Cardiac Rhythm Disturbances and ST-Segment Depression Episodes in Patients With Obstructive Sleep Apnea-Hypopnea Syndrome and Its Mechanisms

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Abstract and Introduction

Abstract

Study Objectives: To compare the frequency of daytime and nocturnal cardiac arrhythmias and ST-segment depression episodes among patients with obstructive sleep apnea-hypopnea syndrome (OSAHS), snoring subjects, and healthy subjects, and to analyze the relationship between the cardiac disturbances, sleep characteristics, and sympathetic tone in patients with OSAHS.
Patients and Interventions: Twenty-one consecutive patients with OSAHS, 12 snorers without hypersomnolence, and 15 healthy subjects were selected. Polysomnography, 24-h Holter ECG recording, and urinary catecholamine determination were simultaneously performed on all subjects.
Results: Patients with OSAHS had more daytime and nocturnal episodes of sinus and supraventricular arrhythmias and couplets than the snoring and control groups. Moreover, nocturnal ST-segment depression episodes were more frequent in the OSAHS group than in control subjects (0.565 ± 0.826/h vs 0 ± 0/h [mean ± SD]). In patients with OSAHS, arousal index and daytime epinephrine levels were related to daytime and nocturnal ST-segment depression episodes, whereas minimum arterial oxygen saturation was related to nocturnal sinus bradycardia and supraventricular tachycardia. Epinephrine and norepinephrine urinary concentrations correlated with sinus and supraventricular arrhythmias.
Conclusions: Patients with OSAHS have a higher frequency of cardiac rhythm disturbances and ST-segment depression episodes than snoring and control subjects. Moreover, ST-segment changes are related to sympathetic tone and sleep fragmentation, whereas most of the rhythm disturbances in patients with OSAHS are associated with sleep fragmentation, nocturnal hypoxemia, and sympathetic tone.

Introduction

Obstructive sleep apnea-hypopnea syndrome (OSAHS) is characterized by periodic reduction or cessation of breathing due to narrowing of the upper airways during sleep. Prevalence surveys estimate that 2% of women and 4% of men of middle age are affected by this syndrome.[1] The main symptoms are daytime sleepiness, cognitive deficits, and impaired mood. OSAHS has been recognized as an important medical condition producing severe morbidity and appreciable mortality.[2] There is growing research evidence for an independent association between OSAHS and cardiovascular disease,[3] mainly hypertension,[4] but an association has also been found with stroke, ischemic heart disease, and congestive heart failure.[5]

Nocturnal ST-segment changes consistent with myocardial ischemia are quite common among patients with OSAHS

and coexisting coronary artery disease.[6] However, there is uncertainty as to whether OSAHS causes nighttime ischemia in the absence of coronary disease. In one study,[7] no evidence of ischemic episodes was found; in another study,[8] ST-segment depressions were reported in 30% of patients.

Cardiac arrhythmias are a prevalent finding in patients with OSAHS undergoing Holter ECG or polysomnography, and they can be successfully controlled by continuous positive airway pressure (CPAP) therapy or after a tracheostomy.[9,10] However, the incidence of pathologically significant rhythm disturbances, such as heart blockage, supraventricular tachycardia (SVT), and ventricular arrhythmia, is less clear-cut. Furthermore, some studies[11] found no clear epidemiologic evidence for a causal relation between OSAHS and arrhythmia when confounders were considered.

While a bradycardic response to obstructive apneas is related to intrathoracic pressure swings, parasympathetic activity, hypoxia, and sleep phase, postapneic tachycardia could be an effect of hypoxia and sympathetic discharge due to arousal reaction.[12] In spite of the research done on sinus arrhythmia mechanisms during sleep, the role of sympathetic activity and sleep characteristics in daytime supraventricular and ventricular arrhythmias as well as myocardial ischemia has not been adequately evaluated.

The aim of the present study was to compare the frequency of daytime and nocturnal cardiac arrhythmias and ST-segment depression episodes among patients with OSAHS, snoring subjects, and healthy subjects. We have also analyzed the relationship among these 24-h ECG monitoring events, sleep characteristics, and sympathetic tone in patients with OSAHS.

