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Review Article

Should We Screen All Elderly Patients with AF for Sleep-Disordered Breathing?

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Abstract

Atrial fibrillation (AF) is associated with a multitude of adverse outcomes. The arrhythmia is associated with increased risk for stroke and heart failure (HF), reduced quality of life and increased shortness of breath. In addition, previous research has found a high prevalence of AF in patients with sleep-disordered breathing (SDB) and the two conditions appear inextricably linked. Traditionally, cardiologists could stand accused for neglecting the strong association between AF and SDB. The precise pathophysiological mechanisms that connect these conditions remain poorly defined and are of interest. There is strong evidence supporting adequate treatment of OSA to improve AF outcomes and also for non-pulmonary vein triggers of AF in such patients, thereby complicating ablative strategies. This paper analyses the connection between the two conditions in detail and also provides a proposal for screening all elderly patients with AF for SDB (regardless of Epworth score) in order to improve management of these patients.

Keywords: *Sleep-Disordered Breathing; Atrial Fibrillation*

Introduction

"Sleep-disordered breathing" is an umbrella term for a group of pathophysiological mechanisms. The group are bound by the common finding of interruption of breathing for at least 10 seconds (apnoea) or a significant reduction in respiration with accompanying oxygen desaturation (either > 3% or > 4% reduction in oxygen saturation depending on national definition) or waking reactions (hypopnoea) [1].

Obstructive sleep apnoea (OSA) is the most common form of SDB with an estimated prevalence in the general population of between 1% to 2% [2,3]. The condition is characterised by obstruction of the upper respiratory tract during the night which leads to suspension of breathing and hypoxaemia. Since circa 2000 there has been evidence from prospective studies that OSA is an independent risk factor for the development of arterial hypertension [4]. It is also well-established that hypertension is the most common co-morbidity in patients with atrial fibrillation (AF) [5]. OSA is a condition characterised by obstructed breathing during sleep causing sleep fragmentation and intermittent hypoxaemia. Longitudinal cohort studies have shown that people with OSA are at increased risk of all-cause and cardiovascular mortality as well as incident stroke and coronary heart disease.

In recent years, and particularly in cardiac patients, another group of sleep-related breathing disorders has gained attention, namely central sleep apnoea (CSA) [6]. CSA is characterised by a lack of drive to breathe during sleep, resulting in repetitive periods of insufficient ventilation and compromised gas exchange. CSA also results in hypoxaemia. In this disorder, there is typically a periodic increase and decrease in depth of respiration with intermittent phases of apnoea followed by hypoxaemia. It is known that there is a high prevalence of CSA in patients with an impairment of left ventricular systolic impairment which is another risk factor for the development of AF [7,8].

AF and SDB are undoubtedly linked. The prevalence of OSA in patients with AF have been reported to range anywhere from 21% to just over 80% and increases with age [1,2]. The common risk factor profiles of the two conditions is the most obvious explanation for the connection. However, this paper analyses the physiological mechanisms that link OSA and AF. The prevalence of CSA in patients with AF is less well defined, but appears to be particularly high in patients who also have HF and a reduced left ventricular ejection fraction (LVEF). We also aim to analyse the pathophysiology between CSA and AF.

AF and sleep-disordered breathing

Perhaps the most straightforward explanation for the association is that patients with AF and SDB share a number of comorbidities, including age, male sex, hypertension (HTN), congestive HF and coronary artery disease (CAD) [7,8]. However, more evidence is emerging for a true physiological connection. It is well established that co-existing OSA reduces the effectiveness of rhythm-control treatment of AF (including direct current cardioversion and AF ablation) and there is an increased risk of arrhythmia recurrence in the presence of SDB. Treating OSA with continuous positive airway pressures (CPAP) therapy has shown the potential to decrease the incidence of AF, improve the effectiveness of AF interventions, and decrease the risk of arrhythmia recurrence, although data from large randomised-controlled clinical trials are lacking.

Various mechanism mediated adverse electrical and structural changes have been proposed to explain the increased risk of AF in patients with OSA. Multiple studies have also observed a greater risk of AF recurrence after cardioversion and catheter ablation in patients with untreated OSA. The epidemiological and pathophysiological associations between OSA and AF have significant implications on the treatment outcomes of rhythm-control strategies for AF. Adequate screening and optimal management of OSA are of key importance to help improve the clinical outcomes following cardioversion and catheter ablation.

In this review, we sought to explore the pathophysiological association between AF and OSA in detail and to determine how treatments for AF can be effective in improving SDB.

Sleep-Disordered Breathing and Atrial Fibrillation in Heart Failure

OSA has consistently been shown to be an independent risk factor for AF in patients with and without HF [9-11]. In addition, Kangala., *et al*. observed a higher recurrence rate of AF after cardioversion in patients with untreated OSA compared to patients with continuous positive airway pressure (CPAP) treated OSA [12]. In contrast to OSA, the relationship between CSA and AF remains less clear. There are, however, multiple studies addressing the association [8,13-19]. These studies reported a high prevalence of CSA in patients with left ventricular systolic dysfunction, ranging from 25% to 64%. This wide range of CSA frequency in HF patients may be explained by a number of variables in including patient selection, HF severity and aetiology, age, gender, HF medication and various AHI cut-offs used to define CSA.

