Obstructive Sleep Apnea Patients With Atrial Arrhythmias Suffer From Prolonged Recovery From Desaturations

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Abstract*—*Objective: **We aimed to investigate how acute and long-term effects of atrial arrhythmias affect the desaturation severity and characteristics determined from the oxygen saturation signal in obstructive sleep apnea (OSA) patients.** ***Methods:*** **520 suspected OSA patients were included in retrospective analyses. Eight desaturation area and slope parameters were calculated from blood oxygen saturation signals recorded during polysomnographic recordings. Patients were grouped based on whether they had previously diagnosed atrial arrhythmia (i.e., atrial fibrillation (AFib) or atrial flutter) or not. Furthermore, patients with a previous atrial arrhythmia diagnosis were sub-grouped based on whether they had continuous AFib or sinus rhythm during the polysomnographic recordings. Empirical cumulative distribution functions and linear mixed models were utilized to investigate the connection between diagnosed atrial arrhythmia and the desaturation characteristics.** ***Results:*** **Patients with previous atrial arrhythmia diagnosis had greater desaturation recovery area when the 100% oxygen saturation baseline reference was considered (β = 0.150–0.127, $p \leq 0.039$) and more gradual recovery slopes ($\beta = -0.181$ to -0.199, $p < 0.004$) than patients without a previous atrial arrhythmia diagnosis. Furthermore, patients with AFib had more gradual oxygen saturation fall and recovery slopes than patients with sinus rhythm.** ***Conclusion:*** **Desaturation recovery characteristics in the oxygen saturation signal contains essential information about the cardiovascular response to hypoxemic periods.** ***Significance:*** **More comprehensive consideration of the desaturation recovery section could provide more detailed information about OSA severity, for example when developing new diagnostic parameters.**

***Index Terms*—Atrial arrhythmias, intermittent hypoxemia, obstructive sleep apnea, oxygen saturation, signal analysis.**

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I. Introduction

CARDIORESPIRATORY and cardiovascular systems are linked both functionally and through several anatomical structures and pathophysiological interactions [1], [2]. These connections are highly sensitive for the autonomic nervous system (ANS) activations as well as cardiovascular and respiratory disturbances [1], [2]. For example, hypoxemia, caused by respiratory disruptions, activate several ANS mechanisms leading to cardiac responses [3], [4]. In turn, cardiac rhythm disturbances impact respiration activity and function [5]. Consequently, cardiovascular diseases (CVDs) and respiratory disorders often appear simultaneously and have a significant association; however, the association is not completely understood at the pathophysiological level [2], [6].

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder that affects globally nearly a billion people and disrupts cardiorespiratory activations [3], [7]. OSA-related complete (apnea) and partial (hypopnea) repetitive upper airway collapses can lead to intermittent hypoxemias (i.e., repetitive desaturations), reoxygenations, substantial heart rate, and blood pressure variation as well as intrathoracic pressure fluctuations. These consequences can further trigger atrial arrhythmias [8], [9]. Thus, OSA patients have over twice the risk for atrial arrhythmias compared to individuals without OSA, and the risk increases with increasing OSA severity [10], [11]. Several studies have investigated the pathophysiological pathways of how intermittent hypoxemias lead to cardiac arrhythmias in OSA patients [6], [9]. However, even though atrial arrhythmias are associated with flow abnormalities and endothelial dysfunction [12], it is not fully understood how atrial arrhythmias are related to the severity and morphology of hypoxemic episodes in OSA patients.

Currently, the apnea-hypopnea index (AHI) is used to assess the severity of OSA, estimating the average number of respiratory events per hour of sleep [13]. However, several studies show that AHI is not the best parameter in OSA severity estimation, as it does not consider the characteristics of the breathing disruptions [14], [15], [16], [17]. Furthermore, it has been shown that different oxygen desaturation thresholds for hypopnea scoring lead to different associations between OSA and CVDs [18], [19]. Instead, the desaturation event characteristics have been shown to describe the connection between OSA severity and OSA-related outcomes better compared to the AHI [15], [20], [21]. Moreover, desaturation areas, characterizing the depth and the duration of desaturations, are associated with severe OSA-related health consequences, such as increase in mortality rate and cardiovascular morbidity [22], [23]. Currently, desaturations are determined as a $\geq 3\%$ drop in the oxygen saturation (SpO_2) signal [13]. However, no standard scoring rules exist for the desaturation endpoint placement, even though differences in the desaturation endpoints substantially affect the value of related desaturation area parameters [24].

Based on the prominent connection between cardiac arrhythmias and intermittent hypoxemias, we hypothesized that suspected OSA patients with a history of atrial arrhythmias (atrial fibrillation or flutter) have more severe desaturation events. Secondly, we hypothesized that OSA patients with previous atrial arrhythmia diagnosis have slower reoxygenation processes leading to larger desaturation recovery areas. Thus, our first aim was to investigate how previously diagnosed atrial arrhythmia in OSA patients is related to desaturation severity and morphology estimated from SpO_2 signal. Additionally, we investigated the acute effects of atrial arrhythmias on the severity and morphology of desaturation events in OSA patients with a previous atrial arrhythmia diagnosis.

II. Methods

A. Dataset

The initial study population consisted of 933 consecutive patients who underwent complete overnight polysomnography (PSG) between January 2015 and December 2017 at the Sleep Disorders Centre, Princess Alexandra Hospital, (Brisbane, Australia) due to clinical suspicion of OSA. PSGs were conducted and scored retrospectively using the Compumedics Grael acquisition system and the Compumedics ProFusion PSG 4 software (Compumedics, Abbotsford, Australia). Recordings were scored manually in conformity with the American Academy of Sleep Medicine 2012 scoring rules [13]. The specific scoring protocol of apneas, hypopneas, and desaturations are delineated in earlier publications [20], [25]. The Institutional Human Research Ethics Committee of the Princess Alexandra Hospital approved the use of this retrospective data (HREC/16/QPAH/021 and LNR/2019/QMS/54313).

