Thorac Res Pract. 2023; 24(2): 76-84 DOI: 10.5152/ThoracResPract.2023.22130

Original Article

Effect of Continuous Positive Airway Pressure Therapy on Pro-Brain Natriuretic Peptide, C-Reactive Protein, Homocysteine, and Cardiac Markers in Patients with Obstructive Sleep Apnea

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Cite this article as: Güngördü N, Börekçi Ş, Çulpan HC, Coşkun E, Ayan F, Mutlu B. Effect of continuous positive airway pressure therapy on pro-brain natriuretic peptide, C-reactive protein, homocysteine, and cardiac markers in patients with obstructive sleep apnea. *Thorac Res Pract.* 2023;24(2):76-84.

Abstract

OBJECTIVE: Obstructive sleep apnea is associated with increased morbidity and mortality, especially cardiovascular and cerebrovascular, and affects a significant proportion of the population. The study was aimed to determine the levels of pro-brain natriuretic peptide, C-reactive protein, homocysteine, and cardiac markers (creatine kinase, creatine kinase isoenzyme MB, troponin T) and evaluate the effectiveness of continuous positive airway pressure therapy in patients with obstructive sleep apnea.

MATERIAL AND METHODS: Pro-brain natriuretic peptide, C-reactive protein, homocysteine, and cardiac markers (creatine kinase, creatine kinase isoenzyme MB, troponin T) were assessed in blood samples collected before and after continuous positive airway pressure treatment from the 30 patients included in the study, and their results were compared.

RESULTS: There was a significant decrease between the baseline pro-brain natriuretic peptide and the 6-month pro-brain natriuretic peptide values after continuous positive airway pressure therapy ($P < .05$). There was a significant increase in creatine kinase-MB and troponin T values 6 months after continuous positive airway pressure therapy compared to baseline values ($P < .05$).

CONCLUSIONS: A significant decrease was observed in pro-brain natriuretic peptide values after continuous positive airway pressure therapy in obstructive sleep apnea patients without cardiac failure, while a more significant decrease was especially observed among hypertension patients. This finding suggests that pro-brain natriuretic peptide may be used as an early indicator of cardiac dysfunction in obstructive sleep apnea patients without any heart diseases except for hypertension.

KEYWORDS: Obstructive sleep apnea, pro brain natriuretic peptide, continuous positive airway pressure

Received: *July 21, 2022* ***Accepted:*** *October 7, 2022* ***Publication Date:*** *March 28, 2023*

INTRODUCTION

Obstructive sleep apnea (OSA) is a disease characterized by recurrent episodes of partial or complete upper airway obstruction resulting in hypoxia and arousals during sleep.[1] This disease is associated with increased morbidity and mortality, especially cardiovascular and cerebrovascular, and affects a significant proportion of the population.[2] Recurrent apnea in OSA can cause nocturnal hypoxemia and sympathetic hyperactivity; sympathetic hyperreactivity may lead to an increase in systemic blood pressure followed by endothelial dysfunction due to this increase, while endothelial dysfunction causes systemic inflammation. Therefore, cardiovascular diseases (CVDs) such as congestive heart failure, hypertension, arrhythmia, and coronary artery diseases (CADs) are prevalent among these patients.[3] Obstructive sleep apnea is considered to be a risk factor for progressive heart failure. Continuous positive airway pressure (CPAP) therapy forms the basis of a treatment to eliminate obstructive events and prevent daytime sleepiness and cardiovascular complications.

Brain natriuretic peptide (BNP) is a cardiac neurohormone secreted by myocytes after myocardial hypoxemia and ventricular volume expansion. Since ventricular load in the apneic period results in ventricular strain, increased BNP level is regarded as a prognostic marker in patients with OSA. Studies have revealed increased secretion of N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) in cardiac problems such as heart failure, CAD, and cardiac hypertrophy and is associated with poor prognosis. Studies have also shown that BNP levels are affected in different ways in OSA patients.[2,4-7] Serum C-reactive protein (CRP) is an inflammatory marker and is reported to be elevated in patients with OSA.[8,9] Various studies have reported that homocysteinemia due to intermittent hypoxia may be observed in OSA patients.[10,11] Elevated levels of cardiac biomarkers in serum are expected following ischemia or damage/necrosis of myocytes. Studies investigating troponin levels in the blood of patients with OSA have reported varying results.[7,12,13]

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In this study, we aimed to evaluate the effects of recurrent apnea and hypoxia on pro-BNP, CRP, homocysteine, and cardiac biomarker levels in OSA patients and the responses of these effects to CPAP therapy.

