

## It Happened While You Were Sleeping

L. Kristin Newby, MD, MHS

Predicting short- and long-term risk for adverse outcomes after an acute coronary syndrome (ACS; ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction, and unstable angina) has been the focus of numerous modeling efforts over many years. Nevertheless, risk models can reflect only the variables that were systematically available in the population databases used to derive the models. The most widely used models for risk stratification of ACS patients in clinical practice today are limited to a handful of clinical and laboratory data routinely available in the context of clinical care. As we enter the “big data era,” the numbers, types, and availability and novelty of descriptive variables for any given population will expand rapidly through multiple sources (eg, electronic health records, social media, geospatial information systems, and continuous monitoring via wearable devices). As new bioinformatics and analysis methods evolve to integrate this increasing volume and variety of data, the potential exists to inform the components of risk models in both expected and unexpected ways and, perhaps, to suggest new targets for intervention to mitigate risk.

The pathophysiology of sleep disturbances and the importance of information gathered while we are sleeping are dimensions of cardiovascular risk that have been explored<sup>1,2</sup> but not fully appreciated or integrated into risk assessment previously. In this issue of the *Journal of the American Heart Association*, Mazaki and colleagues expanded what is known of the relationship between sleep-disordered breathing and adverse cardiovascular outcomes to long-term follow-up

(median 5.6 yr) of patients with ACS.<sup>3</sup> Among 257 consecutive post-ACS patients who were treated with percutaneous coronary intervention at a single center in Japan, 241 had full data from an overnight sleep study conducted within 1 week of the index ACS event. Interestingly, more than half (52%) of this population had sleep-disordered breathing (defined as an apnea–hypopnea index of  $\geq 5$  events per hour of apnea [at least 10 seconds] or oxygen desaturation [at least 4%]). Using this definition, sleep-disordered breathing was associated with a significant increase in death, recurrence of ACS, nonfatal stroke, and hospital admission for congestive heart failure in multivariable modeling (hazard ratio 2.28, 95% CI 1.06–4.92). Despite the limited number of events available for modeling, these observations were consistent using a number of statistical approaches and sensitivity analyses, including multivariable modeling in a propensity score–matched cohort and incorporating the apnea–hypopnea index as a continuous variable.

Because sleep-disordered breathing is potentially treatable, and given the high prevalence of sleep-disordered breathing observed among ACS patients, the findings of the study by Mizaki et al are not simply of academic interest. In this regard, however, their study did not distinguish obstructive sleep apnea from central sleep apnea, which may have different relationships with outcomes and necessitate different modes of treatment. Furthermore, the presence of clinical heart failure was not reported, but the mean left ventricular ejection fraction in the group with sleep-disordered breathing was  $53 \pm 10\%$ . Consequently, although the majority of patients had a normal left ventricular ejection fraction, 15% to 20% of patients had a left ventricular ejection fraction  $\leq 45\%$ ; treatment with continuous positive airway pressure has not been shown to be effective in this group, and adaptive servoventilation may be harmful.<sup>4,5</sup> In the Treatment of Sleep Disordered Breathing with Predominant Central Sleep Apnea by Adaptive Servo Ventilation in Patients with Heart Failure (SERVE-HF) trial, compared with no treatment, the use of adaptive servoventilation resulted in an increase in all-cause mortality (hazard ratio 1.28, 95% CI 1.06–1.55) and cardiovascular mortality (hazard ratio 1.34, 95% CI 1.09–1.65) among symptomatic patients with chronic heart failure (left

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From the Division of Cardiology, Department of Medicine and Duke Clinical Research Institute, Duke University Medical Center, Durham, NC.

**Correspondence to:** L. Kristin Newby, MD, MHS, P.O. Box 17969, Durham, NC 27715-7969. E-mail: kristin.newby@duke.edu

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ventricular ejection fraction  $\leq 45\%$ ) and sleep-disordered breathing (mean apnea–hypopnea index of 6.6 events per hour). The Cardiovascular Improvements with Minute Ventilation-targeted Adaptive Sero-Ventilation [ASV] Therapy in Heart Failure (CAT-HF) trial,<sup>6</sup> which was stopped early after the results of the SERVE-HF trial results were presented, included patients with both reduced and preserved left ventricular ejection fraction with central, obstructive, or mixed sleep apnea and may provide additional insights into the risks and benefits of treatment of sleep-disordered breathing in cardiovascular patients. Ultimately, the effect of intervention to treat sleep-disordered breathing to mitigate this risk of adverse outcomes after ACS would need to be demonstrated in randomized clinical trials and may depend on the subclass of sleep-disordered breathing, comorbidities, and treatment approach.

Perhaps equally important, there has been a proliferation of wearable devices that simply and relatively inexpensively obtain physiological variables continuously (eg, heart rate and oxygen saturation) and determine sleep/wake time, time spent in rapid eye movement, and light and deep sleep and deliver this information to smartphone “apps” or study databases. These devices promise to greatly accelerate our understanding of the physiology of sleep and the relationships of sleep disturbances of many etiologies with health outcomes and quality of life. Evolution of technology and data science has given us an exciting opportunity to understand, at an individual level and at a population scale, what happened while we were sleeping.

## Disclosures

Dr Newby reports no conflicts of interests related to the content of this editorial. All of her relationships with industry are available at <https://www.dcri.org/about-us/conflict-of-interest>.

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