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Obstructive Sleep Apnea Treatment and Atrial Fibrillation: a need for definitive evidence.

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Abstract

Prevalence rates of atrial fibrillation (AF) and obstructive sleep apnea (OSA) are rising on a global scale. Epidemiological data have consistently demonstrated an independent association

between the two conditions. Investigators pose that pathophysiologic features of OSA enable progression of the AF substrate; these features include abnormalities of gas exchange, autonomic remodeling, atrial stretch and inflammation. Furthermore, many of the mechanistic perturbations that impact the AF substrate in OSA can be substantially attenuated by effective treatment with continuous positive airway pressure (CPAP). Clear associations of OSA treatment and improved AF control have been observed across multiple clinical contexts. However, the precision and generalizability of these findings are unclear in view of the data's observational nature. Although risk factor management has emerged as a critical component of AF treatment, effective control of many AF risk factors can be challenging in the longer term. In view of the efficacy and sustainability of CPAP therapy, OSA raises its profile as a prime candidate for intervention. However, translation of this strategy to the broader framework for AF management requires robust data from randomized controlled trials.

Keywords:
atrial fibrillation
obstructive sleep apnea
continuous positive airway pressure

Prevalence of AF and OSA:

Atrial fibrillation (AF) is the commonest sustained cardiac arrhythmia in humans and has been estimated to affect up to 33.5 million people worldwide. [1] Its exponential growth in global prevalence carries profound implications for community health and sustainability of existing

health structures. [2-4] Similarly, obstructive sleep apnea (OSA) has become increasingly diagnosed, with large cohort studies placing its prevalence at 6.9% to 9% in women and 17% to 31% in men. [5, 6] Alarmingly, a recent study suggests that up to 23% of women and 49% men have moderate to severe OSA.[7] The concomitant rise of AF and OSA may reflect their close association with the evolving global obesity epidemic.

OSA has been consistently identified as an over-looked cardiovascular risk factor[8]. Associations of sleep apnea and its treatment with cardiac arrhythmia and arrhythmia burden have long been observed. [9] However, the profound role of OSA in AF pathogenesis and treatment has only recently become a focus. This review will survey the epidemiological data for a relationship of OSA with AF, discuss potential mechanistic links and evaluate the role of OSA treatment in AF management, within the broader scientific and clinical paradigm for AF.

Epidemiological links between AF and OSA:

Epidemiological studies have shown associations of cardiovascular disease with OSA. In the Wisconsin Sleep Cohort, 1522 patients were followed for 18 years. The adjusted hazard ratio for cardiovascular mortality in patients with untreated OSA was 5.2 (95% CI 1.4, 19.2).[10] The Sleep Heart Health Study (SHHS) correlated the results of 6424 patients having overnight, unattended sleep studies, with self-reported cardiovascular disease to discern potential links.[11] OSA severity was independently associated with increasingly prevalent cardiovascular disease. [11] Hypertension[12-14], left ventricular hypertrophy[15, 16] and early atherosclerosis[17], with a concomitant decline in left ventricular function[16], have all been associated with OSA. In a recent meta-analysis, OSA significantly increased AF risk after coronary artery surgery (OR 1.86 (1.24, 2.80) p=0.003).[18]

OSA and AF share multiple risk factors: advancing age, male gender, obesity, hypertension and heart failure. [19-22] Associations of OSA and AF in cross-sectional studies can be difficult to interpret due to overlap of comorbidities and patient characteristics.

The association of sleep disordered breathing (SDB) and incident AF was explored by the SHHS, which after regression analysis that adjusted for common risk factors, determined a 4-fold increased risk of nocturnal AF associated with SDB.[23] Gami et al retrospectively analyzed 3542 sleep study patients to determine the impact of OSA on incident AF.[24] OSA strongly predicted incident AF within ~ 5 years of diagnosis (HR 2.18 (1.34, 3.54) p=0.002), and greater OSA severity conferred a proportionally higher AF risk (1.31 per AHI unit (1.14, 1.50) p=0.0001). The association persisted in patients < 65 years even after adjusting for obesity.