MATERIAL AND METHODS

This study was conducted as a prospective study in the sleep laboratory of an accredited university. Approval was obtained from the Ethics Committee of the Cerrahpaşa Faculty of Medicine at İstanbul University (No: 20908). Informed consent was obtained from each recruited participant.

Study Participants

Thirty-three patients who were diagnosed with moderate and severe OSA by polysomnography (PSG) and received CPAP treatment were prospectively followed up for 6 months. Inclusion criteria were diagnosis of OSA and recommendation of a CPAP device, an average daily CPAP use ≥4 h/day during the 6-month follow-up period, consent to study participation, normal pulmonary function test (PFT) and chest radiography, and ejection fraction (EF) of ≥60% on echocardiography. Exclusion criteria were refusal to participate in the study, previous diagnosis of heart failure or detection of heart failure, diastolic failure or right heart failure on echocardiography, abnormal PFT, and recent facial trauma/operation. Two patients with signs of heart failure on echocardiography and 1 patient who did not show up to follow-up were excluded from the study.

Demographic and Clinical Characteristics

A data collection form was developed to evaluate the age, gender, additional diseases, and medications of each patient. In addition to physical examination, neck circumference, weight, and height were measured. Body mass index was calculated as kilograms per square meter. Posteroanterior chest radiography, electrocardiography (ECG), and respiratory function tests were performed. The EF was used to exclude >60% cardiac failure. Complete blood count, routine biochemical analysis, and thyroid hormone levels were studied.

Polysomnography and Continuous Positive Airway Pressure Therapy

Polysomnography was performed using the SOMNOscreen™ Plus PSG device. Measurements were taken and recorded during nocturnal sleep for 5-8 hours. Polysomnography consisted of 2 electroencephalography (C3A2-O2A1), 2 electrooculogram, 1 chin and 1 leg electromyogram, 1 ECG recording, oronasal thermistor, hemoglobin oxygen saturation with fingertip pulse oximetry, position evaluation, and thoracic and abdominal movements. Synchronous video recording was taken during sleep with the help of a body position sensor and nasal pressure sensor. The sleep scores of the patients were scored in 30-second epochs according to the 2012 American Academy of Sleep Medicine guidelines. Apnea was defined as cessation of the airflow for at least 10 seconds, while hypopnea was defined as ≥50% decrement in airflow with accompanying arousal and/or ≥3% arterial oxygen desaturation.[14] Patients were classified as having mild, moderate, and severe OSA by apnea–hypopnea index (AHI) 5-15, 15-30, and ≥30, respectively. Patients who were recommended CPAP therapy were instructed on how to use the device and summoned to 1-month, 3-month, and 6-month outpatient follow-ups; patients living outside the city were interviewed over the phone. In these follow-ups, patients were asked whether they had any difficulties with the devices, whether they were comfortable with the pressure settings, and how many hours they used the device. Patients who did not regularly use the device or who could not be reached over phone were excluded from the study.

Analysis of Blood Samples

A total of 6 cc of blood was drawn from the patients before the PSG when CPAP titration was performed and after 6 months of CPAP treatment. Blood samples were collected between 9:30 AM and 11:00 AM after 12 hours of fasting using the standard venipuncture technique. After the blood samples were centrifuged at 5000 rpm for 5 minutes, the separated serum was stored at −80°C to study pro-BNP, CRP, homocysteine, and cardiac markers (CK, CK-MB, troponin T). The serum samples were removed from −80°C storage on the day of study. Pro-brain natriuretic peptide was studied with the electrochemiluminescence method in the Cobas E170 modular system device, homocysteine with the immunonephelometric method in the Siemens BN ProSpec device, CK with the enzymatic (N-acetyl-L-cysteine) method in the Cobas Hitachi-modular DPP device, CK-MB with the immunoinhibition method in the Cobas Hitachi-modular DPP device, and troponin T was studied with the electrochemiluminesc ence method in the Cobas e 411 device.

