Effect of short-term continuous positive airway pressure on pulmonary and heart function, quality of life in patients with obstructive sleep apnea

TRUMPALAIKIO GYDYMO NUOLATINIU TEIGIAMU SLĖGIU POVEIKIS PLAUČIŲ IR ŠIRDIES FUNKCIJAI BEI GYVENIMO KOKYBEI PACIENTAMS, SERGANTIEMS OBSTRUKCINE MIEGO APNĖJA

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Summary. Laima Kondratavičienė successfully defended a doctoral dissertation "Effect of short-term continuous positive airway pressure on pulmonary and heart function, quality of life in patients with obstructive sleep apnea" at the open session of the Medical Research Council of the Lithuanian University of Health Sciences on June 1, 2023. The Dissertation has been prepared at Department of Pulmonology of Faculty of Medicine of Lithuanian University of Health Sciences during the period of 2018–2022 year. The article presents the main results of the dissertation.
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INTRODUCTION

Obstructive sleep apnea (OSA) is a chronic condition characterized by recurrent breathing pauses during sleep, followed by episodes of hypoxia and fragmented sleep [1, 2]. Although OSA is the most common cause of respiratory diseases when sleeping, its incidence rate is unknown. According to the Wisconsin Sleep Cohort Study, 4% of middle-aged men and 2% of middle-aged women had OSA [3], but the incidence of it varies in different studies [4]. The exact incidence rate of OSA in the Lithuanian population is not known.

Upper airway obstruction is associated with considerably lower intra-thoracic pressure during inspiration. This drop in pressure results in an enhanced return of

venous blood to the heart as well as higher wall stress on both the atrium and ventricles [5]. Hypoxia can affect the tissue remodeling processes and the severity of cardiovascular diseases (CVD) [6]. This association may have several underlying pathogenetic causes, some of which include oxidative stress, endothelial dysfunction, sympathetic hyperactivity, systemic inflammation, and hemodynamic alterations [7]. As a consequence, OSA has been demonstrated to be a significant risk factor for CVD, such as coronary artery disease, myocardial infarction, heart failure (HF), arterial hypertension (AH), cardiac arrhythmias, and stroke [8].

The standard treatment for moderate to severe OSA is continuous positive airway pressure (CPAP) therapy [9]. Several studies have looked for potentially helpful biomarkers that may be used for OSA screening; however, there are only a few that might be used to assess the effectiveness of CPAP therapies for the cardiovascular system in OSA patients. Although CPAP is a gold standard, adherence to treatment remains a problem. Response to therapy is a major challenge, as patients often perceive only subjective changes, for example, daytime symptoms. Therefore, it is very important to demonstrate improvement in patients using objective data, such as a change in serum biomarkers and an improvement in cardiac function, as examined in our study.

The cardiopulmonary exercise test (CPET) is an additional diagnostic method for evaluating exercise tolerance by monitoring cardiovascular and respiratory capabilities. The CPET provides data on the muscles, metabolic activity of interconnected tissues during exercise, and the cardiopulmonary and oxygen transport systems [10]. Questionnaires are another tool to assess compliance and adherence to CPAP therapy. Typically, questionnaires are used for OSA screening. However, it is more important to ensure the treatment's efficacy for patients using CPAP. It is crucial to closely monitor patient care and track treatment results. To assess sleep efficiency and health-related quality of life (HRQL), questionnaires are straightforward and low-effort methods.

The aim of this study was to evaluate the short-term effect of CPAP therapy on pulmonary function and heart function, quality of life in patients with OSA. In order to complete this aim, these subjects were raised:

1. To evaluate lung volumes, diffusing capacity, and exercise tolerance before and after three months of CPAP treatment in patients with moderate and severe OSA.
2. To assess geometry, function, and deformation parameters of the heart using two-dimensional speckle-tracking echocardiography (2D ST echocardiography).
3. To visualize subtle changes in the right heart using cardiac magnetic resonance imaging (MRI) in patients with OSA who have been treated with CPAP for a short period of time.
4. To analyze changes in blood serum biomarkers (galectin-3, soluble suppression of tumorigenesis-2 (sST2), and endothelin-1 (ET-1) associated with cardiovascular dysfunction and their impact on adherence to CPAP treatment in OSA patients.
5. To examine the sleep structure, its fragmentation, and HRQL during short-term CPAP treatment for moderate and severe OSA patients

METHODS

Study population and design

Newly recruited subjects who had never been studied before made up the entire study population. Between January 2020 and June 2021, a total of 34 patients who had been diagnosed with moderate to severe OSA were enrolled in the study. After a course of CPAP therapy lasting for three months, the final evaluation was performed on seventeen patients. The diagnostic steps of the clinical trial included quality of life and sleep assessment (using three different questionnaires [11–17]: Epworth sleepiness scale, Short Form 36 Medical Outcomes Study questionnaire (SF-36), and Pittsburgh sleep quality index (PSI), pulmonary function tests (CPET (18), spirometry, pulmonary diffusion test, and whole-body plethysmography), 2D ST echocardiography [19–23], cardiac MRI [24–25], and blood serum biomarker (galectin-3, sST2, and ET-1) testing. The design of the study can be seen in Figure 1.

