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재발성 양성돌발체위현기증의 임상적 특성: 후향적 코호트 연구

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Clinical Characteristics of Recurrent Benign Paroxysmal Positional Vertigo: A Retrospective Cohort Study

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Objectives: Benign paroxysmal positional vertigo (BPPV) is a potentially recurrent disease even after successful canalith repositioning maneuvers. However, the exact recurrence rate or any clinical factors affecting the recurrence of BPPV still need to be elucidated.

Methods: We recruited patients diagnosed as BPPV in a tertiary hospital for 3 years. We retrospectively reviewed the clinical information of the patients including baseline demographics, comorbidities and predisposing factors through the electronic medical records. We performed a telephone survey or direct interview 3 to 6 years later from the initial diagnosis of BPPV was made. To determine the factors associated with the recurrence, we divided study population into two subgroups; 'recurrence group' vs. 'recurrence-free group.' Then, intergroup comparative analyses were performed.

Results: Among 397 patients who were originally eligible for the study, we performed a telephone survey or direct interview in 289 patients (72.8%) to determine the recurrence of BPPV. The overall recurrence rate was 29.4% (85 of 289). Baseline demographics except female gender (p=0.014) were not different between subgroups. Neither clinical characteristics nor vascular comorbidities were associated with the recurrence. However, patients with low bone mineral density (BMD; T-score below −1, osteopenia/osteoporosis) showed significantly higher recurrence than those with normal BMD (40.6% vs. 0%, p=0.009).

Conclusions: Female gender and low BMD (T-score below −1) were associated with the recurrence of BPPV in this study. Further researches in various clinical settings with larger sample size are warranted to identify the factors affecting the relapse of BPPV.

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Keywords: Benign paroxysmal positional vertigo; Recurrence; Osteoporosis; Women

INTRODUCTION

Benign paroxysmal positional vertigo (BPPV) is one of the most common vestibular disorders causing positional dizziness/vertigo [1]. With the development of current concept of diagnosis and treatment based on the inner ear pathophysiology, BPPV could be successfully treated by relatively simple bedside canalith repositioning maneuvers (CRMs) [2]. However, despite the high success rate of CRMs (70%–80%), BPPV often recurs in a 15% to 30% of all patients [1,2]. And in cases of recurrent BPPV, they may lead to disability due to frequent falling or other complicating dizzy syndrome such as persistent postural-perceptual dizziness [1-4].

Although, BPPV is known to be caused by dislodged otoconia mostly composed of calcium carbonate, the exact pathomechanisms of BPPV are still uncertain [1]. BPPV is more common among the aged and female population, and the people with previous head trauma, osteoporosis and osteopenia [1,5,6]. Furthermore, several studies reported the association of BPPV with inner ear diseases including vestibular neuritis, Menière's disease as well as vascular risk factors (e.g., hypertension, diabetes mellitus) [7]. Previous studies on the recurrence and long-term prognosis of BPPV conducted by domestic and international investigators have shown that similar factors that increase the risk of BPPV might be associated with the recurrence of BPPV as well [8-12]. However, the results were considerably inconsistent among studies and still need to be elucidated.

We aimed to estimate the overall recurrence rate of BPPV and identify the factors affecting the recurrence (e.g., demographic factors, vascular comorbidities) by studying the clinical aspects of patients who were diagnosed with BPPV at a single tertiary hospital during 36 months and followed at least 36 months up to 72 months.

MATERIALS AND METHODS

1. Study Design and Population

This is a retrospective cohort study of patients with BPPV. We systematically reviewed the electronic medical records (EMR) at Dizziness Clinic of Chonnam National University Hospital in Gwangju, Korea (single tertiary hospital) during the 36-month period from January 2007. Patients with BPPV were initially identified by a computerized disease code search using Korean Standard Classification of Diseases (H81.1).

For evaluating the recurrence from the cohort, we performed either a direct interview or telephone survey with a selected questionnaire (Supplementary material) for whom could not visit the hospital during the 2-month follow-up period from October 2012. The interview was performed by two well-trained neurologists (JMK, JKL). All the results from the interviews were discussed/supervised with an experienced neuro-otologist (SHL).

During the 36-month baseline period, a total of 397 patients with BPPV were originally eligible. Among the selected disease cohort, we excluded the patients who were unable to evaluate the recurrence of BPPV: (1) if they neither answer the call nor visit the hospital (n=61); (2) who refused to do the interview (n=41); (3) who could not remember their vertigo symptoms or related events (n=3); and (4) non-responder to CRMs who complained persistent dizziness after the diagnosis of BPPV (n=3) (Fig. 1). During the 2-month follow-up period, 289 patients with BPPV were finally enrolled in this study.