There is considerable evidence linking sleep apnea with AF in heart failure. However, central sleep apnea (CSA) features as the predominant apnea subtype in this population. In a study by Jahaveri et al of 81 heart failure patients, 40% had CSA and 11% OSA. AF prevalence was significantly higher among sleep apnea patients.[25] A larger retrospective study of 450 patients with heart failure also found an association between AF and sleep apnea and was further specified as being central rather than obstructive sleep apnea.[26] Two studies, one in males with systolic heart failure[27] and the other in stable outpatients with congestive heart failure[28], also demonstrated an association between both central and obstructive sleep apnea and AF.

Multiple studies have evaluated the prevalence of OSA among AF populations across a variety of clinical contexts.[29, 30] However, OSA diagnosis has been inadequate in many studies, with reliance placed on patient reports [31, 32] or OSA questionnaires[29, 33] without objective adjudication

by overnight polysomnogram (PG). Despite prior validation of questionnaires (such as the Berlin Questionnaire) that identify patients at high-risk of OSA, their utility remains unclear in an AF population that is already at high risk for OSA and whose symptoms are often indistinguishable.

Notwithstanding these limitations, studies of multiple patient cohorts have consistently demonstrated higher OSA prevalence among AF populations. [29, 30, 32, 34] Stevenson et al confirmed these trends by screening 90 consecutive AF patients and 50 matched controls from the general cardiology non-AF population with PG.[35] Significant OSA (defined as AHI> 15) was independently associated with AF (OR 3.04 (1.24, 7.46) p=0.02). Additionally, the relationship of OSA severity with AF frequency[35], AF persistence[34, 35] and treatment efficacy[34, 36] suggest a dose dependent relationship of OSA severity with the AF substrate. Furthermore, the impact of OSA on the AF substrate appears compounded by presence of other AF risk factors.[33, 37]

Strong epidemiologic data confirm a close relationship of OSA with AF, suggestive of a mechanistic link amenable to intervention.

Mechanisms of AF in OSA:

Moe et al posed a model for AF that consisted of multiple wavelets that dynamically coalesce and diverge across the atrial myocardium. [38] The later seminal observation by Haissaguerre et al of spontaneous pulmonary vein ectopy is central to our understanding of AF pathophysiology and remains the cornerstone for curative ablation.[39, 40]

While paroxysmal AF is primarily driven by pulmonary vein ectopy, persistent AF appears to be sustained by a complex interaction of triggers and atrial substrate. [41] High-density mapping studies that utilize complex signal processing techniques have implicated focal atrial sources of repetitive activity, termed 'rotors' or 'driver domains' in persistent AF.[42-45] However, their temporal stability remains contentious. A recent study of explanted human hearts utilized simultaneous endo- and epi-cardial atrial mapping to demonstrate that AF can be driven by intramural micro re-entry facilitated by discontinuities of fiber orientation and microscopic conduction barriers.[46] The complex interplay of multiple substrate factors highlights the limitations of trigger- based treatment strategies to achieve durable rhythm control. A sophisticated approach that addresses the arrhythmogenic substrate and its progression appears essential.

The substrate for AF in OSA has been defined with respect to a number of mechanisms. These include abnormalities of gas exchange, autonomic nervous system modulation (ANS), atrial stretch and inflammation. [47-50]. These factors can act as both triggers and perpetuators and may explain the limited efficacy of arrhythmia controlling interventions in untreated OSA. (Figure 1)

Animal data evaluating the impact of apnea on atrial electrophysiology demonstrated slowed atrial conduction and increased atrial refractoriness. Temporal differences of normalization of these factors after apnea cessation enable a window for heightened AF vulnerability. [51, 52] Changes in electrophysiology appear to be driven by hypercapnea but not hypoxia.[51] However, data on the impact of hypoxia/hypercapnea on human cardiac electrophysiology are limited. In clinical studies the risk of incident AF was proportional to the magnitude of nocturnal desaturation (HR 3.29 per 0.5 U Log change (1.35, 8.04)).[24] Similarly, Tanigawa et al correlated the number of oxygen desaturation events < 3% obtained during PG with AF prevalence in 1763

men.[49] After adjustment for covariates, the odd ratios for AF were 2.47 (0.91, 6.69) for those with 5 to 15 events per hour and 5.66 (1.75, 18.34) for those with >15 events per hour. In the SHHS a clear association of SDB and nocturnal AF was identified. Furthermore, a SDB event conferred a 4-fold risk of nocturnal AF, implying a direct temporal relationship between the two. [23, 50] The aggregate of this data suggest that abnormalities of gas exchange, which characterize apneas/hypopneas in OSA, impact the AF substrate.

