



# Comorbidities and the Effect of Comorbidities on Recurrence in Benign Paroxysmal Positional Vertigo

## Benign Paroksizmal Pozisyonel Vertigoda Komorbiditeler ve Komorbiditelerin Rekürrens Üzerine Etkisi

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### Abstract

**Aim:** Our study aims to investigate comorbidities and the effect of comorbidities on recurrence in posterior canal benign paroxysmal positional vertigo (P-BPPV).

**Materials and Methods:** Fifty-four patients diagnosed with P-BPPV were included in the study. Demographic characteristics of the patients, smoking, alcohol use, P-BPPV side, comorbid diseases, menopausal status, previous head trauma history, body mass index (BMI) and biochemical parameter results were recorded. Reposition maneuver (Epley) was applied to the patients, and the patients were followed up for six months. Fifty-four patients followed were divided into two groups according to P-BPPV recurrence. Twenty-three patients with relapsed P-BPPV were included in group I, and 31 patients with non-relapsed BPPV were included in group II.

**Results:** There was no difference between the two groups in terms of age, comorbid diseases, menopausal status, gender, BMI, smoking, alcohol use and biochemical parameters ( $p>0.05$ ). The recurrence rate was lower in P-BPPV patients with right ear involvement ( $p<0.05$ ).

**Conclusions:** Recurrence is observed less frequently in individuals with P-BPPV whose right ear is affected than in those whose left ear is affected. Our study shows that P-BPPV, comorbid diseases and abnormal biochemical parameters, which are more common in advancing ages, are observed together coincidentally.

**Keywords:** Benign paroxysmal positional vertigo, vertigo, relapse, comorbid diseases, biochemical parameters

### Öz

**Amaç:** Çalışmamızın amacı, posterior kanal benign paroksizmal pozisyonel vertigoda (P-BPPV) komorbiditeleri ve komorbiditelerin nüks üzerindeki etkisini araştırmaktır.

**Materyal ve Metot:** P-BPPV tanısı alan 54 hasta çalışmaya dahil edildi. Hastaların demografik özellikleri, sigara ve alkol kullanımı, P-BPPV tarafı, komorbid hastalıkları, menapoz durumu, geçirilmiş kafa travması öyküsü, vücut kitle indeksi (BMI) ve biyokimyasal parametre sonuçları kaydedildi. Hastalara repozisyon manevrası (Epley) uygulandı ve hastalar altı ay takip edildi. Takip edilen 54 hasta nüks etme durumuna göre iki gruba ayrıldı. P-BPPV'si nüks eden 23 hasta grup I'e BPPV'si nüks etmeyen 31 hasta grup II'ye dahil edildi.

**Bulgular:** İki grup arasında yaş, komorbid hastalıklar, cinsiyet, menapoz durumu, BMI, sigara, alkol kullanımı ve biyokimyasal parametreler açısından bir fark yoktu ( $p>0.05$ ). Sağ kulağı tutulan P-BPPV hastalarında nüks oranının daha az olduğu saptandı ( $p<0.05$ ).

**Sonuçlar:** Sağ kulağı etkilenen BPPV'li bireylerde nüks, sol kulağı etkilenen P-BPPV'li bireylere göre daha az gözlenmektedir. Çalışmamızdan ilerleyen yaşlarda daha sık görülen P-BPPV, komorbid hastalıklar ve anormal biyokimyasal parametrelerin tesadüf olarak birlikte gözlendiği çıkarılabilir.

