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RESPONSE TO LETTER

Letter to the Editor Regarding: "Association Between Metabolic Score for Insulin Resistance (METS-IR) and Risk of Obstructive Sleep Apnea: Analysis of NHANES Database and a Chinese Cohort" [Response to Letter]

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Dear editor

We are very pleased to hear from Professor Shan Qingqing and Professor Li Yangke. In the letter, the two professors put forward many constructive comments on the methodology part of our article, and hereby reply as follows:

First, in the NHANES cohort, we utilized standardized sleep questionnaires to identify individuals at high risk of OSA. These tools are not intended to diagnose OSA but are widely accepted in epidemiological studies as proxies for identifying populations at increased risk, especially when polysomnography (PSG) data are unavailable. Therefore, the 49.8% prevalence reported reflects the proportion at high risk for OSA based on questionnaire data—not the true PSG-confirmed prevalence. Previous validation studies have shown that commonly used OSA screening questionnaires (eg, Berlin Questionnaire, STOP-Bang, STOP, and Epworth Sleepiness Scale) have generally high sensitivity but relatively low specificity.[1] These findings are consistent with our results and suggest that overestimation of OSA risk using questionnaires is an expected limitation, but acceptable for population-level screening and risk stratification. Importantly, in our Chinese cohort, OSA diagnosis was based on Ultra-Wideband (UWB) bio-radar sleep monitoring—a validated portable device—thus improving diagnostic accuracy in that part of the study.[2]

Second, OSA is characterized by two core pathological features: intermittent hypoxia and sleep fragmentation. Our study primarily focused on the relationship between METS-IR and hypoxia-related indices (eg, AHI, ODI, and T90), which have well-established metabolic relevance. While sleep duration is inherently reflected in these parameters, sleep fragmentation involves a distinct physiological mechanism, and its impact on metabolism may require a dedicated investigation beyond the scope of this study. In the Chinese cohort, we collected participants' baseline medication information—covering major drug categories such as antihypertensive, lipid-lowering, and antidiabetic medications—to reduce the influence of pharmacological confounders. However, data on specific agents such as glucocorticoids or β-blockers were not available, which we acknowledge as a limitation for this work. We agree that the relationship between OSA and insulin sensitivity remains complex. Notably, emerging studies, such as the work by Polonsky et al, suggest that OSA is associated with peripheral insulin resistance—particularly in skeletal muscle and adipose tissue—without impairing insulin secretion. These findings align with our emphasis on insulin resistance, as captured by METS-IR, rather than β-cell dysfunction.[3]

Third, thank you for your valuable comment. We acknowledge that the cross-sectional nature of both the NHANES dataset and our sleep center data precludes the ability to establish causal relationships between OSA and METS-IR. However, we would like to clarify that our primary aim was not to infer causality, but rather to explore the associative

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relationship between METS-IR and OSA risk. Given that METS-IR and OSA-related measures were assessed simultaneously, our focus was to evaluate whether METS-IR could serve as a potential predictive or screening marker for OSA in clinical practice. We believe this finding has practical value, especially in settings where sleep studies are not readily available. Data on CPAP treatment were lacking in the NHANES database, but we excluded patients who used CPAP before inclusion in the analysis to avoid metabolic interference with CPAP in the Chinese population. Your suggestion gives us important direction, and prospective cohort studies will be considered in the future to clarify the causal relationship and evaluate the effect of CPAP intervention on metabolic parameters.

Forth, thank you for your insightful comment regarding gender differences in the predictive value of METS-IR. We agree that sex-specific physiological and metabolic traits may contribute to the observed findings. As supported by previous research, women generally exhibit higher insulin sensitivity, greater subcutaneous fat accumulation, and lower visceral adiposity compared to men during their reproductive years. These factors may attenuate the association between METS-IR and OSA risk in females. In contrast, men are more prone to visceral fat accumulation, insulin resistance, and metabolic dysfunction, which may strengthen the predictive utility of METS-IR in this group.[4] We fully agree that future studies should further explore these sex-based physiological differences, including the roles of sex hormones, fat distribution, and tissue-specific insulin sensitivity, to better understand their impact on OSA and metabolic risk stratification.

Finally, we would like to thank Professor Shan and Professor Li for their valuable suggestions, which are very instructive for our future research design.

Author Contribution

Beini Zhou and Yan Yao: Conceptualization, Writing - original draft. Yuhan Wang, Wuriliga Yue, Jingyi Zhang, Yang He, Qingfeng Zhang, Yixuan Wang: Conceptualization, Writing - review & editing. Ke Hu: Supervision, Writing - review & editing. All authors have reviewed and agreed on the journal to which the article will be submitted. They have contributed to and approved all versions of the article before submission, during revision, the final version accepted for publication, and any significant changes introduced at the proofing stage. All authors have agreed to take responsibility and be accountable for the contents of the article.

Disclosure

The authors declare no conflicts of interest in this communication.

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