LETTERS TO THE EDITOR

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Obstructive Sleep Apnea and Osteoporosis Risk

Response to Upala et al. Obstructive sleep apnea is not associated with an increased risk of osteoporosis: a systematic review and meta-analysis. J Clin Sleep Med 2015;11:1069–1070.

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We thank Upala et al. for sharing the results of their meta-analysis on osteoporosis risk in obstructive sleep apnea (OSA) in their letter.[1]

The meta-analysis included 5 recently published studies (1) a retrospective study including 66 patients with chronic obstructive pulmonary disease (COPD) in whom bone mineral density (BMD) was significantly lower at the lumbar spine in those who additionally had OSA compared to COPD patients who did not snore[2]; (2) a retrospective cohort study including 1,377 OSA patients (diagnosed by ICD codes) followed over 6 years, in whom the risk of osteoporosis (diagnosed by ICD codes), was 2.52 times the risk in 20,655 matched controls[3]; (3) a retrospective cohort study including 846 individuals with OSA, showing increased incident osteoporosis with an adjusted hazard ratio of 2.98 over 10 years in individuals with OSA compared to 89,380 controls with no sleep disorders[4]; (4) a cross-sectional community-based study including 800 individuals who underwent polysomnography and BMD DXA scan and found inverse relationship between apnea-hypopnea index and femoral neck T-score, and a positive association between oxygen desaturation index and femoral T-score[5]; and (5) an editorial[6] referring to a cross-sectional study by Uzkeser et al. who found a significantly lower BMD at the spine and femoral neck in 26 men with OSA, compared to 21 healthy male controls.[7]

We agree with the authors that a systematic review and meta-analysis would significantly enhance the knowledge on the association between OSA and bone loss. However, the meta-analysis of these five studies had significant limitations. Three studies were from Taiwan, one study from Turkey, and the fifth was from France. The studies included participants of variable age, an important predictor of bone density. Two studies included middle-age and young adults, age < 65 years,[3,4,7] while the other studies included older individuals, > 65 years.[2,5] Furthermore, comorbidities known to affect the skeletal system, such as diabetes and COPD, were variably included, and sometimes were not evenly distributed between participants with and without OSA. Such differences in the pooled samples would result in variability in BMD and osteoporotic fracture risk. The control group was heterogeneous including community-based healthy volunteers,[5,7] patients with COPD,[2] or controls drawn from national health insurance databases.[3,4] The definition of OSA and osteoporosis was based on polysomnography and DXA scan, respectively, in 3 studies,[2,5,7] while it was based on ICD codes in two studies.[3,4] Indeed, all these differences result in a high heterogeneity, as translated in a high heterogeneity index (I^2) in the meta-analysis of Upala et al.[1] Accordingly, pooling the results of these studies is not advised, and the conclusion from this meta-analysis should be interpreted very cautiously.

Furthermore, four of these studies have consistently found an inverse relationship between OSA and BMD at the hip or spine, in support of our descriptive review.[8] Only one study showed mixed results.[5] It is therefore surprising that Upala et al. concluded that there is no association between OSA and BMD; findings possibly attributed to the high heterogeneity of the pooled studies and/or other methodological limitations. The results were very briefly described in the *Letter to the Editor* and they were not published elsewhere. The protocol of this systematic review was not published in any registry. Therefore, readers cannot easily identify the preset outcomes and methods. In addition, the report did not describe the eligibility criteria of the included studies such as the characteristics of the population included (age, severity of OSA, other comorbidities, medical therapy) and the characteristics of the controls (i.e., completely healthy individuals versus patients with other chronic respiratory disorders). The databases searched were defined. However, the search strategy was not available to identify the Mesh terms and the keywords used. Bias assessment was not discussed. Accordingly, the requirements of the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) that dictates standards for transparency in reporting systematic reviews were not met.[9]

In conclusion, in view of the all the aforementioned differences in the studied samples, study design, and definition of variables (OSA and osteoporosis), a meta-analysis of the current studies is significantly limited and its results may be misleading. High-quality prospective studies are needed to better evaluate the likely deleterious effect of OSA on bone density.

CITATION

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DISCLOSURE STATEMENT

The authors have indicated no financial conflicts of interest.