**Anahtar Kelimeler:** Benign paroksizmal pozisyonel vertigo, vertigo, nüks, komorbid hastalıklar, biyokimyasal parametreler

## INTRODUCTION

Benign paroxysmal positional vertigo (BPPV) is the most commonly diagnosed type of vertigo that occurs as a result of the fall of otoconia in the utricle into the semicircular

canals (SCC) (1). Displaced otoconia can move freely in SSCs or attach to the cupula. Thus, excitations or inhibitions occur in the head movements in the axis of the affected canal, which abnormally stimulate the vestibulo-ocular reflex. Patients apply to their outpatient clinics

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with the complaint of vertigo, which is triggered by head movements and lasts for seconds. Sudden onset of BPPV and causing severe true-vertigo can be very distressing and frightening for the patient. The type of BPPV and the affected ear are detected by the characteristic nystagmus that occurs with maneuvers such as Dix Hallpike or supine roll. Patients' symptoms often improve with successful maneuvers. However, despite effective treatment in BPPV, recurrences can be seen within months and years. For this reason, researchers have carried out some studies to understand the factors affecting relapse in BPPV and to prevent relapses. Although it was stated in these studies (2-7) that characteristics such as gender and age, and chronic diseases such as hypertension, diabetes mellitus (DM), and cardiovascular diseases, which are common in the community, may be associated with BPPV disease and its recurrence, the findings are contradictory.

This study aims to investigate comorbidities and the effect of comorbidities on recurrence in BPPV.

## MATERIAL AND METHOD

This prospective cross-sectional study was carried out on patients aged between 18 and 80 years who applied to the otolaryngology clinic with a complaint of vertigo. Detailed anamnesis was taken from the patients, and otorhinolaryngological examination was performed. In the case of observing characteristic nystagmus for P-BPPV in the applied Dix Hallpike maneuver (Vertical and clockwise rotation in left Dix Hallpike test - vertical and counterclockwise rotation in right Dix Hallpike test), the patients are treated with Epley maneuver was performed. Thirty minutes later, the control maneuver was applied to the patients. The results of previous examinations in the hospital system of the patients who did not have vertigo/

nystagmus in the control maneuver and whose complaints improved were checked. Fifty-four patients who had a blood test in the last three months and whose vertigo improved as a result of the Epley maneuver we applied were included in the study. Age, gender, affected side, previous head trauma, smoking-alcohol use, menopausal status, comorbid diseases, height (cm) and weight (kg) of these patients were recorded and body mass index (BMI) was calculated (<18.50kg/m<sup>2</sup> underweight, between 18.50-24.99kg/m<sup>2</sup> normal, 25.00-30.00kg/m<sup>2</sup> overweight and >30 kg/m<sup>2</sup> obese). These patients were followed for six months and were divided into two groups according to their P-BPPV recurrence. 23 patients (42.5%) with P-BPPV recurrence were included in group I, and 31 (57.5%) patients without P-BPPV recurrence were included in group II. Patients with chronic dizziness and vertigo due to another reason and patients with tympanic membrane perforation were not included in the study. Written and verbal consent was obtained from all patients. Permission was obtained from the university's ethics committee for the study (2020/308).

## Lab Tests

In the last three months, leukocyte, erythrocyte, thrombocyte and haemoglobin levels were recorded in the hemogram. Biochemistry tests include glucose, urea, creatine, ast, lower, albumin, total bilirubin, direct bilirubin, alkaline phosphatase, sodium, potassium, chlorine, calcium, iron, iron-binding capacity, cholesterol, triglyceride, very low-density lipoprotein (VLDL) and high-density lipoprotein (HDL) levels were recorded. Ferritin, thyroid-stimulating hormone (TSH), free T3 and T4, vitamins D and B12, folate, and HbA1C values were recorded from hormone tests. Values considered normal are shown in Table 1.

