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Predicting Incident Atrial Fibrillation Using Single Channel Nocturnal Oximetry: Can Necessity Become the Mother of Intervention?

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Obstructive sleep apnea (OSA) is fast becoming a global health crisis, with prevalence rates rising throughout the developed and developing world in parallel with the increasing prevalence of obesity (1). Several large, well-designed prospective cohort studies incorporating diverse groups of patients from around the world have consistently linked OSA with a greater burden of cardiovascular disease in general and with incident and prevalent atrial fibrillation (AF) in particular (2–5). These studies have shown that patients with OSA are more likely to develop AF and suffer more often from its consequences, such as stroke and premature death, than comparable subjects without OSA (6, 7). The argument that OSA may directly contribute to the development of AF is biologically plausible, and a growing body of basic science evidence points to hypoxemia and autonomic dysregulation, often manifested clinically through heart rate variability, as likely culprits (8, 9). Unfortunately, there are disparate levels of awareness of the relationship between OSA and AF between general practitioners, sleep medicine specialists, and cardiologists, and uniform guidelines for screening patients with OSA for AF (and vice versa) are lacking (10).

In an ideal world, all patients at risk for OSA would be appropriately screened and

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referred for attended polysomnography (PSG), which is the current gold standard for the diagnosis of OSA and other sleep disorders where multichannel physiologic data, including continuous electrocardiography (ECG) monitoring, are collected. Unfortunately, the demand for OSA testing greatly exceeds in-laboratory PSG availability, a problem that has only been worsened by the current global coronavirus disease (COVID-19) pandemic (11). Out of necessity, simplified home respiratory polygraphy (RP) devices that measure only airflow and single-channel pulse oximetry have become the faster route to OSA diagnosis in many centers.

In this issue of *AnnalsATS*, Blanchard and colleagues (pp. 1043–1051), on behalf of the ERMES study group in France, ask a straightforward question: Are indices of hypoxemia and pulse rate variability (PRV), a measure of heart rate variability derived from single-channel nocturnal oximetry, associated with incident AF in a real-world population of patients referred for OSA screening with no preexisting AF (12)? Their study population consisted of 7,205 patients from several medical centers in France who underwent PSG or RP in nearly equal proportions to screen for OSA. The study population is well described and similar to other Western OSA cohorts, with a majority representation of older obese men and an expected prevalence of hypertension, diabetes, and cardiovascular disease. Primary independent variables included the time spent with oxygen saturation below 90% (T90) and PRV. Other metrics of OSA severity such as the apnea–hypopnea index (AHI), oximetry nadir, and oxygen desaturation index were also reported. Based on AHI, 41.5% of studied subjects were considered to have severe OSA, although the cohort was minimally sleepy with a mean Epworth Sleepiness Score of 10. PRV was derived from oximetry data using the root mean square of successive normal–normal beat interval differences (RMSSD) in subjects undergoing RP and from both RMSSD and standard deviation from normal to normal beat intervals derived from ECG in subjects studied with PSG. A spectral analysis of the frequency domains of the normal–normal intervals was also used to generate a ratio of normalized low-frequency/high-frequency power (as a surrogate measure of sympathetic/parasympathetic tone). The study's single dependent variable was incident AF, with the majority (72%) of AF diagnoses being confirmed from a centralized hospital diagnosis database.

Outpatient diagnoses were derived from chart review and review of new medication prescriptions for anticoagulants, antiarrhythmic drugs, and atrioventricular node blocking agents; this is the study's sole significant limitation.

Over a median follow-up period of 5.3 years, the authors report an overall AF incidence of 4.6 per 1,000 patient-years. Spearman's correlation coefficient analysis revealed a strong correlation between PRV obtained from oximetry and ECG waveform analysis ($r = 0.61$, $P < 0.001$). After adjusting for confounding clinical variables and using Cox proportional hazard modeling, both T90 and PRV assessed using RMSSD were significantly associated with incident AF, and this risk increased across quartiles for both measurements. Subjects in the highest quartile for both T90 and PRV measured by RMSSD had the greatest risk for AF with an incidence of 13 per 1,000 patient-years (Table 4 in the article by Blanchard and colleauges) (12). Lower low-frequency/high-frequency ratios were also significantly related to incident AF after adjustment for confounders and other variables. There was no difference in the Epworth Sleepiness Score between subjects who developed AF and those who did not.

The findings of this well-designed and well-presented trial are important for two reasons. First, these results lend further support to the theory that physiologic events related directly to the presence of OSA, such as sustained hypoxemia and autonomic dysregulation, play a causal role in the development of AF. This observation should resonate with physician scientists who care for patients with OSA to be more cognizant of the risk for AF in their patients and to prompt the design of mechanistic studies of hypoxemia and autonomic dysregulation in OSA to advance our understanding of how these entities interact and what measures can be taken to reduce collective risk.

The second important finding in this study is that meaningful predictors of AF risk in patients with OSA can be obtained from simple single-channel oximetry studies. This finding is of particular interest given that greater numbers of patients are being referred for home sleep apnea testing because of the growing need for testing and the limited availability of attended PSG. Thus, there is the potential for improved data extraction from these simplified studies beyond the basic metric of the respiratory disturbance index or AHI and lowest oxygen saturation. With the application of artificial intelligence to single channel oximetry, sleep laboratories could potentially report measures of heart rate variability and autonomic dysfunction in addition to basic respiratory and oxygenation data. If these added metrics are assessed in the context of results from studies similar to the work by Blanchard and colleagues, this could lead to the prospective study of risk prediction models for AF derived from these oximetry-derived data. Should such models prove to be reliable, then patients with sleep apnea may be better informed of their risk for incident AF, and their providers may be more inclined to stratify that risk with diagnostic screening tools such as ambulatory telemetry monitoring and echocardiography. Earlier detection and treatment of AF in these higher-risk patients with OSA would almost certainly improve patient outcomes. ■

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