The ANS plays a critical role in AF pathogenesis. Alterations of autonomic tone during apneic episodes commonly cause surges in blood pressure, increased cardiac volume and increased cardiac afterload. Negative tracheal pressure abbreviates the atrial ERP and increases AF inducibility.[53] Although these changes appear to be refractory to commonly used antiarrhythmic drugs,[53] they are remediable by blocking or attenuating the influence of the ANS [54]. Ghias et al further highlighted the role of the ANS.[55] In a canine model of OSA, atrial pacing was used to precipitate AF while simultaneously recording ganglionic plexi (GP) activity at the right pulmonary vein (PV). While progressive escalation of GP activity heralded the onset of AF, targeted GP ablation suppressed AF inducibility.

Secondly, increased sympathetic tone and diastolic impairment, both of which have been linked with OSA[56], causes atrial stretch. Stretch has been shown to remodel the atrial substrate and predispose to AF. Slowed conduction, increased electrogram complexity, low voltage regions denoting scar and impaired sinus node reserve characterize the human atria in stretch.[57-65]. Walters et al described increased signal complexity and altered conduction at the PV-atrial junction in response to transient stretch.[66] Studies of atria in OSA have identified a similarly remodeled substrate and suggest that OSA can induce both temporary and persistent substrate changes.[67-69] (Figure 2a)

Inflammation has been observed in both OSA and AF, prompting speculation of an inflammatory link. Chung et al observed > 2 fold higher CRP levels in patients with AF compared with sinus rhythm. CRP titers correlated with AF burden and persistence.[70] Similarly, investigators have demonstrated raised inflammatory markers, which include CRP, TNF alpha and IL-6, in patients with OSA.[47, 71-73] Shamsuzzaman et al measured CRP levels in 22 OSA patients and 20 matched controls. CRP and CRP levels were independently associated with OSA and OSA severity, respectively.[47] These associations appear to persist even after adjusting for confounding disease states including obesity.[73, 74] An inflammatory mechanism for AF is supported by data drawn from MRI[75, 76], electrophysiologic[77, 78] and histologic studies[79-81], which correlate scar/fibrosis burden with the extent of atrial remodeling. Although the cause of elevated CRP levels in AF and OSA remain unknown, it may reflect an inflammatory state that promotes the persistence of AF.

A poor understanding of fundamental AF mechanisms, especially with regard to persistent AF, have led to sub-optimal treatment options. [82] Both clinician and patient continue to search for alternative management paradigms that extend beyond pharmacological, DCR and ablative therapies. Past investigators have observed a remodeled atrial substrate in lone AF[83] that continues to progress even after apparent successful curative ablation.[84] These studies provide strong support for unrecognized or overlooked risk factors that contribute to substrate progression. The rationale for substrate modification by risk factor treatment can be drawn from previous observations where atrial remodeling was reversed after elimination of inciting factors.[61, 64, 77, 85, 86]

Recent studies have evaluated the impact of sustained weight loss on AF profile. Abed et al[87] demonstrated improved AF burden, AF symptom scores and cardiac structure following weight

loss and cardio-metabolic risk factor management in obese patients. Subsequently, the ARREST-AF cohort[88] extended the benefits of weight loss and risk factor management to the ablation context; patients without risk factor management were 2.3 times more likely to fail AF ablation.

Despite compelling data in support of weight loss, durable weight loss can be difficult to accomplish. Patient compliance presents the most significant obstacle to sustained weight loss.[89] Most patients regain up to one-third of weight lost within a year of treatment and approach baseline at 3 to 5 years following treatment.[90, 91] These trends appear to persist even when pharmacological strategies are utilized. Weight fluctuation has been observed to increase AF risk and even ameliorate reduction of risk achieved by previous weight loss.[92] In light of the significant limitations of weight loss for AF management, OSA presents a prime target for sustainable and feasible treatment.