**Table 1. Normal ranges of parameters and abnormal biochemical parameters by groups**

Parameters (Abnormal)	Group I (n:23)	Group II (n:31)	p Value	Normal Range of parameters
Hemoglobin	2 (8.7%)	4 (12.9%)	0.511 <sup>b</sup>	(11-16 g/dL)
Leukocyte	5 (21.7%)	3 (9.7%)	0.558 <sup>b</sup>	(4-10 10 <sup>9</sup> /L)
Erythrocyte	1 (5.3%)	3 (9.7%)	0.663 <sup>b</sup>	3.5-5.5 10 <sup>6</sup> /uL)
Triglycerides	2 (8.7%)	3 (9.7%)	0.545 <sup>b</sup>	(0-250 mg/dL)
HDL	2 (8.7%)	2 (6.4%)	0.643 <sup>b</sup>	(33-90 mg/dL)
TSH	1 (4.3%)	2 (6.4%)	0.612 <sup>b</sup>	(0.35-5.5 uIU/ml)
HbA1C	5 (21.7%)	6 (19.3%)	0.721 <sup>a</sup>	(4-6 %)
Vitamin B12	1 (4.3%)	4 (12.9%)	0.362 <sup>b</sup>	(211-911 pg/mL)
Vitamin D	5 (21.7%)	8 (25.8%)	0.730 <sup>a</sup>	30-100 ng/mL)
Folate	1 (4.3%)	4 (12.9%)	0.362 <sup>b</sup>	(5.38-17 ng/ml)
Fe	5 (21.7%)	5 (16.1%)	0.563 <sup>a</sup>	(50-175 ug/dL)
TIBC	2 (8.7%)	4 (12.9%)	0.563 <sup>a</sup>	(120-370 ug/dL)
Ferritin	7 (30.4%)	10 (32.2%)	0.447 <sup>a</sup>	(22-322 ng/mL)
Glucose	7 (40.4%)	11 (35.4%)	0.717 <sup>a</sup>	(74-106 mg/dL)
Urea	2 (8.7%)	1 (3.2%)	0.569 <sup>b</sup>	(10-49 mg/dL)
Creatinine	3 (13.0%)	4 (12.9%)	0.623 <sup>b</sup>	(0.5-1.3 mg/dL)
AST	1 (4.3%)	1 (3.2%)	0.675 <sup>b</sup>	(5-34 u/L)
ALT	0 (0%)	1 (3.2%)	0.584 <sup>b</sup>	(10-49 u/L)

<sup>a</sup>: Chi Square Test <sup>b</sup>: Fisher Exact test

### Statistical analysis

SPSS 21 program was used for data analysis. Descriptive statistics were given with n (%), mean±sd, and median (minimum and maximum). The Chi-square test was used to compare categorical variables. Normality distribution was evaluated with the Shapiro-Wilk test. T-test was used for the data conforming to the normality assumption, and Mann Whitney-U test was used for the data not. P<0.05 was considered statistically significant.

### RESULTS

The mean age of group I was 49.03±14.12 (23-76), while the mean age of group II was 51.95±15.05 (22-74). Ten (43.4%) of the individuals in group I were male, and 13 (56.6%) were female, 12 (38.7%) of the individuals in group II were male, and 19 (61.3%) were female. There was no significant difference between the groups regarding age and gender (p>0.05, Table 2).

The most common comorbid diseases in patients with BPPV were 15 (28.3%) hypertension, 12 (22.6%) DM, 6

(11.3%) cardiovascular disease, 6 (11.3%) hypothyroidism, 4 (7.5%) migraine, 4 (7.5%) osteoporosis, 3 (5.6%) hyperlipidemia, 2 (3.7%) chronic obstructive pulmonary disease and 1 (1.8%) hyperthyroidism. There was no difference between the groups regarding comorbid diseases, BMI, menopause, smoking and alcohol use, and previous head trauma (p>0.05, Table 3). However, left ear involvement was higher in relapsed patients than in non-relapsed patients (p<0.05, Table 3). There was no difference between the groups regarding abnormal biochemical parameters (p>0.05, Table 1).

**Table 2. Age and gender distributions by groups**

	Group I (n:23) Mean±ss	Group II (n:31) Mean±ss	P value
Age (Years)	49.03±14.12	51.95±15.05	0.699 <sup>a</sup>
Gender (n)			0.724 <sup>b</sup>
Female	13 (56.5%)	19 (61.3%)	
Male	10 (43.5%)	12 (38.7%)	

a: T test, b: Chi Square test

**Table 3. Comorbid diseases, menopausal status, head trauma status, body mass index (BMI), smoking and alcohol use, and affected side by groups**

