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Unilateral mimicking bilateral BPPV- a forgotten entity? Characteristics of a large cohort of patients, comparison with posterior canal BPPV and clinical implications

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ABSTRACT

Objective: Unilateral mimicking bilateral benign paroxysmal positional vertigo (umb-BPPV) was attributed to inappropriate head positioning during testing of the posterior canal. Despite its inclusion in the Diagnostic criteria for the classification of vestibular disorders of the Bárány Society, the clinical characteristics and treatment responsiveness of this BPPV subtype have not been intensively studied.
Methods: Records of patients with BPPV seen at a single outpatient dizziness clinic during the years 2000–2020 were reviewed. Eighty seven patients with umb-BPPV and 86 random patients with posterior canal BPPV (p-BPPV) were retrieved. Their demographics and BPPV characteristics were analyzed.
Results: Patients' and BPPV characteristics were similar in umb- and p-BPPV except for the prevalence of males in the umb-BPPV group. No differences were found between treatment responsiveness and recurrences in both groups. The recurrence rate of umb-BPPV was not influenced by age, gender, BPPV side, duration of symptoms or treatment responsiveness during the first attack.
Conclusions: In accordance with our hypothesis about mixed canalo- and cupulolithiasis as the underlying mechanism of umb-BPPV, patients did not differ in characteristics and treatment responsiveness from p-BPPV patients. Recognition of umb-BPPV is important since inappropriate treatment can cause an unnecessary delay in therapy success.

1. Introduction

Posterior canal BPPV (p-BPPV), the most common type of BPPV, is caused by canalolithiasis [von Brevern et al., 2007]. Otoconia displaced from macula of the utricle into the posterior semicircular canal move accordingly to gravity and cause inappropriate stimulation of the vestibular end organ during head movements, resulting in vertigo. During the diagnostic Dix- Hallpike maneuver posterior canal containing otoliths is placed by 45° head rotation in the vertical plane to achieve maximal flow velocity of the endolymph during head reclination. Centrifugal endolymph flow then activates ampullar receptors producing nystagmus that beats to the down most ear [von Brevern et al., 2015; Hain et al., 2005; Honrubia et al., 2001; Five et al., 2008].

We often see patients with a mildly asymmetric, bilaterally positive Dix Hallpike test suggestive of bilateral p-BPPV. However, after treatment of the more prominent side, symptoms and nystagmus disappear on both sides. This phenomenon has been reported in the past as unilateral mimicking bilateral BPPV (umb-BPPV) [Steddin et al., 1994]. It was attributed to inappropriate head positioning of the tested posterior canal, leading to gravitation of the otoliths on the cupula and causing ampullopetal flow and geotropic nystagmus on Dix-Hallpike maneuvre of the opposite ear. Other authors were able to distinguish true bilateral BPPV from umb-BPPV by measuring the rotation vector of nystagmus in three dimensions and its time constant [Imai et al., 2008]. Patients with umb-BPPV had a single rotation axis indicating involvement of a single posterior canal. Short time constant of the nystagmus in one ear corresponded to canalolithiasis on this side while long time constant in the opposite ear reflected transient cupulolithiasis of the opposite, firstly tested, ear.

Despite the inclusion of the umb-BPPV in the Diagnostic Criteria

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Table 1
Characteristics of patients with umb- BPPV and p-BPPV.

Characteristics	p-BPPV	umb - BPPV	P-value
	n = 86	*n = 87*	
	mean ± SD	mean ± SD	
Age (years)	63.51 ± 14.90	60.63 ± 16.53	0.265
Gender			
females n (%)	62 (72.1)	48 (55.2)	**0.021**
males n (%)	24 (27.9)	39 (44.8)	
BPPV characteristics			
duration of symptoms before diagnosis (months)	38.98 ± 53.30	36.17 ± 40.31	0.825
side			
left n (%)	41 (47.4)	43 (49.4)	0.818
right n (%)	45 (52.3)	44 (50.6)	
treatment maneuvers (n)	2.20 ± 3.49	2.33 ± 2.69	0.419
minimum treatments (n)	1.98 ± 3.52	1.65 ± 1.63	0.933
maximum treatments (n)	2.68 ± 3.68	3.22 ± 3.96	0.395
Recurrence characteristics			
number of recurrences per year	2.57 ± 1.63	2.11 ± 1.34	0.206
follow up (years)	3.49 ± 5.54	5.05 ± 13.21	**0.037**

for the Classification of Vestibular disorders of the Bárány Society, reports about this BPPV subtype are surprisingly rare and their clinical characteristics and treatment responsiveness have not been intensively studied [von Brevern et al., 2015]. We collected a large cohort of patients with umb- BPPV and compared them to p- BPPV patients trying to draw some implication for the clinical practice.