To identify the factors affecting the recurrence of BPPV, we divided the study subjects into two subgroups (recurrence group vs. recurrence-free group) according to whether they had experienced the recurrent events of BPPV. And we also compared demographic, clinical characteristics between the two subgroups.

This study was performed in accordance with the recommendations of the Institutional Review Board of the Chonnam National University Hospital (CNUH-2012-160). Informed consent was obtained from all subjects involved in the study. The authors declare that they acted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

2. Diagnosis of Benign Paroxysmal Positional Vertigo

A diagnosis of BPPV was made when having both brief, recurrent episodes of positional vertigo and typical positional nystagmus documented by Video-Frenzel glass system (SLMed, Seoul, Korea). For example, a diagnosis of horizontal canal BPPV (HC-BPPV) was based on the following features: (1) a

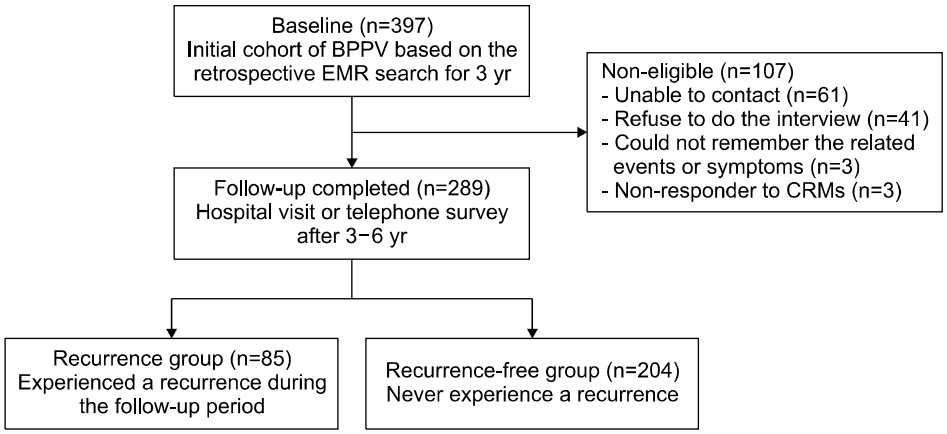

Fig. 1. Study flow sheet of the study participants. BPPV, benign paroxysmal positional vertigo; EMR, electronic medical records; CRM, canalith repositioning maneuver.

history of brief episodes of vertigo provoked by head motion; (2) direction changing horizontal nystagmus during the head-rolling tests, which may beat toward the lowermost (geotropic) or uppermost ear (apogeotropic); and (3) no other identifiable disorders of the central nervous system [13]. Patients with a history of inner ear diseases or other vestibular disorders (e.g., vestibular neuritis) were excluded from this study.

According to the diagnostic criteria, each BPPV subtype was also differentiated, including posterior canal BPPV (PC-BPPV), canalolithiasis, and cupulolithiasis of HC-BPPV, and anterior canal BPPV (AC-BPPV) [1]. After the diagnosis, patients were treated CRMs designed for each BPPV subtype: (1) Epley or Sermont maneuver for PC-BPPV; (2) Gufoni or head shaking maneuver for cupulolithiasis of HC-BPPV; (3) Gufoni or barbecue maneuver for canalolithiasis of HC-BPPV; and (4) reverse Epley maneuver for AC-BPPV [1]. Multiple-canal BPPV was diagnosed when two or more semicircular canals were involved [1].

3. Electronic Medical Record Abstraction

From a systematic review of the EMR, we investigated the disease information, baseline characteristics including vascular risk factors (i.e., hypertension, diabetes mellitus, smoking, and previous history of stroke), accompanied otologic symptoms (i.e., hearing impairment, tinnitus, and ear fullness), and recent (within 1 week) history of upper respiratory infection, head trauma. Bone mineral density (BMD) measured by Dual-Energy X-ray Absorptiometry (Hologic Inc., Marlborough, MA, USA) at the lumbar spine was also evaluated in available patients to determine the association with the recurrence of BPPV. The results were given as a T-score for comparison. Osteopenia was defined when the T-score ranged from −2.5 to −1.0, whereas osteoporosis was defined when the T-score was below −2.5.

4. Statistical Analyses

Statistical analyses included intergroup comparisons of the chi-square test for dichotomous variables and the *t*-test for continuous variables. All analyses were performed using IBM SPSS Statistics ver. 21.0 (IBM Corp., Armonk, NY, USA), and *p*-values of <0.05 were considered statistically significant.

