Letter to the Editor

Comment to the Editorial by KS Park and EW Kang "Is only fixed positive airway pressure a robust tool for kidney protection in patients with obstructive sleep apnea?"

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We thank doctors Park and Kang for their editorial that well summarized our article. Our common belief is that one of the possible consequences of untreated obstructive sleep apnea (OSA) is an accelerated deterioration of kidney function, and that more knowledge would be necessary on the possible protective effects of OSA treatments (1,2).

To our knowledge, so far the only OSA therapy whose effects on renal function have been tested is continuous positive airway pressure (CPAP), and most (3-6), although not all studies (7), have demonstrated its benefits. Our own study, while confirming benefits of fixed CPAP, has demonstrated little effect of auto-adjusting CPAP (APAP) (2). This finding may be of relevance as, at present, OSA treatment by APAP is largely used. Then, should we ban APAP as a therapeutic modality for patients with renal problems?

Most studies comparing fixed CPAP and APAP have focused on correction of respiratory events during sleep, relief of sleepiness, tolerability and patients' compliance in subjects with typical pure OSA (8). In fact, APAP devices have been designed as treatment tools for this subgroup of patients, and not for patients with comorbid OSA with other types of respiratory disorders. Accordingly,

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current guidelines do not recommend APAP therapy for OSA patients with comorbidities like chronic obstructive pulmonary disease (COPD) or congestive heart failure (9) although, more recently, small studies have been published suggesting effectiveness of APAP in patients with both OSA and COPD (overlap syndrome) (10,11). Other diseases are not specifically mentioned in guidelines as contraindications to APAP. However, efficacy of OSA treatment should not be evaluated just in terms of polysomnographic parameters or symptoms, but also for its ability to prevent or counteract OSA deleterious effects on various organs and functions. In that respect, many studies have been published about effects of CPAP treatment, but few of them compared effects of fixed CPAP and APAP. We are aware of some studies comparing effects of these treatment modalities on blood pressure, autonomic activity or insulin resistance (12-17). Most of them showed superiority of fixed CPAP but, altogether, they are few, and more data would be required. Inflammatory activation and enhanced renin aldosterone angiotensin system activity in OSA may contribute to accelerate the age-related decline in estimated glomerular filtration rate (eGFR). Several, although not all, studies suggested beneficial effects of CPAP treatment on those factors (18-22), but to our knowledge possible differential effects of fixed CPAP and APAP have not been investigated, and could account for a different evolution of renal function in patients treated by each CPAP modality. Investigations should be extended to effects of APAP devices working with different algorithms. Besides, effects of setting different pressure ranges on the APAP machines, implying different degrees of variability of the administered pressure, should be tested.

Although changes in eGFR over time differed significantly between our patients treated by fixed CPAP and APAP, standard deviations of changes were large in both groups (2). This finding suggests that the rate of eGFR decline may show high interindividual variability in treated OSA patients. What could make an OSA patient more susceptible to renal injury is not entirely clear. One longitudinal study showed that spending ≥12% of sleep time with an oxygen saturation <90% was associated with a faster eGFR decline (23). In a cross-sectional analysis, we previously found an association between the lowest oxygen saturation during sleep and eGFR <60 mL/min/1.73m^2 (24). However, in subsequent longitudinal analysis, we found that untreated patients with mild OSA had a worse eGFR evolution than treated patients with moderate to severe OSA, suggesting that even mild respiratory disorders could exert detrimental effects on the kidney (2). The role of sleep fragmentation on kidney function is poorly known. Actigraphic measurements suggested that it may be associated with kidney disease (25,26), but there are no polysomnography-based data yet. Usefulness of some molecules as possible biomarkers for kidney injury in OSA is currently under study (27,28).

In conclusion, we believe that in OSA patients with, or at risk of, chronic kidney disease, APAP should not be used as a first choice for treatment. More data are necessary to better identify risk factors for kidney disease and predictors of unfavourable eGFR evolution in OSA. Future research should be addressed to better clarify mechanisms by which OSA may harm the kidneys and understand why APAP may be less protective from kidney dysfunction than fixed CPAP. Until then, preference for OSA treatment should be given to fixed CPAP.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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