Impact of OSA treatment on AF:

The impact of OSA treatment on AF has been the subject of investigation of several small observational studies. (Table 1) Continuous positive airway pressure (CPAP) therapy, the accepted standard of treatment for significant OSA, has been the focus of evaluation thus far. Although limited by study quality, the bulk of evidence suggests that CPAP therapy improves control of AF irrespective of the rhythm control modality employed: AAD's[36], DC cardioversion (DCR) [32] or catheter ablation. [37, 93-95] In the absence of CPAP therapy, treatment response appears to be proportional to OSA severity.[36] (Figure 3)

In the recent 'Outcomes Registry for Better Informed Treatment of Atrial Fibrillation' (ORBIT-AF), 10,132 AF patients, of which 1,841 had OSA, were enrolled and followed for 2 years.[96] AF

patients with OSA had worse symptoms and required more hospitalizations than patients without OSA. Treatment with CPAP therapy decreased the risk of transition from paroxysmal to persistent AF among OSA patients (HR 0.66 CPAP use versus non-use (0.46, 0.94), p= 0.021). These observations imply a dynamic interaction between OSA and the AF substrate, capable of attenuation by treatment.

Observational studies suggest that OSA treatment facilitates maintenance of sinus rhythm following DCR. Kangala et al prospectively evaluated the impact of CPAP on 39 OSA patients having DCR with a diagnosis of OSA confirmed by overnight PG.[32] Twelve patients were classed as CPAP users based on history or CPAP compliance, while the remaining 27 patients were classed as CPAP non-users. Additionally, 79 patients without a history of OSA formed a control group to assess the impact of treatment on arrhythmia recurrence. Freedom from AF was superior among CPAP users compared with non-users (CPAP users 58% versus CPAP non-users 18%, p=0.013). Additionally, recurrence rates among CPAP users was comparable to the non-OSA group. In another study of DCR candidates, higher atrial ectopy burden following cardioversion correlated with obstructive respiratory events during sedation. Alleviation of obstruction by nasopharyngeal tube insertion resulted in reduction of ectopy burden.[97]

The impact of OSA treatment has been extended to the ablation context and results remain consistent with non-ablation studies. [30, 33, 34, 37, 94, 98] Fein et al prospectively evaluated a cohort of 62 patients with OSA having pulmonary vein isolation.[95] CPAP therapy was associated with both superior single (65.6% vs. 33.3%; p=0.02) and multi- procedure success rates (71.9% vs. 36.7%; p=0.01). (Figure 4) Similar to the DCR cohort, therapy improved success rates among OSA patients to a level comparable with patients without OSA. Notably, in the absence of treatment, catheter ablation delivered results equivalent to AAD or DCR alone. In a later study, Szymanski

et al observed that increasingly severe OSA was associated with progressively higher rates of AF recurrence following ablation (non-OSA 45.6% vs. mild OSA 66.2% vs. moderate OSA 57.6% vs. severe OSA 81.8%; p for trend=0.005).[34] Correlations between procedural failure and an increasingly remodeled atrial substrate in the general literature[75, 76] imply OSA severity has a proportionate impact on the AF substrate.

However, most studies including ORBIT-AF[96], Kanagala et al[32] and Fein et al[95], did not systematically exclude OSA among control group patients; in view of high rates of OSA in AF populations, the control group likely comprised an admixture of patients. Lack of a robust control population makes it difficult to quantify the impact of OSA on the AF substrate and to precisely determine the extent of substrate modification mediated by CPAP therapy. Pooled data of patients having pulmonary vein isolation place patients with OSA at ~31% increased risk of procedure failure compared with non-OSA patients.[99] CPAP therapy reduces the risk of procedure failure by ~57-58%.[99, 100] Further evidence for CPAP therapy impacting on substrate progression can be discerned from AF cohorts with OSA having ablation for CTI dependent atrial flutter. Following CTI ablation alone, patients treated with CPAP were less susceptible to recurrent AF.[98] In light of mounting evidence that common triggers are responsible for AF and atrial flutter[101, 102], CPAP may quiet atrial/PV triggers from initiating AF.

