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Original Article

Risk Factors and a Nomogram Model for Residual Symptoms of Cured Benign Paroxysmal Positional Vertigo

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BACKGROUND: We aimed to analyze the independent risk factors that affect the treatment outcomes of residual symptoms of cured benign paroxysmal positional vertigoand to construct a nomogram model.

METHODS: A total of 186 benign paroxysmal positional vertigo patients who were treated in our hospital from June 2019 to August 2021 were selected. According to whether there were residual symptoms, they were divided into a group with residual symptoms (n = 82) and a group without residual symptoms (n = 104). The logistic regression model was used to analyze the independent risk factors affecting the treatment outcomes, and the results were incorporated into R software to establish a nomogram model for verification.

RESULTS: The incidence rate of residual symptoms in the 186 patients was 44.09% (82/186). Logistic regression analysis showed that age, course of disease, number of maneuvers, anxiety state, diabetes mellitus, and hypertension were independent risk factors affecting the treatment outcomes of residual symptoms after cured benign paroxysmal positional vertigo. The area under the receiver operating characteristic curve of the nomogram model was 0.938. The calibration curve was fitted well ($\chi^2 = 8.165$, $P = .417$).

CONCLUSION: The nomogram model constructed based on age, course of disease, number of maneuvers, anxiety state, diabetes mellitus, and hypertension had a high predictive value for the treatment outcomes of residual symptoms in benign paroxysmal positional vertigo patients.

KEYWORDS: Risk factor, cure, residual symptom, nomogram model

INTRODUCTION

Benign paroxysmal positional vertigo (BPPV) occurs due to the displacement of otolith crystals from the utricle into one or more semicircular canals. When the head moves relative to gravity, the otolith also moves, activating the semicircular canal afferents and producing false sensations such as head rotation and nystagmus.[1] Benign paroxysmal positional vertigo is characterized by transient recurrent episodes of vertigo, and it leads to 24.1% of visits for dizziness/vertigo.[2] The onset duration of BPPV is generally short, lasting for a few seconds or 1-2 minutes each time.[3] Despite a clinical response rate of 90%-96%, residual symptoms are still found in 38%-61% of BPPV patients, which will persist for several days or even months, and are complicated with emotional disorders, sleep disorders, fall risks, and even death.[4] Therefore, it is crucial to analyze the risk factors for residual symptoms following the cure of BPPV for relieving symptoms and preventing recurrence.

Global researchers have focused on the risk factors for the onset of BPPV,[5] influencing factors for post-treatment residual dizziness[6] or risk factors for post-treatment recurrence.[7] However, the clinical studies on predicting post-cure residual symptoms are still

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lacking. The nomogram model is an intuitive representation of the mathematical model. It is characterized by displaying the quantitative relationships among predictive factors in the linear regression prediction model, visualizing complex statistical regression equations, and giving individualized prediction of results.[8]

Thus, the aim of this study was to analyze the risk factors for the residual symptoms after the cure of BPPV and to construct a nomogram prediction model, aiming to provide valuable evidence for clinical prevention and treatment.

MATERIAL AND METHODS

Subjects

A total of 186 BPPV patients treated in our hospital from June 2019 to August 2021 were enrolled, and they all met the diagnostic criteria for BPPV and efficacy evaluation criteria.[9] There were 68 males and 118 females aged 24-75 (53.39 ± 7.59) years. This study has been approved by the ethics committee of Ningbo Yinzhou No. 2 Hospital (Approval no: NY2H201906003), and written informed consent has been obtained from all patients.

The inclusion criteria were as follows: (1) patients who were successfully cured and stopped medication, (2) those with no history of ear disease or ear surgery, and (3) those who were successfully followed up.

The exclusion criteria included: (1) patients complicated with sudden deafness or other vestibular diseases; (2) those with hearing impairment; (3) those with head trauma in the last month, (4) those complicated with systemic musculoskeletal diseases; (5) those with severe organic diseases; (6) those complicated with cervical vertigo, brain space-occupying lesion, cerebrovascular malformation, or central vertigo; or (7) those with involvement of multiple semicircular canals.

