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Letter to the Editor

## **In Order to Reliably Assess the Vitamin-D / Benign Paroxysmal Positional Vertigo Relationship, Confounding Variables and Differential Diagnoses must be Taken into Account**

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### **Letter to the Editor**

We read with interest the article by Kwak *et al.* on a nested case-control study investigating the association between benign paroxysmal positional vertigo (BPPV) and its recurrence rate, as well as vitamin D deficiency, osteoporosis, obesity, and vitamin D supplementation, using a dataset of 507,744 individuals collected through the Korean National Health Insurance Service [1]. The overall recurrence rate of BPPV was 22%, and 25% in patients with vitamin D deficiency [1]. The risk of recurrence was increased in postmenopausal women with osteoporosis and in individuals supplementing with vitamin D and calcium [1]. The study warrants further discussion.

First, it was not described how differential diagnoses of BPPV were effectively ruled out [1]. BPPV is frequently mistaken for vertigo that is not caused by otolith displacement. Differential diagnoses for BPPV include Meniere's disease, vestibular migraine, vestibular neuritis, central positional vertigo due to brainstem or cerebellar lesions, electrolyte disturbances, endocrine disorders, hemodynamic abnormalities, and peripheral neuropathy, particularly sensory polyneuropathy [2]. Until these differential diagnoses are systematically excluded from the analysis, the results and their interpretation should be treated with caution.

Second, ICD codes have been used to identify patients with BPPV. However, recruiting patients via electronic diagnoses has several drawbacks, as this coding system was designed for administrative billing rather than scientific purposes [1]. The disadvantages of the ICD system include low sensitivity and specificity, a lack of clinical detail, an administrative rather than clinical focus, coding delays, a lack of context, and the rarity of the code [3]. Furthermore, coding accuracy depends heavily on the diligence and competence of the coding physicians. Because vitamin D deficiency is often considered an insignificant diagnosis, it is frequently not included or coded in final reports.

Third, the factors influencing vitamin D levels have not been sufficiently investigated. In addition to the measurement method, other factors influence vitamin D levels, including sun exposure, geographic location, season, skin pigmentation, the type of clothing, diet, conditions such as malabsorption due to Crohn's disease, gastric bypass, or ulcerative colitis, and genetic factors [4]. Hyperparathyroidism and hypoparathyroidism are two such factors that were not considered in the analysis. Since parathyroid hormone significantly influences vitamin D levels by stimulating the kidneys to convert inactive vitamin D to its active form or calciferol, the effect of vitamin D on BPPV cannot be assessed without considering parathyroid function [5].

The fourth point is that otolith dysfunction and displacement can be related not only to vitamin D levels, osteoporosis, and obesity, but also to numerous other factors. These include the function of the epithelial cells of the utricle and saccular maculae, which produce an organic matrix that concentrates calcium and carbonate to facilitate crystal formation; the available amount of otoconin-90 and otolin-1, the main components of the organic matrix; the turnover rate in adulthood; and the regenerative capacity of the otoliths formed during late embryonic development [6]. Furthermore, otoliths are embedded in a complex matrix and do not float freely. This matrix serves as a structural scaffold of proteins and proteoglycans that binds calcium carbonate crystallites. If the production and localization of this matrix are impaired, otolith function may be affected, even if their composition is normal.

As long as interfering factors that influence vitamin D levels, factors that determine otolith production and turnover, are not included in the analysis, and differential diagnoses of BPPV are not sufficiently excluded from the analysis, the results obtained and their interpretation remain unreliable overall.

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