Materials and Methods

Study Subjects

Twenty-one consecutive patients with OSAHS, 12 consecutive snorers without hypersomnolence (Epworth sleepiness scale < 5), and 15 age- and body mass index (BMI)-matched healthy subjects were selected for study. Patients were excluded from the study for the following reasons: (1) unwillingness or inability to perform the testing procedure; (2) obstructive or restrictive lung disease demonstrated on pulmonary function testing; (3) known valvular heart disease or hypertension, based on the mean of three readings taken on two separate visits (between 1 week and 2 weeks apart) ≥ 140/90 mm Hg[13,14]; (4) current (< 3 months) myocardial infarction or cerebrovascular accident; (5) diabetes (fasting blood sugar > 140 mg/dL) or hypercholesterolemia (fasting serum cholesterol > 200 mg/dL); (6) current use of digoxin, antiarrhythmic agents, hypnotic drugs, or any other drug that could alter the ST segment; (7) current drug or mechanical treatment for sleep apnea; (8) known neuromuscular disease; (9) abnormal thyroid function; and (10) morbid obesity (body weight > 150% ideal). Control subjects were judged healthy by history, physical examination, ECG, basal spirometry, and chest radiography.

Subjects were asked not to eat for 4 h before the exploration, and they were also asked to refrain from coffee, tea, and alcohol for ≥ 12 h, and tobacco for ≥ 2 h before each study. The Institutional Ethics Committee at the hospital approved the study. All subjects gave their written informed consent prior to enrollment.

Polysomnography

Healthy subjects and patients with OSAHS underwent polysomnography from 11 PM to 7 AM. EEG (C3-A2, C4-A1), electro-oculogram, chin electromyogram, electromyograms of the tibialis anterior of both legs, and ECG were continuously recorded. Breathing was monitored using nasal cannulas with a pressure transducer system, oronasal thermistors, and thoracoabdominal stain gauges. Simultaneously, arterial oxygen saturation (SaO_2) was monitored with a pulse oximeter (Pulsox DP-8; Minolta; Osaka, Japan). Sleep was analyzed using the standard criteria[15] for epochs of 20 s, and the following sleep variables were calculated: total sleep time, wake time after sleep onset, and sleep efficiency, defined as the ratio of total sleep time to sleep episode duration. Microarousals were scored according to the American Sleep Disorders Association definition.[16] An obstructive apnea/hypopnea event was characterized by a > 50% decrease from baseline in the amplitude of breathing for ≥ 10 s associated with either oxygen desaturation of > 3% or an arousal in the presence of continued respiratory efforts.[17] The apnea-hypopnea index (AHI) was established as the number of apneas/hypopneas per hour of sleep. OSAHS was defined as excessive daytime sleepiness (a score ≥ 10 in the Epworth sleepiness scale) unexplained by other factors plus five or more obstructed breathing events per hour during sleep.[17] As indexes of nocturnal oxygen saturation, mean

SaO_2 throughout the night, mean low SaO_2 (mean of the minimum value for SaO_2 in each 30-s epoch), and minimum SaO_2 (lowest value recorded during sleep) were computed.

24-h ECG Monitoring

A 24-h Holter ECG recording was simultaneously performed on all patients to screen for cardiac arrhythmias. A two-channel tape recorder (Micro AM, KI 5600 model; Kontrom Instruments; München, Germany) was used, recording leads V_2 and V_5. The ambulatory monitors were fitted to the patients by experienced staff. The recordings were analyzed with computerized equipment (Kontrom Instruments) with manual verification at 60 times normal speed and printed out by experienced medical staff (F.O.) blinded to the results of polysomnography. Nocturnal period was defined according to sleep duration by polysomnography. During daytime monitoring, subjects were instructed to avoid strenuous exercise.

All deviations from normal sinus rhythm were recorded.[18] For the purposes of the present study, rhythm disturbances contemplated included sinus tachycardia, sinus bradycardia (SB), pauses of > 2 s, premature supraventricular beat (PSVB), SVT, and complex ventricular ectopy, including salvoes of three beats or more (couplets) or recurrent bigeminy. An ST-segment depression episode was defined as flat or down-sloping ST-segment depression > 1 mm (sinus tachycardia slope < 59°) from baseline for ≥ 0.08 s after the J point, lasting for at least 1 min and separated from the next episode by at least 1 min. Only one lead showing the largest number of ST-segment depression episodes was used for analysis.

Catecholamines in Urine

Catecholamines were determined as previously described.[19] Subjects were requested to collect separate urine samples from 8 AM until going to bed (day) and all urine during the night and the first one after getting up in the morning (night). Urine specimens for each sample were collected in polyethylene containers, acidified with HCl 6 mol/L as preservative and stored at – 40°C before analysis.