	Group I (n:23)	Group II (n:31)	p Value
<b>Comorbid Diseases (n)</b>			
Hypertension	7 (30.4%)	8 (25.8%)	0.707 <sup>a</sup>
Diabetes Mellitus	4 (17.4%)	8 (25.8%)	0.462 <sup>a</sup>
Cardiovascular Disease	1 (4.3%)	5 (16.1%)	0.242 <sup>b</sup>
Chronic Obstructive Pulmonary Disease	1 (4.3%)	1 (3.2%)	0.675 <sup>b</sup>
Osteoporosis	2 (8.7%)	2 (6.4%)	0.643 <sup>b</sup>
Hypothyroidism	3 (13.0%)	3 (9.7%)	0.512 <sup>b</sup>
Hyperthyroidism	1 (4.3%)	0 (0%)	0.426 <sup>b</sup>
Hyperlipidemia	1 (4.3%)	2 (6.4%)	0.612 <sup>b</sup>
Migraine	2 (8.7%)	2 (6.4%)	0.643 <sup>b</sup>
<b>BPPV Side (n)</b>			0.022 <sup>a</sup>
Left	13 (56.5%)	8 (25.8%)	
Right	10 (43.5%)	23 (74.2%)	
<b>Menopause (n)</b>	9 (39.1%)	9 (29.0%)	0.436 <sup>a</sup>
<b>Head Trauma (n)</b>	2 (8.7%)	1 (3.2%)	0.569 <sup>b</sup>
<b>BMI (n)</b>			0.371 <sup>a</sup>
Normal Weight	5 (21.7%)	12 (38.7%)	
Overweight	12 (52.1%)	14 (45.1%)	
Obese	6 (26.0%)	5 (16.1%)	
<b>Smoking</b>	7 (30.4%)	8 (25.8%)	0.707 <sup>a</sup>
<b>Alcohol</b>	2 (8.7%)	2 (6.4%)	0.643 <sup>b</sup>

a: Chi Square Test b: Fisher Exact test

## DISCUSSION

Otoconias falling from the utricle to the SCCs can move freely within the canals (canalolithiasis) or adhere to the cupula of the SCCs (cupulolithiasis). According to the characteristics of the nystagmus that occurs during provoking maneuvers, it can be easily understood whether the otoconia move freely or adhere to the cupula. In the cupulolithiasis form, the latency of nystagmus is very short or absent and lasts longer than in canalolithiasis. In canalolithiasis, nystagmus has a latent period. However, the same cannot be said for the aetiology of BPPV, and it is sometimes difficult to determine the aetiology. In most patients with BPPV, the etiology cannot be determined and it is called idiopathic BPPV. Head trauma, vestibular neuritis, stapes surgery, Meniere's disease and osteoporosis have been implicated in the aetiology of secondary BPPV (8). None of the patients included in our study had Meniere's disease, vestibular neuritis, or stapes surgery histories and findings. Three patients included in our study had a history of head trauma. In our research, BPPV recurrence was detected in 42.5% of the patients. It has been reported in the literature that the recurrence rate of BPPV is between 7% and 50%, similar to our study (9-12).

Kansu et al. (11) examined 118 patients with BPPV in their study and stated that the most common aetiology was idiopathic with 46.6%, and recurrence occurred in 33.1% of the patients. According to this study, patients with a history of head trauma were more likely to relapse than patients with other etiologic causes. Recurrence was observed in 2 of 3 BPPV patients with head trauma who participated in our study. However, there was no difference in terms of head trauma between patients who relapsed and those who did not.

The risk of BPPV increases with advancing age and female gender. However, it is controversial whether there is a relationship between BPPV recurrence and age and gender. In some of these studies, it was stated that relapses were higher in the elderly and females (13,14,15), while in others, it was noted that age and gender were not a factor for recurrence (4,14,16). In our study, 59.3% of the patients were female, 40.7% were male, and the female-to-male ratio was found to be 1.4. However, there was no difference in age and gender between our study's relapsed and non-relapsed groups.

