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ORIGINAL PAPER

# Characteristics of sleep-disordered breathing in patients with atrial fibrillation and preserved left ventricular ejection fraction

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**Abstract**
*Background* Sleep-disordered breathing (SDB) represents a common and highly relevant co-morbidity in patients with atrial fibrillation (Afib). Obstructive sleep apnea (OSA) has been identified as an independent risk factor for developing Afib and for Afib recurrence after treatment, but the role of central sleep apnea (CSA) is less clear. This study investigated characteristics of SDB in Afib patients with preserved left ventricular ejection fraction (PEF).
*Methods and results* Consecutive patients (07/2007 to 03/2016) with documented Afib at hospital admission and PEF undergoing 6-channel cardiorespiratory polygraphy (PG) screening were retrospectively analyzed. A total of 211 patients were included (146 men; age 68.7 ± 8.5 years). Only 6.6% of patients had no SDB (apnea-hypopnea index [AHI] < 5/h). When moderate-to-severe SDB (AHI ≥ 15/h) was classified based on the predominant type of apneas and hypopneas, OSA (≥ 80% obstructive events) was found in 15% of patients, CSA (≥ 80% central events) in 10%, and 36% had mixed sleep apnea. For patients with Cheyne–Stokes respiration (CSR; 34%), time spent in CSR increased significantly as total AHI increased ($p < 0.001$); total CSR duration was 20, 50, and 117 min, respectively, in patients with mild, moderate, and severe SDB.
*Conclusions* SDB was highly prevalent in this cohort of patients with Afib and PEF. The proportion of patients with moderate-to-severe OSA, for whom treatment is recommended by current guidelines, was about 15%. With 36% of patients presenting with moderate-to-severe mixed sleep apnea and almost 10% of patients having CSA, treatment guidelines for these types of SDB in the setting of Afib are needed.

**Keywords** Atrial fibrillation · Preserved ejection fraction · Obstructive sleep apnea · Central sleep apnea · Cheyne–Stokes respiration

## Introduction

Atrial fibrillation (Afib) is one of the most common cardiac arrhythmias, affecting approximately 1% of the general population and up to 10% of those aged 80 years and older. The aging population demographic means that the number of patients with Afib is estimated to increase 2.5-fold by 2050 [1], with an associated significant rise in costs to the healthcare system [2].

There are a number of recognized independent risk factors for development of Afib, including increasing age, arterial hypertension, heart failure, coronary disease, and obstructive sleep apnea (OSA) [3–6]. OSA is the most common type of sleep-disordered breathing (SDB) [7, 8] and is characterized by partial (hypopnea) or complete (apnea) collapse of the upper airways resulting in negative intrathoracic pressure swings, oxygen desaturation, and hypoxemia, as well as initial vagal stimulation followed by activation of the sympathetic nervous system [9].

OSA has both short- and long-term effects on Afib. Even short-term episodes of negative intrathoracic pressure can

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trigger Afib in animal models [10], probably mediated by sympathico-vagal-imbalance [11]. In an in vitro model, hypoxia increased atrial vulnerability to re-entrant arrhythmias via alteration of conduction properties [12]. The long-term effects of OSA include sympathetic activation, oxidative stress, and systemic inflammation, along with comorbidities resulting in structural and electrical remodeling of the atria, and the left atrium in particular. Thus, OSA might create an arrhythmogenic substrate and be a trigger for Afib onset at the same time [13, 14]. OSA has been shown to be an independent predictor of Afib development and of arrhythmia recurrence after antiarrhythmic treatment or intervention [15–20]. Therefore, recent European and US guidelines recommend screening for OSA and implementation of effective treatment in patients with Afib [21, 22].

Central sleep apnea (CSA), another form of SDB, is characterized by interruption or reduction of ventilatory effort combined with oxygen desaturation and is thought to promote Afib independently of congestive heart failure (CHF) [23]. There is a lack of data on pathogenetic mechanisms of CSA in Afib [24, 25], although CSA has been shown to be associated with incident Afib [26] and successful cardioversion of Afib can moderately decrease central SDB events and the corresponding apnea-hypopnea index (AHI) [27]. Cheyne–Stokes respiration (CSR) is a subtype of CSA and is characterized by a crescendo-decrescendo alteration of breathing amplitude. CSR has been established as an indicator of worse outcome in heart failure (HF) patients [28].