Out of the 933 patients, 385 were excluded based on incomplete PSG recordings, demographic information, or desaturation event information, having AHI < 5, chronic obstructive pulmonary disease (COPD), or having suffered a cardiac failure. The exclusion criteria are detailed in Fig. 1, (Exclusion, Step 1). The patients with COPD or cardiac failure were excluded as overlapping COPD and OSA, or overlapping cardiac failure and OSA, have a deteriorative effect on cardiorespiratory function and oxygen saturation [5], [26]. For the remaining 548 patients, nocturnal atrial arrhythmias were evaluated based on nocturnal electrocardiogram (ECG) signals from the overnight PSG

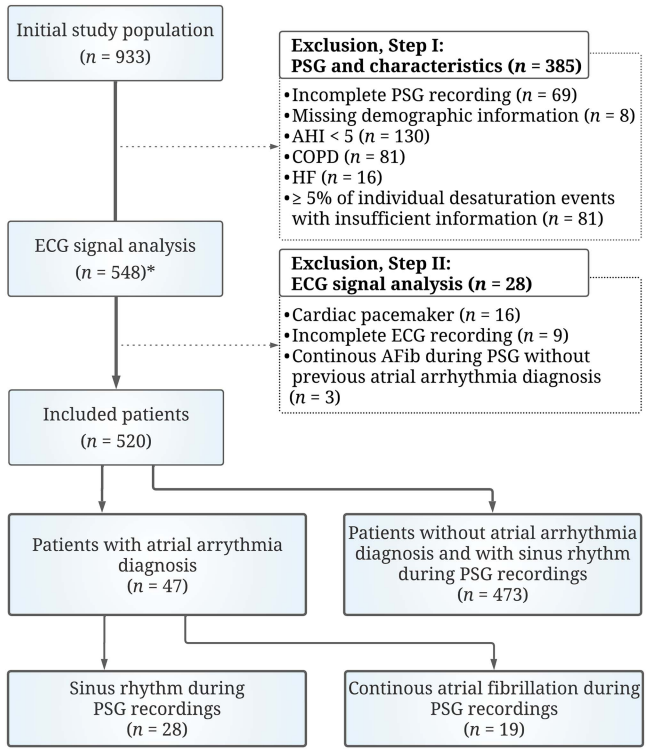

Fig. 1. Flowchart describing patient exclusion and sub-grouping. ECG: electrocardiogram, AHI: apnea-hypopnea index, AFib: atrial fibrillation, COPD: chronic obstructive pulmonary disease, HF: heart failure, PSG: polysomnography. Successful desaturation scoring information required the inclusion of both the fall and recovery parts of the individual desaturation. Only patients having sinus rhythm during PSG recordings were included in the patient-group without atrial arrhythmia diagnosis.

TABLE I
DEMOGRAPHIC AND POLYSOMNOGRAPHIC INFORMATION OF THE INCLUDED PATIENTS ($N = 520$), PRESENTED AS MEDIAN (INTERQUARTILE RANGE) FOR CONTINUOUS VARIABLES AND N (%) FOR CATEGORICAL VARIABLES

Parameter	Without previous diagnosis of atrial arrhythmias	With a previous diagnosis of atrial arrhythmia		
		All	SR	AFib
Subject, *n* (male %)	473 (55.8)	47 (80.9)	28 (71.4)	19 (94.7)
Age, years	53.3 (43.8–63.3)	65.0 (58.5–72.6) *	62.7 (56.5–73.6) *	66.6 (62.7–2.3) *
BMI, kg/m^2	35.6 (30.8–41.4)	35.2 (30.6–42.0)	35.4 (30.6–42.4)	34.0 (30.8–42.0)
Smoker, *n* (%)	86 (18.2)	3 (6.4) *	3 (10.7)	0 (0.0)
Hypertension, *n* (%)	203 (43.0)	22 (46.8)	10 (35.7)	12 (63.2)
T2DM, *n* (%)	98 (20.8)	17 (36.2) *	5 (17.9)	12 (63.2) #
AHI, events/h	22.3 (11.9–46.4)	29.9 (13.6–51.5) *	26.7 (11.9–48.1)	31.2 (17.4–57.9)
ODI, events/h	15.3 (5.3–33.0)	17.0 (7.6–39.9)	15.9 (7.9–30.4)	27.7 (6.6–42.8)
Desaturation events, *n*	53219	5025	3170	1855
Desaturation depth (%)	6.1 (4.0–10.3)	6.1 (3.9–9.6) *	6.1 (3.8-10.5)	6.1 (4.1–8.7) #, *
Desaturation depth with 100% baseline (%)	10.5 (7.9–15.2)	11.6 (8.4–17.3) *	13.3 (8.8–20.1) *	10.2 (8.1–13.5) #, *
Desaturation duration (s)	31.0 (22.1–42.0)	31.0 (21.0–45.0)	27.1 (19.0–37.0) *	41.1 (27.0–53.0) #, *
TST, min	312.3 (257.5–361.0)	269.0 (229.6–306.5) *	279.5 (240.0–347.8)	243.5 (193.8–289.4) *
T90, min	7.0 (0.8–41.0)	9.4 (1.3–75.8)	11.7 (0.4–82.5)	9.1 (4.0–48.6)
Average SpO_2, %	93.1 (90.6–95.1)	93.1 (91.2–95.0)	93.2 (88.8–95.1)	93.0 (91.7–94.9)
Minimum SpO_2, %	81.0 (72.0–86.1)	80.0 (73.2–86.2)	83.9 (71.5–87.1)	79.5 (73.2–84.6)

BMI: body mass index, T2DM: type 2 diabetes mellitus, AHI: apnea-hypopnea index, ODI: oxygen desaturation index, TST: total sleep time, T90: time below 90% of oxygen saturation levels, SpO2: oxygen saturation, SR: sinus rhythm, AFib: atrial fibrillation. * Statistically significant ($p < 0.05$) difference compared with the patients without atrial arrhythmia. # Statistically significant ($p < 0.05$) difference compared with the patients with SR. Continuous variables were compared using the Wilcoxon rank-sum test and categorical variables using the Chi-square test.

which were analysed by two trained specialists using Kubios HRV Premium 3.4.1 software [27]. In the ECG signal analysis, we found that 16 patients had pacemakers, nine patients had incomplete ECG recordings, 22 patients had continuous atrial fibrillation (AFib), and 501 patients had sinus rhythm (SR) throughout the whole night. Paroxysmal AFib or other clinically significant arrhythmias were not found. The 16 patients with pacemakers, nine patients with incomplete ECG recordings, and three patients with continuous AFib but without previous atrial arrhythmia diagnosis (28 patients in total) were excluded from further analysis (Fig. 1, Exclusion, Step 2).

