

Research Article

Obstructive Sleep Apnea and Atrial Fibrillation

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Abstract

Obstructive sleep apnea (OSA) is a sleep breathing disorder affecting millions of people worldwide. It is medically significant because it has been shown to be a risk factor for the development of various cardiac pathologies, including atrial fibrillation (AF). Several studies have shown a correlation between OSA and AF and disparities of OSA occurrence in different ethnic and racial groups. We have undertaken a literature review to determine the correlation between OSA therapy and risk of AF recurrence. The results strongly suggest a positive relationship between OSA treatment and reduction in the risks and symptoms of AF and argue for the development of AF therapeutic strategies that target OSA.

Keywords

- Obstructive sleep apnea
- Atrial fibrillation
- Continuous positive airway pressure
- Pulmonary vein isolation

ABBREVIATIONS

OSA: Obstructive Sleep Apnea; AF: Atrial Fibrillation; PAVI: Pulmonary Vein Antrum Isolation; CPAP: Continuous Positive Airway Pressure

INTRODUCTION

Obstructive sleep Apnea (OSA) is the most common sleep-breathing disorder (SBD), affecting almost 12 million Americans. OSA is associated with various cardiac conditions and is a strong risk factor for heart failure, arrhythmia, atrial fibrillation (AF), coronary artery disease, hypertension, pulmonary hypertension, venous thromboembolism and stroke [1-8]. AF is a common condition in people with OSA, with the prevalence of 4.8%. OSA is an independent risk factor for AF in patients without other underlying cardiac disorders [1]. Patients with AF have an irregular heart rate, a condition that is associated with increased overall morbidity and mortality. Therefore, conversion into sinus rhythm (SR) is a common clinical practice in the management of AF and the effectiveness of cardioversion depends on the treatment of underlying conditions especially OSA. Due to strong association between OSA and AF, it is imperative to identify and treat underlying OSA to successfully treat AF. The present review examines the association between OSA and AF, the pathophysiology of this association, differences in the prevalence of OSA among various racial and ethnic groups, and effective therapy for OSA in patients with AF.

METHODS

English language articles relating to OSA and AF were identified using a PubMed search through February 2017. The search was performed using MeSH terms "atrial fibrillation"

and "obstructive sleep apnea" or "breathing disorder" in various combinations. Abstracts were reviewed, and articles relating to OSA and AF were examined in detail. In this review we included articles with following criteria. (1) Articles that discussed association between OSA and AF, (2) reported disparities of OSA between different ethnic group and sex, (3) discussed pathophysiology of development of AF in OSA, and (4) discussed treatment of OSA and AF.

Association of AF and OSA

OSA is a common disorder affecting 10% of the adult population. It is characterized by the collapse of the pharyngeal airway during sleep, leading to hypoxemia, hypercapnia, variations in intrathoracic pressure and increased catecholamine [9]. These physiological changes in turn lead to arrhythmogenesis and development of AF. Severe OSA with AHI (apnea hypopnea index) increases the odds of arrhythmia by more than 30 times [1]. The risk of developing AF is twice as high in patients with OSA compared with non-OSA individuals. A study by Guilleminault et al., in 1983 found an increase in the incidence of AF of 3% in OSA patients compared with the general population [11]. In a large longitudinal multi-center study by Mehra et al, it was reported that the occurrence of AF was more common in people with SBD (4.8%) compared with normal individuals (0.9%) [10]. Gami et al reaffirmed the association between AF and OSA by finding a 49% probability of OSA in AF patients [2]. Recent literature also presents OSA as a significant risk factor by almost 2-fold for the development of AF after cardiac surgery [12]. Long-standing OSA leads to chronic changes in atrial anatomy, causing atrial fibrosis, remodeling, enlargement, electrophysiological alteration and left atrial dysfunction and ultimately AF [13,14]. A summary of some recent association studies is presented in (Table 1).