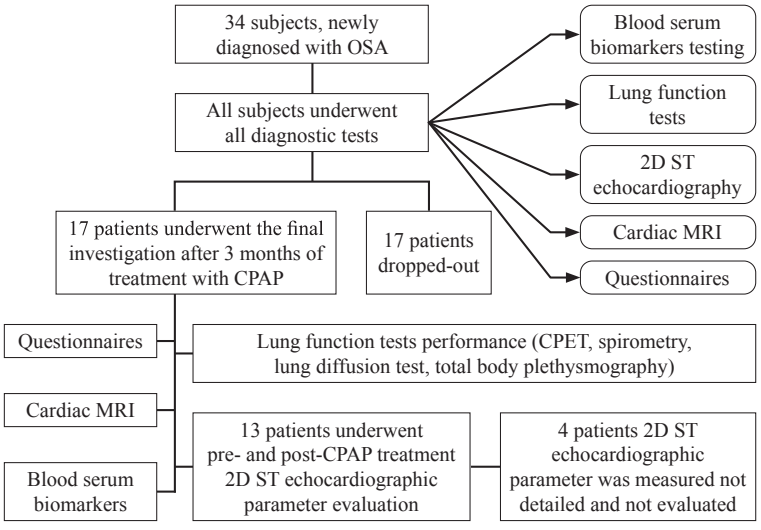

Figure 1. Study design.

Inability to tolerate CPAP, widespread outbreak of coronavirus (COVID-19), and financial concerns (CPAP devices are not reimbursed in Lithuania) were the primary factors that led to the discontinuation of the study.

The following were the inclusion criteria: age between 18 and 65 years old, a diagnosis of moderate to severe OSA, BMI ≥ 30 kg/m^2, and a signed informed consent form from the patient.

The following were considered as exclusion criteria: subjects younger than 18 years and older than 65 years; significant mental and/or internal organ disease that could interfere with the study protocol; absence of signed informed consent. Also, patients with significant ischemic heart disease (class ≥ 3 based on the New York Heart Association (NYHA) Functional Classification), severe valvular heart disease (grade ≥ 3), or uncontrolled AH (an average systolic blood pressure ≥ 140 mmHg or an average diastolic blood pressure ≥ 90 mmHg while taking or not antihypertensive medicaments) were not included in the study.

All of the individuals were put through an extensive clinical examination, during which their symptoms, medical and surgical histories, and comorbidities were documented. Additionally, a full physical assessment was carried out on each participant. Patients were evaluated at the Hospital of Lithuanian University of Health Sciences Kauno Klinikos Outpatient Clinic, and an otolaryngologist consulted each patient to rule out the possibility of any nasal disease (e.g., nasal polyposis, deviated nasal septum, insufficiency of the nasal valve). Complaints were recorded on the first visit, and the ESS was used to evaluate the patient's level of subjective daytime sleepiness.

Those who were suspected of having OSA were referred to the Sleep Laboratory in the Hospital of Lithuanian University of Health Sciences Kauno Klinikos Pulmonology Department for overnight diagnostic polysomnography. This study was performed using the Alice 6 LDx diagnostic sleep system (Philips Respironics, Murrysville, PA, USA). The absence of airflow for more than 10 s was defined as apnea, and the decrease in airflow for at least 10 s, accompanied by a 3% reduction in SpO_2 or arousal as hypopnea. The apnea-hypopnea index (AHI) is the combined average number of apneas and hypopneas recorded per hour of sleep during the study. Patients with OSA were classified according to the AHI: mild OSA was defined as AHI ≥ 5 but < 15, moderate OSA as AHI ≥ 15 but < 30, and severe OSA as AHI ≥ 30 [26, 27].

After OSA diagnosis, each patient spent another night in the sleep laboratory for CPAP titration to select the optimal pressure at which the CPAP device eliminated abnormal breathing events. Patients diagnosed with moderate or severe OSA were invited to participate in the clinical study.

The Regional Ethics Committee for Biomedical Research of the Lithuanian University of Health Sciences (LSMU) in Kaunas approved the study protocol (Protocol no. BE-2-23, 19 May 2020, Kaunas, Lithuania). After being informed of the ongoing investigation, each participant provided signed informed consent.

Control groups

This clinical study included two control groups: one for comparison of 2D ST echocardiographic parameters, and the second for comparison of MRI parameters.

The control group for the 2D ST echocardiographic parameters included thirteen patients. All of the subjects in this control group went through the exact same diagnostic procedures as the subjects in the OSA group. The inclusion criteria were: age 18–65 years old, diagnosis of mild OSA (AHI ≥ 5 but < 15) or no OSA diagnosis after diagnostic overnight PSG (AHI < 5), body mass index (BMI) ≥ 30 kg/m^2, and signed informed consent form.

A second control group was selected for the purpose of comparing the cardiac MRI characteristics. This group consisted of 17 healthy patients who were not obese (their BMI was less than 30 kg/m^2) and who did not have any other disorders at the same time. The people in the control group had a cardiac MRI because it was thought that they might have myocardial pathology. However, the results of the examinations showed that there was no evidence of myocardial injury. This included good general systolic function in both ventricles, good regional contraction, unchanged valvular anatomy and function, and no evidence of myocardial fibrosis in the late gadolinium enhancement sequence.

Patients with moderate or severe OSA (AHI ≥ 15) who were not treated were not included as a control group in the study because it would be unethical not to suggest treatment to these patients.