Studies in the literature have reported that right ear involvement is more common in P-BPPV patients (14,17). In the study of Çakır et al. (17), it was found that 67% of the patients habitually took a lateral head position during bed rest, and in 86% of these patients, the side affected by BPPV was compatible with the side-lying on the head during bed rest. In our study, 61.1% of the patients had right ear involvement, which was consistent with the literature, but left ear involvement was significantly higher in patients with relapsed BPPV.

Singh et al. (18) investigated the relationship between

cardiovascular risk factors and BPPV in a 4-year follow-up study with 628 patients with BPPV. No significant relationship was found between BPPV recurrence and dyslipidemia, BMI, hypertension and DM in the study. Chen et al. (4) stated that vitamin D deficiency, DM, hypertension and osteoporosis were possible risk factors for BPPV recurrence in a meta-analysis including 14 studies. However, it was reported that age, head trauma, Meniere's disease and migraine should be investigated further. In addition, it was stated in the study that most of these studies were conducted in Asia, and it would be wrong to generalise to the world. Akkoca et al. (7) reported that recurrent attacks were more common in patients with hypertension, with 72 BPPV patients in their study. They did not find a significant relationship between DM and other comorbidities and BPPV attacks. De Stefano et al. (19) evaluated 1092 patients and found a significant correlation between the number of comorbidities and recurrences. In the study, it was reported that when comorbidity increased, recurrence also increased. They suggested that the presence of the systemic disease may cause more frequent otolith rupture. However, there was no difference between the groups in our study in terms of comorbid disorders. In addition, there was no significant relationship between smoking and alcohol use and relapse rates in our research. In the literature, similar to our study, it was stated that there was no relationship between relapse and alcohol use. At the same time, it was reported that smoking significantly reduced the recurrence of BPPV (20). The study stated that smoking protects dopaminergic neurons by inhibiting monoamine oxidase, and dopamine release protects inner ear functions.

In the study by Webster et al. (21), the glucose-insulin test was applied to 72 BPPV patients. According to the results, they divided the patients into groups normal, glucose intolerance, hyperinsulinemia, and hyperglycemia. They found that hyperinsulinemia and hyperglycemia are risk factors for BPPV recurrence, while normal glucose test is protective against BPPV. In the study of Yüceant et al. (22), the bone mineral density of 67 BPPV patients and 78 healthy volunteers were examined. No significant difference was found between the two groups regarding osteoporosis prevalence. In the study, BPPV patients were also divided into two groups according to their relapse status. There was no significant difference between the relapsed and non-recurring groups in terms of osteoporosis prevalence. They stated that the higher incidence of osteoporosis in the elderly than in the normal population might cause BPPV and osteoporosis to be seen together coincidentally.

In the study by Talaat et al. (23), T scores and vitamin D levels of 80 BPPV patients and 100 healthy individuals were compared. T scores and vitamin D levels of BPPV patients were lower than the control group. When analysed according to relapse status, a significant difference was found between the two groups in terms of vitamin D levels. However, no significant relationship was found between T score and relapse. In the meta-analysis of Yang et al. (24), serum vitamin D levels were significantly lower in the group

with BPPV than in the healthy group. In comparing the vitamin D levels of the relapsed and non-relapsed groups, the vitamin D level was found to be significantly lower in the relapsed group. It was concluded that vitamin D is an independent risk factor for BPPV. Unlike these studies, there was no difference between the groups in terms of biochemical parameters in our study.

Ogun et al. (25) analysed 1.377 BPPV patients and showed that perimenopausal women are particularly susceptible to BPPV. They noted that hormonal fluctuations might increase the tendency to develop BPPV. When 32 female BPPV patients included in our study were examined in terms of menopausal status, it was found that 18 patients were in menopause, 9 in the relapsed group and 9 in the non-relapsed group. There was no difference in menopause between relapsed and non-relapsed BPPV patients.

## CONCLUSION

Recurrence is observed less frequently in individuals with BPPV whose right ear is affected than in those whose left ear is affected. Our study shows that BPPV, comorbid diseases and abnormal biochemical parameters, which are more common in advancing ages, are observed together coincidentally.

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