Table 1: Summary of studies showing association between Obstructive Sleep Apnea and Atrial Fibrillation

Author	Study Population	Design	Outcome Measure	Comments
Mehra et al. (2006) [10].	228 with SBD and 338 without SBD	Cohort	Prevalence of arrhythmia in SBD	Odd ratio of AF was 4 times in SBD compared to non-SBD
Tanigawa et al. (2006) [14].	1763 AF patients underwent NOD to assess SBD	Prospective	SBD and prevalence of AF	Odd ratio of mild SBD was 2.47 compared to 5.66 moderate-severe SBD in AF patients
Gami et al. (2004) [2].	151 AF patients and 312 without AF, underwent PSM for diagnosis of OSA	Prospective	Prevalence of OSA in AF	Prevalence of OSA was higher in AF group vs. control (49% vs. 32%)
Javaheri et al. (1998) [15].	81 HF patients underwent PSM	Prospective	Prevalence of SBD in HF	SBD was more prevalent in AF (22% vs 5%)
Won et al. (2015) [11].	545 cardiac surgery patients, 226 developed POAF; 72 had OSA and 473 without OSA	Retrospective	If OSA is risk factor for POAF	Risk of POAF was higher by 1.83 in OSA compared to non-OSA

Abbreviations: AF: Atrial Fibrillation; HF: Heart Failure; NOD: Nocturnal Oxygen Desaturation OSA: Obstructive Sleep Apnea; SBD: Sleep-breathing Disorder; PSM: Polysomnography; POAF: Postoperative Atrial Fibrillation

Disparities in OSA prevalence

Several studies have compared the prevalence of OSA across racial groups and have found significant differences based on race and sex. African Americans (AAs) have the highest prevalence of OSA. An AA is 88% more likely to have OSA compared with a white person [16], and AA tends to be younger [17]. However, age is a limiting factor, as the elderly population (>65 years of age) of both races have similar rate of OSA but there is a higher rate of severe OSA in AA populations [18]. Asians have a lower prevalence of OSA than whites [19]; while this has been attributed to the lower obesity rates among Asians, another study found an Asian background to be an independent risk factor in the development of OSA in older men [20]. Studies regarding the prevalence of OSA among Hispanics and Native Americans are scant but generally it is a higher or similar rate compared to whites [20,21]. OSA is primarily associated with men, with 2-3 times higher prevalence compared with women [22]. The reasons are probably anatomical and physiological differences, such as characteristics of the upper airway, craniofacial morphology and pattern of fat deposition [23]. The prevalence of OSA in the elderly [18] is similar in men and women as menopause is also an independent risk factor for OSA [24].

Mechanism of OSA induced AF

OSA is characterized by a disturbance in the breathing pattern due to airway obstruction leading to apnea, which results in physiological and anatomical changes. Acute apneic episodes lead to hypoxemia, hypercapnia, alteration in intrathoracic pressure, increased sympathetic tone, and autonomic dysregulation [25-27]. Acute apneic events during sleep has been directly linked to paroxysm of AF [30]; therefore, such physiological changes as mentioned above are associated with arrhythmogenesis and AF [30]. Schlatter et al. showed that the variations in intrathoracic pressure stimulated by OSA lead to premature atrial beats that increase the risk of AF [31]. Long-term OSA has been shown to cause atrial fibrosis with down regulation of connexin and electrophysiological alteration [14,28,29]. In a rat model of OSA, the incidence of AF was higher by 56% compared with control rats and OSA rats showed down regulation of connexin and atrial fibrosis [29]. Down regulation of connexin and fibrosis is shown to cause electrophysiological alteration and AF [14]. Long-term

OSA can lead to atrial dilatation, increased sympathetic tone and increased in inflammatory markers, such as C-reactive protein, which are precursors for AF [13,14,32-34]. The magnitude of oxygen desaturation also plays a vital role in OSA and is an independent risk factor for AF [35].

Coexistence of AF and OSA and the Need for Therapeutic Strategy

Due to a high co-existence of AF and OSA, the effectiveness of AF treatments often depends on simultaneous treatment of OSA. The recurrence rate of AF is higher in OSA patients without treatment compared to non-OSA patients [36,37]. OSA is a collapse of airway and continuous positive airway pressure (CPAP) is a treatment of choice that applies continuous air pressure to keep airways continuously open. CPAP therapy has been shown to be the most effective therapy to ameliorate cardiac arrhythmia in severe OSA patients [38].