Interventions and follow-up

Three months after CPAP therapy began, study participants were asked to return for a follow-up appointment. Data downloaded from the CPAP device was used to evaluate CPAP therapy compliance. We defined treatment compliance as using the CPAP device for more than 4 hours per night for more than 70% of the nights and having an AHI of less than 5.

After three months of CPAP use, lung function tests (spirometry, lung diffusion tests, and whole-body plethysmography), CPET, 2D ST echocardiography, and cardiac MRI were performed, blood samples were taken, and questionnaires were completed.

For the control groups, 2D ST echocardiography and cardiac MRI were performed just once as baseline (as no treatment with CPAP was initiated).

Statistical analysis

IBM Corp.'s SPSS Statistics for Windows version 27.0 (Armonk, New York, USA) was used for statistical analysis. For describing quantitative variables, the mean and standard deviation, as well as the median at the 25th–75th percentiles, were chosen.

Non-parametric statistical methods were applied for non-parametric data analysis. The Wilcoxon matched-pairs signed-rank two-sided test was applied for dependent groups. Mann–Whitney two-sided U-test was applied for significant differences between two independent groups. The Wilcoxon signed-rank test was used to compare the results with the hypothetical value. The minimum limit for statistically significant values – $p < 0.05$.

Table 1. Baseline characteristics of subjects and sleep data

		Before treatment (n = 17)	3 months after CPAP treatment (n = 17)	p-value*
		Mean (standard deviation)		
Gender, %	Male	15 (88.2)	–	–
	Female	2 (11.8)	–	–
Age, years		52.15 (8.89)		
Concomitant diseases, %	Arterial hypertension	14 (82)	–	–
	Type 2 diabetes	7 (50)	–	–
	Gout	4 (24)	–	–
	Rheumatoid arthritis	1 (6)	–	–
	Well-controlled asthma	1 (6)	–	–
BMI, kg/m^2		39.23 (6.1)	38.3 (5.5)	> 0.05
Polysomnography	AHI, per h	76.14 (24.32)	67.73 (26.64)	**0.049***
	ODI	71.42 (23.95)	29.24 (31.05)	**0.001***
	Mean SpO_2, %	91.53 (2.26)	92.56 (2.19)	0.144
	Minimum SpO_2, %	66.42 (12.84)	72.00 (11.21)	0.099
	TST, min	361.74 (61.25)	348.54 (55.44)	0.356
	Non-REM, %	80.14 (6.53)	85.25 (5.21)	**0.017***
	REM, %	19.96 (7.37)	14.75 (7.45)	**0.016***
	Sleep efficiency, %	76.93 (12.61)	82.05 (12.01)	**0.037***
	Arousal index, per h	75.82 (23.39)	72.28 (23.91)	0.309

*p-value < 0.05, according to the nonparametric Wilcoxon test. CPAP: continuous positive airway pressure; AHI: apnea-hypopnea index; BMI: body mass index; ODI: oxygen desaturation index; TST: total sleep time; REM: rapid eye movement.

RESULTS

Characteristics of subjects and sleep data

Seventeen individuals with newly diagnosed moderate or severe OSA (15 men and 2 women, mean age 52.15 ± 8.89) were included in this study. The included subjects' mean baseline BMI and AHI were 39.23 ± 6.1 kg/m^2 and 76.14 ± 24.32 events/hour, respectively. CPAP therapy for three months resulted in no change in BMI ($p > 0.05$). Concomitant diseases and baseline characteristics are shown in Table 1.

After three months of starting CPAP therapy, the oxygen desaturation index (ODI) and AHI significantly changed from baseline values ($p = 0.049$ and $p = 0.001$, respectively). During the three-month CPAP therapy period, the sleep architecture, which is comprised of REM and non-REM sleep phases, changed. After starting CPAP therapy, the length of REM sleep reduced but the length of non-REM sleep increased ($p = 0.016$ and $p = 0.017$, respectively). Before and after three months of CPAP therapy, other polysomnographic data did not alter (Table 1).

The effect of CPAP treatment on pulmonary function and the change in CPET data

Table 2 shows the findings that were obtained from the CPET test. Before beginning therapy with CPAP, the primary VO_2 max was calculated to be 84.36 ±

Table 2. CPET data

	Before treatment (n = 17)	3 months after CPAP treatment (n = 17)	p-value*
Maximum load, %	79.86 (15.8)	85.5 (16.35)	0.093
Maximum load, W	170.36 (39.25)	174.29 (45.18)	0.662
VO_2, L/min	2.14 (0.41)	2.23 (0.44)	0.706
VO_2, %	84.36 (18.08)	87.21 (17.48)	0.706
VO_2, mL/kg/min	17.52 (3.79)	18.6 (3.40)	0.255
VO_2/kg, %	83.77 (18.68)	88.92 (18.36)	0.195
VCO_2, L	2.61 (0.61)	2.67 (0.67)	0.889
VCO_2, %	93 (20.21)	93.86 (18.63)	1
HR rest, beats/min	86.08 (10.10)	88.83 (12.47)	0.906
HR max, beats/min	135.5 (20.66)	132.38 (18.13)	0.432
HR max, %	90.25 (12.74)	88 (12.14)	0.283
O_2 pulse, mL/beat	16.69 (3.11)	16.46 (3.66)	0.925
O_2 pulse, %	72.64 (16.57)	72.14 (16.53)	0.826
VE_{AT}, L/min	44.51 (10.59)	38.60 (7.52)	**0.03***
VE_{AT}, %	43.21 (21.19)	37.86 (17.77)	**0.028***
VE max load	74.53 (20.04)	69.81 (17.77)	0.51
VE max load, %	68.84 (22.18)	66.36 (24.24)	0.615
VE/VCO_2	23.47 (2.73)	20.63 (3.52)	**0.042***
RER max load	1.19 (0.14)	1.21 (0.09)	0.109