A 5-mL aliquot of a urine sample was filtered; 3.4 dihydroxybenzylamine (internal standard) and 0.1% ethylenediamine tetra-acetic acid were added to the filtrate, adjusted to 6.5 pH and subsequently placed on a cation exchange column (Biorex 70; Bio-Rad; Munich, Germany). After the sample completely entered the resin, the column was washed with distilled water and the catecholamines were eluted with 10 mL 0.65 mol/L boric acid. After this procedure, 20 µL effluent were injected into an high-performance liquid chromatography (HPLC) system composed of an HPLC pump (model 510; Waters Corporation; Milford, MA), an injection valve (20 µL) [Rheodyne; Rohnert Park, CA], HR-80 chromatographic column (RP-C18; ESA; Chelmsford, MA), a coulometric detector (Coulochem II; ESA), and a highsensitivity analytical cell (model 5011; ESA) and conditioning cell (model 5021; ESA). Concentrations of detected compounds were computer calculated using 712 HPLC system controller version 1.2 integration software (Gilson; Middleton, WI) which measures the heights of the peaks and relates them to external standards.

Intra-assay coefficients of variation were 3% for norepinephrine, 3% for epinephrine, and 1.5% for dopamine. Interassay coefficients of variation were 9% for norepinephrine, 10.5% for epinephrine, and 6.4% for dopamine. Results were expressed in terms of micrograms per gram of creatinine.

Lung Function Study

Arterial blood gas values were measured with subjects in a seated position breathing room air. Spirometry was performed by means of a pneumotachograph (MasterLab 4.1; Erich Jaeger GmbH; Würzburg, Germany), according to European Respiratory Society standardization.[20]

Statistical Analysis

The differences between the means of variables in the study group were analyzed using one-way analysis of variance. *Post hoc* analysis was performed using the Dunnett T3 test for multiple comparisons. The χ^2 test was used for evaluating frequencies. Correlations between polysomnographic findings, lung function parameters, catecholamines, and arrhythmias were determined by linear regression analysis[21] using Pearson correlation

coefficient. A multiple logistic regression analysis was performed to identify the factors determining nocturnal arrhythmias or ST-segment depressions. The independent variables included in the model were gender, age, BMI, tobacco habit, AHI, arousal index (ARI), minimum SaO_2, and urinary catecholamines. These analyses were performed using the Statistical Package for the Social Sciences for Windows Release 8.0 software (SPSS; Chicago, IL). In all cases, p values < 0.05 were considered to be significant. Data are expressed as mean ± SD.

Results

Anthropometric characteristics sleep architecture, lung function, and BP in patients with OSAHS, snorers, and control subjects are given in Table 1 . There were no significant differences in gender, age, weight, height, BMI, or smoking habit among the three groups. The mean values of forced expiratory lung volumes, arterial blood gases, pH, hemoglobin concentration, and office BP were similar in all groups.

Daytime and nocturnal catecholamine concentrations in urine are also shown in Table 1 . Compared with snoring and control subjects, patients with OSAHS had higher mean nocturnal norepinephrine, epinephrine, and dopamine urine concentrations. No significant difference in daytime catecholamine concentrations in urine between the three groups was found.

Table 2 and Table 3 show the results of the 24-h Holter ECG recordings. The results are subclassified into daytime and nocturnal findings. No difference in daytime and nocturnal rhythm disturbances was found between snorers and healthy subjects.

Eighteen patients with OSAHS had daytime SB, and 20 patients had nocturnal SB. Patients with OSAHS had more daytime and nocturnal SB than the snorers and the control group. The number of daytime and nocturnal pauses and bigeminy per hour was not significantly different between the study groups. Relationships were found between nocturnal SB and AHI ($r = 0.408$, p = 0.033) and nocturnal minimum SaO_2 ($r = – 0.789$, p = 0.000). Minimum SaO_2 during sleep was also related to daytime SB ($r = – 0.522$, p = 0.023) and nocturnal pauses ($r = – 0.547$, p = 0.017). Daytime epinephrine urinary concentration had significant correlations with diurnal SB ($r = 0.642$, p = 0.001) and daytime and nocturnal pauses ($r = 0.534$, p = 0.006, and $r = 0.504$, p = 0.010, respectively). Patients with OSAHS had more daytime and nocturnal sinus tachycardia, PSVB, SVT, and couplets than the snorers and the control group (Table 2 and Table 3).

