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Long-term exercise parameter outcomes in obstructive sleep apnea patients with and without positive airway pressure therapy

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Abstract:

BACKGROUND: Short-term studies have shown that positive airway pressure (PAP) therapy increases exercise capacity in obstructive sleep apnea syndrome (OSAS). In this study, we investigated the effect of PAP therapy on exercise parameters in OSAS patients who were followed for 2 years.

MATERIALS AND METHODS: This prospective cohort study included patients recently diagnosed with moderate-to-severe OSAS. The patients underwent cardiopulmonary exercise testing and pulmonary function testing (PFT) at the start of the study and at follow-up visits. Outcomes of patients who adhered to regular treatment were compared with those who refused treatment.

RESULTS: Thirty-one patients who attended follow-up were included in the analysis and evaluated as a treated group (n = 16) and untreated group (n = 15). Although patients in the treated group had more comorbidities, the proportion of smokers was higher in the untreated group (P = 0.36 and P = 0.36, respectively). Of the PFT parameters, there were no changes in forced vital capacity and forced expiratory volume in 1 s in both the groups (P = 0.85, P = 0.59 and P = 0.92, P = 0.90, respectively). In the treatment group, there were decreases in resting heart rate (HR) and oxygen saturation compared to baseline levels (P = 0.01 and P = 0.02). A statistically significant decline in breathing reserve was observed in the untreated group (P = 0.03).

CONCLUSION: Our study suggests that PAP treatment does not make any difference in exercise parameters and PFT in long term. However, it supports the fact that PAP treatment may have a positive effect on some cardiac parameters, such as HR rest.

Keywords:

Cardiopulmonary exercise testing, exercise, obstructive sleep apnea syndrome, positive airway pressure therapy

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Introduction

Obstructive sleep apnea syndrome (OSAS) is an increasingly common health problem which is characterized by recurrent partial or complete pharyngeal collapse (hypopnea or apnea) during sleep and affects 4% of middle-aged men and 2% of middle-aged women.[1,2] Hypoxia resulting from this repeated airway collapse

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leads to systemic inflammation, oxidative stress, and endothelial dysfunction. OSAS is also accompanied by autonomous nervous system dysfunction (increased sympathetic activity and reduced parasympathetic activity). Increased sympathetic nervous system activation may lead to many complications, including those involving the cardiovascular system. Positive airway pressure (PAP) treatment seems to be the best option for preventing and managing complications related to OSAS.[3-5]

Cardiopulmonary exercise testing (CPET) is used to differentiate between the myriad causes of exercise limitation, such as cardiac, pulmonary, and muscular disorders. The impact of OSAS on exercise is variable. Exercise limitation in these patients has been associated with disease severity and comorbidities.[6,7]

The beneficial effect of PAP therapy on exercise capacity in OSAS has been demonstrated previously in short-term studies. However, no data are available regarding the influence of PAP therapy on exercise capacity in the long term. The aim of this study was to evaluate the long-term effects of PAP therapy on exercise parameters in patients with OSAS.

Materials and Methods

Study design

This single-center prospective cohort study was conducted in a tertiary hospital among patients who presented to a sleep laboratory between the years 2016 and 2018. Informed written consent was obtained from all patients included in the study, and a local ethics committee approved the study design.

Study population

Eighty patients were initially evaluated. Of these, 12 patients who were lost to follow-up and eight patients who were unable to perform the exercise test were excluded. Thirty-one of the 60 patients included in the study completed all pre- and posttreatment evaluations [Figure 1]. The patients were divided into two groups: the treated group (n = 16) and the untreated (n = 15) group. The inclusion criteria for the 60 patients in the study were being newly diagnosed with moderate/severe OSAS, aged 18–65 years, able to perform the exercise test with sufficient effort, and having body mass index (BMI) <40 kg/m^2. Patients with concomitant severe respiratory failure, chronic obstructive pulmonary disease, asthma, cardiac failure, unstable angina pectoris, history of myocardial ischemia, or neurological, psychological, and cooperation problems that would affect good participation, those previously diagnosed with and treated for OSAS, and those with orthopedic problems that prevented CPET were excluded from the study. Ultimately, 31 patients who attended follow-up and volunteered to participate in the study were included in the analysis. Sixteen of these patients underwent regular PAP therapy lasting ≥6 h a day. The compliance of these patients was evaluated according to the device record. The rate of use of continuous PAP (CPAP) was measured by the time counter built into the CPAP device. Fifteen patients who refused PAP treatment and other treatment options (surgery, device, etc.) were evaluated as a control group.