Statistical Analysis

Number Cruncher Statistical System 2007 and Power Analysis and Sample Size 2008 Statistical Software (Utah, USA) were used for statistical analysis of the data. Descriptive statistical methods (mean, standard deviation, median, frequency, 25th-75th percentile, frequency, percentage) were used to analyze and present the data. Shapiro–Wilk was used to test normality distribution of the data. Wilcoxon signed-rank test was used for the evaluation of the non-normally distributed parameters to compare 6-month follow-up values to the baseline values. Mann–Whitney *U*-test was used for comparing continuous parameters between 2 groups. Categorical parameters were compared by using Fisher exact test. McNemar-Bowker test was used for comparing OSA groups before and after the CPAP treatment. Results were evaluated at significance level of $P < .05$.

RESULTS

Demographic, clinical, and anthropometric characteristics of the 30 patients are presented in Table 1.

Twenty-four patients had severe OSA and 6 patients had moderate OSA. Of 30 patients with OSA, 7 (23%) had hypertension while 5 (16.7%) had diabetes mellitus. Demographic, clinical, and anthropometric characteristics of the 30 patients with moderate and severe OSA are presented in Table 2.

Demographic data are shown in Table 3 according to the presence of hypertension in OSA patients.

Mean AHI was 51.4 at baseline and 5.9 after CPAP therapy. The decrease after treatment was statistically significant (Table 4).

Table 1. Patient Characteristics

Characteristics	(n = 30) Mean ± SD Median (25th-75th Percentile)
Age (years)	46.5 ± 9.8
	47.5 (38.8-53.3)
Height	168.1 ± 10.2
	167.5 (159.8-177.3)
Weight	96.5 ± 17.5
	94.5 (84.8-105)
Body mass index	34.2 ± 5.8
	94.5 (84.8-105)
Apnea–hypopnea index	51.43 ± 25.1
FVC (%)	101.3 ± 12.5
	102.5 (90.8-107.3)
FEV1 (%)	98.4 ± 12.8
	97.5 (87.8-110)
FEV1/FVC	80.3 ± 4.3
	97.5 (87.8-110)
	n (%)
Gender	
Male	24 (80)
Female	6 (20)
Smoking history	
No	19 (63.3)
Yes	5 (16.7)
Quit	6 (20)

FEV, forced expiratory flow; FEV1, forced expiratory flow in 1 second; FVC, forced vital capacity; SD, standard deviation.

Table 2. Characteristics of the 30 Patients with Moderate and Severe OSA

Characteristics	Moderate OSA (n = 6) Mean ± SD Median (25th-75th Percentile)	Severe OSA (n = 24) Mean ± SD Median (25th-75th Percentile)	*P* *
Age	49 ± 7.6	45.9 ± 10.3	.561
	47.5 (43.5-55.8)	47.5 (37.3-53)	
Height	171.5 ± 8	167.3 ± 10.7	.347
	172 (164.5-177.8)	165.5 (159-17.8)	
Weight	97 ± 12.6	96.4 ± 18.8	.667
	97.5 (84.8-108.5)	94.5 (81.5-104.8)	
BMI	33 ± 3.7	34.5 ± 6.3	.743
	32.5 (30-36.9)	33.4 (30.9-37.1)	
FVC (%)	98.8 ± 7	101.9 ± 13.6	.667
	99.5 (93.3-104.3)	105 (90.3-108.5)	
FEV1 (%)	97.8 ± 8.6	98.5 ± 13.8	.820
	96 (92-106.3)	98 (87.3-110)	
FEV1/FVC	80.8 ± 4.8	80.1 ± 4.3	.781
	81 (78.3-83.5)	80 (77.3-84)	
	n (%)	n (%)	*P* **
Gender			
Male	6 (100)	18 (75)	.302
Female	0	6 (25)	
Smoking history			
No	4 (66.7)	15 (62.5)	1
Yes	1 (16.7)	4 (16.7)	
Quit	1 (16.7)	5 (20.8)	

BMI, body mass index; FEV, forced expiratory flow; FEV1, forced expiratory flow in 1 second; FVC, forced vital capacity; OSA, obstructive sleep apnea; SD, standard deviation.
*Mann–Whitney *U*-test.
**Fisher exact test.

There was a statistically significant difference between baseline and post-CPAP AHI groups; while 73% of patients were in the severe OSA group at baseline, they were in the moderate obstructive sleep apnea syndrome (OSAS) group after treatment, while 17% of the patients were in the moderate OSA group at baseline and were in the mild OSA group after treatment (Table 5).

