

# Screening for Obstructive Sleep Apnea in Patients with Atrial Fibrillation

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## KEYWORDS

• Obstructive sleep apnea • Atrial fibrillation • Screening • Questionnaires • Home sleep testing

## KEY POINTS

- Atrial fibrillation (AF) is a common arrhythmia associated with adverse health outcomes and elevated health costs. Obstructive sleep apnea (OSA) is common among AF patients.
- OSA may contribute to the occurrence and recurrence of AF. Screening for OSA among AF patients is justified by the adverse impact OSA may cause.
- Appropriate screening strategies should be used due to the high prevalence of OSA among AF subjects and variable symptomatology.
- OSA questionnaires may have limited performance among patients with high pretest probability, such as the AF population.
- Home sleep testing (HST) is a promising alternative for screening and diagnosing OSA in AF patients. The cost-effectiveness of such approach, however, needs to be studied.

## INTRODUCTION

OSA is characterized by repetitive upper airway obstruction during sleep. The most common symptoms of OSA are snoring, fatigue, disrupted sleep, and excessive daytime sleepiness.<sup>1</sup> Obesity, male gender, and increasing age are the most important risk factors for OSA.<sup>2</sup> There is growing evidence, however, that a significant proportion of OSA patients are minimally symptomatic and frequently also not obese. OSA may present several distinct phenotypes,<sup>3</sup> which points to the potential necessity of simple and cost-effective diagnostic methods.

OSA is common in the general population and strikingly common among patients with

established cardiovascular disease. The high prevalence of OSA is largely due to OSA and cardiovascular disease sharing several risk factors, including male gender, obesity, sedentary life, and increasing age. In addition, OSA may independently contribute to poor cardiovascular outcome.<sup>4</sup> Obstructive events during sleep cause (1) large swings in intrathoracic pressure during the futile efforts to breathe, (2) arousals from sleep, and (3) intermittent hypoxia.<sup>5</sup> These 3 primary mechanisms occurring during sleep trigger a cascade of intermediate mechanisms, which may ultimately contribute to the development or recurrence of AF. There is no definitive evidence, however, that the diagnosis and treatment of OSA reduce the incidence of AF or conversely that the recognition and

The authors have nothing to disclose.

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Sleep Med Clin ■ (2016) ■-■

<http://dx.doi.org/10.1016/j.jsmc.2016.10.009>

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treatment of OSA among patients with established AF have a positive impact on the cardiovascular outcome. On the other hand, the recognition and treatment of OSA may also have a positive impact on quality of life.<sup>6</sup> In clinical practice, OSA remains largely under-recognized among patients with established cardiovascular disease.<sup>7</sup> The reasons for such low recognition include the possibility that several symptoms associated with OSA may overlap with symptoms associated with the underlying cardiovascular disease. In addition, the diagnosis of OSA has traditionally been restricted to full sleep studies, creating a potential barrier. This observation raises the question of how to recognize OSA among patients with AF.

To provide a clinical rationale to justify the screening of OSA among AF patients, the epidemiology of OSA and AF and the mechanisms by which OSA may contribute to AF are reviewed. Possible strategies to screen for OSA are then reviewed and discussed.

### PREVALENCE OF ATRIAL FIBRILLATION

AF is a common arrhythmia associated with adverse consequences and high health-related cost. The clinical risk factors for AF include advancing age, diabetes, hypertension, congestive heart failure, valve disease, and myocardial infarction.<sup>8</sup> The prevalence of AF in the general population is between 1% and 2% and is higher in men than in women.<sup>9</sup> The risk of developing AF increases dramatically with age, and the estimated lifetime risk of developing AF is 1 in 4 for men and women ages 40 years and above.<sup>9</sup> AF is the most common arrhythmia in patients older than 65 years.<sup>10</sup> For instance, data from a cross-sectional study of adults ages 20 years or older who were enrolled in a large health maintenance organization in California estimated that the prevalence of AF increased from 0.1% among adults younger than 55 years to 9.0% in persons ages 80 years or older.<sup>10</sup> Aging heart, characterized by myocardial fibrosis and atrial dilation, is a main risk factor for AF. Structural heart disease enforces atrial chamber abnormality, and this explains the higher prevalence of AF in patients with underlying cardiovascular conditions.<sup>11</sup> Other risk factors for AF, such as obesity and diabetes, are also steadily increasing in society. AF not only is a marker of an underlying cardiovascular disease but also, once established, an independent risk factor for stroke as well as increased mortality. The high lifetime risk of AF and increased longevity underscore the important public health burden posed worldwide.<sup>12</sup> The cost of AF is escalating. A systematic review of recent literature estimated the direct

costs of AF at \$2,000 to \$14,200 per patient-year in the United States and €450 to €3000 per patient-year in Europe.<sup>13</sup> This is comparable to costs associated with other chronic conditions, such as diabetes. Hospitalizations were the main contributors to the high direct cost of AF.<sup>13</sup>