2. Methods

Medical records of patients with idiopathic BPPV seen at single outpatient dizziness clinic during the years 2000–2020 were reviewed. Eighty seven patients with umb-BPPV and 86 random patients with p-BPPV were retrieved. The diagnosis of BPPV was established according to the characteristics of the nystagmus evoked by positioning testing - nystagmus guided strategy.

The diagnosis of p-BPPV was based on a history of positional vertigo and a normal neurotological examination except for a positive Dix-Hallpike test. The latter demonstrated a torsional/vertical nystagmus beating toward the lower ear with latency, had a crescendo-decrescendo course, fatigability and reversal [von Brevern et al., 2015; Hain et al., 2005; Honrubia et al., 2001; Five et al., 2008]. Patients were treated by the Epley repositioning maneuver at a weekly interval until disappearance of the nystagmus on positioning testing [Five et al., 2008].

Patients with a bilaterally positive, mildly asymmetric Dix-Hallpike test in whom the nystagmus disappeared after treatment of the more prominent side exclusively, were diagnosed with umb-BPPV. Patients in whom contralateral nystagmus persisted after successful treatment of the opposite side were considered to have true bilateral BPPV and were excluded from the study. Patients with horizontal canal BPPV as well as patients with mixed canal BPPV also were excluded.

The demographics and BPPV characteristics of patients with umb-BPPV were analyzed and compared to patients with p-BPPV. We also looked for predisposing factors for umb-BPPV as such as well as for number and type of its recurrences.

Statistical methods: The patients' characteristic and BPPV recurrences were compared using univariate nonparametric tests: Mann Whitney for numerical independent variables, and Chi-square for nominal variables. Logistic regression was performed to assess the association between independent variables found to be associated with outcome (p-value < 0.1). The distribution of recurrences in umb-BPPV followed the Poisson distribution and enabled us to examine the association between the number of recurrences and independent variables using Negative Binomial Regressions.

Ethical approval: The study was approved by the Ethical review board of the institution according to the principles of the Helsinki Declaration.

3. Results

The characteristics of patients with umb-BPPV and p-BPPV are summarized in Table 1 and were similar in both groups except for the prevalence of males in the umb-BPPV group. Male gender was also found to be independently associated with a higher probability of having umb-BPPV [Table 2].

No differences were found between the frequency of right and left side in p- BPPV vs umb-BPPV. The mean duration of vertigo prior to first treatment was comparable in both groups of patients. Patients with umb-BPPV were cured after 2.20 Epley maneuvers per attack on average, similarly to p-BPPV patients cured by 2.33 maneuvers [Table 1].

Patients with umb-BPPV were longer in follow up than p-BPPV since the latter were randomly chosen from a large group of about two thousand patients. However, the mean number of recurrences did not differ between both groups (Table 1). The average time period between the first and second as well as the second and third BPPV attack were similar in both groups [Fig. 1].

We further searched for factors influencing recurrences in the umb-BPPV group. Age, gender, BPPV side, mean duration of symptoms until treatment or the number of treatments in the first attack were not associated with the recurrence rate in this group [Table 3].