The final population of 520 patients (with a total of 58244 desaturation events) was divided into two groups based on whether the patient was previously diagnosed with atrial arrhythmia (i.e., AFib or atrial flutter) or not. Patients with a previous diagnosis of atrial arrhythmia were further divided into two subgroups, based on whether the patient had SR or continuous AFib during the overnight PSG. Comorbidities were reported based on the medical history of the patient and an interview in the sleep clinic. Patient demographics and polysomnographic information are presented in Table I. A flowchart describing the subgrouping of the patients is presented in Fig. 1.

B. Signal Processing and Calculated Desaturation Area and Slope Parameters

Eight different desaturation parameters were calculated from the SpO_2 signal: desaturation area, fall area, recovery area, desaturation area with a 100% baseline (i.e., desaturation area with a baseline reference at 100%), fall area with a 100% baseline, recovery area with a 100% baseline, fall slope, and recovery slope (Fig. 2). The desaturation areas with and without a 100% baseline were integrated over the whole desaturation, the fall areas with and without a 100% baseline were integrated from the desaturation onset to the nadir, and the recovery area with and without a 100% baseline from the nadir to the endpoint of the desaturation (Fig. 2). All desaturation area parameters were integrated numerically utilizing the trapezoidal method. The fall slope was calculated by dividing the saturation difference between the onset and the nadir with the time difference between these points and the recovery slope was calculated similarly between the nadir and the endpoint of desaturation (Fig. 2). In addition, median values of desaturation area and slope parameters were calculated for each patient.

C. Statistical Analysis

Differences in the desaturation area and slope parameters between the patients with and without diagnosed atrial arrhythmia were investigated using empirical cumulative distribution functions (CDFs) and linear mixed model analysis. The CDFs of the desaturation area and slope parameters were calculated separately in patients with and without diagnosed atrial arrhythmia using the medians of each patient. In addition, the CDFs of desaturation area and slope parameters were calculated separately in patients with continuous AFib and normal SR using all desaturation events. Statistical significance of the differences between the CDFs were calculated using a two-tailed Kolmogorov-Smirnov test.

In linear mixed model analyses, three different models were constructed. Model 1 was unadjusted, Model 2 was adjusted with age, gender, body mass index (BMI), and smoking, and

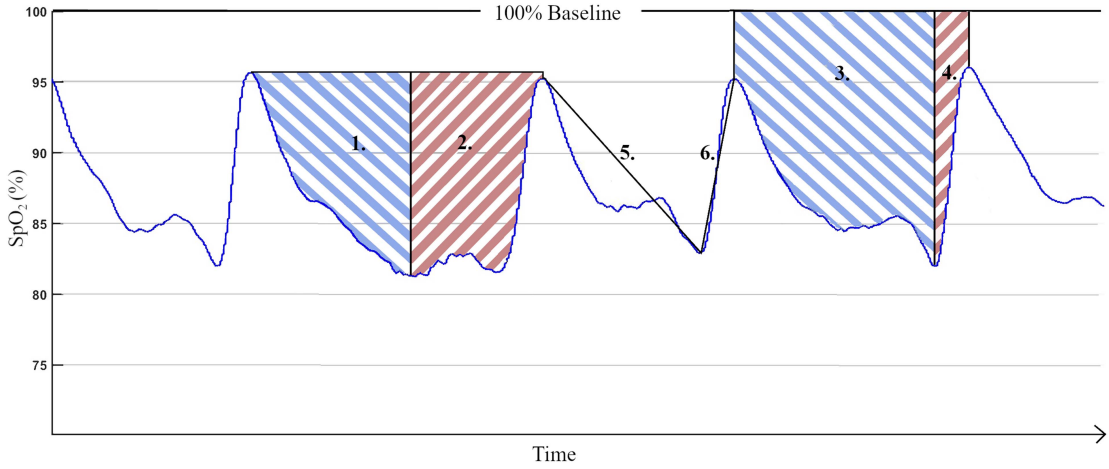

Fig. 2. Illustration of the calculated desaturation area and desaturation slope parameters. 1. fall area, 2. recovery area, 3. fall area with 100% baseline, 4. recovery area with 100% baseline, 5. fall slope, 6. recovery slope. Desaturation area includes both fall area and recovery area. Desaturation area with 100% baseline includes both fall area with 100% baseline and recovery area with 100% baseline. SpO_2: oxygen saturation.

