

## 1-MINUTE CONSULT

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BRIEF ANSWERS  
TO SPECIFIC  
CLINICAL  
QUESTIONS

## Q: Should I evaluate my patient with atrial fibrillation for sleep apnea?

**A:** Yes. The prevalence of sleep apnea is exceedingly high in patients with atrial fibrillation—50% to 80% compared with 30% to 60% in respective control groups.<sup>1-3</sup> Conversely, atrial fibrillation is more prevalent in those with sleep-disordered breathing than in those without (4.8% vs 0.9%).<sup>4</sup>

Sleep-disordered breathing comprises obstructive sleep apnea and central sleep apnea. Obstructive sleep apnea, characterized by repetitive upper-airway obstruction during sleep, is accompanied by intermittent hypoxia, rises in carbon dioxide, autonomic nervous system fluctuations, and intrathoracic pressure alterations.<sup>5</sup> Central sleep apnea may be neurally mediated and, in the setting of cardiac disease, is characterized by alterations in chemosensitivity and chemoresponsiveness, leading to a state of high loop gain—ie, a hypersensitive ventilatory control system leading to ventilatory drive oscillations.<sup>6</sup>

Both obstructive and central sleep apnea have been associated with atrial fibrillation. Experimental data implicate obstructive sleep apnea as a trigger of atrial arrhythmogenesis,<sup>7,8</sup> and epidemiologic studies support an association between central sleep apnea, Cheyne-Stokes respiration, and incident atrial fibrillation.<sup>9</sup>

### ■ HOW SLEEP APNEA COULD LEAD TO ATRIAL FIBRILLATION

In experiments in animals, intermittent upper-airway obstruction led to forced inspiration, substantial negative intrathoracic pres-

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sure, subsequent left atrial distention, and increased susceptibility to atrial fibrillation.<sup>10</sup> The autonomic nervous system may be a mediator of apnea-induced atrial fibrillation, as apnea-induced atrial fibrillation is suppressed with autonomic blockade.<sup>10</sup>

Emerging data also support the hypothesis that intermittent hypoxia<sup>7</sup> and resolution of hypercapnia,<sup>8</sup> as observed in obstructive sleep apnea, exert atrial electrophysiologic changes that increase vulnerability to atrial arrhythmogenesis.

In a case-crossover study,<sup>11</sup> the odds of paroxysmal atrial fibrillation occurring after a respiratory disturbance were 17.9 times higher than after normal breathing (95% confidence interval [CI] 2.2–144.2), though the absolute rate of overall arrhythmia events (including both atrial fibrillation and nonsustained ventricular tachycardia) associated with respiratory disturbances was low (1 excess arrhythmia event per 40,000 respiratory disturbances).

### ■ EFFECT OF SLEEP APNEA ON ATRIAL FIBRILLATION MANAGEMENT

Sleep apnea also seems to affect the efficacy of a rhythm-control strategy for atrial fibrillation. For example, patients with obstructive sleep apnea have a higher risk of recurrent atrial fibrillation after cardioversion (82% vs 42% in controls)<sup>12</sup> and up to a 25% greater risk of recurrence after catheter ablation compared with those without obstructive sleep apnea (risk ratio 1.25, 95% CI 1.08–1.45).<sup>13</sup>

Several observational studies showed a higher rate of atrial fibrillation after pulmonary vein isolation in obstructive sleep apnea patients who do not use continuous positive airway pressure (CPAP) than in those who do.<sup>14-17</sup> CPAP therapy appears to exert benefi-

The prevalence of sleep apnea is very high in patients with atrial fibrillation

cial effects on cardiac structural remodeling; cardiac magnetic resonance imaging shows that patients with sleep apnea who received less than 4 hours of CPAP per night had larger left atrial dimensions and increased left ventricular mass compared with those who received more than 4 hours of CPAP at night.<sup>17</sup> However, a need remains for high-quality, large randomized controlled trials to eliminate potential unmeasured biases due to differences that may exist between CPAP users and non-users, such as general adherence to medical therapy and healthcare interventions.