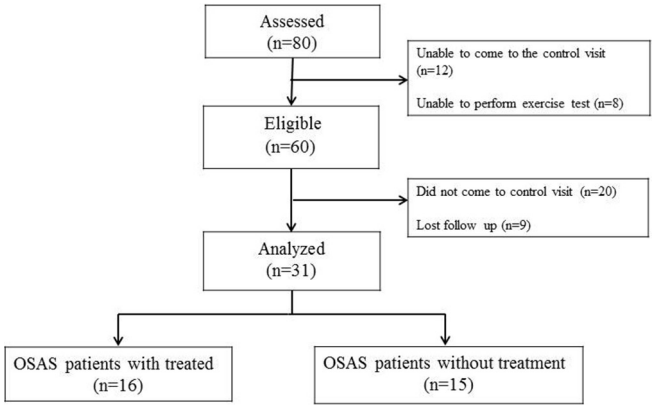

Figure 1: Consort diagram of patients

Sleep study

Full polysomnography (PSG) monitoring was performed using the Compumedics E-series Sleep System (Compumedics Sleep: Melbourne, Australia). Electroencephalography (EEG), electrooculography (EOG), electromyography (EMG), and electrocardiography were performed simultaneously. Surface electrodes were used to record EEG channels, right and left EOGs, and submental EMG. Ventilatory flow, either at the nose or at both the nose and mouth, was measured with airflow. Respiratory movements of the chest and abdomen, as well as the body position, were monitored by inductive plethysmography bands. Arterial oxygen saturation was measured transcutaneously with a finger oximeter. Apnea was defined as a continuous cessation of airflow for ≥10 s, and hypopnea was defined as at least 50% reduction of airflow for ≥10 s, with an oxygen desaturation of ≥3% or an EEG arousal from sleep. Apneas were classified as obstructive, central, or mixed according to the standard criteria of the American Academy of Sleep Medicine.[8]

During the second night of the baseline PSG, all study group patients underwent manual CPAP titration in the laboratory. The same CPAP device (Weinmann, Lowenstein/Germany) and a comfortably fitting nasal mask were used for all patients. The level of nasal CPAP was rapidly increased above the starting level of 4 cm H_2O until apneas and snoring were abolished. The median, highest, and optimal pressures were recorded.

Follow-up

Patients diagnosed with moderate-to-severe OSAS then underwent pulmonary function test and CPET with cycle ergometer and were admitted overnight for device calibration. The patients were invited for outpatient follow-up visits every 3 months, and treatment adherence was assessed. At 24 months, the patients underwent follow-up CPET and pulmonary function testing (PFT).

Exercise testing

Patients underwent CPET before starting PAP therapy (pretreatment) and again after 24 months of treatment (posttreatment). Spirometry and maximum voluntary ventilation were performed before the exercise test. The exercise protocol and reference values used were based on the American Thoracic Society/American College of Chest Physicians guidelines.[9] A cycle ergometer (Ergoselect Ergoline Viasprint 150P) was used for the test. The symptom-limited exercise test was applied to all patients while wearing a facemask (Rudolph Face Mask for Exercise Testing; Hans Rudolph Inc., Kansas City, MO, USA). A 3-min resting period was followed by a 3-min warm-up period (60 rpm maintenance pedaling rate) and then incremental work (10–15 W increase per minute).[10] An automated exercise testing system (Desktop Diagnostics/CPX; Medical Graphics Corporation, St. Paul, MI, USA) was used to collect data. The maximum work rate sustained for at least 30 s was recorded. Continuous monitoring of 12-lead electrocardiography, blood pressure, and pulse oxygen saturation was performed during CPET. Peak oxygen uptake (mL/kg/min), peak CO_2 output, carbon dioxide production/oxygen uptake (VCO_2/VO_2), heart rate (HR) reserve, and dead space/tidal volume ratio were assessed. Symptoms experienced by the patients at the end of the test, including fatigue, dyspnea, and dizziness, were also noted.

Statistical analysis

Data were analyzed using SPSS for Windows version 18.0 (SPSS Inc., Chicago, IL, USA). The Wilcoxon signed-rank test was used to compare pre- and posttreatment data. All results are expressed as mean ± standard deviation. $P < 0.05$ was considered statistically significant.

Results

A total of 31 patients were analyzed. Of these, 25 were male and 6 were female, with a mean age of 43.6 ± 9 years. Comparison of the demographical and clinical features of the two groups at baseline revealed no significant differences in terms of age, BMI, apnea–hypopnea index, or OSAS severity. Although patients in the treated group had more comorbidities pretreatment, the proportion of smokers was higher in the untreated group. The demographical and clinical features of the patients are shown in Table 1.

