Author's response to reviews

Title: Association between osteoporosis and benign paroxysmal positional vertigo: a systematic review

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Author's response to reviews:

Dear Editor and Reviewers:

Thank you for your and reviewers’ comments concerning our manuscript entitled “Association between osteoporosis and benign paroxysmal positional vertigo: a systematic review”. I think that is very important for the enhancement of our manuscript. The following are our responses to your comments.

Response to comments of reviewer 1:

1. The results section does not specifically discuss the findings of reference 13 (Mikulec 2010) even though on page 7, line 20 refers to its findings.
Response: That has been added in results section.

2. Page 7, lines 18-20 seems overstated. I think the studies reviewed show and association between osteoporosis and BPPV and that certainly suggests osteoporosis/osteopenia as a cause but does seem strong enough to "confirm" the causal relationship
Response: That sentence has been revised.

3. Page 8, line 8. I think along with the Vibert 2008 study (ref 20), the authors should include Jang YS1, Hwang CH, Shin JY, Bae WY, Kim LS.Age-related changes on the morphology of the otoconia. Laryngoscope. 2006 Jun;116(6):996-1001.
Response: That reference has been added.

4. Page 14 in References. Reference 1 and 9 should state von BREVERN M instead of von BM.
Response: That has been revised.

5. Figure 1. At the bottom indicates 8 controlled trials but text says there were 7.
Response: That has been revised in figure.
6. On page 5, line 13, rephrase "All studies were non randomised... to "None of the trials were randomized controlled trials (RCTs).
Response: That has been revised.
7. Page 8, line 3. change to "observational study and is not a long-term ...".
Response: That has been revised.
8. Figure 1. bottom right the word "studies" should be capitalized to be consistent with other inclusion criteria.
Response: That has been revised.

Response to comments of reviewer 2:
1. The use of the terms “cohort study” and “case-control study” is problematic in this paper. The authors denominate several studies they have included in their review as cohort studies. I have checked references 12 and 15, which aren’t cohort studies but case-control studies. A cohort study is a longitudinal study that follows a group of people (see also below).
Response: That has been revised.
2. On page 5 the authors write that only one study had a follow-up that was long enough (ref. 12). However, this study was a case control study without any follow-up.
Response: That sentence has been deleted.
3. Page 3, line 12: Osteoporosis might be a risk factor for BPPV. It is not the cause of BPPV.
Response: That has been revised.
4. Page 3, line 18: “exception” instead of “exemption”.
Response: That term has been revised.
5. The authors should specify whether the included studies were prospective or retrospective.
Response: That term has been added.
6. Page 5, line 11: The number of 1631 patients with BPPV reads impressive. However, one study (ref. 17) with 1092 patients might better be removed from this review as in this study only 13 patients had osteoporosis. It is highly likely that this retrospective study did not examine systematically for osteoporosis. Thus, the association between BPPV and osteoporosis can hardly be examined with this study. Furthermore, according to Fig. 1, studies examining multiple associations (as ref. 17) were an exclusion criterion in this review.
Response: That study (ref. 17) included 1092 BPPV patients. In these patients, 13 BPPV patients had osteoporosis. The primary objective of this study was to find a statistical link between the most worldwide comorbidities (hypertension, diabetes, osteoarthrosis, osteoporosis and depression) and recurrent episodes of BPPV. Osteoporosis is one of comorbidities. That similar with other studies(such
as ref 16.). This study truly include 1092 patients with BPPV. We think should not removed these patients. That studies (ref. 17) also didn't examine multiple associations, only examined the associations between BPPV and other comorbidities (osteoarthrosis, etc.) So we shouldn't exclude that from this review.

7. Page 5, line 17: “In all of four cohort studies, no one study had adequacy of follow-up, only one study followed long enough for outcomes to occur.” This is a contradiction. What do the authors consider as long enough for follow-up?
Response: That has been revised. "only one study followed long enough for outcomes to occur." had been deleted.

8. Page 5, line 19: “All of these three studies selected patients as controls.” What diagnosis had these patients?
Response: That has been revised to " None of these five studies selected community as controls"

9. Page 5, line 20: why were the cases not representative?
In these two studies, the case were not consecutive or obviously representative series of cases, or didn't stated how to select cases.

10. Page 6, line 2: what do the authors mean with “apparent correlation”. Was there a statistical significant association or not? The authors have used the term “apparent correlation” several times throughout the paper.
Response: Many studies showed " apparent correlation between BPPV and osteopenia or osteoporosis", such as in study of Vibert 2003. Therefore, we used tern “apparent correlation’. It have data in these studies to certify that. But we can't perform a meta-analysis to certify that. So we deleted some “apparent correlation”.

11. Page 6, line 4: What is meant with “prognosis of BPPV”? The rate of recurrence or the response to treatment or something else?
Response: The rate of recurrence.

12. Page 6, line 15: This sentence does not make sense: “While one study found no correlation between serum vitamin D levels and the presence of BPPV.”
Response: This sentence has been revised.

13. Page 7, line 6: “Only one study assessed the association between biochemical markers of bone turnover and BPPV, and found that patients with BPPV had higher amino-terminal propeptide of procollagen type I levels, and that level of biochemical markers of bone turnover correlated with the presence of BPPV.” These levels were higher compared to what?
Response: Compared to OSTEO subjects (13 women with history of osteopenia/osteoporosis)

14. Page 7, line 14: "...and that the medications used to treat these conditions may be able to prevent the occurrence and recurrence of BPPV." Is there any data in these 7 studies that support this statement or is this speculation?
Response: It have data in one study (Mikulec2010). From data in other study, we
also can drive this conclusion.

15. Page 7, line 17: “recurrence rate for BPPV of about 27%”. This number is meaningless, unless you define the time of follow up; e.g. recurrence rate of xy% per year.
Response: This sentence have been revised.

16. Page 7, line 19: osteoporosis is not the cause of BPPV
Response: We don't know the meaning and the cause of that question.

17. Table 1: does the age refer to patients with BPPV? How about controls? Was the age similar in patients and controls? Does the ratio female to male refer to patients with BPPV? Concerning Ref 13: was there any association between osteoporosis and BPPV?
Response: In that table, the age refer to the age of the subjects and control. some study showed the age with subjects and control respectively ,then we will also showed respectively. The ratio female to male was similar with the age. In Ref 13, it found there was a negative association between BPPV and treated osteoporosis in women. Osteoporosis, or the medication used to treat it, may provide protection against BPPV.

18. References 1, 9 and 10: spelling has to be checked.
Response: That has been revised.

19. Can the authors quantify the association between osteoporosis and BPPV?
Response: In present, we can't quantify the association between osteoporosis and BPPV, because we were unable to perform a meta-analysis because of the lack of RCTs included in this review.

Thank you and best regards.

Yours sincerely,
Qirong Wang