An additional consideration is that the overall utility and value of obtaining a diagnosis of obstructive sleep apnea strictly as it pertains to atrial fibrillation management is affected by whether a rhythm- or rate-control strategy is pursued. In other words, if a patient is deemed to be in permanent atrial fibrillation and a rhythm-control strategy is therefore not pursued, the potential effect of untreated obstructive sleep apnea on atrial fibrillation recurrence could be less important. In this case, however, the other beneficial cardiovascular and systemic effects of diagnosing and treating underlying obstructive sleep apnea would remain.

■ **POPULATION STUDIES**

Epidemiologic and clinic-based studies have supported an association between sleep apnea (mostly central, but also obstructive) and atrial fibrillation.<sup>4,18</sup>

Community-based studies such as the Sleep Heart Health Study<sup>4</sup> and the Outcomes of Sleep Disorders in Older Men Study (MrOS Sleep),<sup>18</sup> involving thousands of participants, have found the strongest cross-sectional associations of both obstructive and central sleep apnea with nocturnal atrial fibrillation. The findings included a 2 to 5 times higher odds of nocturnal atrial fibrillation, particularly in those with a moderate to severe degree of sleep-disordered breathing—even after adjusting for confounding influences (eg, obesity) and self-reported cardiac disease such as heart failure.

In MrOS Sleep, in an older male cohort, both obstructive and central sleep apnea were associated with nocturnal atrial fibrillation, though central sleep apnea and Cheyne-Stokes respirations had a stronger magnitude of association.<sup>18</sup>

Further insights can be drawn specifically from patients with heart failure. Sin et al,<sup>19</sup> in a 1999 study, found that in 450 patients with systolic heart failure (85% men), the prevalence of sleep-disordered breathing was 25% to 33% (depending on the apnea-hypopnea index cutoff used) for central sleep apnea, and similarly 27% to 38% for obstructive sleep apnea. The prevalence of atrial fibrillation in this group was 10% in women and 15% in men. Atrial fibrillation was reported as a significant risk factor for central sleep apnea, but not for obstructive sleep apnea (for which only male sex and increasing body mass index were significant risk factors). Directionality was not clearly reported in this retrospective study in terms of timing of sleep studies and other assessments: ie, the report did not clearly state which came first, the atrial fibrillation or the sleep apnea. Therefore, the possibility that central sleep apnea is a predictor of atrial fibrillation cannot be excluded.

Yumino et al,<sup>20</sup> in a study published in 2009, evaluated 218 patients with heart failure (with a left ventricular ejection fraction of  $\leq 45\%$ ) and reported a prevalence of moderate to severe sleep apnea of 21% for central sleep apnea and 26% for obstructive sleep apnea. In multivariate analysis, atrial fibrillation was independently associated with central sleep apnea but not obstructive sleep apnea.

In recent cohort studies, central sleep apnea was associated with 2 to 3 times higher odds of developing atrial fibrillation, while obstructive sleep apnea was not a predictor of incident atrial fibrillation.<sup>9,21</sup>

Although most available studies associate sleep apnea with atrial fibrillation, findings of a case-control study<sup>22</sup> did not support a difference in the prevalence of sleep apnea syndrome (defined as apnea index  $\geq 5$  and apnea-hypopnea index  $\geq 15$ , and the presence of sleep symptoms) in patients with lone atrial fibrillation (no evident cardiovascular disease) compared with controls matched for age, sex, and cardiovascular morbidity.

But observational studies are limited by the potential for residual unmeasured confounding factors and lack of objective cardiac structural data, such as left ventricular ejection fraction and atrial enlargement. Moreover, there can be significant differences in

**Sleep apnea seems to affect the efficacy of a rhythm-control strategy for atrial fibrillation**

sleep apnea definitions among studies, thus limiting the ability to reach a definitive conclusion about the relationship between sleep apnea and atrial fibrillation.