Favorable structural cardiac remodeling in response to CPAP therapy has been observed in the general OSA population.[103] However, evidence for structural change in response to OSA treatment in AF is sparse. Neilen et al[31] assessed cardiac structure and function using a pre-procedurally acquired MRI in 720 AF patients having ablation. One hundred and forty-two patients with a self-reported diagnosis of OSA were classified as 'treated' versus 'untreated' based on median CPAP times, while remaining patients were assumed OSA-free and comprised

a reference group. Compared with the untreated group, OSA treatment was associated with favorable (atrial and ventricular) cardiac dimensions and superior freedom from AF. Furthermore, the treated and reference groups were comparable. However, in the absence of serial imaging studies and definitive diagnosis/exclusion of OSA by PG, only speculative conclusions can be drawn about the impact of CPAP on structural remodeling and the AF substrate.

Conclusion:

Epidemiologic data demonstrates a strong relationship of OSA with AF. Furthermore, mechanistic studies together with correlations of apnea severity with AF persistence/burden imply that OSA directly impacts the AF substrate. Thus, treatment of OSA carries the potential to modify the AF substrate and improve its clinical profile. Difficulties of effective long-term control of other AF risk factors, strengthens the case for OSA management in AF.

However, studies that have evaluated the impact of CPAP therapy on AF have been small and observational in nature with multiple study limitations. Notably, variable techniques have been utilized to diagnose OSA, control groups are frequently unscreened and CPAP compliance data are not evaluated. Notwithstanding these limitations, considerable treatment benefits in favor of CPAP therapy are evident from pooled data, regardless of clinical context.

The existing evidence base advocates for screening and treatment of OSA in cases of newly diagnosed AF. However, there is an urgent need for high quality data in the form of a randomized trial that definitively demonstrates the benefit and effect size of CPAP therapy. Strong evidence has the potential to profoundly impact the framework for AF management by

mandating OSA diagnosis and treatment. Such strategies proffer new hope to stem the rising tide of AF where conventional therapies appear to have reached their limits.

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Table 1.

Study	**Population**	**Mode of OSA diagnosis**	**AF surveillance**	**Result**
Kanagala et al (2003) Prospective observational study Follow up: 12mths	DCR for AF/AFL OSA: 39 (30M, 65±10yrs) - CPAP users: 12 - CPAP non-users: 27 Control: 79 (51M, 67±13yrs)	43 patients identified with OSA based on previous SS. Data regarding CPAP therapy available in 39: 27 non-users (based on non-use/inappropriate use). Cohort compared with 79 patients not screened for OSA.	Questionnaires, medical record review and telephone interviews.	CPAP non-use associated with higher recurrence rates compared with CPAP use (82% vs 43%, p=0.013) and controls (54%, p=0.009).
Jongnarangsin et al (2008) Prospective observational study	AF ablation OSA: 32 (M 246, 57±11yrs) - CPAP therapy: 18	Patients with OSA had prior SS confirmed diagnosis. OSA was not excluded in all patients in the control group.	Patients that remained arrhythmia free at 3-6 months had 30day triggered event monitors. Surveillance was otherwise symptom based	63% of patients without OSA and 41% with OSA were free from recurrent AF without antiarrhythmic therapy (P = 0.02). OSA was the

Follow up: 7±4mths	- No CPAP therapy: 14 No OSA: 292		and clinic visit.	strongest predictor of recurrent AF (OR=3.04, 1.11–8.32, P= 0.03). 50% OSA patients treated with CPAP versus 29% untreated patients remained free from AF.
Patel et al (2010) Prospective observational study Follow up: 32±14mths	AF ablation OSA 640 (M 475, 51±10yrs) - CPAP 315 - No CPAP 325 No OSA: 360	Patients with OSA had prior SS confirmed diagnosis. All patients did not have SS to diagnose or exclude OSA.	During the first 5 months after ablation, cardiac event monitoring was used with rhythm transmission (3/day and during symptoms). In addition 48-hour Holter monitoring at 3, 6, 9, and 12 months (6 monthly thereafter).	79% of the non-CPAP and 68% of the CPAP group were free of AF (P=0.003).
Naruse et al (2013) Prospective observational study Follow up: 18.8±10.3mths	AF ablation M 128, 60±9yrs OSA: 116 - CPAP use confirmed: 82 - presumed CPAP non-use: 34 No OSA: 37	SS performed 1 week following ablation.	Surveillance consisted of 3mthly clinic follow up, 24hr Holter monitoring (1, 3, 6 and 12 mths), symptom led ECG and twice daily portable ECG monitoring on 3 consecutive days (1, 3, 6 and 12 mths).	OSA diagnosis (HR 2.61; 1.12–6.09) and CPAP use (0.41; 0.22–0.76) were associated with AF recurrence.