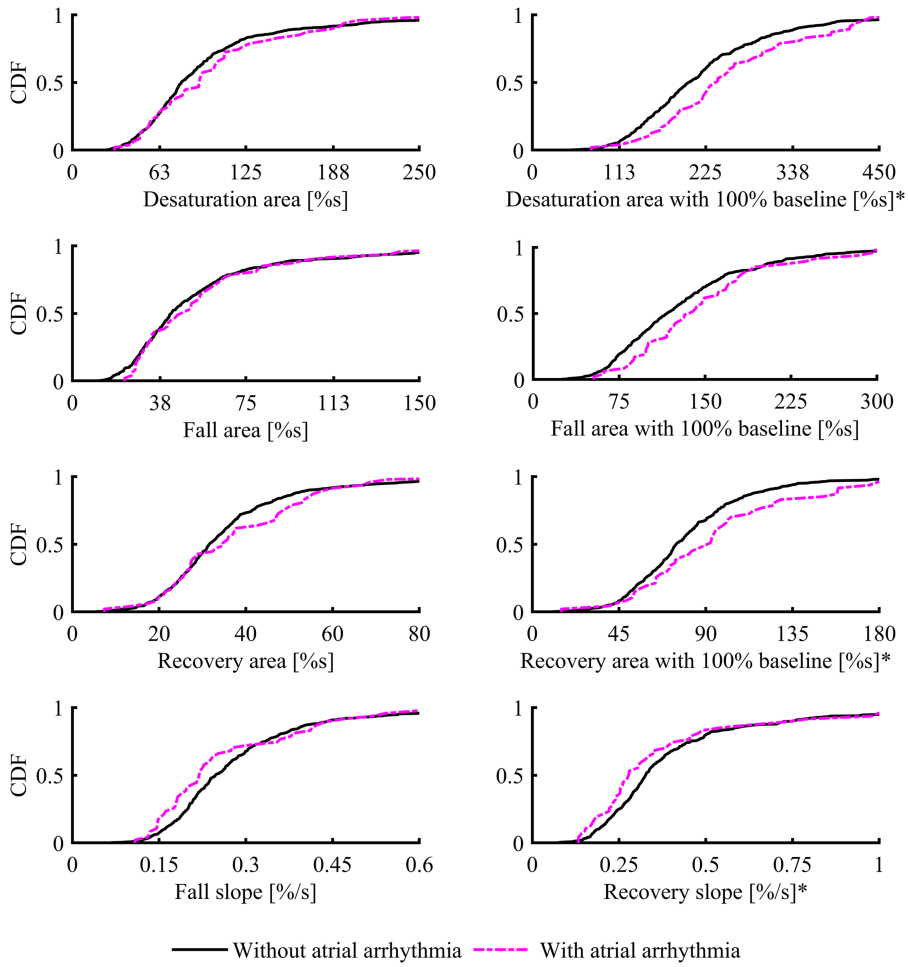

Fig. 3. Results of empirical cumulative distribution functions (CDFs) of desaturation area and slope parameters in OSA patients with ($n = 47$) and without ($n = 473$) previous diagnosis of atrial arrhythmia. The CDFs include the median values of calculated parameters of each patient. * Significant difference ($p < 0.05$) between the CDFs evaluated by the Kolmogorov-Smirnov test. The outliers (i.e., value of CDF > 0.95) are not included in the figure. *Notice different scales for each parameter.*

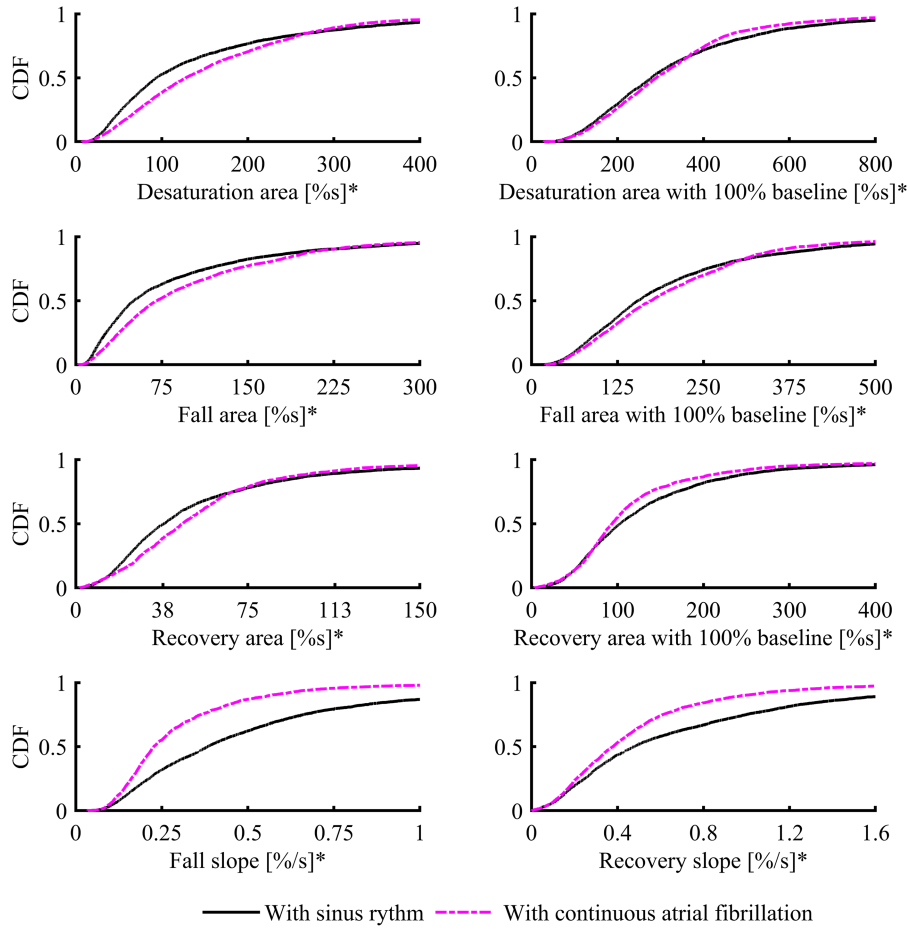

Fig. 4. Results of empirical cumulative distribution functions (CDFs) of desaturation area and slope parameters in OSA patients with previous diagnosed atrial arrhythmia sub-grouped based on whether a patient had continuous atrial fibrillation (AFib) or sinus rhythm (SR) during the PSG. CDFs includes calculated parameters from all events (continuous AFib $n = 1855$ vs. SR $n = 3170$). * Significant difference ($p < 0.05$) between the CDFs evaluated by the Kolmogorov-Smirnov test. The outliers (i.e., value of CDF > 0.95) are not included in the figure. *Notice different scales for each parameter.*

Model 3 was adjusted with the AHI, type 2 diabetes mellitus (T2DM), and hypertension. Desaturation area and slope parameters were inputted separately as response variables in each model. The parameter distributions were logarithmically transformed to ensure normal distribution before linear mixed model analyses. The previous diagnosis of atrial arrhythmia and the adjusted variables were used as fixed effects and the patient research numbers were used as a random effect. Furthermore, the normality of residuals of the linear mixed model analyses was verified visually. The limit of statistical significance was set at $p < 0.05$. All calculations and statistical analyses were performed using MATLAB software (version R2019b; MathWorks; Natick, MA, USA).

