

## Should We Treat Nonsleepy Patients with Obstructive Sleep Apnea and Atrial Fibrillation with CPAP?

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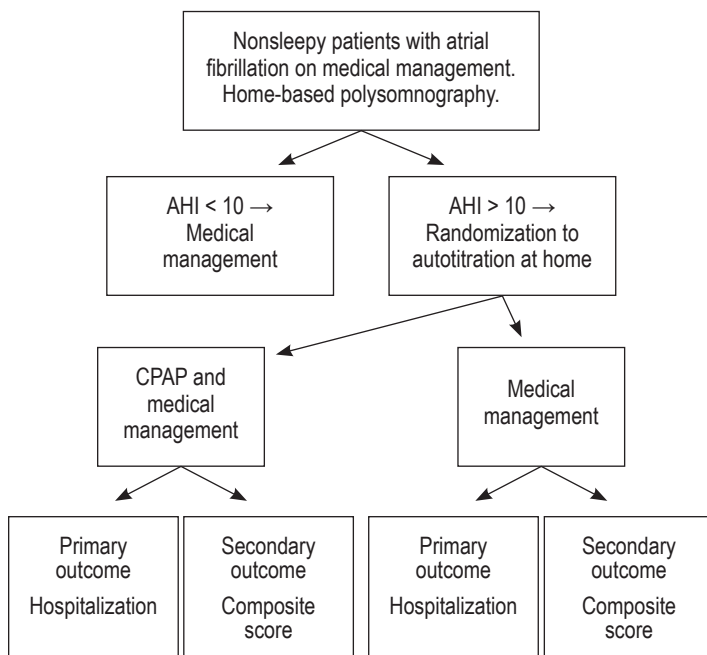
Obstructive sleep apnea (OSA) is a common sleep disorder characterized by partial or complete collapse of the airway leading to abnormal gas exchange, autonomic system imbalance, and frequent arousals during sleep. It occurs in 2% to 7% of our adult population.<sup>1</sup> Atrial fibrillation (AF) is the most common arrhythmia in adults and has an estimated prevalence of 1% to 2%. OSA and AF share several comorbid conditions, such as obesity and advancing age, and OSA is more prevalent in patients with AF after adjusting for other cardiovascular conditions.<sup>2-4</sup> The prevalence of AF is expected to increase 2.5-fold by 2050 as our population ages, and the economic burden it poses will rise accordingly, with a significant fraction of the cost attributed to increased hospitalization rates.<sup>4,5</sup> New therapeutic options are needed to reduce the morbidity and healthcare costs associated with AF, and the treatment of concomitant OSA offers one potential option.

Even mild unrecognized sleep disordered breathing is associated with cardiovascular events.<sup>6</sup> Stevenson et al. demonstrated that patients with AF had an increased rate of sleep disordered breathing compared to matched controls (68% vs. 38%) in a case-control study using polysomnograms.<sup>7</sup> However, one of the cardinal symptoms used to identify OSA by clinicians is excessive daytime somnolence, a physiological state that is difficult to characterize using questionnaires and is affected by other comorbidities like depression.<sup>8</sup> Recent studies in heart failure patients with OSA have demonstrated that the episodes of apnea do not correlate with sleepiness; this is thought to be caused by an increased sympathetic activity produced by the cardiac dysfunction.<sup>9</sup> This could also occur in patients with AF since somnolence and sense of fatigue may be altered by many factors like hypertension, heart failure, psychiatric and thyroid disorders. A recent meta-analysis demonstrated that OSA was a significant predictor of recurrent atrial fibrillation when OSA was diagnosed with polysomnograms, but not with the Berlin Questionnaire.<sup>10</sup> Since screening tools like the Berlin Questionnaire use daytime somnolence as part of their scoring system, questionnaires may not adequately identify OSA in atrial fibrillation patients. Therefore, some studies have tested the effects of CPAP therapy in nonsleepy patients by using outcome measures which did not depend on symptom assessment. To date, these studies have not shown a significant decrease in blood pressure or major cardiovascular events.<sup>11-14</sup>

However, treating nonsleepy OSA in patients with AF may have beneficial effects for the following reasons. Several

studies have demonstrated that the presence of OSA increases the risk for recurrent AF after using antiarrhythmic drugs, electrical cardioversion, and invasive procedures, such as pulmonary vein isolation for restoring sinus rhythm.<sup>10,15,16</sup> It has been suggested by some authors that the presence of OSA should be considered as a risk factor for stroke in patients with atrial fibrillation.<sup>17</sup> This is based on several prospective cohort studies that have found a significantly increased risk for stroke in patients with OSA. The association of OSA with age, hypertension, atrial fibrillation, and endothelial dysfunction could explain its association with cerebrovascular events. In addition, OSA might increase the risk of stroke by left to right shunting, increases in intracranial pressure, and reduced cerebral blood flow.<sup>18-20</sup>

We think that a randomized controlled pilot study that uses CPAP in patients with permanent atrial fibrillation and abnormal sleep studies independent of sleepiness symptoms could answer important questions about the relationship between the treatment of OSA and AF control and AF outcomes, such as stroke (**Figure 1**). Home-based portable sleep tests can identify sleep apnea and auto titration algorithms can provide effective OSA management at lower costs and greater convenience.<sup>21</sup> Important outcomes would include the rate of cerebrovascular events, cardiac events (CHF, myocardial infarction, hospitalization), AF management (days of hospitalization, number of antiarrhythmic drugs used, interventions), and a quality of life survey. The outcome assessment would likely require a weighted composite score since the event rate for thromboembolic events in patients with AF on anticoagulation prophylaxis is only 2% per year. Alternatively, the outcome could be based on hospitalization rate. In the AFFIRM trial 76.6% of the patients were hospitalized over a three and one-half year period.<sup>22</sup> If CPAP treatment reduced the rate by twenty percent per year, a sample size of 1,200 would be needed for a two-year study. Randomizing nonsleepy patients with OSA into a treatment group and a non-treatment group should not present an ethical dilemma since most of the benefit with CPAP occurs in sleepy patients with OSA, and its role in nonsleepy patients is unknown. A study like this will have difficulties with patient compliance since nonsleepy patients may not perceive symptomatic benefit. Patient education and frequent follow-up could reduce this problem. However, the possibility of reducing the medical and cost burden of atrial fibrillation is a very attractive and warrants consideration.

**Figure 1—Pilot study for CPAP treatment**

Composite score: deaths, stroke, myocardial infarction, and quality of life, based on reference 22.

## CITATION

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