Sleep-Disordered Breathing
A Heart-Changing Experience?

Increasingly, sleep-disordered breathing (SDB) is recognized as an important risk factor for coronary atherosclerosis and heart disease. Several large epidemiologic studies have demonstrated that SDB increases the risk of heart disease by approximately twofold to fourfold, independent of other risk factors. While the exact mechanisms responsible for this association are largely unknown, there is credible evidence to indicate SDB can increase systemic BP and sympathetic drive. It may also elevate circulating levels of fibrinogen and C-reactive protein, triggering a cascade of events that eventually leads to thrombus formation in the coronary vasculature. Treatment of SDB, usually with continuous positive airway pressure, leads to significant improvements in these physiologic parameters.

Despite these data, there are still major gaps in knowledge. In this issue of CHEST (see page 936), Hayashi and coworkers present intriguing new information that provides additional support for the role of SDB in the pathogenesis of atherosclerosis. They performed nocturnal pulse oximetry on 59 consecutive patients with coronary artery disease who were admitted to the hospital for coronary angiography. They found that patients with an elevated nocturnal oxygen desaturation index (ODI) had a higher clot burden than those with a normal ODI. More importantly, they observed this relationship to be “dose dependent,” such that those with the highest ODI had the largest clot burden while those with the lowest ODI had the lowest clot burden. Traditional risk factors such as hyperlipidemia and hypertension contributed very little to the model, after adjustments for ODI. Indeed, in their analysis, ODI by itself explained 13% of the variations in the Gensini score (p = 0.005), suggesting that events leading to nocturnal oxyhemoglobin desaturation are powerfully related to atherosclerosis. This carefully conducted epidemiologic study, therefore, suggests a “biological” gradient between severity of SDB and atherosclerotic burden among individuals with heart disease. This work adds to a growing body of literature supporting a causal link between SDB and ischemic heart disease.

The work by Hayashi and coworkers, however, raises some important questions; they used ODI to detect SDB, which assumed that apneas and hypopneas during sleep were responsible for the dips in oxyhemoglobin saturation in their cohort. However, the concordance between ODI and apnea-hypopnea indexes (AHIs) is far from perfect. In one report, ODI had a sensitivity of only 51% and a specificity of 90% in identifying patients with SDB (defined by an AHI of ≥ 15 on polysomnography). In another study, the sensitivity was < 50%, and the correlation coefficient between AHI and ODI was only 0.58, indicating only a modest association. In other studies ODIs have been demonstrated to have moderate-to-high sensitivity but poor specificity in identifying patients with sleep apnea. False-positive

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findings were especially prominent among individuals with airflow obstruction.13

Given the suboptimal concordance between ODI and AHI, there is some uncertainty as to whether the patients with elevated ODI in the study by Hayashi and coworkers had obstructive sleep apnea. This doubt is further fueled by the observation that most of these patients were elderly and had normal or near-normal body mass indexes. Although individuals with normal body weight can acquire obstructive sleep apnea, it would be extremely unusual (and, indeed, unlikely) that obstructive sleep apnea would be found in >70% of nonobese patients, as reported by Hayashi and coworkers.

Could some of the patients with elevated ODI in the study by Hayashi and coworkers have had central sleep apnea or Cheyne-Stokes respiration (CSA-CSR)? CSA-CSR has been reported to be common in patients with ischemic heart disease but, in most cases, such patients have evidence of left ventricular systolic dysfunction.14 In the study by Hayashi and coworkers, the patients had well-preserved left ventricular systolic function. Moreover, they only had a modest elevation in brain natriuretic peptide levels, making it unlikely that these patients had CSA-CSR.

In the study by Hayashi and coworkers, over half of the patients were current or former smokers. The average cigarette exposure time per patient was 23 to 27 pack-years, raising the possibility that some patients may have had impairments in lung function from obstructive airways disease. Although patients had normal daytime oxyhemoglobin saturation, this by no means precludes the possibility of subclinical obstructive airways disease. Patients with reduced lung function may have normal oxyhemoglobin saturations during wakefulness, but nocturnally they may experience significant dips in their oxyhemoglobin saturation even in the absence of discernible upper airway obstruction.15 Importantly, there are strong epidemiologic data to indicate that reduced lung function increases the risk of coronary atherosclerosis and heart disease by twofold to threefold.16

Notwithstanding these concerns, the work of Hayashi and coworkers represents a major step forward in our understanding of the relationship between respiratory events during sleep and atherosclerosis. A severity-dependent association between ODI and clot burden provides further evidence of a causal link between SDB and ischemic heart disease; however, future work is needed to better define the factors responsible for nocturnal oxyhemoglobin desaturations in ischemic heart disease. In this sense, polysomnographic and spirometric data would be very helpful in further strengthening the notion that SDB is, indeed, a “heart-changing” experience.