While continuous positive airway pressure (CPAP) is recommended for the first-line treatment of OSA and has been shown to reduce Afib recurrence after antiarrhythmic therapy [29–31], adaptive servo-ventilation (ASV) is a more appropriate treatment for patients with CSA and preserved left ventricular ejection fraction (PEF) [32]. However, just as more information is needed on the pathophysiological links between CSA and Afib, definitive therapeutic recommendations for the treatment of CSA/CSR in Afib cannot be made based on available data [21].

This explorative study investigated different phenotypes of SDB, and their prevalence and characteristics, in patients with Afib. The aim was to provide more detailed characterization of apneas and hypopneas in a large group of patients to offer qualified treatment decisions. To reduce bias, patients with impaired left ventricular ejection fraction (LVEF) and those who had undergone specific antiarrhythmic treatment were excluded.

## Methods

### Patients

This study included all patients with documented Afib on admission (12-channel ECG on admission) and preserved left ventricular ejection fraction [PEF; ejection fraction ≥ 55% on standardized echocardiography (modified Simpson method)] who underwent routine 6-channel cardiorespiratory polygraphy (PG) screening for SDB between July 2007 to March 2016. Of 22,135 entries in our database 1,220 met these criteria. Exclusion criteria included hemodynamically relevant valvular diseases (> grade 2), valvular reconstruction or replacement surgery, any kind of implanted pacemaker or defibrillator apart from event recorders, previous cardiac surgery or interventional arrhythmic therapy, acute decompensation of heart failure, chronic obstructive pulmonary disease (GOLD > 2) or other structural lung diseases (oxygen saturation < 90% at rest), pregnancy, and age < 18 years. After analysis for exclusion criteria, 211 patients meeting all inclusion criteria and presenting none of the exclusion criteria were included.

All patients gave informed consent and the study was approved by the local institutional review board.

### Cardiorespiratory polygraphy

SDB was evaluated using high-quality 6-channel PG as described previously [33]. A minimum of 240 min of artifact-free recording time was chosen based on guidelines from several European countries stating that a minimal length of 4 h is sufficient [34].

Respiratory events were classified by a single investigator using the American Academy of Sleep Medicine (AASM) 2012 criteria [35]. Events were classified as apnea if there was a drop in peak nasal airflow by ≥ 90% of pre-event baseline lasting for ≥ 10 s. Apnea was scored as obstructive if apnea criteria were met in association with continuation of, or increase in, inspiratory effort during the event. Central apnea was defined as apnea according to the above definition in the absence of associated inspiratory effort, and mixed apnea was characterized by absence of inspiratory effort during the first part of the event and recommencement in the later part of the event. Events were classified as hypopnea if there was a drop in peak nasal airflow by ≥ 30% of pre-event baseline lasting for ≥ 10 s in combination with an oxygen desaturation of ≥ 3% from pre-event baseline (ODI3%). Hypopneas were classified as obstructive if there was either snoring at the time of the event or an increase of inspiratory flattening of nasal airflow, or occurrence of associated thoracoabdominal paradox during, but not before, the event; central hypopnea was scored if none of the obstructive hypopnea criteria were met [35].

SDB was defined as an AHI of ≥ 5/h. SDB severity was classified as mild (AHI 5–14/h), moderate (AHI 15–29/h), or severe (AHI ≥ 30/h) [36]. Current guidelines recommend treatment when AHI is ≥ 15/h [30]. Therefore, patients with an AHI of < 15/h were classified as having none–mild SDB (nmSDB) for this analysis.

Cheyne–Stokes respiration (CSR) was defined as ≥ 3 successive episodes of central apneas and/or hypopneas connected by a crescendo–decrescendo variation in breathing amplitude with a cycle length (CL) of ≥ 40 s [35]. In addition, the breathing pattern had to occur in five central apneas and/or hypopneas per hour in 2 or more hours of recorded time. CSR CL was calculated as the period between commencement of a central hypopnea or apnea to termination of ventilation, and circulatory delay (CD) was assessed as the period between completion of central apnea or hypopnea to nadir of oxygen saturation [37].

Moderate-to-severe SDB (AHI ≥ 15/h) was classified according to the predominant type of apneas (> 80% central events as CSA; > 80% obstructive events as OSA) or as mixed sleep apnea (20–80% of events central or obstructive respectively). This definition was also used in a previous study [20], but it is more restrictive than some current guidelines referring to the association between OSA and Afib [20].

PG recordings were analyzed using RemLogic-E version 3.2. by Embla systems (Broomfield, CO, USA) or DOMINO version 2.6.0 by Somnomedics (Randersacker, Germany).