Conversion of AF to sinus rhythm is the cornerstone of the AF management which is by electrical and/or pharmacological methods. An emerging therapy for AF uses pulmonary vein antrum isolation (PVI), an invasive catheter procedure to ablate and to achieve sinus rhythm. The effectiveness this procedure is measured by AF-free survival after PVI and it is greatly affected in patients with OSA. CPAP use in OSA patients has shown to increase AF-free survival by twice as much compared with non-CPAP group after PVI and anti arrhythmic drugs [39]. A prospective study showed that the recurrence of AF one year after electrical cardioversion therapy was better with CPAP: 42% with CPAP for OSA compared to 82% in untreated OSA and 53% in patients without underlying OSA [40]. Patel et al., found that the success rate of the PVI procedure for AF increased by 8 times with the use of CPAP compared to noCPAP in OSA patients [41]. A summary of studies comparing the efficacy of CPAP to other therapies is presented in (Table 2).

CONCLUSIONS

From our literature review on the association between OSA and AF, we have concluded that AF frequently co-exists with OSA. The prevalence of AF is significantly higher in patients with concurrent OSA and vice versa. It was therefore reasonable to expect that a successful treatment of OSA would have a positive

Table 2: Summary of studies comparing the efficacy in treatment of Atrial Fibrillation in patients with Obstructive Sleep Apnea.

Author	Study Population	Design	Outcome Measure	Comments
Farrehi et al. (2015) [42].	247 AF patients underwent ablation, 94 had diagnosis of OSA. Off 153 without OSA, 121 had high risk for OSA on STOP-BANG questionnaire	Prospective	1) To determine the prevalence of OSA in AF patients getting ablation 2) its relation to recurrence of AF	Success rate of ablation was higher in low risk of OSA compared to known OSA and high score OSA (91%, 70%, and 77% respectively) Prevalence of OSA is 79% in AF patients going for ablation
Mohanty et al. (2014) [43].	1257 AF patients underwent ablation	Prospective	Ablation success rate in AF with OSA and MS	Recurrence rate of AF in OSA group was 38% compare to non-OSA/MS group.
Naruse et al. (2013) [44].	153 drug refractory AF patients underwent PVI; 116 had OSA	Prospective	Recurrence of AF with CPAP usage after ablation	Recurrence of AF was higher in non-OSA to CPAP to non-CPAP (22%, 30% and 53%, respectively)
Fein et al. (2013) [39].	426 AF patients underwent PVI. 62 were diagnosed OSA with PSM	Retrospective	Recurrence rate of AF with CPAP usage after PVI	Recurrence of AF was lower in CPAP group (36.7% vs 71.9%)
Matiello et al. (2010) [45].	174 AF patients underwent ablation. Based on BQ and PSM, 17 had non-severe OSA and 25 had severe OSA	Retrospective	Effect of OSA on AF ablation	AF free survival was higher in low risk OSA compared to non-severe OSA and severe OSA (48.5%, 30.4%, and 10.3% respectively)
Patel et al. (2010) [41].	3000 AF patients underwent PVAI, 640 had OSA	Retrospective	CPAP improves PVAI success rate.	PVAI treatment failure was common in non-CPAP vs CPAP users (78% vs 69%)
Jongnarangsin et al. (2008) [46].	324 AF patients underwent ablation, 32 had OSA diagnosed by PSM	Retrospective	Effectiveness of ablation in AF based on BMI and OSA	AF free events were higher in non-OSA to OSA patients (63% vs 41%)
Kanagala et al. (2003) [40].	118 AF patients underwent cardioversion; 39 had OSA and 79 control. 27/39 not using CPAP, 12/39 were using CPAP	Prospective	Recurrence rate of AF after cardioversion in OSA patients	Recurrence rate AF was 82%, 42% and 53% in non CPAP users vs. CPAP users vs. control, respectively.

Abbreviations: AF: Atrial Fibrillation; BQ: Berlin Questionnaire; CPAP: Continuous Positive Airway Pressure; MS: Metabolic Syndrome; OSA: Obstructive Sleep Apnea; PSM: Polysomnography; PVAI: Pulmonary Vein Antrum Isolation; PVI: Pulmonary Vein Isolation; STOP-BANG: Snore at night; Tired during daytime; Observed stop breathing; Hypertension treatment; BMI >35 kg/m², Age > 50 years; Neck circumference > 40 cm; Male gender

effect on the treatment of AF. Taken together, future therapeutic and management strategies of AF should take into account the status of any accompanying sleep breathing disorder.

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