ARI correlated with daytime and nocturnal sinus tachycardia ($r = 0.447$, p = 0.036, and $r = 0.484$, p = 0.025, respectively), whereas daytime sinus tachycardia also correlated with AHI ($r = 0.528$, p = 0.010). A relationship between nocturnal PSVB and nocturnal minimum SaO_2 ($r = – 0.517$, p = 0.024) and daytime epinephrine urinary concentration ($r = 0.550$, p = 0.005) was found.

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Nocturnal SVT was related to minimum SaO_2 ($r = – 0.687$, p = 0.002), nighttime norepinephrine ($r = 0.458$, p = 0.018), and daytime epinephrine urinary concentration ($r = 0.574$, p = 0.003). However, diurnal SVT correlated significantly with daytime epinephrine urinary concentration ($r = 0.780$, p = 0.000) and diurnal and nocturnal norepinephrine concentration ($r = 0.640$, p = 0.001, and $r = 0.544$, p = 0.005, respectively). No correlations were found among couplets, bigeminy and polysomnographic findings, lung function parameters or catecholamine concentrations in urine. In the logistic regression model, the occurrence of cardiac rhythm disturbances was not predicted by any of the variables included (gender, age, BMI, smoking status, AHI, ARI, minimum SaO_2, or urinary catecholamines).

Twelve patients with OSAHS, 2 snorers, and 1 control subject had diurnal ST-segment depressions. Moreover, we found nighttime ST-segment depressions in 16 patients with OSAHS and 6 snorers, and no nocturnal ST-segment changes were found among healthy subjects (Table 3). Seven of the 16 patients with OSAHS and nocturnal ST-segment depressions had marked ST-segment depression (≥ 2 mm), but there were no marked ST-segment episodes in the snorers and control subjects.

The number of episodes of ST-segment depression per hour was higher during the daytime in patients with OSAHS than in snoring and control groups. Indeed, patients with OSAHS had more nocturnal ST-segment decrease episodes (0.565 ± 0.826/h) than snorers (0.096 ± 0.140/h) and control subjects (0 ± 0/h). We found a direct relationship between the ARI and daytime and nocturnal ST-segment depression episodes (r = 0.607, p = 0.003, and r = 0.608, p = 0.03, respectively) [Fig 1]. However, in the logistic regression model, nocturnal ST-segment depression was only predicted by daytime epinephrine (r^2 = 0.460, p = 0.049).

