

# Are We Sure That Obstructive Sleep Apnea Is Not a Risk factor for Atrial Fibrillation in the Elderly Population ?

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## Abstract

Obstructive sleep apnea is an independent risk factor for atrial fibrillation in the middle- aged population. Furthermore, the prevalence of obstructive sleep apnea is much higher in the elderly then in the middle-aged population. However, in the elderly, the effect of obstructive sleep apnea on atrial fibrillation is not clear due to the nonspecific presentation of obstructive sleep apnea, lack of awareness of the condition among physicians, and subsequent underdiagnosis of obstructive sleep apnea.

## INTRODUCTION

The role of obstructive sleep apnea (OSA) in atrial fibrillation (AF) has been established by numerous studies in the past two decades. The prevalence of atrial fibrillation (AF) is significantly higher in patients with obstructive sleep apnea (1, 2). OSA increases the risk of atrial fibrillation by 2- to 3- fold (1). OSA has gained immense recognition as a significant distinct disorder for which treatment can decrease the risk of AF in the middle aged population. OSA presentation is different in the elderly population compared to the middle aged groups though this difference has not yet been clearly described (3). Certain studies have mentioned that the elderly patients with OSA are likely to be at a lower risk for cardiovascular disease than middle-aged and younger patients with OSA (4, 5). However, there is no clear explanation offered for this reduction in effect of OSA in the elderly population. The clinical significance of OSA in the elderly remains controversial. Possible reasons for varied and different presentation of OSA in the elderly are age-related changes in the body. The atypical presentation has resulted in the underdiagnosis of OSA in the elderly population (6). Investigators in the field are uncertain regarding the level of risk OSA poses for cardiovascular disorders in general, and AF in particular, in the elderly. In this article, we will explore and offer insight into the role of OSA in AF in the elderly population.

## PREVALENCE OF OBSTRUCTIVE SLEEP APNEA IN THE ELDERLY

The prevalence of OSA increases with age. OSA is a common disorder in the elderly population, with prevalence

as high as 30% to 80%, compared to only 2% to 4% in the middle-aged population (7-10). Ancoli-Israel et al. demonstrated that the prevalence of sleep-disordered breathing (SDB) is as high as 44% in the elderly (11). Interestingly, the number of women with sleep apnea is higher in the elderly age group than in the middle-aged population. The discrepancy between sexes, evident in middle-aged groups, is absent in the elderly (8, 10). In the middle-aged groups, fewer women develop sleep apnea (12). The reason for fewer females with OSA in middle-aged population could be the underdiagnosis of OSA, or alternatively, gender may play a role in the development of OSA (13).

## PREVALENCE OF ATRIAL FIBRILLATION IN THE ELDERLY

AF is the most common arrhythmia in the elderly. At least 2.3 million patients are affected by AF, of which 1.85 million patients are 65 years of age and older (14). These numbers are likely to increase and estimates show that by year 2050, 4.97 million elderly patients (88 % of the total patients with AF); will be diagnosed with AF (14).

## RISK FACTORS FOR OBSTRUCTIVE SLEEP APNEA IN THE ELDERLY

While the traditional risk factors for OSA in the middle-aged group are male gender, obesity, snoring and neck circumference (6, 12), in the elderly there are no clear data regarding the risk factors for OSA. Habitual snorers are reported to be at higher risk for sleep disordered breathing (SDB) (12). In the elderly population, snoring is less

prevalent compared to those who are middle-aged. Kobayashi et al. has cited impact of age-related decrease tone of skeletal muscles, genioglossal muscles, and upper airway dilating muscles as well as decreased upper airway compliance as possible causes of sleep apnea in the elderly (3, 15, 16). One study has reported the association between denture use and occurrence of OSA in the elderly (17). The role of obesity in OSA in the elderly is not clear. In the past, one study reported that a higher basal metabolic index (BMI) is associated with OSA in the middle-aged and elderly (13). However, the occurrence of OSA is common even in the absence of obesity in the elderly population. Furthermore, studies have shown that there is a weak association between obesity and OSA in the elderly (6). An age-related decrease in the activity of the upper airway muscles that keep the airway patent could be an important factor in the cause of OSA in the elderly (6).

### **ATYPICAL PRESENTATION OF OBSTRUCTIVE SLEEP APNEA IN THE ELDERLY**

The pattern of presentation and clinical characteristics of OSA in the elderly are not clear.

Atypical presentation is an important factor in the under diagnosis of OSA in the elderly. OSA in the elderly has been described as a condition distinct from that of the middle-aged population (18). When compared to the middle-aged persons who present as being overweight, and with loud snoring, tiredness and fatigue, mild daytime sleepiness, the presentation of the elderly may be quite varied based on their body habitus, fitness and associated comorbidities. One of the important issues that clinicians need to keep in mind is the fact that the elderly population is extremely diverse with patients ranging from very active individuals and living in the community to institutionalized demented individuals.

