-BPPV after successful CRP. These findings imply that canal paresis, osteoporosis, and older age in a patient with BPPV increase the risk of RD after successful CRP. Martellucci *et al.*[7] reported a similar relationship between RD and age. Older patients are commonly affected by deterioration of the visual and proprioceptive systems, but also a global impairment in vestibular function.[30–32] Nevertheless, there may also be relationships between the age-associated decline in the vestibular system, a decline in bone metabolism with age, and the occurrence of RD after CRP. Previous studies have shown that osteoporosis is a risk factor for the occurrence and recurrence of BPPV.[9–11] However, although osteoporosis was identified to be an independent risk factor for RD in the present study, no association was found between BPPV recurrence and RD. In other words, patients with pc-BPPV and RD were no more likely to relapse than those without RD. These findings indicate that the causes of recurrence of BPPV and RD are different and complex.

Previous experimental findings have shown that otoconia exist in a dynamic state.[33,34] Zucca *et al.*[35] demonstrated that the capacity for otoconia dissolution decreases with increasing free calcium concentration in the endolymph in frogs. Calcium metabolism is involved in the synthesis and absorption of otoliths, and thus defects in systemic calcium/bone metabolism may also have an impact in the inner

ear.[36–38] Thus, a significant loss of BMD, indicating osteopenia or osteoporosis, might increase the probability that debris persists in the canal, to an extent that is insufficient to provoke noticeable positional nystagmus, but sufficient to induce RD.[28]

The present study had a few limitations. First, the participants were recruited at a single center. In addition, although it was prospective, it was an observational cohort study, and no randomization was performed. Furthermore, the follow-up period was short (12 months) for a thorough investigation of the relationship between RD and recurrence. Moreover, no Dizziness Handicap Inventory, postural, balance, or biochemical tests were performed to provide further insights into the occurrence of RD. Therefore, additional studies are warranted to comprehensively investigate the occurrence of RD after CRP.

Conclusion

This study has revealed a high prevalence of RD after CRP (52.2%). Significantly reductions in BMD (T-scores <-1 SD), a positive C-test, and older age were shown to be independently associated with RD in patients with pc-BPPV after successful CRP.

Acknowledgement

The authors acknowledge the invaluable contributions of the participants.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

This work was supported by the Zhejiang Province Health Department (grant numbers 2014kyb126, 2014kyb125, and 2014kyb129).

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