Pro-brain natriuretic peptide, CRP, homocysteine, and cardiac biomarkers before and after CPAP treatment are presented in Table 4. An average decrease of 0.4 units was detected in 6-month follow-up CRP values after CPAP therapy, though the difference was not statistically significant ($P > .05$). There was a significant increase in creatine kinase-MB (CK-MB) and troponin T values 6 months after CPAP therapy compared to baseline values ($P < .05$). A statistically significant correlation was not observed between homocysteine and creatine kinase (CK) values at 6-month follow-up compared to baseline values ($P > .05$). There was a statistically significant decrease in pro-BNP values 6 months after CPAP therapy compared to baseline values ($P < .05$). Patients who had hypertension had significantly higher baseline pro-BNP levels ($P < .05$) compared to patients without hypertension; however, this difference disappeared after 6 months of CPAP therapy ($P > .05$). There was a significant difference in pro-BNP values both before and after treatment between patients with hypertension and without hypertension (Table 6, Figures 1 and 2).

DISCUSSION

According to the results of our study, a significant decrease was observed in pro-BNP and a significant increase in troponin T and CK-MB values after 6 months of CPAP treatment compared to baseline values in patients with moderate and severe OSA without heart failure. No statistically significant difference was observed between CRP, homocysteine, and CK values after 6 months of CPAP treatment compared to baseline values.

Kita et al[6] demonstrated increased serum BNP levels between 02:00 and 06:00 at night in OSAS patients, and this improved after effective CPAP therapy. In another study by Møller

Table 3. Presence of Hypertension in OSA Patients

Characteristics	Hypertension (+) (n = 7) Mean ± SD Median (25th-75th Percentile)	Hypertension (–) (n = 23) Mean ± SD Median (25th-75th Percentile)	*P**
Age	52.6 ± 10.4	44.7 ± 9	.077
	51 (48-64)	45 (38-53)	
Height	163 ± 14.8	169.7 ± 8.2	.245
	159 (150-180)	169 (162-177)	
Weight	99 ± 21.4	95.8 ± 16.7	.886
	93 (80-105)	96 (86-105)	
BMI	37.3 ± 6.2	33.2 ± 5.5	.144
	37.5 (31.6-43.8)	33.3 (28.6-35.1)	
FVC (%)	101.1 ± 15.2	101.3 ± 12	.962
	103 (90-116)	102 (91-107)	
FEV1 (%)	98.1 ± 19.3	98.4 ± 10.7	1
	105 (86-110)	97 (89-110)	
FEV1/FVC	79.9 ± 4.1	80.4 ± 4.4	.811
	80 (79-82)	81 (77-84)	
	n (%)	n (%)	*P***
Gender			
Male	3 (42.9)	21 (91.3)	.016
Female	4 (57.1)	2 (8.7)	
Smoking history			
No	5 (71.4)	14 (60.9)	1
Yes	1 (14.3)	4 (17.4)	
Quit	1 (14.3)	5 (21.7)	

BMI, body mass index; FEV, forced expiratory flow; FEV1, forced expiratory flow in 1 second; FVC, forced vital capacity; OSA, obstructive sleep apnea; SD, standard deviation.
*Mann–Whitney *U*-test.
**Fisher exact test.

et al.[15] a significant difference in BNP levels was observed after 14 months of CPAP therapy in patients with moderate OSA. Cifçi et al[7] did not observe a significant change in pro-BNP levels after 6-month CPAP treatment and reported that pro-BNP levels in serum were not associated with the severity of OSA. Colish et al[12] did not find a significant change in pro-BNP levels after 1 year of CPAP therapy compared to baseline values in 47 OSA patients. In another study by Chang et al.[13] CPAP therapy was found to decrease NT-pro-BNP but had a significant effect on troponin-T in patients with moderate and severe OSA. Xu et al[16] demonstrated that CPAP treatment was associated with reduced NT-pro-BNP in nonobese participants with OSA. The results of our study are consistent with the results of studies by Kita et al.[6] Xu et al.[16] and Chang et al[13] but differed from the results of Møller et al.[15] Cifçi et al.[7] and Colish et al.[12]

In a study by Sharma et al.[17] in which the effects of CPAP treatment on serum pro-BNP levels were investigated in acute decompensated heart failure patients with OSA, no significant improvement was found in NT-pro-BNP levels after PAP treatment. In a study by Zhao et al.[18] in which the effects of positive pressure mechanical ventilation treatment on serum pro-BNP levels were investigated in congestive heart failure patients with OSA, plasma pro-BNP levels were found to be significantly decreased in the group treated with CPAP compared to the group receiving only medical treatment, and it was demonstrated that positive pressure mechanical ventilation treatment may be effective in decreasing BNP levels in patients with OSA. As for our study, we observed a significant decrease in pro-BNP with CPAP therapy, despite the fact that participants were OSA patients without heart disease other than hypertension.

