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Determinants of Residual Dizziness in BPPV Patients After Effective Repositioning Maneuvers: The Mediating Role of Blood Lipid Levels in a Single-Center Analysis

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ABSTRACT

Objective: To identify risk factors for residual dizziness in benign paroxysmal positional vertigo (BPPV) patients after repositioning maneuvers and explore the mediation role of lipid indicators.

Methodology: 110 BPPV patients treated from January 2019 to February 2022 were studied. Data on demographics, diseases, behaviors, and lipids were collected. Multivariate logistic regression assessed risk factors, and mediation analyses explored impacts via lipid indicators. Odds ratios (OR) and 95% confidence intervals (CIs) were reported.

Results: Differences between groups with and without residual dizziness included limb weakness, hypertension, nausea, arteriosclerosis, medication, DHI scores, HADS scores, and lipid distributions ($P<0.05$). Significant risk factors were sleep disorders, medication, hypertension, triglycerides, and total cholesterol ($P<0.05$). Total cholesterol mediated 9.1% of the effect of sleep disorders on residual dizziness.

Conclusions: Managing lipid levels and sleep disorders is crucial in treating residual dizziness in BPPV patients after repositioning.

Keywords: Vertigo; Balance; Evidence based medicine

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Introduction

Benign paroxysmal positional vertigo (BPPV) is recognized as the most prevalent episodic vestibular disorder in clinical environments (1). Characterized by short episodes of vertigo, typically lasting less than a minute, BPPV is triggered by specific head movements such as lying down, turning over in bed, looking upwards, or bending forward (2). Although episodes may resolve spontaneously, they can persist for days, weeks, or months without treatment. BPPV is notorious for its tendency to recur, with around 50% of patients experiencing relapses even after successful initial treatment. While generally benign and self-limiting, the episodes can significantly disrupt personal and socioeconomic well-being, also increasing the likelihood of falls (3, 4).

The American Academy of Otolaryngology (AAO) – Head and Neck Surgery Foundation (HNSF), along with the Bárány Society, have established guidelines for diagnosing and treating BPPV (5, 6). Various maneuvers target different semi-circular canals, and the specific nystagmus and vertigo elicited by each maneuver enable clinicians to identify the affected side and understand the underlying pathophysiology (7-9). Consequently, they can select the most appropriate canalith repositioning procedure. These procedures are highly effective in treating BPPV, frequently providing immediate relief to patients (10, 11).

However, often by the time patients reach a vestibular clinic, their symptoms have already subsided into remission, rendering it challenging to confirm the diagnosis (12, 13). The clinical practice guidelines acknowledge the risk of BPPV recurrence and emphasize the importance of educating patients about this possibility. Different maneuvers to reposition canaliths can effectively alleviate

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symptoms, but some patients still experience residual dizziness even after successful repositioning (14, 15). Many studies have shown that patients with residual dizziness after repositioning maneuvers may also suffer from unsteady gait, neck discomfort, and other symptoms, significantly impacting their daily lives (3, 15, 16). To reduce the incidence of residual dizziness after repositioning maneuvers and improve the effectiveness of these treatments, it is crucial to identify the factors influencing residual dizziness post-repositioning (17, 18). Additionally, it remains unclear whether lipid levels are a risk factor for residual dizziness and what role they play in the physiological mechanisms influencing residual dizziness (19, 20).

Based on this, the present study aims to address this research gap and, based on evidence, explore the independent risk factors for residual dizziness in BPPV patients following successful repositioning maneuvers. Additionally, to further investigate the interrelationships and possible mechanisms among various influencing factors, this study intends to examine whether different lipid-related indicators act as mediators between these risk factors and residual dizziness (21).