### Statistical analysis

Patient demographic and clinical characteristics and sleep parameters were described by apnea type and severity (four groups) using mean and standard deviation values or frequencies and proportions. Hypotheses of no difference between the four groups for continuous variables were tested using ANOVA and pairwise tests were performed using *t* tests. Discrete variables were analyzed using a *z* test. Linear regression and Spearman Rank Order correlation were performed for comparison of time spent in Cheyne–Stokes Respiration (tCSR) and the AHI.

Adjusted comparisons of AHI (also dichotomized as < 15 vs ≥ 15/h), time spent with oxygen saturation ($SpO_2$) below 90% ($T < 90\%$), oxygen desaturation index (ODI3%), and obstructive AHI (oAHI) based on the type of Afib were performed using a linear regression model or logistic regression model; comparisons were adjusted for age, sex, body mass index, left atrial diameter (LAD) and history of arterial hypertension (aHTN).

All statistical analyses were explorative and there was no correction for multiple testing. Testing was performed using Stata 14 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP) and SigmaPlot 12.0 by Systat Software Inc.

## Results

After elimination of duplicate entries, PG recordings with < 6 channels, and insufficient recording time, a total of 211 patients previously untreated for SDB met all the inclusion criteria, and none of the exclusion criteria, and were included in this analysis.

The majority presented with persistent Afib. Demographic and clinical data at baseline for the total study population and by type of SDB are shown in Table 1.

None-to-mild SDB (nmSDB; AHI < 15/h) was documented in 85 patients (40.3%), 31 patients (14.7%) had predominant OSA, 20 (9.5%) had predominant CSA, and 75 (35.5%) had mixed sleep apnea (SA). CSR was documented in 71 patients (33.6%), 5 of whom had predominant OSA, 18 had predominant CSA, 44 had mixed SA, and 4 had nmSDB (Fig. 1).

Patients with moderate-to-severe central, obstructive, or mixed SA had a significantly higher body mass index than patients in the nmSDB group. Compared to Afib patients without SDB, those with mixed SA were more likely to be male, and those with CSA were more likely to be male and were younger. Other baseline demographics and clinical characteristics were similar between patient groups.

Overall, nearly 60% of the total AHI was made up of hypopneas. Detailed baseline respiratory parameters for the total study population and by type of SDB are presented in Table 2. As expected, SDB metrics indicated greater SDB severity in patients with moderate-to-severe SDB compared with none or mild SDB. Also consistent with the definition of patient groups, patients with predominant OSA or mixed SA had significantly lower minimum oxygen saturation than other patient groups, and those with predominant OSA had more obstructive apneas and hypopneas compared with the predominant CSA and mixed SA groups. Patients with mixed SA spent significantly more time in CSR than those with OSA. The central apnea index (cAI) was higher in the CSA vs OSA and mixed SA groups, and patients with predominant CSA spent more time in CSR than other patient groups. In addition, CSA patients tended to spend more time with oxygen saturation at < 90% (T90) and had longer CSR CL and CD. For all patients with CSR, time spent in CSR increased significantly as the AHI increased ($\rho < 0.01$) (Fig. 2).

The SDB phenotype tended to vary by the type of Afib (Fig. 3). Patients with paroxysmal Afib seemed to be more likely to have nmSDB, whereas the rate of nmSDB appeared to be lower in those with long-persistent-to-permanent Afib and these patients apparently had the highest rates of

**Table 1** Demographic and clinical characteristics at baseline overall and in patient subgroups by sleep apnea type and severity