The cure criteria involved a negative result in the positional test, no transient paroxysmal vertigo, and no positional nystagmus.[10]

Follow-Up

All patients were followed up 1, 2, and 7 days after cure for residual dizziness or walking instability and then once a month for 2 months.

Data Collection

The following data were collected: patient data (age, gender, and body mass index), BPPV-related data (course of disease, semicircular canal involvement, side, type of onset, number of maneuvers, and onset month), co-morbidities (anxiety state, hyperlipidemia, coronary heart disease, sleep disorders, diabetes mellitus, and hypertension), bad habits (history of alcohol abuse and smoking history), and serum indices (homocysteine and 25-dihydroxy vitamin D_3 [$25(OH)D_3$]).

The anxiety state was assessed using the Self-Rating Anxiety Scale.[11] With 50 points as the cutoff value, a score of less than 50 points indicated a normal state, and a score of more than 70 points indicated anxiety.

Sleep disorders were assessed using the Pittsburgh Sleep Quality Index (PSQI).[12]

The levels of serum homocysteine and $25(OH)D_3$ were detected using the ELISA kits provided by Shanghai Jining Industrial Co., Ltd.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) version 25.0 (IBM SPSS Corp.; Armonk, NY, USA) software was used for statistical analysis. The count data (e.g., number of maneuvers) were described by the case number, and the χ^2 test was performed for comparisons between the groups with and without residual symptoms. The measurement data (e.g., homocysteine, $25(OH)D_3$, and course of disease) were described by ($\bar{x} \pm s$), and the *t*-test was performed for comparisons between the 2 groups. Seven factors, such as diabetes mellitus, number of maneuvers, gender, and type of onset, were incorporated in multivariate logistic regression analysis, and risk factors including age, diabetes mellitus, number of maneuvers, anxiety state, hypertension, and course of disease were introduced into R software to construct a nomogram prediction model for residual symptoms. The efficacy of the model for predicting the post-cure residual symptoms in BPPV patients was evaluated using calibration curves, receiver operating characteristic (ROC) curves, and Hosmer–Lemeshow (H–L) test, respectively. $P < .05$ was considered statistically significant.

RESULTS

Occurrence of Residual Symptoms

After cure, residual symptoms occurred in 82 patients (44.09%) (group with residual symptoms), and the remaining 104 patients had no residual symptoms (group without residual symptoms). In the group with residual symptoms, dizziness occurred in 40 cases (48.78%), walking instability in 32 cases (39.02%), and 2 residual symptoms in 10 cases (12.20%).

During follow-up in the group with residual symptoms, all patients had discomfort symptoms 1 day after cure, and residual symptoms disappeared in 2 and 8 cases 2 and 7 days after cure, respectively. In addition, 13 cases had residual symptoms at 4 weeks, and 3 cases had residual symptoms at 8 weeks.

Univariate Analysis Results

There were no statistically significant differences in gender, body mass index, history of alcohol abuse, smoking history, coronary heart disease, hyperlipidemia, sleep disorders, semicircular canal involvement, homocysteine, side, $25(OH)D_3$ level, or onset month between the groups with and without residual symptoms ($P > .05$). In the group with residual symptoms, age and proportions of cases with diabetes mellitus, hypertension, anxiety state, and canalithiasis were significantly higher, the number of maneuvers was ≥3 times in more

MAIN POINTS

- The incidence rate of residual symptoms in 186 patients with cured benign paroxysmal positional vertigo (BPPV) was 44.09%.
- We established a nomogram model established based on age, course of disease, number of maneuvers, anxiety state, diabetes mellitus, and hypertension.
- This model has good predictive value for post-cure residual symptoms in BPPV.