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Methodology

Participants and Procedures

A retrospective analysis was conducted on the clinical data of 110 patients diagnosed with BPPV and treated with repositioning maneuvers at our hospital between January 2019 and February 2022. These patients met the diagnostic criteria outlined in the 2017 Guidelines for the Diagnosis and Treatment of Benign Paroxysmal Positional Vertigo. Based on the presence or absence of residual dizziness after successful repositioning maneuvers, the patients were divided into two groups: the residual dizziness group (30 cases) and the no residual dizziness group (80 cases).

The ethical standards review for our research methodology, including its objectives and protocols, was comprehensively conducted and approved by our institution's ethics committee. This evaluation ensured the research adhered to high ethical norms, with special emphasis on safeguarding patient confidentiality and rights. The study was carefully designed to meet ethical guidelines, maintaining the integrity and scientific validity of the results. Prior to their participation, informed consent was secured from all individuals involved in the study.

Inclusion and exclusion criteria

To maintain the integrity of our dataset, we enforced strict exclusion criteria, carefully screening out and excluding patients whose written records were unclear or indistinguishable. This thorough screening process was crucial to ensure the reliability of our dataset, strengthening the basis for our later analyses and findings.

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Inclusion Criteria: (I) All patients underwent relevant examinations and met the diagnostic criteria for BPPV. (II) Complete clinical data required for this study. (III) Patients who received and successfully responded to repositioning maneuvers.

Exclusion Criteria: (I) Patients with malignant tumors. (II) Patients with chronic renal, hepatic, cardiovascular, or autoimmune diseases. (III) Patients with coexisting conditions such as Ménière's disease,, vestibular neuritis, central positional vertigo, vestibular migraine or other conditions that could potentially cause vertigo. (IV) Patients who received other treatments (such as medication treatment) during the course of the disease. (V) Patients with bone diseases, gynecological diseases, thyroid diseases, or recent use of hormonal medications.

Data collection

Collect general data and lipid-related data from both groups of patients. General data was collected from questionnaires and included gender, age, BMI, smoking status, alcohol consumption, and the presence or absence of sleep disorders, which were defined as difficulty falling asleep (taking more than 30 minutes), reduced total sleep time (<6 hours), sleep maintenance disorders (waking up at least 2 times per night), early awakening, decreased sleep quality, and associated daytime functional impairment. Additionally, the presence of comorbidities, including hypertension, diabetes, and lower limb arteriosclerosis, was documented. Other collected data included the onset time (expressed as days), clinical symptoms (positional vertigo, nausea, vomiting, limb weakness, and hearing loss), whether medication treatment was administered after repositioning, Dizziness Handicap Inventory (DHI) scores before repositioning, and Hospital Anxiety and Depression Scale

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(HADS) scores before repositioning.

The diagnostic criteria for comorbidities referred to "Hypertension: From Basics to Clinical Practice, From Guidelines to Practice," "2014 American Diabetes Association Guidelines: Standards of Medical Care in Diabetes," and "Guidelines for Diagnosis and Treatment of Lower Extremity Arteriosclerosis Obliterans." The DHI consists of 25 items, with a total score range of 0-100 points, including three subscales: Physical (P, 28 points), Emotional (E, 36 points), and Functional (F, 36 points). Each item is scored as 0 (No), 2 (Sometimes), or 4 (Yes), with higher scores indicating more severe vertigo symptoms. The grading standard is: 0-30 points for mild impairment, 31-60 points for moderate impairment, and 61-100 points for severe impairment. The HADS comprises 14 items divided into two subscales: HADS-A (Anxiety) and HADS-D (Depression), each with 7 items. Based on the total score, results are classified as no symptoms (0-7 points), doubtful symptoms (8-10 points), and definite symptoms (11-21 points), with higher scores indicating more severe anxiety and depression.

For physiological and biochemical indicators, 3 mL of venous blood was collected from all study subjects upon admission. The blood samples were centrifuged at 3,000 rpm for 10 minutes with a centrifuge radius of 15 cm. Serum was extracted and analyzed using an automatic biochemical analyzer (HTSH-3800, Qingdao Han Tang Biotechnology Co., Ltd. In China) to measure the concentrations of serum triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL), and high-density lipoprotein cholesterol (HDL).