4. Discussion

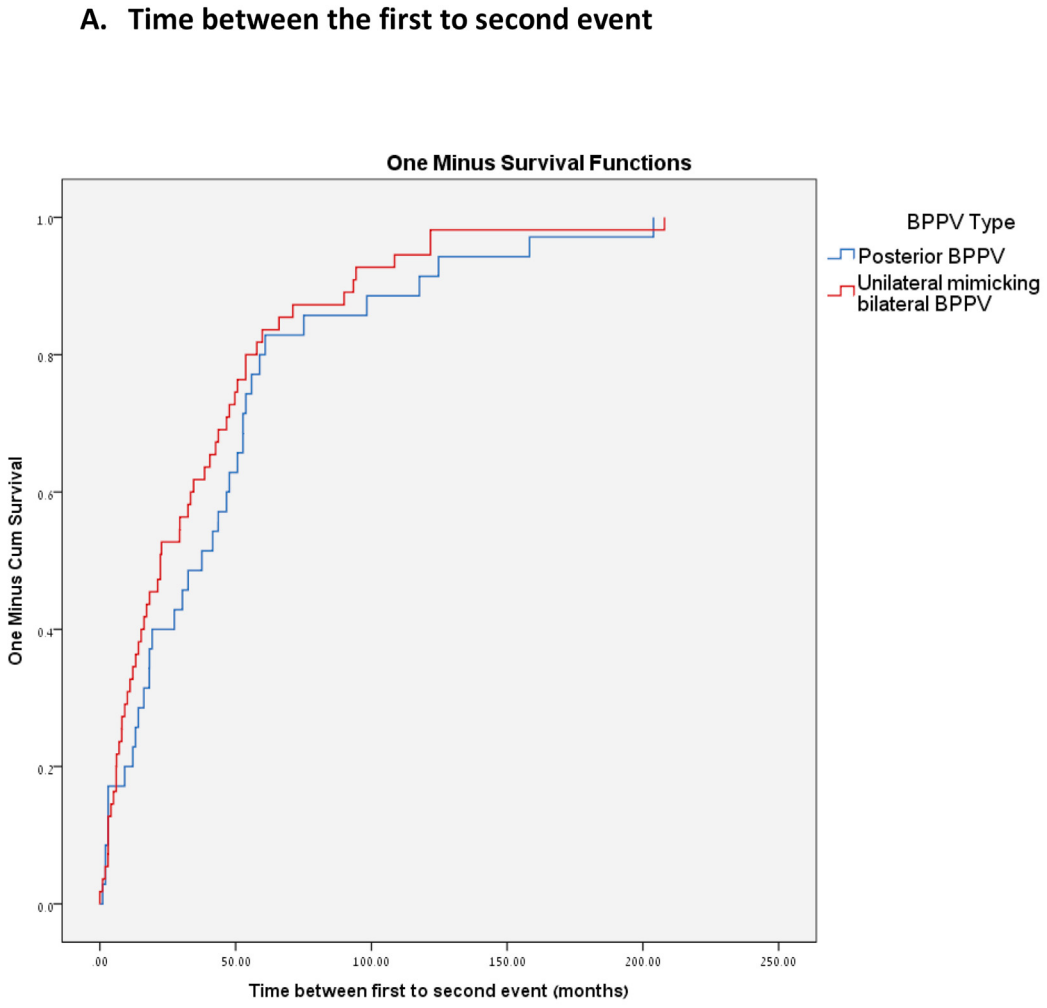
While canalolithiasis is the accepted pathomechanism of p-BPPV, pathological findings of otoliths attached to the cupula of the semicircular canal raised the theory of cupulolithiasis [von Brevern et al., 2015; Shuknecht, 1969]. Detached otoconia fall into the short arm of the posterior semicircular canal and get attached to the utricular side of cupula causing excitation of the receptors in an ampullofugal direction, similarly to the free floating canaloliths. The co-existence of canalo- and cupulolithiasis is difficult to be clinically distinguished [von Brevern et al., 2015; Shuknecht, 1969; House et al., 2003; Imai et al., 2009; Valli et al., 2008; Yatomi et al., 2017; Buckingham, 1999].

Table 2
Logistic regression shows association of umb-BPPV with male gender.

Characteristics	B	S.E	P-value	OR	CI 95% low	CI 95% high
Age	−0.015	0.01	0.132	0.985	0.966	1.005
Gender						
males	0.787	0.327	**0.016**	2.198	1.157	4.173
females	■	■	■	■	■	■

We presume that umb-BPPV is caused by mixed canalo- and cupulolithiasis of the posterior semicircular canal [Fig. 2]. During positioning testing of the involved ear, geotropic nystagmus is obtained, as excepted. On testing the opposite - healthy ear, ampullopetal flow of the otoliths leads to inhibitory stimulation of the vestibular receptors resulting in an apogeotropic nystagmus and mimicking a positive Dix-Hallpike test. This nystagmus lasts longer and is of smaller amplitude than in the opposite ear and is caused mainly by cupulolithiasis since the relatively low weight of canaloliths and their caudal position in the semicircular is not sufficient to evoke vestibular stimulation and nystagmus [Fig. 2]. The posterior semicircular canal cupulolithiasis alone – the heavy cupula- might partly explain the pathophysiology of umb-BPPV. It is assumingly caused by density ration changes between the cupula and surrounding endolymph but the nystagmus is quite persistent with no latency [Asprella Libonati, 2012].

In accordance with the above hypothesis are the similarities between BPPV characteristics in patients with umb-BPPV and p-BPPV found in this study. The treatment responsiveness in the umb-BPPV group was comparable with that of the p-BPPV group. We assume that during testing of the opposite ear cupuloliths get easily removed from the short arm of the semicircular canal due to their proximity to the utricle and do not influence the treatment



The difference between the time from first to second recurrence in the two types of BPPV is not significant (log-rank P-value = 0.385 , χ^2= 0.345).

