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LETTER

Obstructive Sleep Apnea, Circadian Rhythm Disturbance, Hypertension, and Kidney Stone: An Attractive Quadrangle? [Letter]

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Dear editor

We are interested to read the article by Liu et al titled "Link Between Obstructive Sleep Apnea and Kidney Stones: NHANES 2015–2018 and Mendelian Randomization".[1] This study investigated the relationship between obstructive sleep apnea (OSA) and kidney stone disease (KSD) and explored the causal link using Mendelian randomization. Here, we would like to raise a little concern and indicate some clinical implications of this study.

First, the accurate diagnosis of OSA is not available from the NHANES database due to a lack of polysomnography test results, which is the gold standard for diagnosing OSA. Usually, the frequency of self-reported symptoms of OSA is an alternative indicator for OSA.[2] Since the self-reported symptoms were obtained using a questionnaire, recall bias is inevitable, and may reduce the robustness of the final results. The rigor of this study may benefit from emphasizing that the diagnosis of OSA is based on "self-reported symptoms" and related bias in Title or Introduction. In addition, the results about the risk of KSD in OSA patients "OR = 1.29; 95% CI: 1.00–1.66; p = 0.05" may result in decreased statistical reliability due to critical p-value and confidence interval. More covariates may be considered to be adjusted to modify the results, for example, the presence of chronic kidney disease.

Apart from a fly in the ointment, we appreciate this study for both population- and genetic-based evidence unraveling the relationship between OSA and KSD. OSA induces the disruption of the normal circadian clock and is associated with various cardiovascular and metabolic complications.[3] Recently, KSD has been proven to be tightly related to circadian rhythm disturbance (CRD).[4] Unlike previous urinary component analyses, Liu et al confirmed that OSA can promote KSD formation, and their viewpoints support the link between CRD and KSD. Currently, the most widely known link between KSD and CRD is metabolic syndrome (MetS) (type 2 diabetes, obesity), and a new concept "circadian syndrome" was proposed to underline the connection between MetS and CRD.[4] Another biological parameter, blood pressure, is also regulated by the circadian clock, and CRD can cause hypertension, which is a key component in MetS.[5] However, the relationship between hypertension and KSD is still controversial due to opposite results in different cohorts.[5] OSA and hypertension exist in a bidirectional relationship where the presence of one condition increases the risk of the other, and they share some same pathological processes (eg, oxidative stress, excessive generation of reactive oxygen species, and the abnormal activation of renin-angiotensin-aldosterone system).[5] Therefore, OSA has the potential to link hypertension and KSD. Summarily, it is found that OSA, hypertension, and KSD are all related to CRD, and OSA could explain the obscure link between hypertension and KSD. We suspect a "Quadrangle" formed by OSA, CRD, hypertension, and KSD, which elucidates the relationship between CRD and KSD and the potential targets for KSD prevention and therapy.

In conclusion, this article provides valuable insights for KSD pathogenesis associated with CRD and the relationship between hypertension and KSD, which can inspire more about KSD management.

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