Statistical analysis

Firstly, for the characteristics of study participants, continuous variables were expressed using the mean ± standard deviation (SD), and the means between the two groups were compared using the t-test. Categorical variables were expressed using frequency (n) and percentage (%), and the comparisons between groups were made using the χ^2 test. Multivariate logistic regression models were performed to evaluate the risk factors for residual dizziness in BPPV patients following successful repositioning maneuvers. Several models were constructed: Model I was adjusted for age and gender. Model II was Model I additionally adjusted for smoking status, alcohol consumption, BMI, sleep disorders, comorbidities, medication treatment, DHI scores and HADS scores. Model III was Model II with additional adjustment for lipid-related indicators, including TG, TC, LDL and HDL. Odds ratios (OR) and 95% confidence intervals (CIs) were finally reported and calculated.

Through regression-based mediation analyses, a detailed exploration was conducted to determine both the direct effects of statistically significant risk factors on residual dizziness and their indirect effects mediated through lipid-related indicators (TG, TC, LDL, and HDL). This investigation resulted in three key estimations: (i) the total effect, which covers the overall relationship between statistically significant risk factors and residual dizziness, including both direct connections and those mediated by lipid-related indicators; (ii) the direct effect, which isolates and clarifies the link between the statistically significant risk factors and residual dizziness; and (iii) the indirect effect, which reveals the pathways where lipid-related indicators mediate the relationship between statistically significant risk factors and residual dizziness.

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All statistical analyses and figures were produced using R version 4.3.2. We established a significance threshold with a p-value of less than 0.05, a standard that highlights the identification of significant associations within the scope of the study framework.

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Results

Within the scope of this study, a total of 110 eligible participants were included, 80 (72.7%) were no residual dizziness while 30 (27.3%) were with residual dizziness, aged 66.58±9.29 years of all participants, and the majority were male ones (51.8%), no smoking (54.5%); current drinking (56.4%); without sleep disorders (61.8%); without hypertension (68.2%); without diabetes (53.6%); with limb arteriosclerosis (52.7%); with positional vertigo (57.3%); without nausea (58.2%); without limb weakness (59.1%); without hearing loss (59.1%); without medication treatment (71.8%). The age, gender, smoking status, alcohol consumption, whether suffering from diabetes or not, whether suffering from positional vertigo or not, whether suffering from vomiting or not, whether suffering from limb weakness or not, whether suffering from hearing loss or not, onset time, DHI score, TG, BMI have no significant difference between the two groups. In contrast, whether suffering from limb weakness or not, whether suffering from hypertension or not, whether suffering from nausea or not, whether suffering from limb weakness or not, whether suffering from limb arteriosclerosis or not, medication treatment, DHI scores, HADS scores, TC, LDL, HDL are significant different between the two groups (P<0.05). The details are shown in ***Appendix A***.

Appendix B shows the results of risk factors for residual dizziness in BPPV patients following successful repositioning maneuvers based on three models of multivariate logistic regression analysis. According to the regression results adjusted for all confounders (Model III), only sleep disorders, medication treatment, hypertension, TG, and TC were significant risk factors for residual dizziness (P<0.05). **Figure 1** is a forest plot of the subgroup analysis for each factor.