Don D. Sin, MD, FCCP
Edmonton, AB, Canada

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Correspondence to: Don D. Sin, MD, FCCP, 2E4.29 Walter C. Mackenzie Centre, University of Alberta, Edmonton, AB, Canada T6G 2B7; e-mail: don.sin@ualberta.ca

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Collateral Damage
The Effects of Obstructive Sleep Apnea on Bed Partners

While health-related problems have a definite and identifiable effect on patients, the patients’ families are also very much affected. This may reach such a level of intensity that the patient will present to a physician because their family desires that they be evaluated and treated. Most clinicians would agree that sleep apnea is one of those conditions that stimulates familial assertion. The dynamics and repercussions of these encounters on the doctor-patient relationship and the doctor-family relationship may be staggering. The willingness and compliance of a patient with treatment may be a result of familial coercion.

The effect of medical illness on families has been studied in a wide variety of diseases, varying from pediatric cancers to mental illness. Quality-of-life scales and indexes also have been developed but have focused mainly on the patients. Five different categories of measurement can be performed. Measures can be generic, disease-specific, population-specific, dimension-specific, or of utility.1 One such generic scale is the short form-36 (SF-36). This 10-min general health survey looks at the patient’s self-report of the physical and mental distress of having a specific medical illness. The physical component examines physical functioning, role-physical (accomplishment), bodily pain, and general health. The mental component examines vitality (energy), social functioning, role-emotional (accomplishment), and mental health. The reliability and validity of this scale for patients to compare the effect of interventions has been confirmed.1,2 The benefit of using such a generic scale, is that the effect of an illness on a patient can be compared against the effect that other diseases have on patients and against national normative values.

A population-specific scale that also can be used for patients with daytime sleepiness, including those with obstructive sleep apnea, is the Epworth sleepiness scale. This is an eight-item questionnaire that asks patients to rank their drowsiness and likeliness to fall asleep in different routine situations (for example, while watching television). While the utility of this scale as a subjective assessment of daytime sleepiness has been established, it has not correlated well with objective measurements.3,4 Our current objective measurements of sleepiness may, however, benefit from adjustment.5 Finally, a disease-specific scale has been created to assess patients with sleep-disordered breathing. The Calgary sleep apnea quality of life index (SAQLI) was designed at the University of Calgary in 1997. It was based on one-on-one interviews with 40 sleep apnea patients who were asked about the effect of sleep apnea on their life. Specific problems were identified, and were ranked by frequency and importance.6

When the SAQLI was distributed to 100 sleep apnea patients, patients were able to express their frustration and concerns about having sleep apnea. Many complained of a lack of energy and the need to force themselves to accomplish daily routine tasks. There were similar concerns about how bothersome their snoring was to their bed partner. Feelings of depression also surfaced. These complaints then were organized into the following four domains: role functioning; social interactions; emotional functioning; and symptoms.6 The measurement of the specific effect of sleep apnea and its treatment on the bed partners of patients with sleep apnea is the focus of an article in this issue of CHEST (see page 942) by Parish and Lyng from the Mayo Clinic in Scottsdale, AZ. In this article, while there was significant drop-out from the lack of tolerance for treatment with continuous positive airway pressure (CPAP), 54 patients and their bed partners were studied via questionnaires before and after 6 weeks of unmonitored CPAP treatment. The instruments used included the SF-36, the Epworth sleepiness scale, and the Calgary SAQLI. While none of these instruments are designed for the evaluation of the bed partners of sleep apnea patients, they still provide some measure of daytime symptoms and general health.

Previous studies have examined the quality of sleep of bed partners, but this study is novel in that it evaluates daytime functioning and general health. Furthermore, it shows improvement in both with treatment. One of the first published articles looking specifically at how bed partners were affected by patients with sleep apnea was published by Beninati et al7 from the Mayo Clinic. Beninati and colleagues studied 10 married couples with one partner suspected of having sleep apnea due to snoring. Both partners underwent simultaneous sleep studies, with the partner with sleep apnea receiving a split study with CPAP titration during the second portion of the night. Patients in this study had an average apnea-