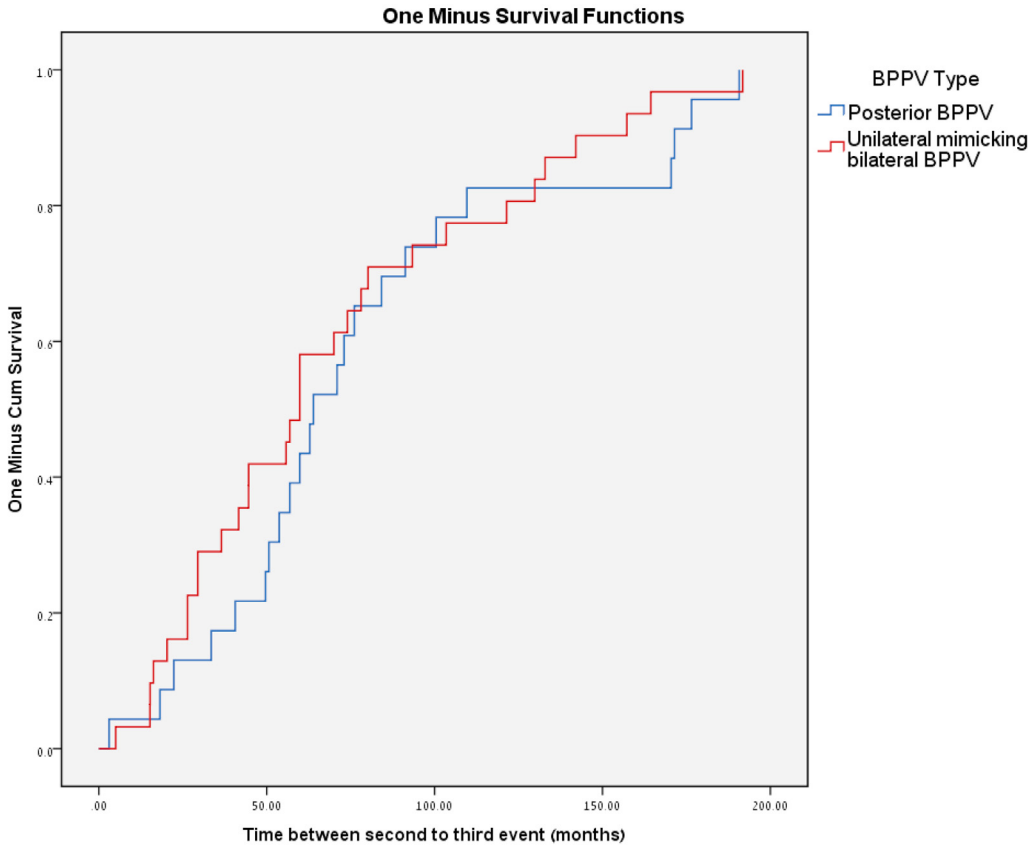
Fig. 1. Time intervals between recurrences in umb-BPPV vs p-BPPV.

outcome.

Similarly, the characteristics of patients were comparable between umb-BPPV and p-BPPV except for gender differences. Males had a predisposition for umb-BPPV as compared to females. This is rather surprising since vestibular disorders in general, and BPPV specifically, were reported to be more common in women [von Brevern et al., 2007; von Brevern et al., 2015]. In a recent study about sexual dimorphism in vestibular function female preponderance was attributed to hormonal and neurochemical differences, female reporting bias or comorbidity such as migraine or depression [Smith et al., 2019]. Osteoporosis and associated changes in otoconia production have also been related to female preponderance of BPPV [Yang et al., 2017; Rhim et al., 2019]. Moreover, anatomical differences in the vestibular system, such as anterior-posterior dimension differences between both sexes, have been recognized [Le Maitra et al., 2017; Cox et al., 2010; Bhattacharya et al., 2008; Welker et al., 2009]. Larger size of some parts of the vestibular system in men could be associated with a predisposition for otoliths displacement into the short arm of the posterior semicircular canal accounting for the prevalence of umb-BPPV in men.