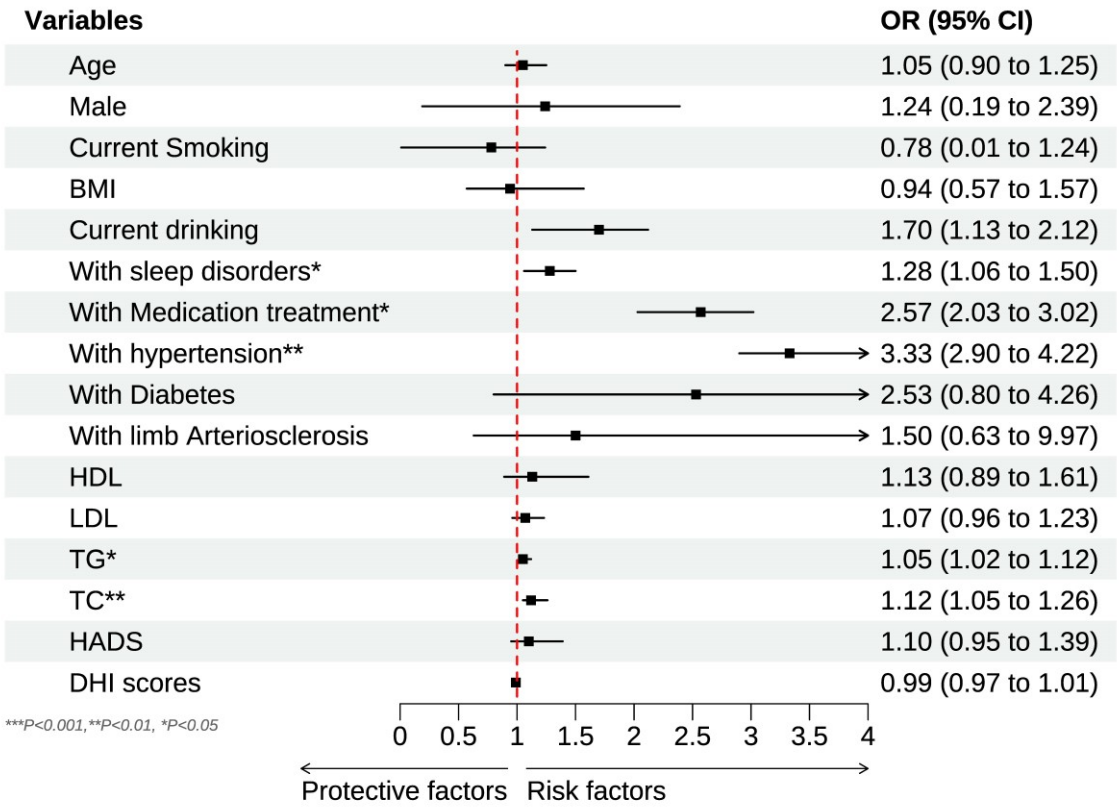

Figure 1. Forest plot of influencing factors for residual dizziness in BPPV patients following successful repositioning maneuvers based on Model III.

The mediation analyses were conducted to explore the role of significant lipid-related indicators (TG and TC) between all other significant risk factors and residual

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dizziness. It was found that only TC had a significant mediating effect between sleep disorders and residual dizziness (all other variable combinations had P>0.05). Specifically, the total effect on residual dizziness was 0.539 [β (95% CI): 0.539 (0.369, 0.690), *P*<0.001], and the indirect effect was 0.091 [β (95% CI): 0.091 (0.118, 0.088), *P*<0.001]. This indicates that a notable indirect effect was detected for TC, contributing to 9.1% of the overall change through the mediating effect of TC.

Figure 2 shows the path diagram of mediation analysis of relationship between sleep disorders, medium TC concentration and residual dizziness.

