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Letter to the Editor

LETTER TO THE EDITOR

Response to "Does renal function decline slower in those with sleep apnea?"

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Dear Editor,

We read with great interest the letter to the editor by Kuo *et al.* in reference to our article entitled "Sleep Apnea and Kidney Function Trajectory: Results From a 20-Year Longitudinal Study of Healthy Middle-Aged Adults" [1]. Kuo *et al.* note the discordance of our findings from other studies of sleep apnea (SA) and kidney function decline. In our retrospective study of middle-aged men and women unselected for sleep disorders, we found that SA assessed by polysomnography was *not* associated with accelerated decline in renal function, after adjustment for confounding variables. Kuo *et al.* expressed concern that the use of renin-angiotensin-aldosterone system (RAAS) blocker medication was greater among those with SA in our cohort. Because RAAS blockade may slow decline of renal function, the use of RAAS blockade may be responsible for the slower decline of renal function among those with SA in our cohort [2]. Indeed, we considered this in our original analyses, as noted in our Results section under "Sleep Apnea and Kidney Function Trajectory" paragraph 3. We will reiterate our findings here. First, we adjusted for any use of RAAS blockade at baseline or during the follow-up period and found that for both outcomes of annualized eGFR decline and odds of rapid eGFR decline, the point estimates did not change from the main analyses (Table 1). We went a step further to exclude those who ever used RAAS blockade (n = 52 or 6% of our cohort) and, again, the point estimate was not meaningfully changed (Table 1). In addition, as in the main analyses, there was no difference in time to development of chronic kidney disease between those with and without SA after excluding those with RAAS blockade (p = 0.71 for log-rank test, data not shown). Thus, our findings suggest that greater use of RAAS blockade among those with SA in our cohort did not explain the slower eGFR decline observed among those with SA.

Kuo *et al.* also present data from a meta-analysis they performed as part of their Letter to the Editor compiling data from three other population-based studies plus our study to suggest that even with our findings, current literature favors a positive association between sleep apnea and renal function decline [3–5]. However, the results of Kuo *et al.*'s meta-analysis should be viewed cautiously, given that two of the three studies they include are cross-sectional studies while our study and that of Jaussent *et al.* are longitudinal studies. As such, interpretation of combined point estimates from these studies is difficult to interpret. Furthermore, not all included studies included presented SA as the predictor of renal function as it was presented in our article [3]. For example, the study by Canales *et al.* presented renal function as the predictor with SA as the outcome [3]. Finally, we note that the three studies added to our data for this meta-analysis do not represent the entirety of population-based estimates of the association between SA and renal function in the literature [6].

To summarize, we found that in our cohort study of middle-aged healthy men and women unselected for sleep disorders or renal disease, SA was not associated with the accelerated decline of renal function after adjusting for multiple factors that may confound this association, including RAAS blockade. In our article, we discuss several possible explanations for the divergence

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Table 1. Estimated annualized change in eGFR and odds of rapid decline as defined as lowest decile (10%ile, >2.2 mL min^{-1} 1.73 m^{-2} $year^{-1}$) in annualized change in eGFR by baseline sleep apnea (AHI ≥ 15) status

	beta: mL min^{-1} 1.73 m^{-2} $year^{-1}$ (SE) [95% CI]			Odds ratio (95% CI)		
Sleep apnea category	Unadjusted	Age, sex, BMI, diabetes*, HTN*, baseline eGFR, RAAS* blockade-adjusted	Excluding RAAS blockade users†: age, sex, BMI, diabetes*, HTN*, baseline eGFR-adjusted	Unadjusted	Age, sex, BMI, diabetes*, HTN*, baseline eGFR, RAAS* blockade-adjusted	Excluding RAAS blockade users†: age, sex, BMI, diabetes*, HTN*, baseline eGFR-adjusted
No sleep apnea N = 765†	0.0 (referent)	0.0 (referent)	0.0 (referent)	1.0 (referent)	1.0 (referent)	1.0 (referent)
Sleep apnea N = 90†	0.20 (0.13) [–0.06 to 0.45]	0.24 (0.13) [–0.01 to 0.50]	0.30 (0.13) [0.11 to 0.69]	0.86 (0.40 to 1.84)	0.65 (0.28 to 1.51)	0.65 (0.25 to 1.68)
p	0.14	0.06	0.02	0.70	0.31	0.37

eGFR, estimated glomerular filtration rate; PAP, positive airway pressure; BMI, body-mass index, HTN, hypertension; RAAS, renin-angiotensin-aldosterone system.
*Reflect ever diagnosis or use during the follow-up period.
†Total sample after excluding RAAS blockade users = 803, *n* = 724 without sleep apnea, and *n* = 79 with sleep apnea.

of our results from published literature and refer the reader to that discussion. Ultimately, we agree with Kuo *et al*. that, given conflicting data from the literature on this topic, the question of SA as a promoter of renal injury requires further study.

Conflict of interest statement. None declared.

References

1. Canales MT, *et al*. Sleep apnea and kidney function trajectory: results from a 20-year longitudinal study of healthy middle-aged adults. *Sleep*. 2018;**41**(1): 1–8. doi:10.1093/sleep/zsx181
2. Jafar TH, *et al*.; AIPRD Study Group. Progression of chronic kidney disease: the role of blood pressure control, proteinuria, and angiotensin-converting enzyme inhibition: a patient-level meta-analysis. *Ann Intern Med*. 2003;**139**(4):244–252.
3. Canales MT, *et al*.; Osteoporotic Fractures in Men (MrOS) Study Group. Reduced renal function and sleep-disordered breathing in community-dwelling elderly men. *Sleep Med*. 2008;**9**(6):637–645.
4. Adams RJ, *et al*. Chronic kidney disease and sleep apnea association of kidney disease with obstructive sleep apnea in a population study of men. *Sleep*. 2017;**40**(1): 1–9. doi:10.1093/sleep/zsw015
5. Jaussent I, *et al*. Impact of sleep disturbances on kidney function decline in the elderly. *Eur Respir J*. 2016;**47**(3):860–868.
6. Ogna A, *et al*. Sleep characteristics in early stages of chronic kidney disease in the hypnolaus cohort. *Sleep*. 2016;**39**(4):945–953.