*p-value < 0.05, according to the nonparametric Wilcoxon test. VO_2: O_2 consumption; VCO_2: CO_2 production; AT: anaerobic threshold; HR: heart rate; O_2 pulse: oxygen pulse; VE: pulmonary ventilation; VE at AT: pulmonary ventilation at the anaerobic threshold; VE/VCO_2: ventilator equivalent for carbon dioxide; RER: respiratory exchange ratio.

18.08 % (a VO_2 max of more than 80% is considered to be a normal result), and the absolute value was 17.52 ± 3.79 mL/kg/min. During therapy with CPAP, there was a trend toward an increase in VO_2 max; however, this trend did not reach statistical significance (after 3 months of treatment, 87.21% and 18.6 mL/kg/min; p = 0.255). The use of CPAP therapy was also associated with an improvement in work performance, but without statistical significance (maximum load increased from 79.86% to 85.5%; p = 0.093). Pulmonary ventilation at the anaerobic threshold (VE_{AT}) was 44.51 L/min (43.21%) during the baseline visit, but it considerably dropped after the treatment period of three months (38.60 L/min and 37.86%; p = 0.03 and p = 0.028, respectively). During the short-term CPAP therapy period, the patient's Ventilator Equivalent for Carbon Dioxide (VE/VCO_2) dropped from 23.47 to 20.63, resulting in a significant reduction (p = 0.042).

The patients' pulmonary function tests were normal and did not change after the three-month CPAP treatment period (Table 3).

Table 3. Lung function test data (spirometry, lung diffusion test, whole body plethysmography) data

	Before treatment (n = 17)	3 months after CPAP treatment (n = 17)		p-value*
		Mean (standard deviation)		
Spirometry	FVC, L	4.43 (0.95)	4.38 (0.72)	0.666
	FVC, %	90.31 (11.84)	89.64 (8.29)	0.906
	FEV_1, L	3.59 (0.78)	3.54 (0.59)	0.906
	FEV_1, %	93.46 (13.79)	92.57 (9.44)	0.969
	FEV/VC	81.12 (3.31)	81.17 (3.78)	0.221
	FEV_1/VC, %	102.92 (4.27)	102.86 (4.46)	0.404
Lung diffusion test	DLCO, %	92.94 (8.57)	93.84 (8.35)	0.683
Whole body plethysmography	sGAW	0.87 (0.27)	1.00 (0.24)	0.099
	sGAW, %	99.67 (30.39)	114.78 (0.43)	0.099
	sRAW	1.24 (0.43)	1.05 (0.27)	0.096
	sRAW, %	109.0 (38.41)	92 (22.08)	0.109
	FRC	2.94 (0.58)	3.06 (0.52)	0.490
	FRC, %	84.21 (15.1)	87.21 (11.53)	0.593
	RV	2.21 (0.36)	2.31 (0.47)	0.49
	RV, %	99.43 (13.23)	102.71 (16.63)	0.638
	TLC	6.49 (0.96)	6.72 (0.96)	0.149
	TLC, %	91.78 (9.98)	95.07 (9.15)	0.116
	RV/TLC	34.33 (5.06)	34.64 (7.04)	1.0
	RV/TLC, %	99.21 (10.49)	99.00 (14.52)	0.925

* p-value < 0.05, according to the nonparametric Wilcoxon test. FVC: forced vital capacity; FEV_1: forced expiratory volume in 1 s; FEV_1/VC: forced expiratory volume in 1 s – vital capacity ratio; DLCO: diffusing capacity of carbon monoxide; sGAW: specific airway conductance; sRAW: specific airway resistance; FRC: functional residual capacity; RV: residual volume; TLC: total lung capacity; RV/TLC: residual volume – total lung capacity ratio.

Impact of CPAP treatment on echocardiographic parameters

LV end-diastolic diameter, volume, and EF were similar in both OSA and control groups, whereas patients in OSA group had higher LV end-systolic volume and lower global longitudinal strain (GLS) (p = 0.015 and p = 0.035, respectively). Indexed by height, OSA group patients had a greater prevalence of LV diastolic dysfunction (p = 0.023) and a higher LV Mmi (p = 0.007). Although there was no difference in LA volume between the groups, patients in the OSA group had significantly reduced LA reservoir strain (p = 0.001).