The shortcoming of this study is its retrospective character with related flaws such as possible information and selection bias. The diagnosis and treatment responsiveness were based on clinical findings without objective measurements such as videoculography which is not applied in our daily clinical practice. The recurrence rate was established only if confirmed by a positive Dix-Hallpike test while undocumented recurrences were not considered, therefore the real recurrence rate might be higher. Finally, p-BPPV patients were randomly chosen from a large group of about two

B. Time between the second and third event

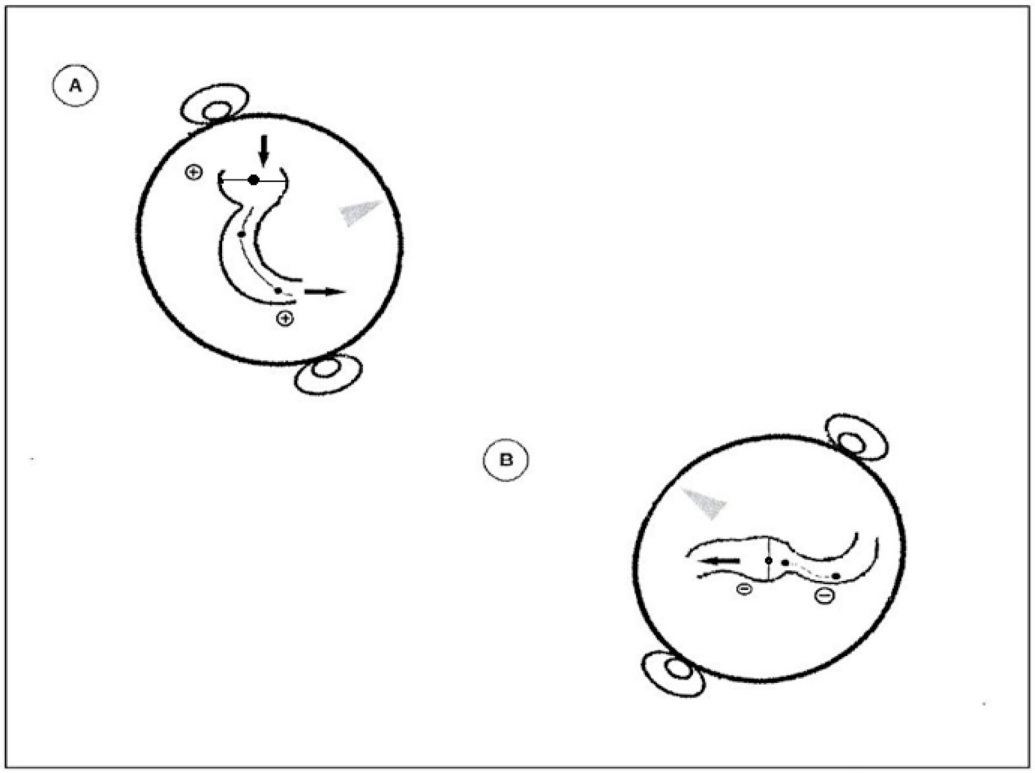


The difference between the time from second to third recurrence in the two types of BPPV is not significant (log-rank P-value = 0.554 , χ^2= 0.351).

Fig. 1. (*continued*).

Table 3
Negative Binomial regression shows independence of umb-BPPV recurrences on the first attack age, gender, BPPV side and treatment responsiveness of the first attack.

Characteristics	B	S.E	P-value	OR	CI 95% low	CI 95% high
Age	−0.01	0.012	0.411	0.99	0.967	1.014
Gender						
males	0.501	0.426	0.239	1.65	0.716	3.799
females	■	■	■	■	■	■
BPPV side						
right	0.275	0.393	0.484	1.317	0.61	2.844
left	■	■	■	■	■	■
Symptoms and treatment						
duration of symptoms until first treatment (days)	−0.004	0.004	0.339	0.996	0.987	1.004
number of treatments in the first attack	−0.081	0.089	0.361	0.922	0.775	1.097



A- Right Dix-Hallpike maneuver: ampullofugal flow of canaloliths and cupuloliths causes excitation of vestibular receptors and geotropic nystagmus.

B - Left Dix-Hallpike maneuver: ampullopetal flow of cupuloliths causes inhibition of vestibular receptors in the right ear resulting in an apogeotropic nystagmus that mimics a positive Dix- Hallpike maneuver on the left side.

Fig. 2. Umb- BPPV of the right posterior semicircular canal.

thousand patients and were not matched according to the follow up period with umb-BPPV patients. However, the mean number of recurrences did not differ between both groups and the average time period between the first and second as well as the second and third BPPV attack were similar in both groups.

It is important to recognize and differentiate umb-BPPV from bilateral BPPV. In umb-BPPV the more prominent side should be treated as long as necessary until disappearance of nystagmus. Treatment maneuvers for the pseudo-positive ear can lead to insufficient clearing of canaloliths from the long arm of the

posterior semicircular canal and be the cause of treatment resistance.

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Declaration of competing interest

The authors report no conflict of interests.

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