Fein et al (2013) Prospective observational study Follow up: 12mths	AF ablation M 85, 57±1.7yrs OSA: 84 - PVI, OSA and CPAP: 32 - PVI, OSA and no CPAP: 30 - no PVI, OSA, CPAP: 22 PVI, no OSA and no CPAP: 30	Patients with OSA had prior SS confirmed diagnosis. All patients did not have SS to diagnose or exclude OSA.	Follow-up consisted of both clinic visits (1, 3, 6, and 12 months) and 2-week trans telephonic monitoring at 3, 6, and 12 months. Additional trans telephonic monitoring performed based on symptoms.	CPAP therapy resulted in higher AF-free survival rate (71.9% vs. 36.7%; p=0.01) and AF-free survival off AADs or repeat ablation following PVI (65.6% vs. 33.3%; p=0.02). AF recurrence rate of CPAP-treated patients was similar to a group of patients without OSA (HR: 0.7, p=0.46).
Neilen et al (2013) Prospective observational study Follow up: 42mths (23-50)	AF ablation M 531, 56±11yrs OSA 142 - Treated 71 - not treated 71 No OSA 578	Berlin questionnaire used to diagnose sleep apnea in all patients. Patients with OSA had diagnosis confirmed by SS. Treatment vs no treatment based arbitrarily on the median CPAP use time.	Symptom based.	OSA (HR 2.79, 1.97 to 3.94, P< 0.0001) and untreated OSA (HR 1.61, 1.35 to 1.92, P< 0.0001) were highly associated with AF recurrence.
ORBIT-AF (2015) Prospective observational registry Follow up: up to 24mths	All patients with AF (without a reversible cause) M 1270, 75 (67-82)yrs	Data regarding OSA diagnosis and CPAP used was obtained by physician history. OSA not diagnosed/excluded by SS in all patients.	AF burden not evaluated. Progression from paroxysmal to persistent AF determined by 6 monthly follow up.	OSA patients using CPAP were less likely to progress to permanent forms of AF compared to patients without CPAP (HR, 0.66; 95% CI, 0.46-0.94; P = 0.021).

	OSA: 1841 - CPAP 1067 - no CPAP: 203 No OSA: 8291			

Table 1. Studies evaluating the association of OSA treatment and AF: study characteristics and results. Studies are observational, often do not diagnose OSA with sleep study and utilize sub-optimal AF monitoring strategies. AF atrial fibrillation, OSA obstructive sleep apnea, SS sleep study, M male.

Figure legends.

Figure 1. Main mechanisms in obstructive sleep apnea that contribute to atrial remodeling. Associated AF risk factors that commonly co-exist with OSA also contribute to the AF substrate. ANS autonomic nervous system, BP blood pressure, ERP effective refractory period, OSA obstructive sleep apnea.