The RV GLS was decreased in OSA patients (p = 0.026), but the conventional RV longitudinal and global function measures (S', fractional area change

Table 4. Echocardiographic parameters of patients in the control group and the OSA group

		Control group (n = 13)	OSA group (n = 34)	p-value*
LV EDD, mm		47.62 ± 3.97	50.08 ± 4.69	0.165
LV EDV, mL		102.55 ± 26.05	142.25 ± 26.84	**0.026***
LV ESV, mL		44.08 ± 12.72	67.06 (14.77)	**0.015***
LV Mmi, g/m^2		79.56 ± 2.92	88.98 ± 13.51	0.084
LV Mmi by height, $g/m^{2.7}$		38.96 ± 5.90	46.11 ± 8.23	**0.007***
IVS, mm		10.6 ± 1.09	11.42 ± 1.32	**0.006***
LV EF, %		56.45 ± 2.35	54.15 ± 3.59	0.055
LV GLS, %		–23.20 ± 2.44	–16.56 ± 3.31	**0.035***
LA diameter, mm		36.23 ± 3.08	43.58 ± 8.19	**< 0.001***
LA volume, mL		64.35 ± 3.09	70.97 ± 13.80	0.191
LA dilatation (volume index by BSA, > 34 mL/m^2)		1 (7.7)	5 (14.70)	0.324
LA dilatation (volume index by height > 18.5 mL/m^2 men, > 16.5 mL/m^2 women)		9 (69.2)	19 (55.88)	0.289
LV diastolic dysfunction	Normal	7 (53.8)	4 (15.4)	0.781
	Grade 1	6 (46.2)	22 (80.8)	**0.023***
	Grade 2	0 (0)	1 (3.8)	0.923
	Grade 3	0 (0)	0 (0)	0
LA reservoir strain, %		31.01 ± 1.56	26.56 ± 1.38	**< 0.001***
RV diameter, mm		35.46 ± 4.23	36.55 ± 4.57	0.419
RA diameter, mm		37.62 ± 4.48	40.58 ± 3.4	**0.043***
RV S', cm/s		13.18 ± 2.27	14.06 ± 6.16	0.941
RV FAC, %		43.72 ± 5.92	41.51 ± 4.66	0.415
RV GLS, %		–25.03 ± 3.21	–19.65 ± 3.75	**0.026***
Mean PAP, mmHg		22.19 ± 7.60	28.59 ± 7.08	**0.037***

Data presented as mean ± SD (standard deviation), N (%). *p-value < 0.05, according to the nonparametric Mann–Whitney U test. OSA: obstructive sleep apnea, LV: left ventricle, EF: ejection fraction, GLS: global longitudinal strain, EDD: end-diastolic diameter, ESV: end-systolic volume, EDV: end-diastolic volume, MM: myocardial mass, LA: left atrial, RV: right ventricle, RA: right atrium, FAC: fractional area change, PAP: pulmonary artery pressure, IVS: interventricular septum.

Table 5. Changes in echocardiographic parameters in individuals with OSA following CPAP therapy

		OSA group (N = 13)		p-value*
		Before treatment	3 months after CPAP treatment	
		Mean (standard deviation)		
LV EDD, mm		50.08 (4.69)	49.75 (3.57)	0.504
LV EDV, ml/L		142.25 (26.84)	127.08 (33.8)	**0.022** *
LV ESV, mL		67.06 (14.77)	53.74 (17.8)	**0.037** *
LV EF, %		54.15 (3.59)	54.83 (3.27)	0.473
LV Mmi, g/m^2		88.98 (13.51)	80.06 (20.79)	0.963
LV Mmi by height, g/m$^{2.7}$		46.11 (8.23)	43.63 (6.29)	0.480
LV GLS, %		−16.28 (3.82)	−18.82 (3.04)	**0.005** *
LA reservoir strain, %		25.82 (7.6)	32.45 (5.64)	**0.008** *
LA volume, mL		64.35 (3.09)	67.56 (11.24)	0.328
LA diameter, mm		43.58 ± 8.19	43.79 ± 2.27	0.874
LV diastolic dysfunction	Normal	4 (15.4)	6 (46.15)	0.657
	Grade 1	22 (80.8)	6 (46.15)	**0.024** *
	Grade 2	1 (3.8)	1 (7.7)	0.973
	Grade 3	0 (0)	0 (0)	0
RV diameter, mm		36.55 (4.57)	39.17 (3.83)	0.411
RA diameter, mm		40.58 (3.4)	41.92 (3.75)	0.623
RV S′, cm/s		14.06 (6.16)	13.62 (3.72)	0.624
RV FAC, %		41.51 (4.66)	43.49 (7.68)	0.104
RV GLS, %		−19.65 (3.75)	−21.15 (4.57)	0.608
Mean PAP, mmHg		28.59 (7.08)	29.62 (8.19)	0.075

* p-value < 0.05, according to nonparametric Wilcoxon test. OSA: obstructive sleep apnea, CPAP: continuous positive airway pressure, EF: ejection fraction, GLS: global longitudinal strain, RS: reservoir strain; EDD: end-diastolic diameter, MM: myocardial mass, LA: left atrial, RV: right ventricle, RA: right atrium, FAC: fractional area change, PAP: pulmonary artery pressure, E: early diastolic transmitral velocity, E′: early diastolic mitral annular velocity, S′: myocardial systolic excursion velocity, IVS: interventricular septum, E/A: the ratio of the early (E) to late (A) ventricular filling velocities, LV LS: left ventricular longitudinal strain.