| | Total ($n=211$) | nmSDB (AHI < 15/h) ($n=85$) | OSA (AHI ≥ 15/h) ($n=31$) | CSA (AHI ≥ 15/h) ($n=20$) | Mixed SA (AHI ≥ 15/h) ($n=75$) |
|---|---|---|---|---|---|
| Age, years | 68.7 ± 8.6 | 68.0 ± 9.4 | 71.1 ± 6.4 | 66.9 ± 7.7 | 69.0 ± 8.4 |
| Male, *n* (%) | 146 (69.2) | 50 (58.8) | 21 (67.7) | 18 (90.5) | 57 (76.0) |
| Systolic BP, mmHg | 136.4 ± 19.9 | 134.0 ± 21.1 | 140.7 ± 24.0 | 133.3 ± 13.3 | 138.1 ± 17.3 |
| Diastolic BP, mmHg | 83.7 ± 13.8 | 82.0 ± 13.5 | 85.7 ± 17.1 | 83.1 ± 11.3 | 85.0 ± 13.0 |
| Body mass index, kg/m$^2$ | 29.6 ± 5.0 | 27.9 ± 4.3[a,b] | 30.7 ± 4.8[a] | 30.0 ± 4.7 | 31.0 ± 5.3[b] |
| ESS score | 7.2 ± 3.6 | 6.8 ± 3.6 | 7.0 ± 3.2 | 7.9 ± 3.3 | 7.5 ± 3.7 |
| Coronary artery disease, *n* (%) | 74 (35.1) | 26 (30.6) | 13 (41.9) | 7 (35.0) | 28 (37.3) |
| Arterial hypertension, *n* (%) | 177 (83.9) | 68 (80.0) | 27 (87.1) | 17 (85.0) | 65 (86.7) |
| Diabetes mellitus, *n* (%) | 57 (27.0) | 19 (22.4) | 8 (25.8) | 5 (25.0) | 25 (33.3) |
| Current/former smoker, *n* (%) | 65 (30.8) | 24 (28.2) | 7 (22.6) | 7 (35.0) | 27 (36.0) |
| Medication use, *n* (%) | | | | | |
| β-Blockers | 158 (74.9) | 58 (68.2)[b] | 25 (80.6) | 12 (60.0)[c] | 63 (84.0)[b,c] |
| Antiarrhythmics | | | | | |
| Class I | 14 (6.6) | 7 (8.2) | 3 (9.7) | 0 (0.0) | 4 (5.3) |
| Class III | 3 (1.4) | 2 (2.4) | 0 (0.0) | 0 (0.0) | 1 (1.3) |
| Dronedarone/amiodarone | 16 (7.6) | 5 (5.9) | 1 (3.2) | 3 (15.0) | 7 (9.3) |
| Calcium antagonists | 62 (29.4) | 18 (21.2) | 12 (38.7) | 6 (30.0) | 26 (34.7) |
| Digitalis | 37 (17.5) | 10 (11.8) | 6 (19.4) | 3 (15.0) | 18 (24.0) |
| Laboratory parameters | | | | | |
| Creatinine, mg/dL | 1.1 ± 0.3 | 1.0 ± 0.2 | 1.2 ± 0.4 | 1.0 ± 0.2 | 1.1 ± 0.4 |
| Echocardiography | | | | | |
| Left atrial diameter, mm | 46.9 ± 7.5 | 45.3 ± 7.4 | 48.4 ± 8.1 | 49.2 ± 99 | 47.5 ± 6.1 |
| Atrial fibrillation, *n* (%) | | | | | |
| Paroxysmal | 39 (8.5) | 19 (22.4) | 7 (22.6) | 4 (20.0) | 9 (12.0) |
| Persistent | 140 (66.4) | 56 (65.9) | 18 (58.1) | 15 (75.0) | 51 (68.0) |
| Long persistent | 13 (6.2) | 4 (4.7) | 4 (12.9) | 0 (0.0) | 5 (6.7) |
| Permanent | 19 (9.0) | 6 (7.1) | 2 (6.5) | 1 (5.0) | 10 (13.3) |

Values are mean ± standard deviation, or number of patients (%)

*AHI* apnea–hypopnea index, *BP* blood pressure, *CSA* central sleep apnea, *ESS* Epworth Sleepiness Scale, *OSA* obstructive sleep apnea, *SA* sleep apnea, *SDB* sleep-disordered breathing

[a] $p < 0.05$ nmSDB vs OSA

[b] $p < 0.05$ nmSDB vs mixedSA

[c] $p < 0.05$ CSA vs mixedSA

moderate-to-severe SDB and CSR. There were no significant differences between patients with different types of Afib with respect to AHI, ODI3%, T90, and CSR metrics (Table 3). The results of an explorative multivariate analysis adjusting for potential confounding factors including age, sex, history of hypertension, and BMI were similar, although no statistically significant associations were found.

## Discussion

The results of this explorative study provide new information about the prevalence and characteristics of SDB in patients with Afib. In addition to identifying a high prevalence of moderate-to-severe SDB (60%), we showed that mixed SA was the most common manifestation of SDB in Afib followed by OSA, while CSA was less common. We also found that hypopneas accounted for the majority of respiratory events, and that time spent in CSR increased in parallel with both increasing SDB severity and persistence of Afib.