III. Results

A. Cumulative Distribution Functions

Significantly ($p \leq 0.032$) larger desaturation and recovery areas were observed in patients with diagnosed atrial arrhythmia compared to patients without a previous atrial arrhythmia diagnosis when the 100% baseline was considered (Fig. 3). Furthermore, the recovery slope was significantly ($p = 0.045$) steeper in patients without a previous atrial arrhythmia diagnosis compared to patients with a previous atrial arrhythmia diagnosis (Fig. 3). In the CDFs of the subgroups of arrhythmia patients, all other area parameters were larger, but the recovery area with the 100% baseline was smaller in AFib patients compared to patients with SR ($p < 0.001$) (Fig. 4). In addition, substantially more gradual fall and recovery slopes were observed in patients with continuous AFib ($p < 0.001$) (Fig. 4).

B. Descriptive Statistical Results of the Desaturation Area and Slope Parameters

The greatest differences between OSA patients with and without previous atrial arrhythmia diagnosis were observed in the desaturation area parameters when the 100% baseline was considered. That is, patients with a previous atrial arrhythmia diagnosis had significantly larger desaturation areas (Table II). Furthermore, patients with previously diagnosed atrial arrhythmia had more gradual fall slope and recovery slopes than patients without a previous atrial arrhythmia diagnosis (Table II). When the comparison was done between patients with SR and continuous AFib during the PSG recordings, AFib patients were

observed to have more gradual desaturation slopes and larger desaturation areas (Table II). As the only exception, the recovery area with the 100% baseline was significantly smaller ($p < 0.05$) in patients with continuous AFib (Table II).

C. Linear Mixed Model Analyses

With the unadjusted model, a previous atrial arrhythmia diagnosis in OSA patients was associated with an increase in desaturation area parameters when the 100% baseline reference was considered ($\beta \geq 0.133$, $p \leq 0.031$, Table III). However, this association diminished in the adjusted models, as recovery area with the 100% baseline was the only statistically significant predictor for the prevalence of an atrial arrhythmia diagnosis in Model 3 ($\beta = 0.127$, $p = 0.039$) (Table III). In contrast, the predictive power of the fall and recovery slopes was higher in the adjusted models compared to the unadjusted model. That is, prevalence of atrial arrhythmia was associated with a decrease in the fall slope (Model 2: $\beta = -0.091$, $p = 0.052$; Model 3: $\beta = -0.145$, $p = 0.003$) and the recovery slope (Model 2: $\beta = -0.199$, $p = 0.004$; Model 3: $\beta = -0.181$, $p < 0.001$) (Table III).

IV. Discussion

In this study, we examined how atrial arrhythmias are related to the severity and morphology of oxygen desaturations in OSA patients. We found that patients with a previous atrial arrhythmia diagnosis had significantly greater recovery area when a 100% SpO_2 baseline reference was considered and more gradual desaturation recovery slope. Moreover, patients who had continuous AFib during the PSG recordings had substantially more gradual desaturation slopes than patients with SR. These results show that the desaturation recovery section and desaturation rates determined from SpO_2 signal contain essential information about the pathophysiological impacts of breathing cessations in OSA patients. Thus, this study suggests that the desaturation events should be scored to include also the desaturation recovery section, not only until the nadir of desaturation. This would lead to utilization of more detailed information on the desaturations in OSA severity estimation and diagnostics. Furthermore, results illustrate that the 100% SpO_2 baseline reference should be considered in the desaturation area calculations as it contains the information on the baseline of the patient's nocturnal oxygen saturation level.

In linear mixed model analysis, the prevalence of atrial arrhythmia diagnosis was associated with an increase in the recovery area with the 100% baseline parameter (Table III). Furthermore, the prevalence of having previously diagnosed atrial arrhythmia was associated with a decrease in the recovery slope parameter. These results support our hypothesis that the reoxygenation from desaturations is prolonged in OSA patients with a previous atrial arrhythmia diagnosis compared to patients without a previous atrial arrhythmia diagnosis. The possible causes behind these findings are manifold. First, the irregular rhythm can cause an acute impairment of the cardiorespiratory regulation and function. Second, OSA-related recurrent desaturations may promote the development of AFib by inducing electrical and structural cardiac remodelling as well as autonomous system dysregulation [6], [28]. Therefore, the homeostasis of the cardiovascular system may be impaired and lack the adequate response to the changes of peripheral oxygenation in OSA patients with a previous atrial arrhythmia diagnosis. These findings provide interesting new insight in understanding the pathophysiological cascade seen in patients with OSA and atrial arrhythmias. Therefore, a more detailed assessment of the clinical history of the patients, the overnight ECG, and the pathophysiology of desaturations, would benefit the clinical decision making and OSA severity assessment.

Previous studies have shown that the desaturation severity describes the severity of OSA and its connection with the related long- and short-term outcomes better than the AHI [14], [15], [25], [29]. For example, we have previously shown that desaturation severity parameters are significant predictors for cardiovascular comorbidity and other health consequences of OSA such as severe excessive daytime sleepiness (EDS) and impaired psychomotor vigilance task (PVT) performance [20], [25], [29]. Therefore, the present results together with the previous findings support the conclusion that the more detailed examination of desaturation characteristics and recovery section in OSA diagnostics could be beneficial to estimate the true severity of OSA. Currently, no uniform guidelines exist for scoring desaturations endpoints [13]. The results of the current study suggest that both the fall, and the recovery parts should be included in the scored desaturations. A uniform way to score desaturations could contribute to achieve more coherent information related to desaturations and assist in finding the best parameters to diagnose OSA.

In accordance with our hypothesis, the present results showed that OSA patients with previously diagnosed atrial arrhythmia have larger desaturation areas. Interestingly, this phenomenon appeared only when the 100% baseline reference in oxygen saturation was considered, and against our hypothesis, the connection between the desaturation severity and a previous diagnosis of atrial arrhythmia was not observed when the areas were restricted to the desaturation onset level (Fig. 3, Tables II and III). In addition, patients with previously diagnosed atrial arrhythmia were observed to have deeper desaturations when either the onset level or the 100% SpO_2 baseline was considered compared to patients without previously diagnosed atrial arrhythmia (Table I). It has been shown that lower levels in the nocturnal oxygen saturation and prevalence of intermittent hypoxemias have major effects on cardiac and vascular dysfunction and are one of the most important pathophysiological consequences of OSA [6], [30]. Furthermore, desaturation area-based parameter which includes 100% SpO_2 baseline has been associated with predicting CVD outcomes of OSA [31]. Together with previous knowledge and results of this study, we support this finding in the case of patients with atrial arrhythmia when developing parameters assessing OSA severity. That is, the baseline reference could be set at 100% SpO_2 value in order to factor differences in baseline blood oxygenation as well as the relative decrease in blood oxygenation.