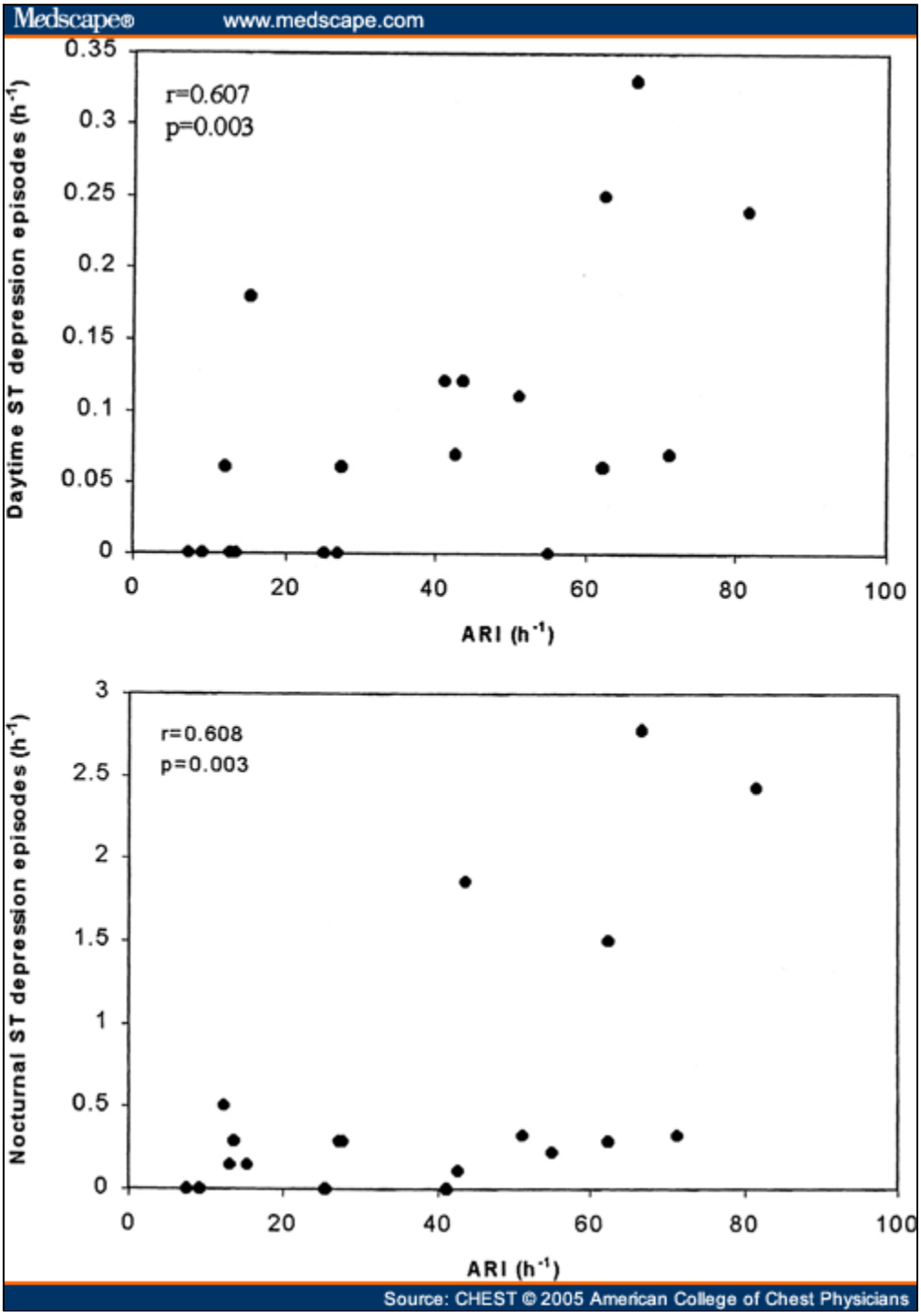

Figure 1.

Relationship between ARI and daytime (top) and nocturnal (bottom) ST-segment depression episodes.

Discussion

The main results of this study are the following: (1) patients with OSAHS have a higher frequency of most of the cardiac arrhythmias analyzed and ST-segment dynamic changes, in comparison with snoring and control subjects; and (2) ST-segment depression episodes are related to sleep fragmentation and sympathetic tone, whereas most of the rhythm disturbances in patients with OSAHS are associated with sleep fragmentation, nocturnal hypoxemia, and urinary catecholamine excretion.

There is uncertainty as to whether OSAHS causes nocturnal myocardial ischemia in the absence of coronary artery disease, but in the present study, patients with OSAHS patients have a higher frequency of nocturnal ST-segment depression episodes in comparison with control subjects. In some studies,[7,22] no evidence of nocturnal ischemic episodes in such patients was reported; in another study,[8] 30% of the patients had ST-segment depression during the night and CPAP treatment significantly reduced the total duration of these events. Moreover, sleep apnea was found in 9 of 10 subjects with severely disabling angina pectoris and nocturnal angina.[23]

It has been reported that periodic respiratory disturbances in OSAHS are associated with nocturnal ischemic heart events.[24] Apneas and hypopneas reduce myocardial oxygen delivery by intermittent hypoxia, but they worsen myocardial oxygen demand by mechanical changes due to reduced intrathoracic pressure. These pressure and volume changes and the sympathetic nervous system activation due to arousals increase left ventricular preload and afterload. Therefore, interventricular septum shift leads to impediment of the diastolic function of the left ventricle and stroke volume.[6] It is also known that hypoxia may directly depress cardiac contractility or reduce cardiac performance indirectly by causing pulmonary vasoconstriction and increasing pulmonary arterial pressure.[24]

We found a direct relationship between the ARI and daytime and nocturnal ST-segment depression episodes in the present study; therefore, we think that sleep fragmentation may play an important role in OSAHS-related myocardial ischemia. It has been hypothesized that repeated nocturnal hypoxemia, abrupt decreases and increases in cardiac output, and sympathetic activation in association with arousals could lead to the creation of oxygen-free radicals and ischemia-reperfusion injury to the vascular wall that may play an important role in the development of atherosclerosis.[24] Moreover, platelet aggregability increases significantly overnight in association with elevated nocturnal catecholamine levels, and both are reduced by CPAP treatment.[25,26] Furthermore, there is evidence of predisposition to clot formation, owing to the increase in hematocrit, fibrinogen levels, and whole-blood viscosity in OSAHS.[24]