Table 6. Cardiac MRI parameters of control and OSA group patients

	OSA (n = 32)	Control (n = 17)	p-value*
	Mean (standard deviation)		
LV parameters			
LV EDVI, mL/m^2	79.44 (21.02)	71.58 (15.59)	0.438
LV ESVI, mL/m^2	30.89 (11.69)	27.47 (10.94)	0.438
LV EF, %	61.62 (5.28)	62.71 (9.45)	0.506
LV GLS, %	−24.86 (4.85)	−23.64 (4.89)	0.532
LV GCS, %	−35.14 (4.67)	−39.11 (7.01)	0.063
RV parameters			
RV GLS, %	−25.72 (10.93)	−21.54 (5.87)	0.096
RV EDVI, mL/m^2	70.46 (14.77)	58.65 (14.31)	**0.042***
RV ESVI, mL/m^2	33.56 (11.67)	22.88 (9.19)	0.069
RV EF, %	53.69 (8.91)	61.35 (9.08)	**0.016***

p-value < 0.05, according to the nonparametric Mann–Whitney U test. OSA: obstructive sleep apnea; LV: left ventricle; RV: right ventricle; LA: left atrium; RA: right atrium; EDVI: end-diastolic volume index; ESVI: end-systolic volume index; EF: ejection fraction; GLS: global longitudinal strain; GCS: global circumferential strain.

Table 7. The effects of CPAP therapy on the cardiac MRI characteristics of individuals with OSA

	Before treatment (n = 17)	3 months after CPAP treatment (n = 17)	p-value*
	Mean (standard deviation)		
LA and LV parameters			
LV EDV, mL	182.68 (43.81)	197.93 (30.28)	0.102
LV EDVI, mL/m^2	75.92 (17.51)	81.79 (10.67)	0.136
LV ESV, mL	70.03 (21.58)	77.66 (16.17)	0.163
LV ESVI, mL/m^2	29.12 (8.86)	32.26 (7.04)	0.193
LV SV, mL	114.43 (26.31)	122.47 (20.14)	0.210
LV SVI, mL/m^2	47.49 (10.14)	50.63 (7.26)	0.246
LV EF, %	61.78 (4.89)	62.08 (5.94)	0.906
LV mass	125.65 (30.39)	120.39 (26.13)	0.266
LA, cm^2	31.61 (9.16)	25.65 (5.13)	0.724
LV GLS, %	−23.76 (4.10)	−24.29 (3.91)	0.981
LV GCS, %	−35.42 (4.79)	−34.88 (5.51)	0.850
LA GLS, %	20.45 (7.25)	26.05 (14.00)	**0.043***
RA and RV parameters			
RV EDV, mL	164.82 (32.57)	180.16 (39.09)	**0.042***
RV EDVI, mL/m^2	68.82 (12.74)	74.81 (14.74)	0.067
RV ESV, mL	78.33 (23.64)	77.45 (21.77)	0.846
RV ESVI, mL/m^2	32.53 (9.27)	32.94 (8.21	0.791
RV EF, %	53.35 (9.36)	57.09 (7.51)	0.151
RA, cm^2	21.94 (2.68)	23.48 (4.19)	0.129
RV GLS, %	−24.21 (7.37)	−27.31 (5.19)	0.480
RA GLS, %	21.04 (7.14)	26.18 (7.17)	**0.043***

p-value < 0.05, according to the nonparametric Wilcoxon test. OSA: obstructive sleep apnea; LV: left ventricle; RV: right ventricle; LA: left atrium; RA: right atrium; EDVI: end-diastolic volume index; ESVI: end-systolic volume index; SV: stroke volume; SVI: stroke volume index; EF: ejection fraction; GLS: global longitudinal strain; GCS: global circumferential strain.

(FAC)) did not differ between the groups. The mean PAP and RA diameter were considerably greater in OSA patients ($p < 0.05$) (Table 4).

Table 5 shows the modifications made to biventricular geometry and function as well as atrial remodeling in individuals with OSA before and three months after the start of CPAP therapy.

Following therapy, there was no change in the LV diameter, Mmi, or LV ejection fraction. The LV diastolic function parameters and the global longitudinal strain of the LV both improved. We discovered that the OSA group had a higher prevalence of LV diastolic dysfunction. After three months, CPAP therapy improved LV diastolic function.

No changes in LA volume were seen during treatment, but three months later, CPAP therapy significantly improved LA reservoir function ($p = 0.008$). The geometry, function, and deformation parameters of the right ventricle remained unchanged.

Impact of CPAP treatment on cardiac MRI parameters

Several statistically significant results were discovered when comparing the baseline cardiac MRI parameters of the OSA group with those of the control group. The left heart's MRI characteristics did not change. In the OSA group, the RV end-diastolic volume was greater than in the control group (70.46 ± 14.77 mL/m^2 and 58.65 ± 14.31 mL/m^2, respectively; p = 0.042). Additionally, it was discovered that the OSA group's RV ejection fraction was lower than that of the control patients (53.69 ± 8.91% and 61.35 ± 9.08%, respectively; p = 0.016) (Table 6).

After three months of CPAP therapy, the LA and RA GLS both improved (20.45 ± 7.25% and 26.05 ± 14.00%, p = 0.043; 21.04 ± 7.14% and 26.18 ± 7.17%, p = 0.049, respectively). Although there was a trend to improve, RV GLS did not significantly change over that time (−24.21 ± 14.32% and −27.31 ± 5.19%, p = 0.642). Additionally, it was shown that CPAP treatment improved the RV end-diastolic volume significantly (164.82 ± 32.57 mL and 180.16 ± 39.09 mL, p = 0.042), even if the RV EF did not change (Table 7).