To study the acute influence of AFib on the desaturations in OSA patients with a history of atrial arrhythmias we further compared patients having continuous AFib to patients having SR during the PSG recordings. Results showed that the patients with AFib had greater desaturation areas. As an exception, the

TABLE II

DESATURATION AREA AND DESATURATION SLOPE PARAMETER VALUES OF THE INCLUDED PATIENT POPULATION ($N = 520$). VALUES ARE GIVEN AS MEDIAN (INTERQUARTILE RANGE)

Parameter	Without previous diagnosis of atrial arrhythmias	With a previous diagnosis of atrial arrhythmia		
		All	SR	AFib
Desaturation area, %s	106.7 (58.6–206.7)	106.9 (58.9–202.9)	93.7 (52.9–189.6) #, *	128.0 (72.5–218.8) *
Fall area, %s	61.3 (30.2–132.2)	58.1 (30.1–124.4) *	50.8 (26.3–114.1) #, *	70.6 (37.5–140.0) *
Recovery area, %s	40.4 (23.2–71.9)	41.5 (24.7–68.6)	38.4 (22.7–68.6) #, *	46.5 (28.2–68.6) *
Desaturation area with 100% baseline, %s	240.5 (158.4–370.7)	282.2 (186.8–417.3) *	278.8 (181.5–428.7) *	290.6 (195.0–404.3) *
Fall area with 100% baseline, %s	143.0 (86.0–240.7)	161.7 (100.1–262.9) *	155.1 (96.6–254.5) #, *	174.3 (106.8–274.2) *
Recovery area with 100% baseline, %s	86.8 (55.6–133.8)	98.7 (65.4–158.6) *	103.0 (64.4–168.8) #, *	93.8 (66.2–138.6) *
Fall slope, %/s	0.325 (0.202–0.535)	0.306 (0.185–0.553) *	0.383 (0.214–0.662) #, *	0.227 (0.162–0.364) *
Recovery slope, %/s	0.490 (0.263–0.914)	0.432 (0.231–0.836) *	0.480 (0.248–1.000) #	0.379 (0.210–0.612) *

SR: sinus rhythm, AFib: atrial fibrillation. * Statistically significant ($p < 0.05$) difference compared with patients without atrial arrhythmia. #Statistically significant ($p < 0.05$) difference compared to atrial arrhythmia patient with AFib. Variables were compared using the Wilcoxon rank-sum test.

TABLE III

RESULTS OF LINEAR MIXED MODEL ANALYSES TO EVALUATE THE DIFFERENCES IN DESATURATION AREA AND DESATURATION SLOPE PARAMETERS BETWEEN SLEEP APNEA PATIENTS WITH AND WITHOUT A PREVIOUS DIAGNOSIS OF ATRIAL ARRHYTHMIA. PATIENTS WITHOUT DIAGNOSED ATRIAL ARRHYTHMIA WERE USED AS A REFERENCE CATEGORY

Parameter	Model 1		Model 2		Model 3	
	β (SE)	*p*-value	β (SE)	*p*-value	β (SE)	*p*-value
Desaturation area	0.067 (0.072)	0.347	0.010 (0.062)	0.867	0.007 (0.060)	0.910
Fall area	0.057 (0.079)	0.468	-0.092 (0.079)	0.247	-0.016 (0.062)	0.797
Recovery area	0.080 (0.067)	0.231	0.081 (0.049)	0.099	0.034 (0.060)	0.569
Desaturation area with 100% baseline	**0.139 (0.059)**	**0.020**	-0.011 (0.050)	0.823	0.087 (0.056)	0.119
Fall area with 100% baseline	**0.133 (0.062)**	**0.031**	-0.035 (0.065)	0.594	0.086 (0.051)	0.091
Recovery area with 100% baseline	**0.150 (0.065)**	**0.020**	0.081 (0.050)	0.107	**0.127 (0.062)**	**0.039**
Fall slope	-0.055 (0.071)	0.437	-0.091 (0.047)	0.052	**-0.145 (0.048)**	**0.003**
Recovery slope	-0.118 (0.083)	0.158	**-0.199 (0.069)**	**0.004**	**-0.181 (0.049)**	**0.000**
Model's Covariates						
Age	-	-	-0.003–0.012 (0.001–0.002)	0.000–0.523	-	-
BMI	-	-	0.004–0.019 (0.002–0.003)	0.000–0.107	-	-
Gender	-	-	0.053–0.272 (0.033–0.047)	0.000–0.110	-	-
Smoking	-	-	0.022–0.093 (0.037–0.058)	0.025–0.638	-	-
AHI	-	-	-	-	**0.003–0.012 (0.001)**	**0.000**
Hypertension	-	-	-	-	-0.060–0.066 (0.022–0.040)	0.062–0.949
T2DM	-	-	-	-	0.005–0.084 (0.034–0.051)	0.056–0.926

BMI: body mass index, AHI: apnea-hypopnea index, T2DM: type 2 diabetes mellitus, β: standardized beta coefficient, SE: standard error. Statistically significant values are marked as bold.
Model 1: unadjusted.
Model 2: adjusted for gender, age, BMI, and smoking.
Model 3: adjusted for AHI, hypertension, and T2DM.
In categorical variables (gender, smoking, hypertension and T2DM), female gender, nonsmoker, patients without hypertension and patients without T2DM were used as a reference category.

