Healthy Sleep for Healthy Kidneys—It Takes a Village

Affecting nearly 700 million people globally, chronic kidney disease (CKD) contributes substantially to disability and reduced survival, with more than 1.2 million directly attributable deaths worldwide in 2017. With cardiovascular disease being a major and often fatal complication of CKD, mortality more than doubles when cardiovascular deaths due to impaired renal function are included. Symptom burden, reduced quality of life, and increased health care expenditures add to the burden of CKD on individuals and societies. To mitigate the significant public health hazard posed by CKD, it is thus critical to concentrate efforts on population-level strategies to preserve kidney function and to slow or to prevent progression of renal disease, which includes identification of renoprotective factors.

Preemptive recommendations focus largely on management of canonical risk factors, such as obesity, hypertension, and diabetes, and encourage behavioral modifications to promote healthy lifestyles, targeting primarily diet and physical activity. However, among the nontraditional indicators of risk for CKD, the significance of sleep is becoming increasingly apparent.

Sleep disturbances are commonplace and have dramatic consequences on health, including on renal function. Disorders such as sleep disordered breathing and insomnia have been linked to accelerated decline in renal function and greater risk of CKD in cross-sectional and longitudinal studies. Sleep difficulties are associated with higher comorbidity burden in patients with CKD and may precipitate cardiovascular events in this population. Evidence is similar for sleep duration, whether excessively short or long, thus highlighting the impact of sleep on renal function.

Geng et al, in the current issue of Mayo Clinic Proceedings, provide an important and novel contribution to the implications of sleep for risk of CKD. Leveraging the UK Biobank data set, the authors developed a composite index for healthy sleep. Five components, or sleep behaviors, were identified from self-reported information at baseline, namely, snoring, insomnia, excessive daytime sleepiness, sleep duration, and chronotype. One point was assigned for each low-risk sleep behavior (defined as no snoring, no frequent excessive daytime sleepiness, no frequent insomnia, sleep duration of 7 to 8 h/d, and morning chronotype), thus yielding a total score ranging from 0 to 5, with higher scores indicating a healthier sleep profile. After exclusion of those with a prior diagnosis of CKD at study entry, Geng et al evaluated incidence of CKD and CKD deaths during a median follow-up of 11 years. In analysis adjusted for demographic, lifestyle, and clinical covariates (including estimated glomerular filtration rate at baseline), an inverse association between healthy sleep score and incident CKD was apparent, with hazard ratios for CKD being progressively lower with increasing scores (namely, healthier sleep patterns). The association was manifest across age, sex, body mass index, smoking status, physical activity, prevalent hypertension, and diabetes strata, although it was interestingly stronger among those 60 years of age or younger and among those without hypertension at baseline. This may be because aging and hypertension are strong predictors of renal dysfunction, thus masking any renoprotective effects of high-quality sleep.

Several aspects of this work deserve further discussion. The traditional approach to the evaluation of sleep in the setting of health outcomes focuses on individual

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characteristics, or specific sleep disorders, as isolated entities. The prognostic power associated with this approach is limited because unhealthy sleep behaviors and sleep symptoms often cluster, yielding additive or even synergistic effects. Furthermore, aside from specific sleep diagnoses, it is increasingly recognized that sleep is a multidimensional construct, with a breadth of characteristics such as duration, efficiency, timing, and regularity of sleep, to name a few, that are cardinal to its integrity. It follows that perturbations in 1 or more dimensions compromise sleep health, causing downstream repercussions for psychological and physical well-being. By devising a composite sleep health score including multiple sleep domains, Geng et al validate the multifaceted nature of sleep health in the context of CKD, with corroborating results. The composite index did indeed convey superior prognostic insights compared with its individual components in multivariable analysis. Cumulative effects were further evidenced by their findings that are indicative of a dose-dependent relation between sleep score and future CKD, with the lowest risk exhibited by those who reported low-risk sleep behaviors in all 5 domains. These data give strength to the ongoing paradigm shift toward addressing sleep within a multidimensional, integrative framework and provide further rationale for interventions directed at improving sleep to ameliorate CKD risk. As impaired sleep is a modifiable risk factor, health promotion strategies not only targeting clinical sleep disturbances but designed to optimize multiple sleep components to maintain or to restore sleep health may provide substantial prognostic advantages, at both the individual and the population levels.

Another innovative aspect of the integrative approach to sleep health adopted by Geng et al is the inclusion of chronotype information in the sleep health index. Chronotype is an expression of personal preferences for time of the day to partake in activities, including sleep, and is typically dichotomized into morning type (“larks,” in lay terms) or evening type (“owls”), although an “intermediate” phenotype also exists. Thought to reflect an individual’s circadian rhythm, the implications of chronotype have been studied in relation to disease risk, and evidence favoring a protective role of morningness for a variety of health outcomes has emerged, including for known cardiometabolic precursors of CKD. Geng et al add to this body of literature first by showing that morning chronotype is independently, albeit modestly, associated with lower risk of CKD, and second by promoting the integration of an indicator of circadian rhythm, namely, chronotype, into an overall index of sleep assessment. Given the prominent role of circadian rhythmicity in regulating sleep behaviors, inclusion of this important information provides for a more comprehensive and hence more relevant sleep health index.

These findings were generated harnessing the resources of the UK Biobank, a very large, prospective cohort study with in-depth assessment of participants’ biological and environmental characteristics and extended follow-up for monitoring of health outcomes. Despite these unquestionable strengths, the population of the UK Biobank is somewhat limited in terms of racial and ethnic diversity. More than 90% of the sample consists of individuals of White descent, raising the question of the generalizability of findings to different ethnic/racial groups. This is of particular relevance to the analysis by Geng et al because of the striking ethnic/racial disparities in both sleep disturbances and CKD risk. Marked inequalities exist in risk factors, diagnosis, incidence, progression, therapy, and outcomes of renal disease. Similarly, despite their greater risk for disordered and insufficient sleep, sleep problems remain underrecognized and undertreated in minorities. Geng et al have provided evidence strongly supportive of a beneficial impact of multidimensional sleep health for kidney function, thus favoring the construct that sleep promotion strategies may help mitigate onset, progression, and complications of CKD. Given the disparities
in disease burden, whether optimal sleep habits carry a comparable protective effect on renal function in racial and ethnic minorities is unknown and warrants investigation. An important corollary to this question is whether and to what degree the greater prevalence of disrupted sleep in African Americans and other minorities may be contributing to their greater vulnerability to renal impairment.

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Potential Competing Interests: Dr Somers has served as a consultant for Baker Tilly, Respica, Bayer, and Jazz Pharmaceuticals and is on the Scientific Advisory Board for Sleep Number Corporation. Dr Covassin and Dr Li report no competing interests.

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REFERENCES