EDITORIAL

Cardiac rhythm disorders and obstructive sleep apnea: a multifaceted relationship

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Cardiovascular comorbidity is highly prevalent in patients with obstructive sleep apnea (OSA), and there is increasing evidence of a bidirectional relationship in this context, especially for heart failure (HF) and stroke.[1] Cardiac rhythm disorders are very common among patients with OSA, and they range from the cyclical fluctuations in heart rate that accompany recurring apneas and hypopneas to pathological arrhythmias that may have adverse prognostic significance. The fluctuating heart rate that is common in OSA has been recognized since the early days of investigation,[2] and has been proposed as a potential diagnostic tool for OSA.[3] However, this rhythm disturbance is a physiological response to the obstructive events, likely as a consequence of several factors that include sympathetic excitation and other vagally-mediated autonomic effects, negative intrathoracic pressure swings during upper airway obstruction, and intermittent hypoxemia,[4] and has little prognostic significance.

Pathological arrhythmias may be atrial or ventricular and the principal atrial arrhythmia in OSA is atrial fibrillation (AF). This arrhythmia is highly prevalent in patients with OSA, and a recent study found moderate or severe OSA in 55% of patients with newly diagnosed AF.[5] OSA is a significant risk factor for the development and recurrence of AF,[6] and a recent scientific statement from the American Heart Association recommends screening for OSA in patients with recurrent AF.[7] Furthermore, AF in the setting of OSA represents an additional risk factor for stroke.[1] A recent report from the Sleep Heart Health Study indicated that incident AF is more strongly associated with central sleep apnea than with OSA.[8] Animal models of OSA implicate atrial distension, remodeling, and fibrosis with associated decreased conduction velocity in the pathophysiology of AF in OSA.[9] Multiple observational studies suggest that continuous positive airway pressure (CPAP) treatment may lower the rate of AF recurrence following electrical cardioversion, and a meta-analysis of 7 prospective cohort studies found that CPAP therapy was associated with a reduction in AF recurrence, irrespective of whether the patients underwent pulmonary vein isolation.[6] However, a recent prospective randomized controlled trial involving 579 patients with paroxysmal AF found that 244 had moderate to severe OSA. As many as 108 patients randomized to CPAP complied with the therapy but there was no difference in percent time in AF between CPAP and control patients over 3 months of follow-up.[10] Other forms of atrial arrhythmias that are prevalent in patients with OSA include sick sinus syndromes, sino-atrial exit block, and tachycardia-bradycardia syndromes, which must be distinguished from the cyclical fluctuation in heart rate that accompanies obstructive events.

Ventricular arrhythmias (VAs) are also common in OSA and may be an important factor in the sudden death that has been reported as more common in patients with OSA.[11,12] Several VAs have been reported in patients with OSA and a report from the Sleep Heart Health Study found evidence of complex ventricular ectopy, nonsustained ventricular tachycardia, in addition to bigeminy and quadrigeminy, with complex ventricular ectopy evident in 25% of patients with OSA.[13] Not surprisingly, VAs associated with OSA are most common during sleep and typically occur during apnea/hypopnea. Patients with OSA and an implantable cardiac defibrillator (ICD) demonstrate significantly higher rate of ICD shocks during sleep.[12] Predictors of propensity to VA on the electrocardiogram include QT interval prolongation and the time interval from the peak to the end of the T wave.[12] CPAP therapy has been reported to be an effective treatment for VAs in patients with OSA,[14] including patients with comorbid HF.[6]

The mechanisms of arrhythmogenesis in OSA are multi-factorial.[11] Increased left ventricular

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afterload due to intrathoracic pressure swings causes acute atrial distension leading to vagal activation and shortening of the atrial effective refractory period, thus promoting arrhythmogenesis. Furthermore, simulating obstructive apnea using the Mueller maneuver in healthy subjects is proarrhythmogenic and results in generation of atrial premature beats and prolongation of ventricular repolarization. Also, ventricular remodeling over time because of repetitive effects of negative intrathoracic pressure is associated with an increased risk of arrhythmias. Additional mechanisms of arrhythmogenesis include sympathetic activation, intermittent hypoxemia, and hypercapnia. Sympathetic excitation, which is an important consequence of recurring apnea / hypopnea,[4] has been shown to be implicated in OSA--associated AF, as well as hypertension, and HF.[1] Intermittent hypoxemia as a direct result of recurring apnea / hypopnea promotes a range of downstream consequences that include inflammation, oxidative stress, enhanced prothrombotic state, and vascular dysfunction, which alone, or in combination, may promote arrhythmia.[11] Furthermore, the intermittent hypoxia itself may be arrhythmogenic, as evidenced by animal studies[11] of acute intermittent hypoxia. This direct pro--arrhythmogenic effect may be particularly evident in the setting of an already ischemic myocardium due to other factors, such as coronary artery disease.

The report of Domaradzki et al[15] adds further insight into the mechanisms of VAs in OSA and their response to CPAP therapy. In an observational study, the authors evaluated OSA patients demonstrating VAs who were treated with CPAP and compared with a similar control population who refused CPAP. VAs decreased in the CPAP-treated group at 3-month follow-up, especially at night, whereas there was no change in the control group. The decrease in arrhythmias was greatest in the patients with the most pronounced nocturnal oxygen desaturations, and nocturnal predominance of arrhythmia was the strongest predictor of benefit from CPAP therapy. As with most previous reports on this topic, this report is limited by its observational design, and the report that the control population represented patients who did not accept CPAP therapy.

The increasing evidence of cardiovascular comorbidity in OSA indicates that cardiac arrhythmias represent an important aspect of this relationship with important implications for clinical outcomes. While observational studies strongly support a beneficial impact of CPAP on cardiac arrhythmias, there is a pressing need for more randomized controlled prospective studies to properly evaluate this relationship.

ARTICLE INFORMATION

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