Impact of CPAP treatment on blood serum biomarkers

After three months of CPAP therapy, concentrations of galectin-3 and sST2 decreased significantly; however, we could not detect any significant changes in the concentration of ET-1 (Table 8).

Evaluation of sleepiness and health-related quality of life

We found a considerable improvement in the patients' HRQL scores after three months of CPAP therapy. The overall SF-36 score increased from 499.8 ± 122.3 to 589.6 ± 124.7 (p = 0.012). After three months of CPAP therapy, the SF-36 scores of role limitation due to emotional problems (p = 0.012), energy (fatigue) (p = 0.035), and general health (p = 0.002) domains significantly improved. After combining the physical and mental component scores from the SF-36 domains, we discovered a substantial improvement in mental component scores in the posttreatment group (p = 0.009) (Table 9).

After three months of CPAP therapy, there were also significant changes in the sleep quality assessment using the PSQI questionnaire: the mean score at baseline was 12.6 ± 2.9, and in the posttreatment group, it was 5.5 ± 2.3 (p = 0.001). Even 53.3% of those who received short-term CPAP therapy reported no sleep problems. None of the pretreatment data fell into this group.

Table 8. Changes in blood serum biomarkers during 3 months of CPAP treatment

	Before treatment	3 months after CPAP treatment	p-value*
	Mean (standard deviation)		
Galectin-3, ng/mL	17.52 ± 1.19	11.64 ± 0,97	**0.001***
sST2, ng/mL	0.56 ± 0.47	0.41 ± 0.56	**0.047***
ET-1, pg/mL	3.82 ± 2.27	3.56 ± 2.27	0.28

*p-value < 0.05, according to nonparametric Wilcoxon test. CPAP: continuous positive airway pressure, sST2: soluble suppression of tumorigenesis – 2, ET-1: endothelin-1.

Table 9. SF-36 domains before therapy and three months after CPAP use

	Pretreatment (n = 17)	Posttreatment (n = 17)	Mean, 95% Confidence Interval of the difference (lower–upper)	p-value
	Mean (standard deviation)			
Physical functioning	67.35 (25.98)	74.12 (22.93)	6.77 (−5.0–20.0)	0.12
Role limitations due to physical health	52.06 (40.04)	73.53 (35.87)	21.47 (0–25.0)	0.102
Role limitations due to emotional problems	54.9 (47.06)	86.28 (23.75)	31.38 (0–66.7)	**0.012***
Energy (fatigue)	58.41 (16.12)	66.76 (12.24)	8.35 (−5.0–20.0)	**0.035***
Emotional wellbeing	67.18 (16.39)	75.52 (13.03)	8.34 (−8–20.0)	0.238
Social functioning	77.39 (21.83)	86.59 (16.92)	9.2 (0–12.5)	0.163
Pain	68.82 (27.94)	72.38 (29.70)	3.56 (10.0–10.0)	0.347
General health	51.18 (14.63)	62.64 (17.06)	11.46 (0–20.0)	**0.002***
Physical component score	60.01 (21.87)	70.67 (22.48)	10.66 (6.25–11.8)	0.058
Mental component score	64.47 (21.49)	78.78 (14.06)	11.31 (0.6–21.4)	**0.009***

*p-value < 0.05, according to nonparametric Wilcoxon test. CPAP: continuous positive airway pressure.

Table 10. PSQI and ESS scores at the beginning of treatment and three months after CPAP use

PSQI	Pretreatment (n = 17)	Posttreatment (n = 17)		
	Frequency (%)			
PSQI ≤ 5	0	53.3		
5 < PSQI ≤ 10	26.7	40		
10 < PSQI ≤ 15	46.7	6.7		
15 < PSQI ≤ 21	26.7	0		
	Mean (standard deviation)		Difference (95% CI)	p-value
PSQI general score	12.6 (2.9)	5.5 (2.3)	7.7 (2.9)	**0.001***
ESS	10.9 (5.7)	5.3 (3.2)	5.6 (5.7)	**0.002***

*p-value < 0.05, according to nonparametric Wilcoxon test. CPAP: continuous positive airway pressure, ESS: Epworth sleepiness scale, PSQI: Pittsburgh sleep quality index. PSQI ≤ 5: no sleep disorder, 5 < PSQI ≤ 10: episodic sleep disorder, 10 < PSQI ≤ 15: moderate sleep disorder, 15 < PSQI ≤ 21: severe sleep disorder.

When analyzing the ESS score during CPAP therapy, the perception of sleepiness also decreased significantly: the pretreatment ESS mean score was 10.9 ± 5.7; after 3 months, it was 5.3 ± 3.2 (p = 0.002) (Table 10).

We found significant PSQI and SF-36 mental component score distributions using the nonparametric Kruskal–Wallis one-way analysis of variance (even though the SF-36 questionnaire domains did not change independently, the physical component score was p = 0.133, and the mental component score was p = 0.047).

The results of the Spearman correlation analysis showed that there was a significant direct link between changes in ESS score and SF-36 (role limitations due to emotional problems domain (r = 0.631, p = 0.012) and the social functioning domain (r = 0.54, p = 0.038)) (Figure 2).

The ESS score also showed a significant increase in the SF-36 mental component score (r = 0.676, p = 0.006), however, this improvement was not seen in the physical component score (r = 0.111, p = 0.693) (Figure 3).