recovery area with 100% SpO_2 baseline was smaller in the patients with continuous AFib (Table II, Fig. 4). However, the patients with continuous AFib had substantially more gradual desaturation slopes (Fig. 4) implying noticeably longer desaturations compared to the patients who had SR during the PSG (Table I). Previously, AFib has been associated with blood flow abnormalities and endothelial dysfunction [12]. These results are in line with the previous findings, showing that oxygenation changes in the peripheral vascular system are highly prolonged in patients suffering AFib during the night. In turn, it has been shown that OSA patients have impaired cardiac response causing acute hypoxia in the body and cerebral circulation [6], [30]. These findings indicate that this phenomenon is exceedingly severe in OSA patients suffering from acute AFib. It is acknowledged that OSA patients with cardiac comorbidity have a higher risk for nocturnal sudden death compared to patients without OSA [32]. Thus, these findings suggest that the identification of OSA patients having acute atrial arrhythmias in the early stage is highly important to reduce these more severe health consequences. For example, as the patients with SR had faster desaturation rates than patients with AFib, the results of this study reveal that rhythm control might be better than rate control in OSA patients suffering from acute AFib. Thus, also the ECG signal measured during PSG should always be analysed in detail for a more comprehensive view of the status of the patient. However, OSA is commonly diagnosed with home sleep apnea testing which can be conducted without ECG making the detection of atrial arrhythmias challenging. The present results suggest that it could be possible to differentiate between OSA patients with and without atrial arrhythmias based in more comprehensive analysis of the SpO_2 signal. Furthermore, it has been shown that detecting arrhythmias and OSA are feasible using ambulatory devices utilizing arterial tonometry measurement alongside oxygen saturation, indicating potential for detailed, at-home diagnosis [33], [34].

In the linear mixed models, the connection between desaturation areas and previously diagnosed atrial arrhythmias diminished when adjusted with demographic parameters. We acknowledge that the study population was relatively old (median = 53.3 years), particularly in the subgroup with a previous diagnosis of atrial arrhythmia (median = 65.0 years). It has been shown that the severity of desaturation increases with increasing age [35]. Furthermore, age is one of the major risk factors for the prevalence of atrial arrhythmias [36]. These, together with the biased sample size ($n = 47$ vs. $n = 473$, respectively) could explain these results (i.e., decreased β-coefficients and increased p-values) in the linear mixed model analysis when considering desaturation area parameters.

This study has some limitations. First, the patient subgrouping was done based on whether the patient had previously diagnosed atrial arrhythmia, and we had no information on whether the patient had paroxysmal or persistent AFib or atrial flutter during the primary atrial arrhythmia diagnosis. Furthermore, the information about the possible treatments and interventions for atrial arrhythmias were not available. Moreover, we lacked the information about the time between the atrial arrhythmia diagnosis and the PSG. It is acknowledged that different arrhythmia types might have different physiological consequences and responses to intermittent hypoxemias [6], [9]. However, in this dataset most of the arrhythmias observed in ECG signals revealed AFib. Therefore, the results can be generally associated with AFib and a more detailed investigation of other types of arrhythmias and their association with desaturation severity is warranted. Second, we acknowledge including patients with a history of multimorbidity as a limitation of the present study since several comorbidities can affect oxygen saturation levels and cardiac function. However, as OSA patients are usually multimorbid, excluding all possible comorbidities would have extensively reduced the number of patients. Therefore, only the most common and potential comorbidities, i.e., COPD and cardiac failure were considered in exclusions. Third, the desaturation values at start points and endpoints of desaturations were not evaluated. However, these values could give valuable information on how well patients recover from desaturations. For example, it is possible that the oxygen saturations do not always recover to the baseline level of the desaturation onset. As this aspect was not considered in this study, it warrants further investigation in the future. Finally, as there are no clinical guidelines for scoring desaturations (besides the minimum depth requirement), some desaturations were scored from the onset to the nadir in this data set. Those desaturations were excluded from analyses to enable the evaluation of the characteristics of fall and recovery areas. However, this study included around 58 000 desaturation events and the number of such events was only 693. Thus, the exclusion of these 693 events has negligible effects on the results.

V. Conclusion

This study revealed that acute and long-term effects of atrial arrhythmias are connected prolonged changes in peripheral SpO_2 levels in OSA patients. This was particularly highlighted in the recovery section of the desaturation. Therefore, both the decrease and the recovery sections of desaturations in SpO_2 signal should be considered in more detail in OSA severity assessment and diagnostics. Thus, uniform desaturation scoring protocols and rules are required to allow the determination of the most appropriate diagnostic parameters beyond the AHI.

References

[1] S. Ahn, J. Solfest, and L. L. Rubchinsky, "Fine temporal structure of cardiorespiratory synchronization," *Amer. J. Physiol. Heart Circulatory Physiol.*, vol. 306, no. 5, pp. H755–H763, 2014.
[2] A. J. Garcia et al., "Cardiorespiratory coupling in health and disease," *Auton. Neurosci.*, vol. 175, no. 1/2, pp. 26–37, 2013.
[3] M. M. Kabir et al., "Cardiorespiratory phase-coupling is reduced in patients with obstructive sleep apnea," *PLoS One*, vol. 5, no. 5, 2010, Art. no. e10602.
[4] D. Zhang et al., "Effects of acute hypoxia on heart rate variability, sample entropy and cardiorespiratory phase synchronization," *Biomed. Eng. Online*, vol. 13, no. 1, pp. 1–12, 2014.
[5] T. J. Cross et al., "The interactions between respiratory and cardiovascular systems in systolic heart failure," *J. Appl. Physiol.*, vol. 128, no. 1, pp. 214–224, 2020.
[6] A. M. May, D. R. van Wagoner, and R. Mehra, "OSA and cardiac arrhythmogenesis: Mechanistic insights," *Chest*, vol. 151, no. 1, pp. 225–241, 2017.

[7] A. V. Benjafield et al., "Estimation of the global prevalence and burden of obstructive sleep apnoea: A literature-based analysis," *Lancet Respir. Med.*, vol. 7, no. 8, pp. 687–698, 2019.

[8] A. Adlakha and J. W. Shepard, "Cardiac arrhythmias during normal sleep and in obstructive sleep apnea syndrome," *Sleep Med. Rev.*, vol. 2, no. 1, pp. 45–60, 1998.