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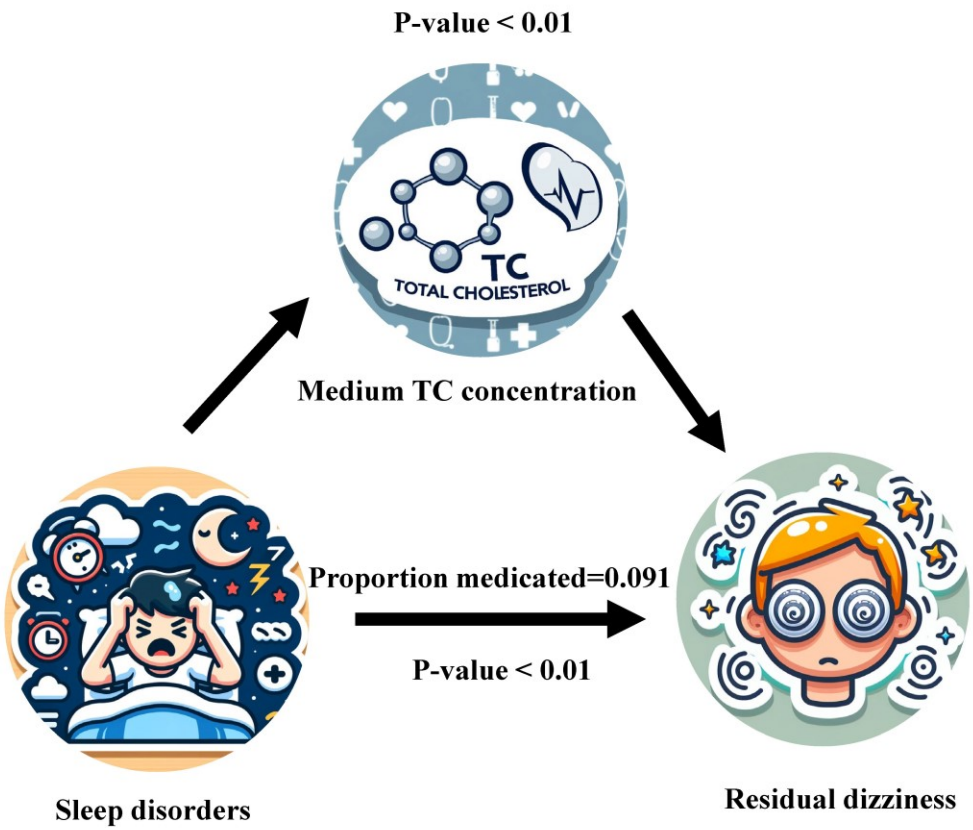

Figure 2. Path diagram of mediation analysis of relationship between sleep disorders, medium TC concentration and residual dizziness

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Discussion

To the best of our knowledge, this is the first study to explore the risk factors for residual dizziness in BPPV patients following successful repositioning maneuvers and to thoroughly analyze the relationship between lipid-related indicators and residual dizziness. We found that whether suffering from limb weakness, hypertension, nausea, or limb arteriosclerosis, medication treatment, DHI scores, HADS scores, TC, LDL, and HDL distributions were significantly different between the groups with and without residual dizziness. Moreover, the results of the multivariate logistic regression analysis further revealed that sleep disorders, medication treatment, hypertension, TG, and TC were all significant risk factors for residual dizziness ($P<0.05$). Simultaneously, we further revealed the mediating effect (9.1%) of total cholesterol blood concentration between sleep disorders and residual dizziness.

Our study found that the more severe the sleep disorders were before repositioning, the less effective the maneuver was, and the higher the probability of residual dizziness. This finding aligns with another single-center retrospective study on sleep disorders in BPPV patients, which reported that BPPV patients experienced sleep disorders before the diagnosis of BPPV, suggesting it as a significant risk factor (22). In BPPV, the detachment and displacement of otoliths can mechanically stimulate the semicircular canal's ampullary ridge, leading to vertigo (23, 24). Regarding the potential mechanisms, some researchers believe that dysfunction in the central nervous system (CNS) increases the excitability of the trigeminal caudate nucleus, solitary tract nucleus, and vestibular nucleus, resulting in vertigo (25, 26). Others propose that abnormal trigeminal neurovascular pathways cause asymmetric release of neurotransmitters, such as serotonin and

norepinephrine, on both sides of the vestibule, also leading to vertigo (27). Therefore, residual dizziness and sleep disorders in BPPV patients may have a bidirectional causal relationship. This finding needs further exploration in future prospective cohort studies.