Tasci et al[5] demonstrated that there was a significant decrease in serum NT-pro-BNP levels with nasal CPAP treatment in patients with hypertensive OSA compared to normotensive patients. In our study, although patients with hypertension had significantly higher baseline pro-BNP levels ($P < .05$); however, this difference disappeared after 6 months of CPAP treatment. This suggests that CPAP therapy is more effective in lowering pro-BNP levels in OSAS patients

Table 4. OSA Classification

Parameters	Overall (n = 30)	Moderate OSA (n = 6)	Severe OSA (n = 24)	Hypertension (n = 7)	No Hypertension (n = 23)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
	Median (25th-75th Percentile)	Median (25th-75th Percentile)	Median (25th-75th Percentile)	Median (25th-75th Percentile)	Median (25th-75th Percentile)
AHI	51.4 ± 25.1	19.7 ± 4.1	59.4 ± 21.5	59.6 ± 22.3	48.9 ± 25.8
	50.4 (33.7-66.8)	19.1 (15.6-24.4)	54.3 (44.6-69)	66.7 (44.6-79.8)	50.2 (32-57.6)
Pressure	7.4 ± 1.8	6.3 ± 2.1	7.7 ± 1.6	6.6 ± 1.4	7.7 ± 1.8
	4.3 (1.9-7.3)	6.5 (4-8.3)	4.6 (2.2-7.5)	4.5 (2.7-7.2)	3.9 (1.8-7.6)
Post-CPAP AHI	5.9 ± 7.5	5.1 ± 9.8	6.1 ± 7.1	4.4 ± 2.6	6.4 ± 8.5
	8 (6-8)	0.8 (0.2-9.2)	8 (6-8)	7 (6-8)	8 (6-9)
*P**	<.001	.046	<.001	.018	<.001

AHI, apnea–hypopnea index; CPAP, continuous positive airway pressure; OSA, obstructive sleep apnea; SD, standard deviation.
*Wilcoxon signed-rank test (comparison of AHI and post-CPAP AHI).

Table 5. OSA Groups After the CPAP Treatment

Baseline	Post-CPAP AHI			
AHI	**Mild**	**Moderate**	**Severe**	***P****
Mild	0	0	0	<.001
Moderate	5 (17%)	1 (3%)	0	
Severe	22 (73%)	1 (3%)	1 (3%)	

AHI, apnea–hypopnea index; CPAP, continuous positive airway pressure; OSA, obstructive sleep apnea.
*McNemar-Bowker test.

with hypertension, thus providing better hypertension management. Msaad et al[19] found that BNP levels significantly decreased in normotensive and especially hypertensive OSAS patients after CPAP treatment, which was consistent with our findings. Brain natriuretic peptide seems to be sensitive enough to detect myocardial stress caused by OSA. As such, it is a potential marker for screening preclinical cardiovascular damage in patients with untreated OSA. This finding suggests that pro-BNP can be used as an early marker of cardiac dysfunction in patients with OSA without any heart disease and can be used in the risk management of patients

Table 6. Comparison of Baseline and 6-Month Pro-BNP, CRP, Homocysteine, and Cardiac Biomarkers After CPAP Treatment