Table 1. Univariate Analysis Results [n, ($\bar{x} \pm s$)]

Influencing Factor		Group with Residual Symptoms (n = 82)	Group without Residual Symptoms (n = 104)	t/χ^2	*P*
Gender	Male	29	39	0.090	.764
	Female	53	65		
Age (years)		56.85 ± 6.72	50.66 ± 6.91	6.139	.000
Body mass index (kg/m^2)		23.25 ± 2.40	23.74 ± 2.02	1.511	.132
Course of disease		10.05 ± 2.93	7.76 ± 1.15	19.397	.000
Semicircular canal involvement	Anterior semicircular canal	29	32	0.537	.765
	Horizontal semicircular canal	25	36		
	Posterior semicircular canal	28	36		
Side	Left	39	46	0.923	.630
	Right	37	53		
	Bilateral	6	5		
Type of onset	Canalithiasis	56	25	36.525	.000
	Cupulolithiasis	26	79		
Number of maneuvers	<3 times	46	83	12.127	.000
	≥3 times	36	21		
Onset month	December to February	30	39	2.054	.561
	March to May	26	24		
	June to August	15	23		
	September to November	11	18		
Anxiety state	Normal	20	69	32.343	.000
	Anxiety	62	35		
Hyperlipidemia	Yes	7	10	0.064	.800
	No	75	94		
Coronary heart disease	Yes	18	24	0.033	.855
	No	64	80		
Sleep disorders	Yes	38	57	1.315	.251
	No	44	47		
Diabetes mellitus	Yes	19	11	5.376	.000
	No	63	93		
Hypertension	Yes	42	29	10.578	.000
	No	40	75		
History of alcohol abuse	Yes	31	39	0.002	.966
	No	51	65		
Smoking history	Yes	25	36	0.354	.552
	No	57	68		
Homocysteine (μmol/L)		11.88 ± 2.37	12.42 ± 2.14	1.629	.105
25(OH)D_3 (ng/mL)		29.41 ± 4.90	30.74 ± 5.46	1.725	.086

cases, and the course of the disease was significantly longer than those in the group without residual symptoms ($P < .05$) (Table 1).

Multivariate Logistic Regression Analysis Results

Based on the results of univariate analysis, 7 factors (including age, diabetes mellitus, hypertension, anxiety state, number of maneuvers, type of onset, and course of disease) were assigned (Table 2). With residual symptoms as the dependent variable (1 = yes, 0 = no), these factors were incorporated into multivariate logistic regression analysis. The results showed that age, course of disease, number of maneuvers, anxiety state, diabetes mellitus, and hypertension were independent risk factors for post-cure residual symptoms ($P < .05$) (Table 3).

Establishment of Nomogram Model

With the 6 risk factors including age, diabetes mellitus, number of maneuvers, hypertension, anxiety state, and course of disease introduced into R software, a nomogram prediction model for post-cure

Table 2. Variable Assignment

Variable	Assignment
Age	Continuous variable
Course of disease	Continuous variable
Diabetes mellitus	No = 0, yes = 1
Anxiety state	No = 0, yes = 1
Hypertension	No = 0, yes = 1
Number of maneuvers	<3 times = 0, ≥3 times = 1
Type of onset	Canalithiasis = 0, cupulolithiasis = 1

residual symptoms was established (Figure 1). The results illustrated that the weight of influence was increased by 5.7 points for every 1-day increase in the course of disease and by 8.8 points for every 5-year increase in age, and the diabetes mellitus, anxiety state, hypertension, and the number of maneuvers ≥3 times increased the weight by 11.2 points, 17.1 points, 14.7 points, and 12.1 points, respectively.

Validation of Nomogram Model

The area under the ROC curve of the nomogram prediction model for post-cure residual symptoms in patients with BPPV was 0.938 (95% CI: 0.905-0.972), suggesting good predictive ability (Figure 2). Moreover, the calibration curve was well fitted, and $\chi^2 = 8.165$ and $P = .417$ in the H–L test, indicating good consistency (Figure 3).

