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COMMENTARY

Can Poor Sleep Cause Kidney Disease? Another Step Closer to the Answer

Commentary on Bo et al. Sleep and the risk of chronic kidney disease: a cohort study. *J Clin Sleep Med.* 2019;15(3):393–400.

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Inflammatory mediators and sympathetic overtone contribute to the development of cardiovascular and renovascular disorders.[1,2] Obstructive sleep apnea, circadian rhythm disorders, hypersomnia, and insomnia have been linked to a multitude of metabolic disturbances. A growing body of evidence suggests that sleep disturbances affect the development of kidney disease, possibly as a result of the inflammatory milieu and sympathetic activation occurring at the renal vascular bed that damage the glomerular basement membrane and the kidney tubular apparatus.[3–6] Most current evidence linking kidney disease and sleep disorders has originated from small epidemiological studies. A previous study by Choi et al. linked longer sleep duration to the development of chronic kidney disease (CKD) in Korean women but findings were not replicated in men.[7] Yamamoto et al. found a U-shaped relationship between sleep duration and progression of CKD to end stage renal disease (ESRD), with individuals sleeping less than 5 hours and over 8 hours at greatest risk for disease progression. This study also revealed that poor sleep quality was associated with the incidence of ESRD.[8] A meta-analysis suggested an association between short sleep duration and proteinuria, a surrogate marker of kidney disease progression.[9] Renal hyperfiltration, a marker of early renal damage, has been linked to short (less than 6 hours) and long (more than 10 hours) sleep duration.[10,11]

A study by Bo et al. in this issue of the *Journal of Clinical Sleep Medicine* adds to the existing body of evidence linking poor sleep quality and the development of CKD.[12] This appears to be the largest epidemiological study of its kind. The development of kidney disease was analyzed in almost 200,000 patients (after excluding preexisting CKD or proteinuria as well as metabolic risk factors such as hypertension, diabetes, cardiovascular disease and cancer). Short sleep and long sleep duration as well as poor sleep quality were associated with the incident development of CKD. CKD was defined using the modification of diet in renal disease (MDRD) study equation. Despite some limitations outlined below, the study has important global health implications and once again emphasizes the importance of good quality and quantity of sleep to overall health. Another important observation is the link of insomnia and/or the use of sedative agents with the development of CKD.

The study population was Asian and mostly well-educated and non-smoking. It is unknown whether the findings of the study carry equally across other populations. Most previous evidence linking sleep and CKD also comes from studies in Asian populations.[7,8,10] Some potential study pitfalls were related to the definition of CKD and the use of a nonvalidated sleep questionnaire. The MDRD calculations used in this study have shown inaccuracy when applied to a Taiwanese population and the MDRDc (MDRD for Chinese) is favored as a more accurate calculation.[13] It is possible that some of the problems with calculation of eGFR and the overestimation and later exclusion of study subjects could have been avoided if additional correction had been performed for the Asian population. Lack of accounting for some of these subjects is of further concern, since glomerular hyperfiltration has been linked to eventual progression of kidney disease and it has been linked to sleep disturbances in prior studies.[10] Furthermore, it would have been appropriate to have serial measurements confirming the existence of CKD instead of a single value with eGFR under 60 mL/min/1.73m^2. As a result, some patients would have had the development of reversible acute kidney injury at the time that laboratory measurements were taken, and these could have been potentially excluded with subsequent measurements.

Sleep quality and quantity were obtained through questionnaires, which is characteristic of a study of this size. The patients were not screened for sleep-disordered breathing, which is a drawback, given the high body of evidence linking obstructive sleep apnea and the development of cardiovascular disease, including renovascular hypertension, diabetes, and progression of CKD.[14–19] The authors used a nonvalidated questionnaire that generated a scale of sleep quality. This presents bias since its validity is unknown and some of the measurements reported may not be additive. It is hard to assign a number to a particular sleep problem and compare it with another, much less compare it between patients. The Epworth Sleepiness Scale, for example, is very good in tracking any given patient over time or patient populations but may become problematic when comparing individual patients.[20]

Benjamin Franklin said, "an ounce of prevention is worth a pound of cure."[21] Health campaigns with widespread ramifications should be a priority for society. This study offers us the hope that if we improve sleep quantity and quality, we can have an impact on the development of CKD. More work needs to be done in the field to validate these findings as identification and treatment of sleep disorders becomes a priority and the natural history of renal disease is better defined.

CITATION

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