Table 1: Baseline characteristics of patients (*n*=31)

	OSAS with treated (*n*=16)	OSAS with untreated (*n*=15)	*P*
Age, mean	43±10	45±8	0.56
Male, sex (%)	75	87	0.65
Current smoker (%)	44	60	0.36
Comorbidity, hypertension (%)	38	26	0.36
AHI	33±26	30±17	0.68
BMI	29±6	31±4	0.28
AMS	92±2	92±1	0.22
SMS	90±2	89±2	0.35
MDS	6±2	5±2	0.49
MHR	75±8	78±9	0.39
MaxHR	151±49	153±39	0.91
OSAS severity (%)			
Severe	31	40	0.63
Moderate	69	60	

Data were presented as mean±SD or percentage, unless otherwise stated. AHI: Apnea-hypopnea index, BMI: Body mass index, AMS: Awake mean saturation, SMS: Sleep mean saturation, MDS: Mean desaturation, MHR: Mean heart rate, MaxHR: Maximum heart rate, SD: Standard deviation, OSAS: Obstructive sleep apnea syndrome

When pre- and posttreatment values were compared, the treated group showed an increase in BMI, but the change was not statistically significant ($P = 0.67$). Of the PFT parameters, there were no changes in forced vital capacity and forced expiratory volume in 1 s (FEV_1) in both groups ($P = 0.85$, $P = 0.59$ and $P = 0.92$, $P = 0.90$, respectively) [Table 2].

In CPET, there were no changes in VO_2 and VT values between the treated and untreated groups ($P = 0.13$, $P = 0.17$ and $P = 0.25$, $P = 0.39$, respectively). Posttreatment HR rest and oxygen saturation were reduced compared to pretreatment values in the treated group ($P = 0.01$ and $P = 0.02$). The reduction in breathing reserve in the untreated group was statistically significant ($P = 0.03$) [Table 3].

Discussion

In our study, we analyzed 2-year follow-up results to determine the effects of long-term PAP therapy on exercise parameters in patients with OSAS. Of the exercise parameters studied, saturation (SO_2) decreased while cardiac parameter (HR rest) improved in the group of treated patients. There was no difference in VO_2, VT, and VE parameters in both the groups following 2-year period.

Numerous factors affect exercise capacity in patients with OSAS. Oztürk *et al*. showed that exercise capacity was limited in moderate/severe OSAS patients, which may

Table 2: Baseline and control spirometric parameters of patients

	OSAS with treated (*n*=16)			OSAS with untreated (*n*=15)		
	Baseline	Follow-up	P	Baseline	Follow-up	P
BMI (kg/m^2)	29±6	32±6	0.67	31±4	30±4	0.87
FVC (percentage predicted)	108±12	109±14	0.85	108±14	107±17	0.92
FEV_1 (percentage predicted)	102±13	104±13	0.59	103±15	103±17	0.90
FEV_1/FVC	79±5	79±2	0.58	79±5	78±6	0.32
FEF_{25} (percentage predicted)	73±28	69±20	0.55	72±26	70±26	0.49
FEF_{75} (percentage predicted)	109±32	101±19	0.26	108±20	105±20	0.62
MVV	115±33	101±43	0.11	114±30	112±38	0.67

Data were presented as mean±SD. Wilcoxon signed-rank test was used. FVC: Forced vital capacity, FEV_1: Forced expiratory volume in 1 s, FEF_{25}: Forced expiratory flow at 25%, FEF_{75}: Forced expiratory flow at 75%, MVV: Maximal voluntary ventilation, SD: Standard deviation, BMI: Body mass index, OSAS: Obstructive sleep apnea syndrome

Table 3: Cardiopulmonary exercise test results of patients

	OSAS with treated (*n*=16)			OSAS with untreated (*n*=15)		
	Baseline	Follow-up	*P*	Baseline	Follow-up	*P*
RER peak	1.34±0.1	1.34±0.1	0.40	1.34±0.1	1.35±0.1	0.86
VCO_2 peak	2081±532	1863±483	0.40	2023±437	2168±563	0.14
VO_2 peak (ml/min)	1530±322	1374±325	0.13	1499±262	1598±372	0.25
VO_2 peak (ml/min/kg)	18±6	15±4	0.12	17±4	18±5	0.17
HR rest	88±9	84±7	0.01	84±5	85±4	0.52
HR max	146±23	145±21	1	148±16	147±15	0.83
VE peak	69±22	62±17	0.28	63±12	68±14	0.09
VT	1931±454	1775±478	0.17	1933±518	1978±501	0.39
BR	42±16	47±11	0.47	46±11	41±16	**0.03**
VD/VT	20±4	19±5	0.86	19±3	18±4	0.34
Work load peak (watt)	160±54	156±51	0.49	162±37	163±44	0.75
Work load peak (%)	93±17	96±25	0.88	97±20	96±19	0.75
SO_2	96±4	95±4	0.02	97±2	97±3	0.52
HRR	35±15	31±18	0.31	31±15	30±14	0.91
TA systolic max	193±25	188±27	0.17	175±31	173±29	0.51
TA diastolic max	106±21	94±18	0.19	100±15	98±10	0.42