A previous study in patients with Afib and PEF documented moderate-to-severe CSA and OSA using PG in 49.4% of patients (half each with OSA and CSA) [38]. This study only used apneas, not hypopneas, to differentiate between central and obstructive events, whereas we also looked at hypopneas. In addition, the previous study defined predominant OSA and CSA as > 50% obstructive and central events, respectively, rather than the more strict ≥ 80%

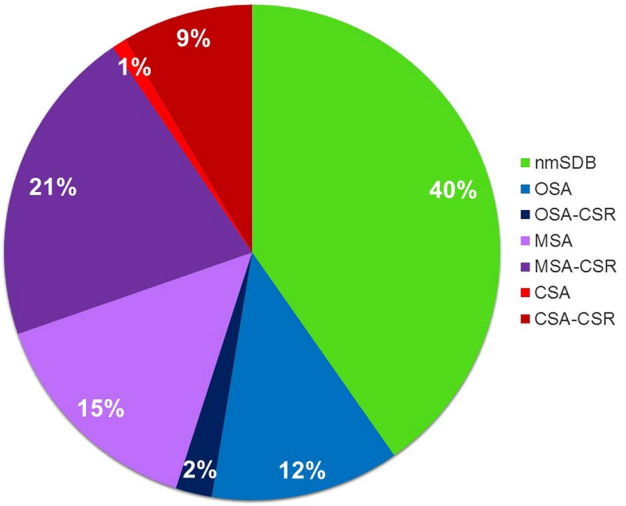


**Fig. 1** Proportion of atrial fibrillation patients with different types of sleep-disordered breathing. nmSDB, none–mild sleep disordered breathing with apnea–hypopnea index < 15/h; *CSA* central sleep apnea, *CSR* Cheyne–Stokes respiration, *MSA* mixed sleep apnea, *OSA* obstructive sleep apnea

definition used in our study. These factors could explain the higher CSA rate compared with the current study. However, our overall prevalence of moderate-to-severe SDB was higher (approximately 60 vs 50%), which may be due to the higher BMI and more advanced age of our cohort. In another study of Afib patients, most of whom had HF with PEF, 50% of patients had an AHI of ≥ 15/h and predominant CSA (≥ 50% central events central or CSR pattern with AHI ≥ 5/h) was seen in 15% [39]. However, the ability to directly compare these results to our study is limited because of the use of different SDB classification criteria and also because oxygen desaturation was defined as > 4% (compared with > 3% as recommended by the current guidelines [35] and done in our study). Reported prevalence rates for OSA in Afib have varied between studies, from 32% (OSA defined as apnea index [AI] ≥ 5/h plus AHI ≥ 15/h) [40] to 80% (OSA defined as AHI ≥ 10/h) [7]. Again, the differences between studies are most likely explained by the different OSA definitions used and differences in patient characteristics between studied populations (e.g., age and BMI).

We found a tendency towards higher proportions of SDB as the duration of Afib increased (approximately 50 vs 60 vs 70% in paroxysmal vs persistent vs long persistent to permanent Afib, respectively). This is consistent with reports showing that SDB is an independent predictor of Afib occurrence [41]. Nocturnal hypoxemia, a consequence of SDB, has been shown to be a risk factor for developing Afib and appears to be one factor responsible for cardiac structural remodeling [11]. The hypoxemic burden (T90) was increased in all patients with SDB in our study. This parameter appears to be a robust and objective predictor of overall mortality in HF with reduced ejection fraction (HF-REF) [42], and this may also be the case in patients with HF-PEF. On average, in our study, patients with SDB spent nearly an hour with oxygen saturation at < 90%, regardless of the type of SDB, suggesting that treatment to reduce hypoxemia would be beneficial across all SDB phenotypes.

Although less marked than the relationship between increasing SDB and persistence of AF, we also showed that the proportion of CSR tended to increase with increasing AF persistence. This is consistent with data showing that both CSA and CSR are associated with a higher incidence of Afib [43]. Conversely, Afib itself has been reported to be a risk factor for CSA/CSR incidence in HF-REF patients [44]. If this also applies in patients with PEF, it will be interesting to further assess the cause-and-effect relationship between increased time in CSR and the duration of Afib. In our study, patients with CSA and CSR showed more severe SDB (higher proportion of CSR, longer time in CSR, and longer CL and CD). CSR has been identified as a predictor of mortality in CHF patients [45] and CSR severity appears to correlate with cardiac impairment [33]. In patients with HF-REF, the phenotype and morphology of CSR is reasonably well understood, and both CL and CD have been established as indicators of cardiac function [37]. To our knowledge, no such research has been conducted in patients with Afib and PEF. Our data on CL and CD in patients with CSR are consistent with those of Wedewardt and colleagues (mean CL 54.7 vs 49.1 s, mean CD 33.4 vs 29.0 s). The slight variations might be a result of the higher number of patients in our study ($n = 72$ vs 21). We found that patients with long-persistent-to-permanent Afib tended to have the longest CL; therefore, it might be worth investigating whether CL correlates with duration of arrhythmias, as well as with cardiac function, in a larger patient group.