## ■ SCREENING AND DIAGNOSIS

The 2014 joint guidelines of the American Heart Association, American College of Cardiology, and Heart Rhythm Society for the management of atrial fibrillation state that a sleep study may be useful if sleep apnea is suspected.<sup>23</sup> The 2019 focused update of the 2014 guidelines<sup>24</sup> state that for overweight and obese patients with atrial fibrillation, weight loss combined with risk-factor modification is recommended (class I recommendation, level of evidence B-R, ie, data derived from 1 or more randomized trials or meta-analysis of such studies). Risk-factor modification in this case includes assessment and treatment of underlying sleep apnea, hypertension, hyperlipidemia, glucose intolerance, and alcohol and tobacco use.

Further study is needed to evaluate whether physicians should routinely use screening tools for sleep apnea in patients with atrial fibrillation. Standardized screening methods such as the Berlin questionnaire,<sup>25</sup> STOP-Bang,<sup>26</sup> and NoSAS<sup>27</sup> (Table 1) are limited by lack of validation in patients with atrial fibrillation, particularly as the symptom profile may be different from that in patients who do not have atrial fibrillation.

Laboratory polysomnography has long been considered the gold standard for sleep apnea diagnosis. In one study,<sup>13</sup> obstructive sleep apnea was a greater predictor of atrial fibrillation when diagnosed by polysomnography (risk ratio 1.40, 95% CI 1.16–1.68) compared with identification by screening using the Berlin questionnaire (risk ratio 1.07, 95% CI 0.91–1.27). However, a laboratory sleep study is associated with increased patient burden and limited availability.

Home sleep apnea testing is being increasingly used in the diagnostic evaluation of obstructive sleep apnea and may be a less costly, more available alternative. However, since a home sleep apnea test is less sensitive than polysomnography in detecting obstructive sleep apnea, the American Academy of

TABLE 1

### Screening tools to identify increased risk of obstructive sleep apnea

Screening tool	Factors assessed
Berlin questionnaire <sup>25</sup>	Snoring, waketime sleepiness or fatigue, obesity, hypertension
STOP-Bang <sup>26</sup>	Snoring, tiredness, observed apnea, high blood pressure, body mass index, age, neck circumference, male sex
NoSAS <sup>27</sup>	Neck circumference, obesity, snoring, age, male sex

Sleep Medicine guidelines<sup>28</sup> state that if a single home sleep apnea test is negative or inconclusive, polysomnography should be done if there is clinical suspicion of sleep apnea. Moreover, current guidelines from this group recommend that patients with significant cardiorespiratory disease should be tested with polysomnography rather than home sleep apnea testing.<sup>22</sup>

Further study is needed to determine the optimal screening method for sleep apnea in patients with atrial fibrillation and to clarify the role of home sleep apnea testing. While keeping in mind the limitations of a screening questionnaire in this population, as a general approach it is reasonable to use a screening questionnaire for sleep apnea. And if the screen is positive, further evaluation with a sleep study is merited, whether by laboratory polysomnography, a home sleep apnea test, or referral to a sleep specialist.

## ■ MULTIDISCIPLINARY CARE MAY BE IDEAL

Overall, given the high prevalence of sleep apnea in patients with atrial fibrillation, the deleterious effects of sleep apnea in general, the influence of sleep apnea on atrial fibrillation, and the cardiovascular and other beneficial effects of adequate treatment of sleep apnea, patients with atrial fibrillation should be assessed for sleep apnea.

While the optimal strategy in evaluating for sleep apnea in these patients needs to be further defined, a multidisciplinary approach to care involving a primary care provider, cardiologist, and sleep specialist may be ideal. ■

**For overweight and obese patients with atrial fibrillation, weight loss and risk-factor modification are recommended**

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