Data were presented as mean±SD or percentage, unless otherwise stated. The statistically significant one is bolded. Wilcoxon signed-rank test was used. RER: Respiratory exchange ratio, Peak: Data at maximum effort during exercise test, Rest: Data at rest before exercise test, VCO_2: Peak of carbon dioxide output during exercise test, VO_2: Peak of oxygen consumption during exercise test, HR: Heart rate, VE: Peak pulmonary ventilation, VT: Tidal volume, BR: Breathing reserve, SO_2: Oxyhemoglobin saturation by pulse oximetry, HRR: Heart rate recovery, TA: Tension arterial systolic and diastolic, SD: Standard deviation, OSAS: Obstructive sleep apnea syndrome, VD/VT: Dead space/tidal volume ratio

be associated with cardiovascular causes or peripheral vascular damage.[11] Obesity is another important factor influencing exercise capacity in OSAS patients.[12,13] Obese patients have increased respiratory energy load at rest and reduced peak oxygen consumption during exercise. In addition, periods of hypoxemia secondary to autonomic nervous system dysfunction in OSAS patients are proposed to affect energy metabolism in the musculoskeletal system, thereby limiting exercise capacity.[14] PAP therapy is the most effective treatment method for completely controlling sleep apnea.[5] Previous studies have shown that this treatment increases exercise capacity in OSAS patients.[7,13,15-21] These studies evaluated exercise capacity of the patients after treatment periods ranging between 1 and 6 months. One of the most important parameters in assessing exercise capacity is peak oxygen consumption. Treatment was shown to increase peak oxygen consumption, and improvements in VE and saturation parameters were also reported. Ozsarac *et al*. showed that a decrease in AT, VE/VCO_2 values in the treated group while VO_2 max, VCO_2, and VE/VO_2 remained unchanged. In contrast to these studies, we compared the 2-year results of PAP therapy.[7] We observed no changes in peak oxygen consumption, VE, and VCO2 parameters in the treated group. There was only a saturation decline in the treated group. This decline may attribute to the increase in BMI compared to the baseline values in this group. Our study results may indicate that the effect of CPAP treatment on exercise parameters may be effective in short term but not lasted for 2 years.

Cardiac complications frequently accompany OSAS. Marin *et al*. demonstrated that the incidence of fatal and nonfatal cardiac complications was significantly higher, particularly in patients with severe OSAS.[22] Previous studies that evaluated CPAP effects in short period found no difference in HR rest.[7,13,16-21] The patients in the present study were followed for 2 years, and we observed improvement in HR rest in the treated group.

This may show that CPAP treatment is important for preventing cardiac complications in OSAS patients.

Pulmonary function parameters may also be altered in OSAS patients. The most widely known spirometric finding is forced expiratory flow at 50%/forced inspiratory flow at 50% ratio > 1 and a sawtooth pattern in the flow–volume curve.[23,24] Obesity may also be the cause of abnormal lung function values in OSAS patients. In another study analyzing the effects of PAP therapy on respiratory function parameters in OSAS patients, a significant decline was observed in FEV_1. That study evaluated the 5-year effects of treatment, and the authors related this decline to high rates of smoking rather than the treatment.[25] Tapan *et al*. also observed a significant decline in functional respiratory parameters, especially FEV_1. However, they stated that the patients did not receive any additional treatment that would explain this decrease.[20] Bonay *et al*. noted a loss of FEV_1 and Forced expiratory flow at 25-75% (FEF_{25-75}) in OSAS patients after CPAP treatment. They stated that long-term CPAP may act as a mechanical alteration of the nasal mucosa and creates a change in small airway resistance through the nasobronchial reflex.[26] In contrast to these studies, we found no changes in functional respiratory parameters after CPAP treatment.

A major limitation of our study was the small patient number. This is due to the low level of patient compliance in this type of clinical study. In addition, the high rate of treatment refusal in our study (48%) made it difficult for us to reach statistically significant results. Nevertheless, our study is the first in the literature to evaluate the 2-year results of PAP therapy in terms of its impact on exercise parameters. Multicenter studies are needed to achieve statistically significant case numbers.

Conclusion

Our study suggests that PAP treatment does not make any difference on exercise parameters and PFT in long term. However, it supports the fact that PAP treatment may have a positive effect on some cardiac parameters, such as HR rest.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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