As described above, OSA and CSA have different pathophysiological mechanisms and etiology. In addition, definitions of OSA vary widely between the previous studies and guidelines. The majority of studies did not differentiate between OSA and CSA [5, 15–17, 40, 44, 46–53] or just used questionnaires for the diagnosis of SDB [18, 54–56]. Only two studies took hypopnea type into account; these defined OSA as > 5 obstructive hypopneas and apneas per hour [4] or when > 80% of apneas were obstructive [20]. In contrast, our study used recommended methods [35, 57] to clearly differentiate between obstructive and central respiratory events, including hypopneas. We chose to classify patients as having predominant OSA or CSA when > 80% of hypopneas and apneas were obstructive or central, respectively, to provide clear discrimination between the two forms of SDB. We also noted a high proportion of patients with mixed SA, who had both obstructive and central events.

**Table 2** Respiratory parameters by sleep apnea type and severity

| | Total, $n=211$ | nmSDB (AHI < 15/h) ($n=85$) | OSA (AHI ≥ 15/h) ($n=31$) | CSA (AHI ≥ 15/h) ($n=20$) | mixedSA (AHI ≥ 15/h) ($n=75$) |
|---|---|---|---|---|---|
| Total recording time, min | 482.5 ± 37.1 | 479.9 ± 36.8 | 476.5 ± 10.8 | 477.1 ± 12,9 | 489.3 ± 46.6 |
| Index time, min | 452.1 ± 48.2 | 454,1 ± 55.3 | 437.8 ± 34.6 | 451.7 ± 20.8 | 455.8 ± 48.4 |
| AHI, $h^{-1}$ | 22.9 ± 16.3 | 8.5 ± 3.3[a,b,c] | 34.6 ± 13.1[a] | 39.2 ± 13.4[b] | 30.2 ± 14.2[c] |
| AI, $h^{-1}$ | 9.6 ± 12.8 | 1.8 ± 1.9[a,b,c] | 13.4 ± 12.5[a] | 23.4 ± 15.3[b] | 13.3 ± 13.9[c] |
| Central AI, $h^{-1}$ | 5.4 ± 9.1 | 0.8 ± 1.1[b,c,d,e,f] | 2.0 ± 2.1[d,e] | 21.6 ± 14.7[b,d,f] | 7.8 ± 8.2[c,e,f] |
| Obstructive AI, $h^{-1}$ | 2.6 ± 5.0 | 0.8 ± 1.1[a,c,d,f] | 8.0 ± 9.6[a,d] | 0.8 ± 0.9[d,f] | 2.9 ± 3.7[c,f] |
| Mixed AI, $h^{-1}$ | 1.6 ± 4.9 | 0.3 ± 1.3[a,b,c] | 3.3 ± 6.7[a] | 1.0 ± 1.4[b] | 2.5 ± 6.5[c] |
| Average apnea duration, sec | 19.2 ± 6.9 | 16.8 ± 6.7[a,b,c] | 21.9 ± 9.5[a] | 19.6 ± 3.6[b] | 20.6 ± 5.4[c] |
| HI, $h^{-1}$ | 13.5 ± 9.1 | 7.0 ± 3.9[a,b,c] | 21.6 ± 10.7[a] | 15.7 ± 10.1[b] | 16.8 ± 7.3[c] |
| Central HI, $h^{-1}$ | 4.7 ± 5.3 | 2.4 ± 2.1[b,c,d,e] | 2.1 ± 1.7[d,e] | 11.9 ± 8.1[b,d] | 6.4 ± 5.5[c,e] |
| Obstructive HI, $h^{-1}$ | 8.2 ± 7.5 | 4.1 ± 2.7[a,c,d,e,f] | 19.1 ± 10.3[a,d,e] | 2.9 ± 1.8[d,f] | 9.8 ± 5.0[c,e,f] |
| Average hypopnea duration, sec | 27.4 ± 5.8 | 29.5 ± 5.9[a] | 25.8 ± 5.1[a] | 25.7 ± 3.7 | 26.1 ± 5.7 |
| ODI, $h^{-1}$ | 22.6 ± 16.2 | 8.5 ± 3.4[a,b,c] | 35.6 ± 13.2[a] | 35.2 ± 16.4[b] | 29.8 ± 13.7[c] |
| Mean oxygen saturation, % | 92.9 ± 1.7 | 93.5 ± 1.7 | 92.3 ± 1.7 | 92.5 ± 1.9 | 92.5 ± 1.5 |
| Minimum oxygen saturation, % | 82.8 ± 6.2 | 85.6 ± 5.3[a,c] | 79.4 ± 6.8[a] | 82.6 ± 5.9 | 81.2 ± 5.6[c] |
| Oxygen desaturation, % | 4.6 ± 1.4 | 3.8 ± 0.4[a,b,c] | 5.2 ± 1.5[a] | 5.4 ± 2.1[b] | 5.0 ± 1.4[c] |
| $T<90\%$, min | 38.5 ± 64.6 | 13.6 ± 30.2[a,b,c] | 58.7 ± 76.9[a] | 65.3 ± 97.7[b] | 51.4 ± 67.2[c] |
| Time spent in CSR, min | 28.8 ± 60.4 | 0.9 ± 4.7[b,c,d,e,f] | 2.7 ± 6.4[d,e] | 140.6 ± 100.4[b,d,f] | 41.4 ± 53.8[c,e,f] |
| CSR cycle length, sec | 54.7 ± 7.6 | 54.1 ± 2.4 | 53.2 ± 8.9 | 54.6 ± 6.6 | 54.5 ± 8.3 |
| CSR circulatory delay, sec | 33.4 ± 6.3 | 32.0 ± 4.6 | 31.4 ± 1.6 | 38.6 ± 6.1 | 31.7 ± 5.8 |