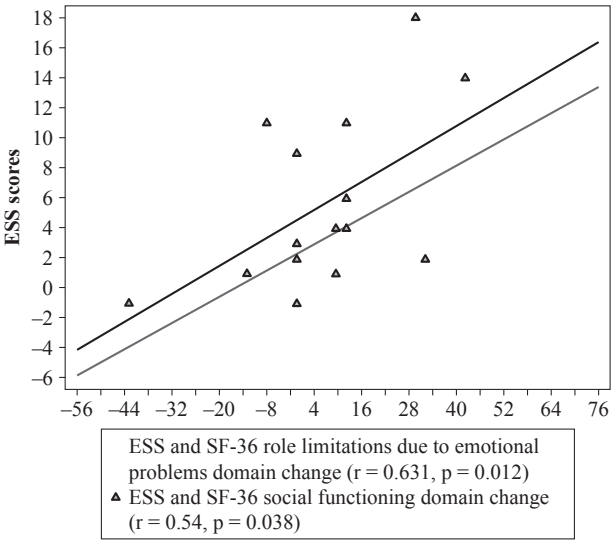

Fig. 2. Scatter plot showing the relationship between changes in SF-36 role limitations due to emotional problems and social functioning domains and the Epworth Sleepiness Scale (ESS)

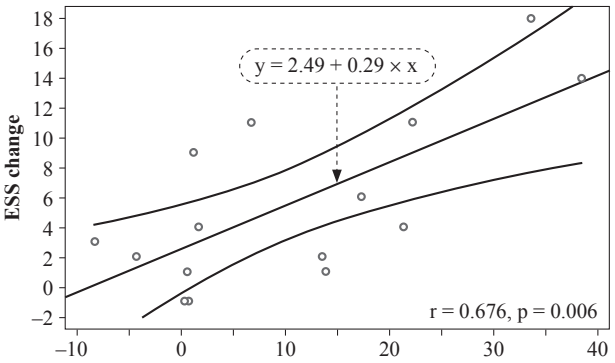

Fig. 3. A scatter plot demonstrating the link between CPAP therapy and changes in the SF-36 mental component score and the Epworth Sleepiness Scale (ESS)

CONCLUSIONS

Although short-term CPAP therapy showed a tendency to improve exercise capacity and pulmonary ventilation, this treatment had no effect on lung volumes measured by pulmonary function tests.

Increased LV myocardial mass index, LV diastolic dysfunction, decreased LV and RV longitudinal strain, and decreased LA reservoir function are all signs of OSA that are linked to the left heart remodeling process. Short-term, 3-month CPAP therapy improved LV global longitudinal strain and LA reservoir function but it had no effect on the geometry of the left heart chambers, assessed by 2D ST echocardiography.

As shown by cardiac MRI FT analysis, three-month CPAP therapy improved the function of both atria (effect of CPAP therapy by improving their global longitudinal strains), as well as RV end-diastolic volume. Cardiac MRI could provide high-resolution images for an accurate and thorough noninvasive evaluation of heart structure, function, and their subtle changes throughout the treatment period.

After three months of CPAP therapy, the concentrations of galectin-3 and sST2 decreased significantly; however, we did not detect any significant changes in the concentration of ET-1. The evaluation of the relationship between echocardiographic measures and galectin-3, sST2, and ET-1 in CPAP therapy requires more research. Blood serum biomarkers could evaluate the efficacy of CPAP treatment and its impact on the cardiovascular system.

In patients with moderate to severe OSA, short-term CPAP therapy improved mental elements of HRQL, as CPAP often restores normal breathing patterns during sleep and mostly relieves symptoms (e.g., snoring, daytime sleepiness, and vigilance). No improvement in the physical component of quality of life in the questionnaire SF-36 was observed. Perception of sleepiness, measured with ESS, and sleep quality, assessed with the PSQI questionnaire, improved.

PRACTICAL RECOMMENDATIONS

The results of the study provided additional knowledge about the pathogenesis of OSA and its impact on quality of life from three different perspectives. We propose to use questionnaires as a tool to assess both HRQL and sleep efficiency in clinical practice to achieve better CPAP compliance. We suggest performing 2D ST echocardiography and cardiac MRI at least three months after starting CPAP therapy to assess the status of the cardiovascular system. When talking about techniques of 2D ST echocardiography, in overweight and obese individuals, LV mass should be routinely indexed to height to prevent a systematic misclassification of cardiovascular risk.

Although further in-depth studies are ongoing, blood serum indicators have the potential to serve as predictive indicators of the interaction between OSA and cardiovascular disease. Assessment of blood serum biomarkers could help to evaluate adherence to CPAP treatment. Further studies with a larger number of patients and more attention in this specific area are needed to better understand the overall effect of CPAP.

PUBLICATIONS, WHERE THE RESULTS OF THE DISSERTATION WERE PUBLISHED

1. **Kondratavičienė L, Padervinskienė L, Lapinskas T, Ereminienė E, Malakauskas K, Žemaitis M, et al.** Effect of Short-Term Treatment with Continuous Positive Airway Pressure on Cardiopulmonary Exercise Tolerance, Pulmonary and Cardiac Function in Patients with Obstructive Sleep Apnea. Medicina (Kaunas). 2023;59(2):326.
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