[9] J. Martí-Almor et al., "Obstructive sleep apnea syndrome as a trigger of cardiac arrhythmias," *Curr. Cardiol. Rep.*, vol. 23, no. 3, 2021, Art. no. 20.

[10] R. Mehra et al., "Association of nocturnal arrhythmias with sleep-disordered breathing: The sleep heart health study," *Amer. J. Respir. Crit. Care Med.*, vol. 173, no. 8, pp. 910–916, 2006.

[11] B. J. Selim et al., "The association between nocturnal cardiac arrhythmias and sleep-disordered breathing: The DREAM study," *J. Clin. Sleep Med.*, vol. 12, no. 6, pp. 829–837, 2016.

[12] A. A. Khan et al., "Endothelial function in patients with atrial fibrillation," *Ann. Med.*, vol. 52, no. 1/2, pp. 1–11, 2020.

[13] R. B. Berry et al., "Rules for scoring respiratory events in sleep: Update of the 2007 AASM manual for the scoring of sleep and associated events," *J. Clin. Sleep Med.*, vol. 8, no. 5, pp. 597–619, 2012.

[14] T. Leppänen et al., "RemLogic plug-in enables clinical application of apnea-hypopnea index adjusted for severity of individual obstruction events," *J. Med. Eng. Technol.*, vol. 40, no. 3, pp. 119–126, 2016.

[15] A. Muraja-Murro et al., "Adjustment of apnea-hypopnea index with severity of obstruction events enhances detection of sleep apnea patients with the highest risk of severe health consequences," *Sleep Breathing*, vol. 18, no. 3, pp. 641–647, 2014.

[16] D. A. Pevernagie et al., "On the rise and fall of the apnea−hypopnea index: A historical review and critical appraisal," *J. Sleep Res.*, vol. 29, no. 4, 2020, Art. no. e13066.

[17] A. Kulkas et al., "Novel parameters indicate significant differences in severity of obstructive sleep apnea with patients having similar apnea-hypopnea index," *Med. Biol. Eng. Comput.*, vol. 51, no. 6, pp. 697–708, 2013.

[18] N. M. Punjabi et al., "Sleep-disordered breathing and cardiovascular disease an outcome-based definition of hypopneas," *Respir. Care*, vol. 177, no. 10, pp. 1150–1155, 2008.

[19] C. H. J. Won et al., "Varying hypopnea definitions affect obstructive sleep apnea severity classification and association with cardiovascular disease," *J. Clin. Sleep Med.*, vol. 14, no. 12, pp. 1987–1994, 2018.

[20] A. Kulkas et al., "Severity of desaturation events differs between hypopnea and obstructive apnea events and is modulated by their duration in obstructive sleep apnea," *Sleep Breathing*, vol. 21, no. 4, pp. 829–835, 2017.

[21] A. S. Gami et al., "Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation," *J. Amer. College Cardiol.*, vol. 49, no. 5, pp. 565–571, 2007.

[22] A. Muraja-Murro et al., "The severity of individual obstruction events is related to increased mortality rate in severe obstructive sleep apnea," *J. Sleep Res.*, vol. 22, no. 6, pp. 663–669, 2013.

[23] A. Azarbarzin et al., "The hypoxic burden of sleep apnoea predicts cardiovascular disease-related mortality: The osteoporotic fractures in men study and the sleep heart health study," *Eur. Heart J.*, vol. 40, no. 14, pp. 1149–1157, 2019.

[24] T. Karhu et al., "Desaturation event scoring criteria affect the perceived severity of nocturnal hypoxic load," *Sleep Med.*, vol. 100, pp. 479–486, Dec. 2022.

[25] S. Kainulainen et al., "Severe desaturations increase psychomotor vigilance task-based median reaction time and number of lapses in obstructive sleep apnoea patients," *Eur. Respir. J.*, vol. 55, no. 4, 2020, Art. no. 1901849.

[26] A. Chaquat et al., "Association of chronic obstructive pulmonary disease and sleep apnea syndrome," *Amer. J. Respir. Crit. Care Med.*, vol. 151, no. 1, pp. 82–86, 1995.

[27] M. P. Tarvainen et al., "Kubios HRV - heart rate variability analysis software," *Comput. Methods Prog. Biomed.*, vol. 113, no. 1, pp. 210–220, 2014.

[28] M. A. Arias et al., "Obstructive sleep apnea syndrome affects left ventricular diastolic function: Effects of nasal continuous positive airway pressure in men," *Circulation*, vol. 112, no. 3, pp. 375–383, 2005.

[29] S. Kainulainen et al., "Severity of desaturations reflects OSA-related daytime sleepiness better than AHI," *J. Clin. Sleep Med.*, vol. 15, no. 8, pp. 1135–1142, 2019.

[30] N. A. Dewan, F. J. Nieto, and V. K. Somers, "Intermittent hypoxemia and OSA: Implications for comorbidities," *Chest*, vol. 147, no. 1, pp. 266–274, 2015.

[31] P. de Chazal et al., "Predicting cardiovascular outcomes using the respiratory event desaturation transient area derived from overnight sleep studies," in *Proc. Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.*, 2021, pp. 5496–5499.

[32] A. S. Gami et al., "Day–night pattern of sudden death in obstructive sleep apnea," *New England J. Med.*, vol. 352, no. 12, pp. 1206–1214, 2005.

[33] R. Tauman et al., "Watch-PAT is useful in the diagnosis of sleep apnea in patients with atrial fibrillation," *Nature Sci. Sleep*, vol. 12, pp. 1115–1121, 2020.

[34] G. Pillar et al., "Detection of common arrhythmias by the watch-PAT: Expression of electrical arrhythmias by pulse recording," *Nature Sci. Sleep*, vol. 14, pp. 751–763, 2022.

[35] T. Leppänen et al., "Severity of individual obstruction events increases with age in patients with obstructive sleep apnea," *Sleep Med.*, vol. 37, pp. 32–37, 2017.

[36] A. S. Go et al., "Prevalence of diagnosed atrial fibrillation in adults: National implications for rhythm management and stroke prevention: The anticoagulation and risk factors in atrial fibrillation (ATRIA) study," *JAMA*, vol. 285, no. 18, pp. 2370–2375, 2001.