DISCUSSION

Following successful treatment of BPPV, residual symptoms may occur due to the following reasons. First, the maneuver may be incomplete. Secondly, BPPV is not only a semicircular canal disease but also an otolith lesion. Otolith dysfunction may be responsible for the transient mild dizziness. Thirdly, other vestibular lesions may coexist with BPPV. Fourthly, it takes time to restore the vestibular function after treatment. Fifthly, patient's anxiety and depression about vertigo also affect the rehabilitation.[13,14] The incidence rate of residual symptoms after maneuver for BPPV is 34%-61%,[15] consistent with the rate in this study [44.09% (82/186)]. In this study, the residual symptoms disappeared or subsided gradually in most patients with

Table 3. Multivariate Logistic Regression Analysis Results

Variable	β	Standard Error	Wald	*P*	Odds Ratio	95% CI
Age	0.132	0.025	26.911	.000	1.141	1.086-1.199
Course of disease	0.516	0.127	16.485	.000	1.675	1.305-2.149
Diabetes mellitus	0.936	0.413	5.149	.023	2.550	1.136-5.723
Hypertension	1.246	0.502	10.652	.013	3.477	1.300-9.300
Anxiety state	1.549	0.500	9.621	.002	4.708	1.769-12.532
Number of maneuvers	1.015	0.512	3.930	.047	2.154	1.012-7.523
Type of onset	0.586	0.559	1.096	.157	1.796	0.600-5.376
Constant	–15.271	0.379	41.000	.000	0.000	

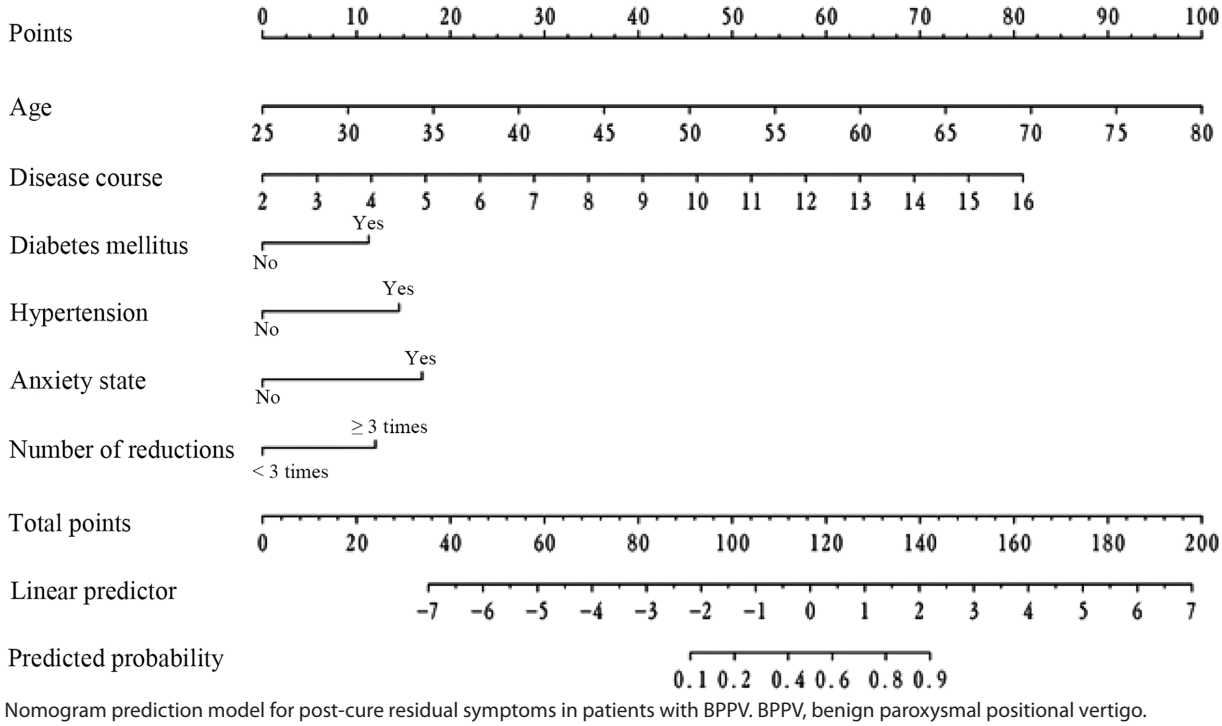

Figure 1. Nomogram prediction model for post-cure residual symptoms in patients with BPPV. BPPV, benign paroxysmal positional vertigo.