### PREVALENCE OF OBSTRUCTIVE SLEEP APNEA AND ASSOCIATION WITH ATRIAL FIBRILLATION

OSA is common in the general population. A landmark Wisconsin cohort initially reported that the estimated prevalence of OSA syndrome in the general population, as defined by an apnea-hypopnea index above 5 events per hour of sleep determined by full polysomnography plus symptoms of excessive daytime sleepiness, was 2% and 4% in adult women and men, respectively.<sup>14</sup> Several factors, however, including the increased capacity to recognize hypopneas with the use of pressure cannula, the recognition that several patients do not have symptoms of excessive daytime sleepiness, and the increasing rates of obesity of the population have led to the recognition that OSA is more common than initially imagined. For instance, the estimated prevalence of OSA among adults of the city of São Paulo, Brazil, and Lausanne, Switzerland, was estimated to be approximately 30% to 50%.<sup>2,15</sup>

The prevalence of unrecognized OSA among patients with established cardiovascular disease is strikingly high. For instance, 1 study evaluated 500 consecutive outpatients from a tertiary cardiovascular university hospital and found that although only 3.1% had a previous diagnosis of OSA, more than half of the population (51.6%) had symptoms suggestive of OSA as evaluated by the Berlin questionnaire. The high prevalence of OSA was further confirmed by HST in a subset of 50 patients.<sup>7</sup>

The prevalence of AF among OSA patients is approximately 5%,<sup>16</sup> which is higher than the prevalence of AF in the general population (1%–2%).<sup>9</sup> On the other hand, studies that assessed the prevalence of OSA in patients with AF showed prevalence ranging from 21% to 81%.<sup>17–20</sup> The impact of OSA on AF incidence, however, remains controversial. One study showed an independent association between OSA and increased AF incidence,<sup>21</sup> whereas another study found an association of AF and central sleep apnea but not with OSA.<sup>22</sup>

### THE IMPACT OF OBSTRUCTIVE SLEEP APNEA ON ATRIAL FIBRILLATION

Although the precise mechanisms by which OSA is linked to arrhythmias are not fully elucidated,

several studies showed an increase propensity of OSA patients to develop AF. As discussed previously, obstructive events during sleep promote reductions in the intrathoracic pressure, intermittent hypoxia, and sleep fragmentation.<sup>5</sup> One or more of the OSA-related components elicits sympathetic surges, atrial distension (due to the increase in atrial transmural pressure gradients), surges in blood pressure, increased systemic inflammation, and oxidative stress. Chronically, these repetitive events may promote structural cardiac changes, including atrial enlargement and fibrosis.<sup>23</sup> Two main factors may contribute to atrial remodeling in OSA: (1) chronic atrial dilation by repetitive changes in intrathoracic pressure<sup>24</sup> and (2) surges in blood pressure. In addition, OSA has been shown to increase aorta stiffness that in turn contributes to increased heart afterload and atrial and ventricular remodeling.<sup>25,26</sup>

In the past 2 decades, growing evidence has suggested the potential role of OSA in the genesis of AF occurrence and recurrence.<sup>27,28</sup> The increased risk of AF among OSA patients seems independent of potential confounding factors, such as age and obesity. The increased risk of recurrence of AF has been also observed in patients who have had catheter ablation.<sup>29</sup> In line with this evidence, one observational study showed that patients with untreated OSA have a higher recurrence of AF after ablation. Appropriate treatment of OSA with continuous positive airway pressure (CPAP) was associated with a lower recurrence of AF.<sup>30</sup> In the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation study, patients with OSA were more symptomatic and more often on rhythm control therapy than patients with AF without OSA.<sup>31</sup> In adjusted analyses, patients with OSA had higher risk of hospitalization. Supporting the impact of OSA, patients with OSA on CPAP treatment were less likely to progress to more permanent forms of AF compared with patients without CPAP.<sup>31</sup>

### ***Circadian Variation of Atrial Fibrillation***

Data from the Sleep Heart Health Study also evaluated paroxysmal AF.<sup>32</sup> The investigators found that the relative risk of paroxysmal AF during sleep was markedly increased shortly after a respiratory event.<sup>32</sup> These results support a direct temporal link between OSA events and the development of AF. The potential implications for these findings rely on OSA associated with increased risk for stroke, and this may be partially explained by the higher occurrence of AF in this population. Patients with OSA who had a stroke had higher rates

of AF even after accounting for potential confounders.<sup>33</sup> Further studies in this important research field are warranted.