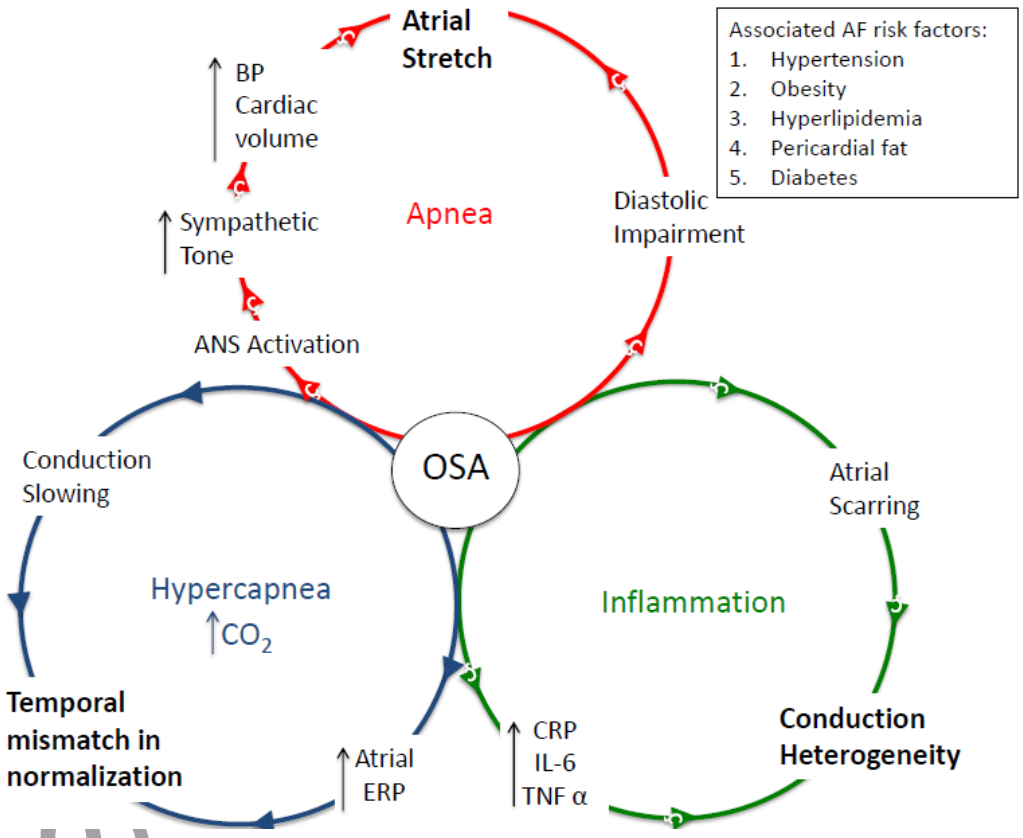

Figure 2. Electroanatomic voltage maps of the right atrium (RA) and the left atrium (LA) in a representative patient with obstructive sleep apnea (OSA) (apnea–hypopnea index = 86; top) and a reference (apnea–hypopnea index < 15; bottom). Color scale is set to "low voltage" (≤0.05 mV) and high voltage (purple) (≥5 mV). There are greater areas demonstrating low-voltage signals (and electrical silence [gray]) as well as complex signals (double and fractionated signals) in the patient with OSA.(Left panel). Regional conduction velocities in each of the atrial regions in reference patients and patients with OSA. (Right panel) From Dimitri et al, Atrial remodeling in obstructive sleep apnea: Implications for atrial fibrillation. Heart Rhythm, 2012;9(3):321–327 (with permission). AF atrial fibrillation, ANT anterior, ARA anterior right atrium, HLRA high-lateral right atrium, HPRA high-posterior right atrium, HSRA high-septal right atrium, INF inferior, LAT lateral, LLRA low-lateral right atrium, LSRA low-septal right atrium, LPRA low-posterior right atrium, POST posterior, ROOF roof, SEPT septal.