The ratio of males to females with OSA is 8:1 in the diagnosed general patient population whereas the ratio is almost equivalent among the elderly (13). Snoring is predictive of sleep apnea in about 65 percent elderly (11). Snoring is a common symptom of OSA and is very sensitive in its diagnosis especially in the middle aged groups. (19). However, studies have shown that the prevalence of snoring decreases with age (20). In an important study, Enright et al. demonstrated that snoring is negatively correlated with age in patients older than 65 years (21).

Nocturia is frequent in the elderly population and is associated with sleep disorders (22, 23). Older adults with

severe sleep disordered breathing had a greater number of nocturia episodes (23). Umlauf et al. have examined the relationship between OSA and nocturia in community dwelling older adults and found that patients with a severe apnea hypopnea index (AHI) had greater urine production and elevated atrial natriuretic peptide levels (ANP) (24).

Excessive daytime sleepiness is a possible presentation symptom. Presentation with this symptom can be confusing for diagnosis as daytime sleepiness may be due to dementia, polypharmacy or poor cognition in the elderly. Furthermore, OSA could cause recurrent falls and accidental falls (25). OSA presenting with falls is atypical and it may be prudent to consider sleep disorders as one of the possible underlying causes.

A case report noted that dementia as a presenting symptom in a patient with OSA (26). OSA can present with delirium due to lack of sleep (27). Fragmented sleep and intermittent hypoxemia, can affect cognitive functioning in elderly. Studies have shown that a causal relationship may exist between SDB and Alzheimer's disease. The association between sleep apnea and the genotype of Alzheimer's disease (apolipoprotein E epsilon E4) was observed in some studies (28, 29). Sleep apnea could also present as depression in both the elderly and the middle aged (11, 30). The causal relationship between OSA and depression is unclear at this point. Sleep apnea and insomnia co-occur and substantial overlap of symptoms of these disorders may make it hard to distinguish and treat accordingly (31).

One factor that has widespread implications is the role of OSA in causing

traffic accidents (32, 33). Multiple studies have reported that OSA may present this way in elderly due to the interplay of multiple factors like poor sleep, decreased cognition, delayed reaction and attention deficit. The role of OSA in occupational accidents has also been reported (34).

In an interesting study Tarasiuk et al. compared the morbidity and healthcare utilization of the middle aged and the elderly population with OSA (8). They found that the elderly had lower total sleep time, sleep efficiency, reports of snoring and apnea hypopnea index (AHI), compared to the middle aged group. The study also reported that lower sleep time and quality among the elderly may be due to the effects of depression, medication effects, anxiety and associated comorbidities. With recent data showing that OSA is an independent risk factor for metabolic syndrome

(MS), one study advises geriatricians to look for the presence of metabolic syndrome in OSA patients and vice versa (35).

It is difficult to identify the elderly patients who have OSA based on any single group of symptoms or age population (11). Properly diagnosing the elderly with OSA is further challenged by the factors such as decreased awareness among physicians about the presence of OSA (36), the multiple nonspecific symptoms of OSA and decreased reporting of symptoms by the patient or bed partner. The wide gap between the huge numbers of undiagnosed sleep apnea patients and available sleep medicine specialists further complicates this situation (37).

### **THE IMPACT OF OBSTRUCTIVE SLEEP APNEA ON THE OCCURRENCE OF ATRIAL FIBRILLATION IN THE ELDERLY**

Various mechanisms have been proposed over the last few years to explain the relationship of OSA to AF in the general population. However, the clinical significance of OSA in the elderly and its role in the occurrence of AF is not clear. The reasons could be many. We have yet to find the exact mechanism responsible for how OSA causes AF. Multiple studies have been performed to explain the possible pathophysiological mechanisms involved.

Regarding how OSA may cause AF, Somers et al. discusses the effect of an increase in sympathetic activity associated with arousals and repeated episodes of arousals (38, 39). More recently Ghias et al suggested that autonomic blockade could prevent AF in patients with OSA (40). Gami et al notes that OSA is strikingly more prevalent in AF patients than in patients with other cardiovascular diseases (2). Furthermore, OSA is more prevalent in patients with chronic persistent and permanent AF (41). A recent study by Stevenson et al. reports that hypercapnia alters the atrial electrophysiology by causing changes in effective refractory period and conduction time thus increasing for the risk of developing AF (42). Pedrosa et al. reported a high prevalence of OSA in patients with Hypertrophic Obstructive Cardiomyopathy ( HOCM) and is associated with left atrial enlargement (43). Drager et al. introduced the mechanism of OSA induced-increased left atrial diameter and atrial remodeling and its potential role in increasing the risk for AF (44). Other possible mechanisms include hypoxemia, increased intrathoracic pressure, increased cardiac wall stress (45, 46) and diastolic dysfunction.