Peker et al[27] studied 62 patients with ischemic heart disease and 62 age-, sex-, and BMI-matched control subjects without history or signs of heart disease, and found that OSAHS increased risk for coronary artery disease prevalence after risk factor adjustment (odds ratio, 3.1; 95% confidence interval, 1.2 to 8.3). At a 5-year follow-up of these patients, the respiratory disturbance index was the only independent predictor of cardiovascular mortality.[28] In two additional case-control studies[29,30] with symptomatic and angiographically verified coronary artery disease, an AHI > 10/h was almost twice as common in male ischemic patients and three times more prevalent in female ischemic patients when compared to age-matched control subjects. In a cross-sectional analysis of the Sleep Heart Health Study[5] cohort of > 6,424 subjects, OSAHS was found to be an independent risk factor for coronary artery disease (odds ratio, 1.27; confidence interval, 0.99 to 1.62). Furthermore, Peker et al[3] found that incompletely treated OSAHS represented a fivefold increased risk for coronary artery disease incidence, after risk factor adjustment, in a consecutive sleep clinic cohort over 7 years of 182 middle-aged men without previous cardiovascular disease.

Patients with OSAHS had more daytime and nocturnal sinus tachycardia, SB, PSVB, SVT, and couplets than the snoring and control groups. Two previous reports[9,31] have demonstrated high prevalence (58% and 48%, respectively) of cardiac rhythm disturbances, significantly higher than nonapneic snorers, among large populations of patients with OSAHS. However, other studies[11,32] have reported a much lower prevalence of rhythm disturbances that was not significantly different from that of nonapneic snorers. It has been argued that such discrepant results can be explained in terms of selection bias, because the control populations for these studies have generally consisted of patients undergoing sleep studies for suspected OSAHS, but who were found not to have significant OSAHS. Accordingly, Valencia-Flores et al[33] found that cardiac arrhythmias were related to the level of sleep-disordered breathing and oxygen desaturation in a morbidly obese population. Furthermore, some studies[10,34] have demonstrated objective benefits with CPAP on cardiac rhythm disturbances.

Rhythm disturbances did not differ significantly in snorers vs control subjects in the present study. Similar results were reported by Hoffstein and Mateika,[31] who showed no difference in the prevalence of arrhythmias between heavy snorers and nonsnorers in a large group of patients.

Heart rate changes depend on the balance of both sympathetic and parasympathetic tone. Thus, stimulation of upper airway receptors may increase parasympathetic efferent activity even in the absence of lung inflation and stretch receptor stimulation.[12] OSAHS-related bradyarrhythmias are due to heightened parasympathetic tone, rather than cardiac structural abnormalities. The mechanisms of this are poorly understood, but rapid eye movement sleep may be one of the major pathogenetic factors contributing powerful vagal stimulation inducing nocturnal heart blockage.[34,35]

As arrhythmias described in patients with OSAHS are generally benign, it is difficult to evaluate the implications of these findings. There are no data evaluating mortality in patients with OSAHS and bradyarrhythmias, nor is there any information on the natural course or evolution of heart blockage in this group. Further studies will be required to assess the cardiovascular morbidity and mortality rates of untreated and undertreated patients with OSAHS-related cardiac arrhythmias. However, arterial hypertension, mostly as a consequence of the autonomic imbalance, in addition to rhythm disturbances, may be the most deleterious cardiovascular effects of OSAHS.

Our results show a significant correlation between minimum SaO_2 and nocturnal SB. It is known that vagally mediated bradycardia is the primary response to hypoxemia and chemoreceptor stimulation. Moreover, hypoxemia has CNS effects, suggesting that heart rate changes in patients with OSAHS may be the result of the simultaneous activation of different reflex pathways.[12,34] Minimum SaO_2 also correlated with nocturnal SVT in the present study, and similar pathways could be related.

An interesting finding of the current study is the relationship between diurnal SB and SVT and daytime urinary catecholamine levels. It could be hypothesized that a sustained high sympathetic tone could play a role in these rhythm disturbances. Accordingly, in the OSAHS group, daytime sinus tachycardia had significant correlations with ARI, and it could be argued that the sleep fragmentation could increase heart rate due to an increase in sympathetic tone by increasing the arousal reaction,[12] but this must be further evaluated.

