SECOND OPINION

Who is Mr. Z?

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In daily practice we deal both with very symptomatic obstructive sleep apnea syndrome (OSAS) patients who come to our labs because they fall asleep in unwanted situations (e.g., at the wheel) at or embarrassing moments (e.g., at the cinema, in a meeting), as well as with patients who deny any symptoms, but reluctantly acquiesce to their partner who is alarmed by the respiratory pauses and excessive movements during sleep—or simply can no longer bear the annoying sound of someone snoring and snorting all night long. It is not unusual that these two types of patients share a similar number of apneas/hypopneas per night. This apnea/hypopnea index, however, provides only a hazy insight into the complex universe of OSAS. While convenient for practical purposes [i.e., a threshold for continuous positive airway pressure (CPAP) reimbursement], the index is but a pale mirror of the full clinical picture.

A recent article by Byxler et al (Am. J. Respir. Crit. Care Med. 1998; 157:144–148) suggests that this index should be considered differently depending on the age of the patient. These authors suggest that in men there exist two types of obstructive events that can occur at different ages: one is age dependent and increases monotonically with age, often becoming apparent only in the seventh decade and representing a lower risk for health. The second obstructive event is age related, peaks around the age of 55, and is accountable for the type of sleep apnea treated in a typical sleep-disorders clinic. When the authors extrapolated data from patients with apnea plus hypopnea index (AHI) $\geq$10 plus daytime sleepiness, hypertension or other cardiovascular complication, they found that the prevalence of these patients changed with age in a quadratic fashion, increasing from over 1% in the youngest age group, to almost 5% in the middle age group, then returning to less than 2% in the oldest subjects. The severity of desaturations caused by respiratory events changed as well; young patients with AHI > 20 had lower desaturations than older patients with a comparable number of events. In the cases with milder disease (i.e., AHI = 5), older patients had lower SaO_2. In other words, there is a slow increase of respiratory events with age associated with a mild decrease of SaO_2, which is consistent with the physiological decrease of PaO_2 with age. Overlapping this trend is a second type of obstructive event that usually climaxes around the sixth decade, causing deeper desaturations and probably causing a greater health threat than the first type. Why do these events decrease after 55 years of age? Instinctively, I would say it is because patients die before entering their sixties. Retrospective data on Stanford patients described by He et al ten years ago demonstrated that in the group younger than 50 years of age, the survival of OSAS patients was significantly lower after 2 years, while in older patients a period of 8 years was necessary to gain statistical significance. Is there more than a causal link between these two observations?

The OSAS patients we deal with in everyday practice exhibit nocturnal trends marked by cyclical blood pressure rises and sleep disruption caused by apneas associated with deep desaturations. Overweight, often smokers, with diabetes, cardiac ischemia or daytime hypertension, these patients usually have a whole host of potentially fatal conditions, and the respiratory events following one another nightly could simply be "the straw that breaks the camel's back." Nevertheless, only a small percentage of these patients suffer the most severe consequences from nocturnal events.

"Syndrome X," a quartet of risk factors (systemic hypertension, insulin resistance, dyslipidemia, central obesity), posing a real threat of cardiovascular complications, is a paradigmatic example of the whole combined risk being greater than the sum of its individual parts. Ian Wilcox et al (Thorax 1998; 53: S25–8) recently proposed adding OSA to this cluster and coining a new term: "Syndrome Z." Obstructive events can influence each of the other factors, adding a further cardiovascular risk. In spite of the controversial results of studies on the association of hypertension with OSAS, there is little doubt that the rise in blood pressure during obstructive events, the surge in neural traffic recorded in peripheral sympathetic nerves, and the higher variability of blood pressure at least during sleep (a factor commonly considered a risk for cardiovascular events) leads to the development of more severe consequences than hypertension alone, at least in some patients. Central obesity is related to both neck circumference (a well known risk factor for OSA) and insulin resistance, but when data on insulin resistance in obese patients are normalized for age, sex, and weight, OSAS still carries an additional risk. Dyslipidemia—increased cholesterol and triglycerides—is linked to atherosclerosis. Plaque rupture is promoted by mechanical stress, and OSA causes dramatic hemodynamic stress on the walls of the vessels, which occurs in the phase when in normal subjects' blood pressure and heart rate decrease and are less variable.

Is the key factor of syndrome Z genetic? Can we predict the relative weight of OSA as a risk factor for cardiovascular disease in a single patient? We are still far from a clear-cut answer to either of these questions, but these two contributions seem to point in the right direction. We need instruments to assess the global health status of our patients. "Quality of life" questionnaires have been validated in other diseases, like chronic obstructive pulmonary disease (COPD), linking together objective signs and symptoms beyond the simple measurements (i.e., FEV_1). In sleep medicine, this is far more difficult because symptoms are often underestimated by patients (mainly before treatment). We are still lacking a reliable instrument to measure hypersomnolence, and neuropsychological tests show such a limited difference between normal and OSAS patients that their usefulness in a single patient assessment is nil. The AHI can be considered like the FEV_1: abnormal in several diseases (i.e., asthma, chronic bronchitis, and emphysema), irreplaceable for severity assessment, but really insufficient to describe the full clinical picture. It is time to examine the full clinical picture: the quest for Mr. Z could be a good starting point.

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