RESULTS

Among a total of 289 patients, the age ranged from 19 to 85 years, with average at 59.6 years (standard deviation, ±13.1 years). One hundred seventy-four patients were female (60.2%), and 85 patients (29.4%) experienced the recurrence of BPPV during the follow-up period. The proportion of women was significantly higher in the recurrence group than in the re-currence-free group (71.8% vs. 55.4%, $p=0.014$). Regarding the demographics, there was no significant difference between the two groups (hypertension, $p>0.999$; diabetes mellitus, $p>0.999$; previous history of stroke, $p=0.46$; smoking, $p=0.19$). Also, the proportion of predisposing factors (recent history of head trauma, $p=0.61$; recent history of upper respiratory infection, $p=0.94$) and accompanied inner ear symptoms ($p=0.62$) were

Table 1. Demographic characteristics of the recruited BPPV patients

Characteristic	Recurrence group (n=85)	Recurrence-free group (n=204)	*p*-value
Age (yr)	60.1±12.4	59.4±13.4	0.68
Female sex	61 (71.8)	113 (55.4)	0.014*
Hypertension	30 (35.3)	72 (35.3)	>0.999
Diabetes mellitus	11 (12.9)	28 (13.7)	>0.999
Previous stroke	4 (4.7)	6 (2.9)	0.46
Smoking	4 (4.7)	19 (9.3)	0.19
Recent head trauma[a)]	3 (3.5)	10 (4.9)	0.61
Recent URI	4 (4.7)	10 (4.9)	0.94
Inner ear symptoms[b)]	11 (12.9)	31 (15.2)	0.62

Values are presented as mean±standard deviation or number (%). BPPV, benign paroxysmal positional vertigo; URI, upper respiratory infection.
[a)]Within 1 week before BPPV occurs. [b)]Inner ear symptoms included tinnitus, ear fullness, and hearing loss.
*$p<0.05$.

Table 2. Comparative analysis of the recurrence rate of benign paroxysmal positional vertigo

Variable	No. of patients	Recurrence	*p*-value
Semicircular canal involvement			0.915
Horizontal canal	179		
Canalolithiasis	78	25 (32.1)	
Cupulolithiasis	101	29 (28.7)	
Posterior canal	92	27 (29.3)	
Anterior canal	4	1 (25.0)	
Multicanal	14	3 (21.4)	
No. of canal			0.764
Single	275	82 (29.8)	
Multiple	14	3 (21.4)	
Bone mineral density[a)]			0.009*
Normal	13	0 (0)	
Low[b)]	32	13 (40.6)	

Values are presented as number only or number (%).
[a)]Measured at the lumbar spine; [b)]T-score below −1.0.
*$p<0.05$.

not different between the two groups (Table 1).

According to subtypes of BPPV, 179 patients (61.9%) had HC-BPPV (78 were canalolithiasis and 101 were cupulolithiasis), 92 (31.8%) had PC-BPPV, 4 (1.4%) had AC-BPPV, and 14 (4.8%) had multicanal BPPV. There was neither significant difference in the recurrence rate among subtypes of BPPV (p=0.915). Moreover, the patients with multicanal BPPV showed similar recurrence rate with single-canal BPPV (21.4% vs. 29.8%, p=0.764) (Table 2).

Among the 45 patients who performed BMD, the recurrence rate of BPPV was higher in patients with abnormal BMD (i.e., T-score below −1.0) with a statistical significance (0% vs. 40.6%, p=0.009) (Table 2).

DISCUSSION

This study described the baseline characteristics and the recurrence rate in patients with BPPV who visited a tertiary hospital during a specific period of time, and we also aimed to identify the factors related to the recurrence rate. The overall recurrence rate of BPPV in this cohort was 29.4%, consistent with the previous study results of 15% to 30% [1,14,15].

In this study, HC-BPPV was the most common subtype, accounting for 61.9% of total BPPV cases. In general, PC-BPPV is known to be the most common subtype and accounts for 60% to 90% of all BPPV cases and HC-BPPV for 5% to 30% of the cases [1]. However, HC-BPPV appears to be more prevalent than was previously thought and the relative proportion of each type of BPPV might depend upon the setting of each clinic [1]. The higher proportion of HC-BPPV in our study might be explained by several reasons: (1) the patients with HC-BPPV were more prone to visit a tertiary university hospital since HC-BPPV might cause more severe and long-lasting vertigo than other subtypes of BPPV [1,2,16]; (2) cupulolithiasis of HC-BPPV might mimic central positional vertigo, especially in cases without other neurologic abnormalities [1,2]; and (3) PC-BPPV might be familiar to primary physician and this enabled them to diagnose and treat more easily than other subtypes.