### **SCREENING OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH ATRIAL FIBRILLATION USING QUESTIONNAIRES**

It is well established that standard overnight polysomnography is the recommended method for the overall diagnosis of OSA. It is expensive, however, and may not be readily available in many places. To simplify and improve the access to OSA diagnosis, screening questionnaires and simplified diagnostic methods performed at home have been proposed. OSA screening questionnaires have been used to screen for OSA among AF patients, to predict the postoperative occurrence of AF, and to predict the recurrence of AF among subjects undergoing catheter ablation and (described later). The characteristics of the most commonly used OSA screening questionnaires are summarized in [Table 1](#).

#### ***Epworth Sleepiness Scale***

Sleepiness can be subjectively assessed through several questionnaires. The most commonly used is the Epworth Sleepiness Scale.<sup>34</sup> Sleepiness is an important symptom of OSA due to its impact on health-related quality of life, accident risk, and productivity. Sleepiness is also associated with adherence to CPAP treatment,<sup>35</sup> although this relationship has not been found in several studies.<sup>36</sup> On the other hand, sleepiness is a common symptom among adults, with several differential diagnoses that include sleep deprivation, major depression, hypothyroidism, and medication side effects. Moreover, sleepiness assessed by the Epworth Sleepiness Scale is only present in approximately 30% of OSA subjects.<sup>37</sup> Sleepiness has been shown to be less prevalent among OSA patients with comorbid cerebrovascular and heart disease.<sup>38,39</sup> Similarly, in a study by Albuquerque and colleagues,<sup>17</sup> the proportion of patients with excessive daytime sleepiness among 151 patients with AF was not different between those with and without OSA. Therefore, active search for excessive daytime sleepiness is not a valid approach to screen for OSA among AF patients.

#### ***Berlin Questionnaire***

The Berlin questionnaire was designed and tested in a primary care setting and showed reasonable performance (sensitivity of 86% and specificity of 77%).<sup>40</sup> The Berlin questionnaire assesses the

**Table 1**  
**Obstructive sleep apnea questionnaires used among atrial fibrillation patients**

Questionnaire	Description	Advantages/Disadvantages
Epworth Sleepiness Scale	Chance of dozing is graded in 8 daily activities to determine sleepiness severity.	<1/3 of OSA patients are sleepy. Sleepiness is common in other disorders.
Berlin questionnaire	Has 3 domains (snoring, tiredness, and presence of obesity or arterial hypertension)	Somewhat complicated to score Low specificity in populations with a high prevalence of OSA
STOP-Bang	8 Questions with a dichotomous (yes/no) format	Simple to answer and score Low specificity

The accuracy of these questionnaires has not been adequately studied among AF patients.

risk of OSA through 3 domains that focus on snoring, tiredness, and the presence of diagnosed arterial hypertension and obesity. The performance of the Berlin questionnaire, however, was shown to be suboptimal in populations with a higher prevalence of OSA. The Berlin questionnaire has been tested in patients with cardiovascular disorders, such as hypertension, coronary artery disease, and hypertrophic cardiomyopathy,<sup>41–43</sup> with sensitivities ranging from 40% to 93% and specificities ranging from 30% to 59%. Tang and colleagues<sup>44</sup> tested the validity of the Berlin questionnaire among 30 patients undergoing radiofrequency ablation for AF compared with polysomnography with a portable device. The investigators reported a sensitivity of 100% but a specificity of 30%. Larger studies are necessary to confirm the Berlin questionnaire as a sensitive screening tool for OSA. Based on the performance of the Berlin questionnaire in other populations with a high prevalence of OSA, however, such as those with other cardiovascular disorders, the specificity most likely is not enough to rule out a diagnosis of OSA.