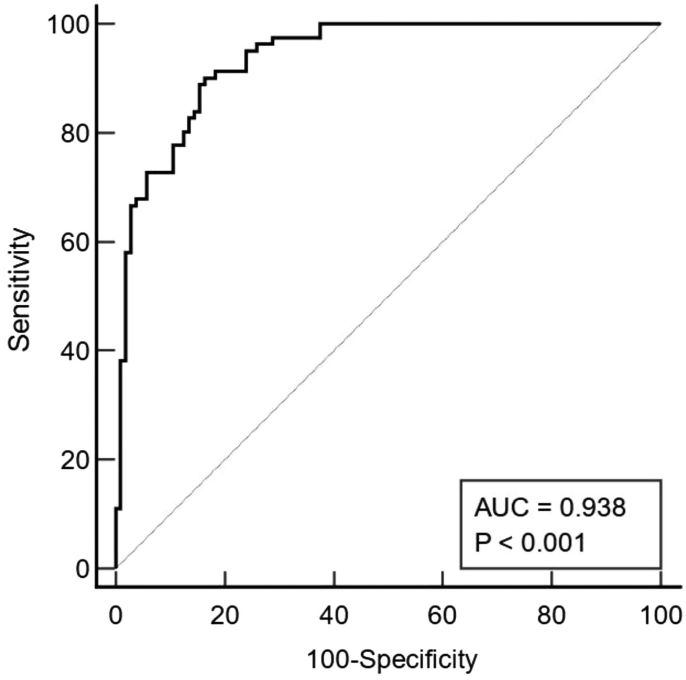

Figure 2. ROC curve of the nomogram prediction model for post-cure residual symptoms in patients with BPPV. BPPV, benign paroxysmal positional vertigo; ROC, receiver operating characteristic.

time, while recurrent BPPV occurred in very few patients. In addition, 6 independent risk factors (including age, diabetes mellitus, hypertension, anxiety state, number of maneuvers, and course of disease) for post-cure residual symptoms in BPPV patients were screened out using the logistic regression model. However, there is a lack of clinical assessment tools for individually predicting post-cure residual symptoms in BPPV patients. The nomogram model established in this paper can help medical staff to intuitively analyze the weight of influence on post-cure residual symptoms in BPPV patients, so as to identify high-risk patients as soon as possible and achieve early prevention and treatment.

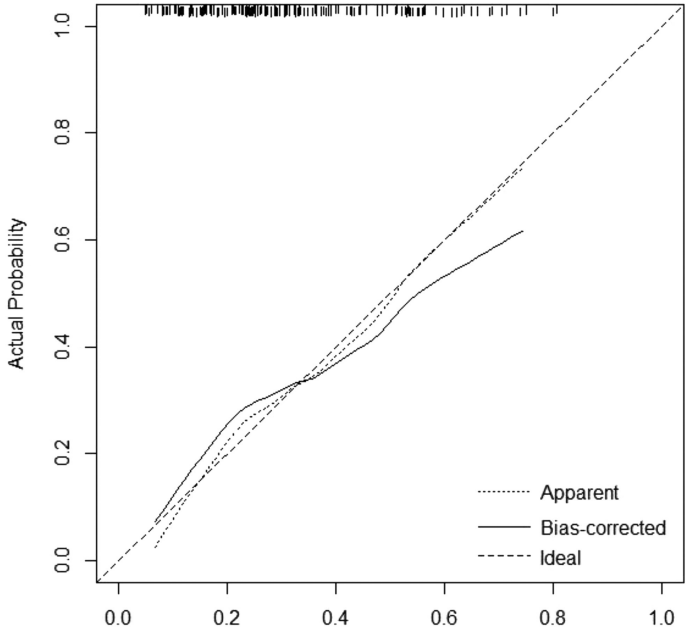

Figure 3. Calibration curve of the nomogram prediction model for post-cure residual symptoms in patients with BPPV. BPPV, benign paroxysmal positional vertigo.