One study proposes that while OSA incidence increases with age, the severity of OSA may be lesser compared to younger age groups (47). Gami et al studied the role of OSA in new-onset AF and found that OSA predicted the onset of AF in patients younger than 65 years but not in those older than 65 years(1). Obesity is strongly associated with AF and is also an independent risk factor for AF (48, 49). OSA was also considered to be the link that could explain the relation between Obesity and AF. While Obesity has been independently associated with AF, this association was not evident in older patients (50, 51). Previous studies have shown that OSA has limited predictive power in cardiovascular morbidity and mortality in elderly patients (4, 5). Males with OSA between the ages of 50 to 79 years have the same mortality rate as the general population (4).

Recently, in an important study by Kobayashi et al (3), these investigators compared OSA in the elderly and middle aged groups and reported that the clinical significance of OSA in the elderly is mild due to a smaller physiologic response to respiratory events. They also suggest that the significance of OSA is mild in the elderly with no co-occurring obesity.

### **TREATMENT OF OBSTRUCTIVE SLEEP APNEA IN PREVENTING ATRIAL FIBRILLATION IN THE ELDERLY:**

Continuous Positive Airway Pressure (CPAP) is the standard treatment for OSA and it is also the most widely accepted treatment modality. Elderly persons with mild OSA have been shown to benefit from CPAP therapy (52). CPAP therapy improves alertness, fatigue and sleepiness (53), management of obesity (54), improves insulin secretion capacity, cholesterol levels (55) and reduces mortality in stroke patients (56). CPAP therapy improves left ventricular ejection fraction in patients with ejection fraction more than 30% (57). Gami et al (1) reported that the use of CPAP did not reduce the risk of new-onset AF in elderly. However the study the limitations of the study may be significant and include lack of data on compliance, frequency of use and the study's retrospective design. The study also notes that CPAP was more likely to be used by patients with severe OSA versus those with mild OSA which prevents determining whether using CPAP at an early state of OSA may help in the prevention of AF. Diagnosing the elderly with mild OSA or at early stages of OSA remains challenging. The use of polysomnogram in the diagnosis of OSA is expensive and perhaps not feasible for use on such a large scale. We need further studies to determine if using CPAP in elderly patients

## ***Are We Sure That Obstructive Sleep Apnea Is Not a Risk factor for Atrial Fibrillation in the Elderly Population ?***

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with mild OSA has potential benefits.

In a recent study involving a large Japanese cohort (58), Abe et al. have studied the efficacy of CPAP therapy in preventing OSA-associated arrhythmias and found that CPAP therapy prevents paroxysmal atrial fibrillation (PAF). Prior to that study, Kanagala et al showed that treatment of OSA with CPAP decreases the recurrence of AF after cardioversion (59). Another study noted the cardio protective effects of CPAP (60). Furthermore, a recent study noted that CPAP therapy improves the sympathovagal balance by decreasing the stiffness of major arteries (61).

The role of patient education and support is vital to ensuring the benefits of clinical treatment. The efficacy of CPAP therapy is dependent upon patient adherence and use of the CPAP machine for at least 4 hours to achieve significant clinical benefits (62). There is no evidence for surgical treatment modalities like maxillomandibular advancement or anterior palatoplasty for preventing the OSA-associated arrhythmias.

### **CONCLUSION**

The data from studies conducted thus far suggests that in the elderly, the significance of OSA in causing AF is limited due to reasons that are as yet unknown. There is a possibility that OSA is milder in elderly due to age-related changes.

Changes in the muscle tone and a reduction in weight due to age-related reasons may limit the impact of obesity on OSA. The data from various studies also raises the question of whether there are obesity subtypes that vary by the morphological patterns in facial shapes and palate shape that predispose some patients to OSA or AF. Life expectancy has increased, with the advancements in medicine and public health, leading to an increase in the elderly population worldwide. OSA has become a public health problem with high cardiovascular morbidity. The presentation of OSA is varied and nonspecific in the elderly population compared to the middle aged population. This presentation variation has resulted in the underdiagnosis of OSA in the elderly. It is already evident that the prevalence of OSA is much higher in the elderly compared to the middle-aged groups. Even mild OSA causes significant morbidity and mortality in the elderly. The next challenge is to identify the atypical presentation of OSA in the elderly by conducting further studies. Uniform specific clinical criteria for identifying OSA in the elderly are needed in order to assemble a large sample size with sufficient statistical power to identify those clinical traits that are predictive. By using CPAP therapy in patients with mild OSA or in the early stages, we can find if treating patients early in the disorder helps to prevent AF in the elderly.

### **References**

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