Values are mean ± standard deviation

*AHI* apnea–hypopnea index, *AI* apnea index, *CSA* central sleep apnea, *CSR* Cheyne–Stokes respiration, *HI* hypopnea index, *OSA* obstructive sleep apnea, *ODI* oxygen desaturation index, *SA* sleep apnea, *SDB* sleep-disordered breathing, *T<90%* time with oxygen saturation < 90%

[a] $p < 0.05$ nmSDB vs OSA

[b] $p < 0.05$ nmSDB vs CSA

[c] $p < 0.05$ nmSDB vs mixedSA

[d] $p < 0.05$ OSA vs CSA

[e] $p < 0.05$ OSA vs mixedSA

[f] $p < 0.05$ CSA vs mixedSA

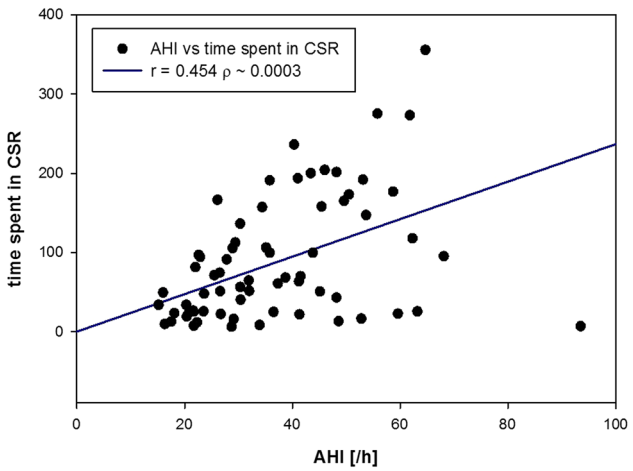


**Fig. 2** Relationship between the apnea–hypopnea index (AHI) and time spent in Cheyne–Stokes respiration (CSR) in patients with moderate–severe sleep-disordered breathing

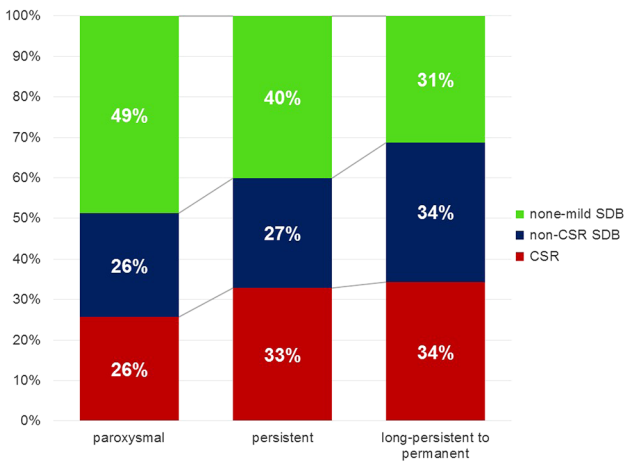


**Fig. 3** Type of sleep-disordered breathing (SDB) in patients with different types of atrial fibrillation

**Table 3** Baseline and nocturnal respiratory parameters in patients with moderate-to-severe sleep-disordered breathing based on the type of atrial fibrillation