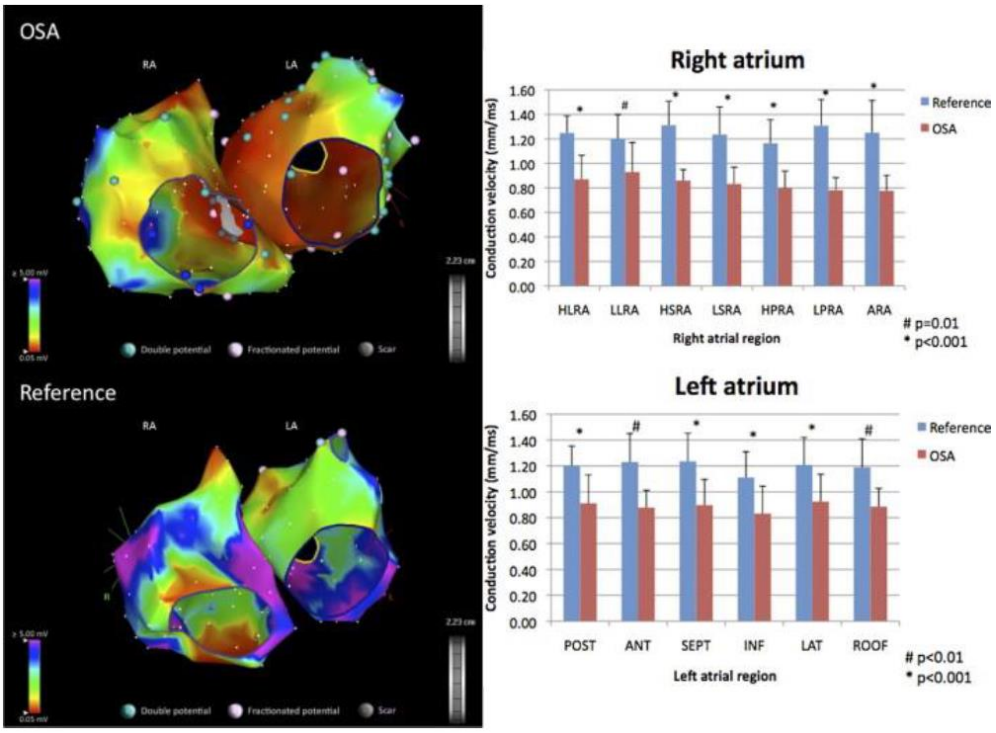

Figure 3. Schematic of the impact of CPAP therapy on the AF substrate, AF burden and clinical symptoms. AF atrial fibrillation, CPAP continuous positive airway pressure, OSA obstructive sleep apnea.

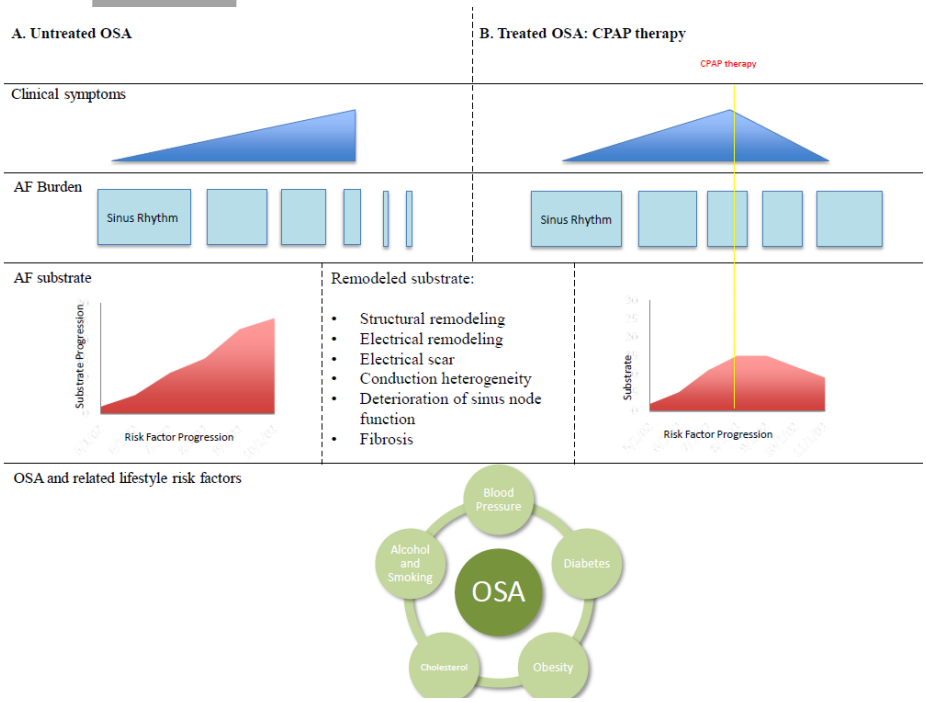

Figure 4. Kaplan-Meier curve demonstrating that freedom from AF are similar among OSA patients having treatment and patients without OSA after PVI. Freedom from AF in OSA patients not treated having PVI are similar to patients not having PVI at all. Kaplan-Meier Survival Curves According to Treatment Group Log-rank p = 0.02. Adapted from Fein et al, Treatment of Obstructive Sleep Apnea Reduces the Risk of Atrial Fibrillation Recurrence After Catheter Ablation. J Am Coll Cardiol. 2013;62(4):300-305 (with permission). AF atrial fibrillation, CPAP continuous positive airway pressure, PVI pulmonary vein isolation.