We conclude that patients with OSAHS have a higher frequency of cardiac rhythm disturbances and ST-segment depression episodes than control subjects, and that snoring alone is not associated with increased frequency of cardiac arrhythmias and diurnal ST-segment depression events. Moreover, ST-segment depression episodes are related to sleep fragmentation and sympathetic tone, whereas most of the rhythm disturbances in patients with OSAHS are associated with sleep fragmentation, nocturnal hypoxemia, and sympathetic tone.

Table 1. Anthropometric Characteristics, Sleep Architecture, Lung Function, BP, and Urinary Catecholamine Excretion in Patients With OSAHS, Snoring Subjects, and Control Subjects*

Variables	Patients With OSAHS (n = 21)	Snorer Subjects (n = 12)	Control Subjects (n = 15)
Male/female gender, No.	19/2	11/1	13/2
Age, yr	54 ± 8	55 ± 12	54 ± 7
Weight, kg	87 ± 15	79 ± 11	81 ± 8
Height, m	1.68 ± 0.08	1.64 ± 0.09	1.66 ± 0.09
BMI	30.9 ± 3.8	29.3 ± 2.4	29.6 ± 2.4
Smokers, %	19	17	20

AHI, /h	41.9 ± 24.6	2.5 ± 1.7†	2.8 ± 1.4†
ARI, /h	38.4 ± 23.7	3.0 ± 1.2†	2.6 ± 1.4†
Mean SaO_2, %	93.4 ± 4.5	95.3 ± 1.1	94.7 ± 1.5
Mean low SaO_2, %	77.5 ± 8.0	90.5 ± 1.4†	90.5 ± 1.7†
Minimum SaO_2, %	74 ± 7	89.4 ± 1.5†	89.1 ± 1.7†
Sleep-onset latency, min	8.1 ± 9.5	34.7 ± 10.2†	36.1 ± 4.6†
Sleep efficiency, %	72.1 ± 6.6	84.5 ± 7.7†	85.2 ± 4.1†
Total sleep time, min	321 ± 66	381 ± 41§	396 ± 19†
Wake time after sleep onset, min	120.7 ± 31.6	32.9 ± 32.8†	28.0 ± 9.0†
pH	7.40 ± 0.03	7.40 ± 0.03	7.41 ± 0.03
PaO_2, mm Hg	73.1 ± 11.2	73.1 ± 6.8	76.4 ± 5.0
$PaCO_2$, mm Hg	39.7 ± 4.3	38.8 ± 3.1	39.0 ± 3.0
Hemoglobin, g/dL	15.5 ± 1.4	15.1 ± 1.6	15.0 ± 1.0
FVC, L	3.66 ± 0.90	3.52 ± 0.84	3.45 ± 0.47
FEV_1, L	2.90 ± 0.93	2.89 ± 0.69	2.81 ± 0.37
FEV_1/FVC, %	78.2 ± 12.9	82.4 ± 9.8	81.4 ± 4.4
Systolic BP, mm Hg	133 ± 16	127 ± 12	125 ± 8
Diastolic BP, mm Hg	83 ± 8	81 ± 7	79 ± 5
Daytime norepinephrine, µg/g	70.9 ± 65.4	63.5 ± 41.3	67.0 ± 35.6
Daytime epinephrine, µg/g	9.0 ± 6.8	8.7 ± 11.5	8.1 ± 5.4
Daytime dopamine, µg/g	313.5 ± 233.3	303.0 ± 91.0	334.9 ± 104.0
Nocturnal norepinephrine, µg/g	48.3 ± 32.3	28.5 ± 10.9	23.5 ± 5.2†
Nocturnal epinephrine, µg/g	3.36 ± 1.55	1.21 ± 1.15†	1.0 ± 0.9†
Nocturnal dopamine, µg/g	307.9 ± 144.9	239.5 ± 47.3	225.3 ± 69.9

* Data are presented as mean ± SD unless otherwise indicated.
† $p < 0.001$ for the comparison with patients with OSAHS.
‡ $p < 0.01$ for the comparison with patients with OSAHS.
§ $p < 0.05$ for the comparison with patients with OSAHS.