| | Type of atrial fibrillation | | |
|---|---|---|---|
| | Paroxysmal ($n=20$) | Persistent ($n=84$) | Long persistent/permanent ($n=21$) |
| SDB (OSA/CSA), *n* | 20 (7/4) | 84 (18/15) | 21 (7/1) |
| AHI, $h^{-1}$ | 32.4 ± 13.2 | 33.0 ± 14.9 | 31.7 ± 12.2 |
| ODI3, % | 30.7 ± 11.2 | 32.4 ± 15.5 | 32.3 ± 11.8 |
| $T<90\%$, % of TRT | 10.3 ± 10.9 | 13.2 ± 16.9 | 11.7 ± 19.0 |
| CSR duration, min | 60.8 ± 77.9 | 45.7 ± 72.0 | 43.3 ± 66.3 |
| CSR cycle length, s | 55.6 ± 5.8 | 53.9 ± 6.8 | 56.6 ± 10.7 |
| CSR circulatory delay, s | 34.0 ± 5.8 | 32.9 ± 6.0 | 34.8 ± 7.6 |
| Left atrial diameter, mm | 43.6 ± 6.4 | 48.6 ± 7.0 | 50.4 ± 8.1 |
| Male sex, *n* | 17 (85%) | 61 (73%) | 18 (86%) |
| Age, years | 70.7 ± 6.1 | 68.4 ± 8.7 | 70.8 ± 5.4 |
| BMI, $kg/m^2$ | 29.5 ± 3.1 | 30.8 ± 5.5 | 31.9 ± 4.7 |
| History of aHTN, *n* | 17 (85%) | 72 (86%) | 20 (95%) |

Values are mean ± standard deviation, or number of patients

*AHI* apnea–hypopnea index, *aHTN* arterial hypertension, *BMI* body mass index, *CSA* central sleep apnea, *CSR* Cheyne–Stokes respiration, *OSA* obstructive sleep apnea, *ODI3* 3% oxygen desaturation index, *SDB* sleep-disordered breathing, $T<90\%$ time with oxygen saturation < 90%

Even though we used a strict classification for OSA and CSA, the prevalence of these conditions in Afib patients was quite high, suggesting an indication for therapy. Afib guidelines recommend CPAP treatment for patients with OSA. For CSA, AASM guidelines favor therapy with ASV in patients with PEF [32], because this provides more effective suppression of CSA and improves sleep quality to a greater extent than first-line therapy with CPAP [58]. The results of the Cardiovascular Outcomes With Minute Ventilation-Targeted Adaptive Servo-Ventilation Therapy in Heart Failure (CAT-HF) study recently indicated that treatment of SDB in post-acute HF-PEF patients might be associated with improved outcome [59]. Moreover, the CAT-HF arrhythmia substudy showed a 16% reduction in Afib burden in ASV-treated patients compared with a 24% increase in the control group who did not receive SDB-specific intervention [60].

While correct differentiation between OSA and CSA is important to identify the most appropriate primary treatment strategy to optimize therapy for every patient, there was a high prevalence of mixed SA in our study and there are currently no clear recommendations on therapy for these patients. In our sample, Afib patients with mixed SA had a high proportion of periodic breathing meeting CSR criteria, which is usually categorized as CSA, meaning that ASV might be the most appropriate treatment option.

### Limitations

A larger patient population, the inclusion of hypopneas in SDB classification, and the use of strict criteria to define predominant OSA and CSA are all strengths of our study. However, there are also a number of limitations that need to be taken into account. The analysis was conducted retrospectively and exploratively using data from a tertiary center, and therefore, the patient population included might not be representative of those found in primary centers. Although use of PG is routine clinical practice for patients with heart diseases in our clinic, it is possible that some Afib patients did not undergo SDB screening. Finally, nocturnal respiratory parameters may have been underestimated by the use of PG, because calculations are based on total recording time rather than total sleep time (which is usually less than recording time).

## Conclusions

Our analysis showed that SDB was highly prevalent in patients with Afib and PEF. Even using the most restrictive definitions for predominant OSA and CSA, a significant number of patients had SDB requiring treatment. Taken together, our findings contribute to better understanding of SDB in Afib and could help guide appropriate treatment strategies for different types of SDB and patient phenotypes.

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**Compliance with ethical standards**

**Conflict of interest** Olaf Oldenburg received honoraria for lectures and travel grants from ResMed, Somnomedics, Novartis, Boehringer

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