### ***STOP-Bang Questionnaire***

The STOP-Bang questionnaire was derived from the Berlin questionnaire and initially tested in the surgical population, showing a sensitivity of 84% and specificity of 56%.<sup>45</sup> The STOP-Bang questionnaire assesses the risk of OSA based on the positive or negative answer to 8 different questions (presence of loud snore, tiredness, observed apneas, body mass index  $\geq 35$  kg/m<sup>2</sup>, age >50 years, neck circumference >16 inches, and male gender). Despite its simplicity, subsequent studies in different patient groups confirmed that the STOP-Bang has a low specificity and, therefore, confirmation of OSA with a sleep test will still be necessary.<sup>46</sup>

### ***Neck Circumference, Obesity, Snoring, Age, and Sex Score***

The NoSAS (neck circumference, obesity, snoring, age, and sex) score has been recently described as a promising OSA screening questionnaire.<sup>47</sup> The NoSAS score was developed using the HypnoLaus cohort and independently validated in the EPISONO cohort and showed better performance than the Berlin and STOP-Bang questionnaires.<sup>47</sup> The NoSAS score has not been tested in populations with high OSA prevalence, however, such as in patients with cardiovascular disorders or AF.

### ***Occurrence of Postoperative Atrial Fibrillation***

Mungan and colleagues<sup>48</sup> tested the Berlin questionnaire and Epworth Sleepiness Scale in 73 patients undergoing coronary artery bypass grafting. Increased subjective sleepiness and a higher percentage of high-risk Berlin questionnaire were found among the 33 patients who developed AF compared with those who did not develop AF.<sup>48</sup> van Oosten and colleagues<sup>49</sup> used a modified Berlin questionnaire (in which subjects with a previous confirmed diagnosis of OSA were considered high-risk) to identify subjects at a higher risk for developing AF after coronary artery bypass graft. The investigators showed a 2-fold increased risk for the development of postoperative AF among patients with high-risk or confirmed OSA.<sup>49</sup> Therefore, patients with high risk of having OSA as determined by the Berlin questionnaire are at increased risk for developing AF. These findings are in line with studies that diagnosed OSA preoperatively using polysomnography and showed that OSA was a risk factor for postoperative AF.<sup>50,51</sup> The significance of being at high risk for OSA in the preoperative setting is limited, however, due to the low specificity of the screening

questionnaires to detect OSA and the need to further confirm the diagnosis and implement therapy.

### **Recurrence of Atrial Fibrillation After Catheter Ablation**

OSA diagnosed through standard polysomnography has been shown to be an independent predictor of AF recurrence after radiofrequency ablation.<sup>30,52</sup> OSA screening questionnaires have been used to identify patients with an increased risk of AF recurrence due to OSA. Both the Berlin and STOP-Bang questionnaires have been tested as predictors of AF recurrence after radiofrequency ablation. A high-risk score for OSA at the STOP-Bang questionnaire was associated with a 3.7-fold increased risk of AF recurrence.<sup>53</sup> Conflicting results have been reported on the performance of the Berlin questionnaire to predict AF recurrence after catheter ablation. Tang and colleagues<sup>44</sup> used the Berlin questionnaire among 178 AF patients undergoing catheter ablation. A high OSA risk was not associated with AF recurrence. In contrast, Chilukuri and colleagues<sup>54</sup> used the Berlin questionnaire and showed that high-risk OSA was independently associated with increased AF recurrence after catheter ablation. Screening using questionnaires to predict those who are more likely to have AF recurrence after catheter ablation can be useful to select those who should undergo confirmation using HST or polysomnography.

### **HOME SLEEP TESTING**

The utility of screening questionnaires for OSA among populations with a known high prevalence of OSA has been questioned.<sup>55,56</sup> HST is becoming increasingly cheaper and more readily available. Devices that only have respiratory channels (nasal pressure cannula, chest and abdominal respiratory effort belts, and oximetry) can be assembled by patients at home with instructions that are simple to follow. Skomro and colleagues<sup>57</sup> showed that the outcomes of HST followed by CPAP titration using an auto-CPAP at home were similar to the traditional laboratory-based approach. HST has become an attractive single-step approach to detect OSA among populations known to have a high OSA prevalence.

### **FUTURE DIRECTIONS**

OSA is a common comorbidity of AF patients and has been shown to adversely influence health outcome and quality of life. Detecting OSA among AF patients seems to decrease AF recurrence after

cardioversion or catheter ablation. Apart from the prevention of AF recurrence, however, it is not clear who among patients with AF and OSA benefits from OSA treatment. Randomized studies on the impact of OSA among AF patients are lacking.

OSA screening questionnaires among AF patients have been used in several studies. The validity of such questionnaires, however, is limited. Additional studies using more accurate diagnostic methods are necessary. One possibility is using a 2-step approach, beginning with screening questionnaires (eg, Berlin and STOP-Bang questionnaires) followed by confirmatory HST (for those identified as at high risk). Conversely, HST alone should be considered an alternative to diagnosing OSA in the AF population. The cost-effectiveness of such approaches, however, needs to be studied.

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