Similarly, our results align with a previous meta-analysis, which suggested that hypertension and hyperlipidemia are risk factors for the recurrence of BPPV (28). This implies that these factors may also contribute to residual dizziness in BPPV patients even after successful repositioning maneuvers. Our findings indeed support this view, showing that higher levels of TG (OR: 1.05, 95% CI: 1.02-1.12), TC (OR: 1.12, 95% CI: 1.05-1.26), and hypertension (OR: 3.33, 95% CI: 2.90-4.22) are significantly associated with residual dizziness. This finding is also consistent with a cross-sectional study from Germany, which reported that hypertension and hyperlipidemia were independently associated with residual dizziness in BPPV patients (2, 29). The reason for this lies in the anatomical positioning of the SCC, which is at the lowest point in the vestibular apparatus when a person is standing (18, 30). Von Brevern et al. discovered that BPPV predominantly affects the right labyrinth, likely due to the common habit among most patients of sleeping on their right side (2, 18). Theoretically, hypertension acts as a vascular risk factor, suggesting that ischemia might be a common predisposing factor for BPPV. However, our study did not identify any association between BPPV and other recognized vascular risk factors, including smoking and alcohol consumption ($P > 0.05$) (17).

BPPV patients exhibit higher TC levels, and elevated TC levels have been identified as a risk factor for the occurrence of BPPV. The relationship between TC levels and BPPV has not been thoroughly

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explored in previous research. Elevated TC levels or hyperlipidemia can cause vascular damage in the inner ear, potentially leading to BPPV (31). Additionally, a recent study discovered an association between the three rs2074880 genotypes of the CACNA1A (Calcium Voltage-Gated Channel Subunit Alpha1 A) gene and elevated cholesterol levels in patients with BPPV (9, 32). Our study results also revealed the mediating role of TC levels in the relationship between sleep disorders and residual dizziness in BPPV patients. This finding highlights the importance of TC levels as a crucial intermediary factor. Elevated cholesterol levels, which are often a consequence of sleep disorders, can cause vascular damage in the inner ear, thus exacerbating dizziness symptoms. This mediating effect of TC levels suggests that managing cholesterol may help mitigate the impact of sleep disorders on residual dizziness (33, 34). For example, interventions aimed at reducing cholesterol levels could potentially disrupt the pathway linking sleep disturbances to dizziness, thereby improving patient outcomes (9, 35, 36). Such evidence underscores the need for comprehensive treatment approaches that address both sleep quality and lipid management in BPPV patients to effectively reduce residual dizziness (37-41).

Several limitations of this study should be noted: (I) the sample size was relatively small, necessitating further validation and support from future research; (II) all the BPPV patients included were from a single location, which could restrict the generalizability of our findings; (III) the retrospective analysis period of this study was relatively short. Future research should utilize large-scale prospective cohort studies to further elucidate the risk factors for residual dizziness in BPPV patients and the interactions between these factors (42-45).

Conclusion

Our findings indicate that sleep disorders, medication treatment, hypertension, TG, and TC as significant risk factors for residual dizziness. Additionally, our study revealed a notable mediating effect (9.1%) of total cholesterol blood concentration on the relationship between sleep disorders and residual dizziness. These insights underscore the importance of addressing lipid levels and sleep disorders in the management of residual dizziness in BPPV patients. Implementing targeted interventions for these factors could significantly improve patient outcomes and enhance the quality of care for those suffering from BPPV-related dizziness.

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Author contribution

The author Guanyu Wang contributed to all work of this study, including but not limited to design, data collection, analysis, and interpretation, drafting and revision of the article, and so on.

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The views expressed in this publication are those of the authors.

Conflicts of Interest

The authors declare no conflict of interest.

Data Availability Statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Availability of data and material

All data are included in the article and are available from the corresponding author.

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