Most of the demographic factors as well as predisposing factors did not affect to the recurrence of BPPV in this study. There have been studies with conflicting results regarding the recurrence of BPPV, since multiple factors including clinical settings, and even genetic backgrounds might have influence on the occurrence of BPPV [10-12,17]. For example, previous studies suggested that the patients with BPPV had higher frequency of vascular comorbidities (i.e., hypertension, diabetes mellitus, and hyperlipidemia), and these might also increase the risk of the recurrence in BPPV [11,17,18]. Vascular damage,

ischemia, or atherosclerosis associated with vascular comorbidities may induce poor inner ear circulation or degeneration of otoconia [11]. Although, including our study, several studies have shown that vascular comorbidities might not increase the recurrence rate of BPPV, clinicians should pay attention to treat vascular comorbidities considering that BPPV and vascular comorbidities are both prevalent in advanced age.

A previous study reported that 23% of patients with BPPV had a history of head trauma and posttraumatic BPPV is more likely to have multiple semicircular canal involvement, require more repeated CRMs than idiopathic BPPV and have a greater recurrence rate [11,19-21]. The authors suggested that trauma-induced microscopic hemorrhage, or tissue shearing might result in biochemical changes that enhance the formation of otoconial clots. And these changes may reactivate the production of new clots, accounting for the recurrence of BPPV [20]. However, including our study, the other studies showed a similar recurrence rate of posttraumatic BPPV compared with idiopathic one [22]. Moreover, type of the involved semicircular canals did not affect the recurrence rate of BPPV in our study, as replicated by other studies [10].

We demonstrated the higher recurrence rate of BPPV among female patients and those with low BMD (osteopenia/osteoporosis), which were consistent with the previous results [10-12,23]. Otoconia are composed of calcium carbonate as calcite crystals and an organic core consisting predominantly of glycoprotein and are connected with protein fibers on hair cells [24]. Otoconia degeneration increases with age and is affected by calcium metabolism in the inner ear [25]. Meanwhile, the incidence of BPPV among women increases dramatically after 60s, and this is assumed to be related to the decrease in estrogen after menopause, which causes a sharp decrease in bone mass [6,23]. Estrogen is one of the main hormones associated with calcium, bone metabolism and estrogen deficiency decrease intestinal calcium absorption, which may lead to degeneration of otoconia [6,23]. Even the exact mechanism of estrogen in BPPV are still to be elucidated, given the peri- and postmenopausal women are especially susceptible to BPPV, estrogen deficiency might have substantial effects on the gender difference in the recurrence of BPPV [6,23]. Low BMD usually suggests the impairment of calcium metabolism and several studies found that patients with osteopenia/osteoporosis had higher recurrence rate of BPPV, both in male and female [23,26]. This result means that the hormonal (estrogen) deficiency is not the sole factor affecting demineralization of otoconia [23]. Indeed, decreased density and increased size of the otoconia in the osteopenic/osteoporotic rats [27].

This study has some limitations. Firstly, we performed a telephone survey to identify the recurrence of BPPV whom could not visit our hospital. In these cases, the patients might answer the questionnaire relied on their self-reported memory. Although several previous studies showed questionnaire-based diagnosis of BPPV as an acceptable tool since BPPV usually have the characteristic symptoms provoked by specific head position [28-30], there are still paucity of data on the recurrence of BPPV assessed by the questionnaire. Other types of mimicking vertigo such as persistent postural-perceptual dizziness that may occur after BPPV should also be carefully discriminated through additional supplementation of the questionnaire in the future. Secondly, retrospective investigations through the EMR might limit to obtain detailed clinical information in some patients. Lastly, this study was performed in a single tertiary hospital and included a relatively small sample size. Thus, the interpretation of our results should be careful and further studies in various clinical settings with larger sample size are warranted for generalization.

From this retrospective cohort study, the recurrence of BPPV were associated with female gender and low BMD (osteopenia/osteoporosis). Even we did not show the difference on the recurrence rate according to the other demographics, vascular comorbidities, and predisposing factors, efforts to identify the factors affecting the relapse of BPPV are warranted for improving the prognosis of the patient as well as better understanding of BPPV.

중심 단어: 양성돌발체위현기증, 재발, 골다공증, 여성

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

SUPPLEMENTARY MATERIALS

Supplementary material can be found via https://doi.org/10.21790/rvs.2021.20.2.45.

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