In this study, the weight of influence was increased by 8.8 points for every 5-year increase in age, thus increasing the risk of residual symptoms. It has been found that the prevalence rate of BPPV in patients above 60 years of age is about 7 times higher than that in patients 18-39 years of age, and the residual symptoms such as dizziness are more common in elderly patients after repositioning maneuver, showing a high recurrence rate.[16] The possible reason is that the vestibular function degrades with age, resulting in an abnormality of dynamic balance between the production and absorption of otolith, and otolith fragments are still left in the ear after maneuver, thus delaying the adaptation of the central system.[17] Moreover, human vision and proprioception are negatively correlated with age, and the impairment of vestibular function weakens the balance ability, thus increasing the risk of residual symptoms.[18] Therefore, elderly patients with BPPV should be paid more attention to before and after treatment. In this study, the weight of influence was increased by 5.7 points for every 1-day increase in the course of disease, consistent with the study result of Luryi *et al.*[19] The reason is that due to a longer course of disease (namely the duration from the onset of vertigo to treatment), the adaptation of the central system will be delayed, and the vestibular compensation and the recovery of the balance system will consume more time, resulting in residual symptoms.[20] For this reason, early detection and prompt treatment of BPPV are conducive to reducing the incidence of residual symptoms. As previously shown, diabetes mellitus and hypertension in patients with BPPV will affect otolith absorption and remodeling, thereby increasing the incidence rate of residual symptoms.[21] In this study, hypertension and diabetes mellitus increased the weight by 14.7 and 11.2 points, respectively. The reason is that hypertension may cause spasms, sclerosis, and stenosis of the internal auditory artery of the inner ear and its branches which can supply nutrients to the inner ear. Diabetes mellitus in BPPV patients will damage the inner ear nerves and blood vessels, resulting in insufficient blood supply. As a result, otolith fragments will detach, and the absorption of fragments will be delayed.[22] Therefore, clinical attention should be paid to BPPV patients with underlying diseases. In addition, anxiety increased the weight by 17.1 points. Anxiety or depression has been reported to be associated with vestibular or balance dysfunction, especially in BPPV patients. Due to fear of falling and symptoms such as nausea and vomiting, patients usually dare not move in daily life and develop anxiety, thus forming a vicious circle of residual dizziness.[23] Repositioning maneuver fails to effectively ameliorate the emotional symptoms of patients. In the case of a high anxiety level, BPPV patients may also suffer from dizziness after vertigo is cured with no otolith and vestibular dysfunction.[24] This suggests that psychological counseling should be given to BPPV patients to overcome fear and anxiety during the treatment. Besides, the number of maneuvers was also an independent risk factor for posttreatment residual symptoms in BPPV patients, and the weight was increased by 12.1 points by the number of maneuvers ≥3 times. To sum up, the risk factors for post-cure residual symptoms in BPPV patients displayed in the nomogram model in this study can be used to individually predict high-risk patients early, and special attention should be paid to such patients to improve the prognosis.

In this study, the nomogram model was further validated using the ROC curve, H–L test, and calibration curve. The results in Figures 2 and 3 and H–L test ($\chi^2 = 8.165$ and $P = .417$) manifested that the nomogram model established based on the results of logistic regression analysis had good predictive value for post-cure residual symptoms in BPPV patients.

In conclusion, the nomogram model established based on age, course of disease, number of maneuvers, anxiety state, diabetes mellitus, and hypertension has good predictive value for post-cure residual symptoms in BPPV. Nevertheless, this study has a limitation. The sample size is small, so the results may have bias. Further studies with larger sample sizes are ongoing in our group to confirm our conclusion.

Ethics Committee Approval: This study was approved by Ethics Committee of Ningbo Yinzhou No. 2 Hospital (Approval No: NY2H201906003, Date: June 4, 2019).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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