Table 2. Daytime and Nocturnal Rhythm Disturbances and ST-Segment Depression Episodes in Patients With OSAHS, Snoring Subjects, and Control Subjects*

Variables	OSAHS Patients	Snoring Subjects	Control Subjects

Daytime sinus tachycardia	3.22 ± 3.041	0.54 ± 1.35‡	0.13 ± 0.18§
Nocturnal sinus tachycardia	8.99 ± 4.52	2.61 ± 3.45‡	0.19 ± 0.17†
Daytime SB	2.00 ± 2.99	0.20 ± 0.27§	0.09 ± 0.13†
Nocturnal SB	14.90 ± 14.06	2.62 ± 5.93‡	0.37 ± 0.46†
Daytime pauses	0.24 ± 0.43	0.03 ± 0.06	0.05 ± 0.06
Nocturnal pauses	3.03 ± 5.38	0 ± 0	0.10 ± 0.12
Daytime PSVB	0.36 ± 0.42	0.25 ± 0.50	0.05 ± 0.05‡
Nocturnal PSVB	3.24 ± 4.66	0.65 ± 1.30	0.06 ± 0.08†
Daytime SVT	0.03 ± 0.05	0 ± 0§	0 ± 0†
Nocturnal SVT	0.63 ± 1.08	0.10 ± 0.33	0.02 ± 0.04§
Daytime couplets	0.55 ± 0.73	0.14 ± 0.26	0.07 ± 0.10§
Nocturnal couplets	2.46 ± 3.64	0.35 ± 0.58§	0.17 ± 0.18§
Daytime bigeminy	0.13 ± 0.27	0.05 ± 0.18	0.00 ± 0.02
Nocturnal bigeminy	0.51 ± 1.02	0.19 ± 0.61	0.02 ± 0.05
Daytime ST-segment depression	0.079 ± 0.097	0.006 ± 0.021‡	0.004 ± 0.0152‡
Nocturnal ST-segment depression	0.565 ± 0.826	0.096 ± 0.140§	0 ± 0†

* Data are presented as mean ± SD unless otherwise indicated.
† $p < 0.001$ for the comparison with patients with OSAHS.
‡ $p < 0.01$ for the comparison with patients with OSAHS.
§ $p < 0.05$ for the comparison with patients with OSAHS.

Table 3. Daytime and Nocturnal Rhythm Disturbances and ST-Segment Depression Episodes in Patients With OSAHS, Snoring Subjects, and Control Subjects*

Variables	OSAHS Patients (n = 21)	Snoring Subjects (n = 12)	Control Subjects (n = 15)	Total (n = 48)
Daytime sinus tachycardia	20 (95.2)	6 (50)	9 (60)	35 (73)
Nocturnal sinus tachycardia	0 (0)	9 (75)	10 (66.7)	19 (39.6)
Daytime SB	18 (85.7)	6 (50)	6 (40)	30 (62.5)
Nocturnal SB	20 (95.2)	6 (50)	8 (53.3)	34 (70.8)
Daytime pauses	11 (52.4)	3 (25)	7 (46.7)	21 (43.8)
Nocturnal pauses	17 (81.0)	0 (0)	7 (46.7)	24 (50)
Daytime PSVB	20 (95.2)	6 (50)	9 (60)	35 (73)
Nocturnal PSVB	19 (90.5)	4 (33.3)	6 (40)	29 (60.4)
Daytime SVT	7 (33.3)	0 (0)	0 (0)	7 (14.6)

Nocturnal SVT	12 (57.1)	1 (8.3)	2 (13.1)	15 (31.3)
Daytime couplets	15 (71.4)	3 (25)	7 (46.7)	25 (52.1)
Nocturnal couplets	19 (90.5)	6 (50)	10 (66.7)	35 (73)
Daytime bigeminy	8 (38.1)	1 (8.3)	1 (6.7)	10 (20.8)
Nocturnal bigeminy	10 (47.6)	2 (16.7)	2 (13.1)	14 (29.2)
Daytime ST-segment depression	12 (57.1)	2 (16.7)	1 (6.7)	15 (31.3)
Nocturnal ST-segment depression	16 (76.2)	6 (50)	0 (0)	22 (45.8)

* Data are presented as No. of subjects (%).

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Abbreviation Notes

AHI = apnea-hypopnea index; ARI = arousal index; BMI = body mass index; CPAP = continuous positive airway pressure; HPLC = high-performance liquid chromatography; OSAHS = obstructive sleep apnea-hypopnea syndrome; PSVB = premature supraventricular beat; SaO_2 = arterial oxygen saturation; SB = sinus bradycardia; SVT = supraventricular tachycardia

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