Sleep-disordered breathing in patients with atrial fibrillation and normal systolic left ventricular function

Leung., *et al*. compared the prevalence of AF in a series of patients with idiopathic CSA (apnoea-hypopnoea index > 10 events per hour, > 50% central events) with that in 60 patients with OSA (apnoea-hypopnoea index > 10, > 50% obstructive events and 60 patients without sleep apnoea (apnoea-hypopnoea index < 10), matched for age, sex, and body mass index [13]. The prevalence of AF among patients with idiopathic CSA was found to be significantly higher than the prevalence among patients with OSA or no sleep apnoea (27%; 1.7% and 3.3%, respectively, $P < 0.001$) [12]. This study implicates the importance of CSA in patients with AF and a normal LV function.

Effect of CPAP Treatment

Numerous prospective studies have shown that the use of CPAP significantly reduces AF recurrence following AF ablation [12,20,21]. The reason for the benefit of CPAP is interesting. Apnoeic episodes can result in wide fluctuations in intrathoracic blood pressure which can, in turn, lead to left atrial stretch via pressure and volume overload and alteration of sympathetic tone [22,23]. Intermittent periods of hypoxaemia and hypercapnic can lead to atrial remodelling with regions of fibrosis [23]. These physiological changes could better explain the link between the two condition.

Rhythm Control AF Treatment and SDB

Naruse., *et al*. found that restoring sinus rhythm by radiofrequency catheter ablation was associated with a decrease in apnoea-hypopnoea index (AHI) (AHI; median, 21, to median 15, P = 0.002) [24]. The effect of OSA and CPAP has also been examined among patients undergoing catheter ablation of AF. Patel et al evaluated 3,000 consecutive patients undergoing pulmonary vein isolation between January 2004 and December 2007, of which 640 (21.3%) were identified as having OSA. Overall, patients with OSA had a statistically significant increase in procedural failures ($p = 0.024$) compared to patients without OSA. Among those with paroxysmal AF, OSA patients had more non-pulmonary vein triggers and posterior wall firing than patients without OSA (20% versus 8%, $p < 0.001$). This was also true in non-paroxysmal AF patients; patients with OSA had more non-pulmonary vein triggers than those without OSA (31% versus 19%, $p = 0.001$). Importantly, treatment with CPAP reduced the rate of AF recurrence (79% versus 68%, $p = 0.003$). The presence of non-pulmonary vein triggers and absence of CPAP use strongly predicted ablation failure (HR 8.81, $p < 0.001$).

Screening patients with AF for SDB

Our proposal to screen all AF patients for SDB arises from the high prevalence of this condition in patients with AF. Given the significant benefits from diagnosing and subsequently treating such patients there would appear to be a number of positive outcomes for this approach. There are few indicators providing clues to underlying SDB in AF patients. This ensures a real challenge to tailor SDB investigations to certain patients and would support screening all patients. Traditionally, Epworth scores provide symptomatic evidence of increased drowsiness which is a feature of SDB. However, patients with AF typically have normal or low Epworth scores as demonstrated by data from our own centre in which 54 patients (without previously diagnosed SDB) aged 66 - 90 with persistent AF underwent sleep tests with the novel Watch Pat device there was an average score of 8.04. According to UK NICE definition 47/54 (87%) had evidence of SDB. 17/54 (31.5%) had severe sleep apnoea vs. 14.3% post AF intervention ($p < 0.05$).

Discussion

AF is independently associated with CSA in patients with both normal and impaired LV systolic function. AF treatment in the form of electrical cardioversion and radiofrequency ablation can reduce AHI. However, no previous study has assessed the impact of different treatments on AHI head to head. SDB in AF patients is of great relevance if a rhythm control strategy is to be pursued. There is statistically more chance of a non-PVI trigger in patients with SDB and AF and this is relevant as it might indicate a potential role for non-PV ablation. In addition, untreated SDB will reduce the chance of success from ablation significantly.

Few clinical trials have assessed the long-term impact, if any, on effective AF treatment on apnoea-hypopnoea index. The purpose of this review is to analyse the available data to determine the true impact of AF treatment on SDB outcomes. Based on available data, inclusion of SDB recognition and management strategies as part of AF management appears to have the potential to reduce the impact of this arrhythmia.

Conclusions

Patients with AF have a high prevalence of SDB. SDB is almost certainly underdiagnosed in AF patients. The association between the two conditions is not fully explained by the common risk factors they share. It remains unknown whether CSA is more common in AF because of diastolic dysfunction or whether the phenomena associated with CSA predispose to AF. The majority of the literature analysing the association between these conditions has evaluated the established benefit of treating SDB on AF outcomes.

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