	Overall (n = 30)	**Moderate (n = 6)**	**Severe (n = 24)**	**Hypertension (n = 7)**	**No Hypertension (n = 23)**	
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	
	Median (25th-75th Percentile)	**Median (25th-75th Percentile)**	**Median (25th-75th Percentile)**	**Median (25th-75th Percentile)**	**Median (25th-75th Percentile)**	***P*****
Baseline CRP	3.8 ± 2.9	1.8 ± 1	4.3 ± 3	4.4 ± 1.9	3.7 ± 3.2	.311
	3.2 (1.4-5.8)	2.1 (0.6-2.5)	4.3 (1.4-6.3)	4.3 (3.2-5.7)	2.2 (1.3-6)	
Control CRP	3.4 ± 2.3	4 ± 3.4	3.2 ± 2	3.8 ± 1.8	3.3 ± 2.5	.471
	3.3 (1.3-5.3)	3.3 (1.3-6.4)	3.3 (1.2-5.3)	3.4 (2.8-5.3)	2.5 (1.3-5.2)	
*P**	.252	.345	.061	.735	.270	
Baseline CK	120.8 ± 71.8	121.5 ± 48.7	120.7 ± 77.4	93.9 ± 37.7	129 ± 78.2	.413
	104 (72.8-138)	128.5 (75.3-147.8)	87.5 (70.3-140)	79 (74-119)	120 (69-141)	
Control CK	127.9 ± 62.5	138 ± 41.8	125.4 ± 67.1	112.6 ± 51.9	132.6 ± 65.7	.532
	118.5 (78.8-157.5)	141.5 (99-178.3)	112.5 (78.3-153)	106 (65-153)	121 (85-162)	
*P**	.136	.249	.271	.090	.420	
Baseline troponin T	4.5 ± 2.6	5.4 ± 2.8	4.2 ± 2.6	5.2 ± 3.9	4.2 ± 2.1	.962
	3 (3-5.2)	4.6 (3-8.3)	3 (3-4.3)	3 (3-9.1)	3 (3-5)	
Control troponin T	5.4 ± 2.6	5.8 ± 2.4	5.3 ± 2.7	6.1 ± 3.7	5.2 ± 2.3	.564
	4.8 (3-6.8)	5.1 (4.3-7.4)	4.6 (3-6.8)	4.9 (3.4-7.6)	4.8 (3-6.8)	
*P**	.027	.917	.006	.116	.112	
Baseline CK-MB	13.1 ± 5.1	13 ± 4	13.2 ± 5.4	8.6 ± 2.1	14.5 ± 4.9	.003
	12 (8.8-17.3)	12.5 (10-17.3)	12 (8.3-17.8)	8 (7-11)	13 (11-18)	
Control CK-MB	15.7 ± 5.4	13.7 ± 2.7	16.3 ± 5.9	14.1 ± 4.6	16.2 ± 5.7	.360
	14 (11.8-18.3)	14 (11.5-15)	15 (11.3-19.8)	13 (11-17)	15 (12-19)	
*P**	.006	.786	.004	.018	.152	
Baseline homocysteine	13.7 ± 3.7	14.6 ± 1.6	13.5 ± 4.1	13.7 ± 4.4	13.7 ± 3.6	.598
	14.1 (11.5-15.7)	14.2 (13.5-16.4)	13.7 (10.6-15.5)	15.3 (12.2-16.7)	14 (11.3-15.6)	
Control homocysteine	13.8 ± 4.6	15.8 ± 4.1	13.3 ± 4.7	12.8 ± 4.9	14.1 ± 4.7	.471
	12.6 (11.1-17.2)	17.4 (11.2-18.9)	12.1 (10-15.3)	11.5 (9.5-18.1)	13.6 (11.6-17)	
*P**	.845	.249	.864	.397	.594	
Baseline pro-BNP	26.8 ± 30.6	21.8 ± 11	28.1 ± 33.9	56.6 ± 48.5	17.7 ± 14.9	.025
	15.7 (7.8-33.8)	22.8 (13.4-30.8)	12.9 (6.7-33.9)	34 (18.5-94.9)	12.8 (6.1-28.5)	
Control pro-BNP	16.7 ± 17.5	15 ± 10.5	17.1 ± 19	27.9 ± 27.6	13.2 ± 12	.245
	7.7 (5-24.3)	12.3 (5-25.9)	5.4 (5-22.8)	12.2 (5-64.4)	5 (5-18.5)	
*P**	.004	.080	.014	.046	.044	

CK, creatine kinase; CK-MB, creatine kinase-MB; CPAP, continuous positive airway pressure; CRP, C-reactive protein; Pro-BNP, pro-B-type natriuretic peptide.
*Wilcoxon signed-rank test (comparison of baseline and post-CPAP values).
**Mann–Whitney *U*-test (comparison of hypertension and non-hypertension).

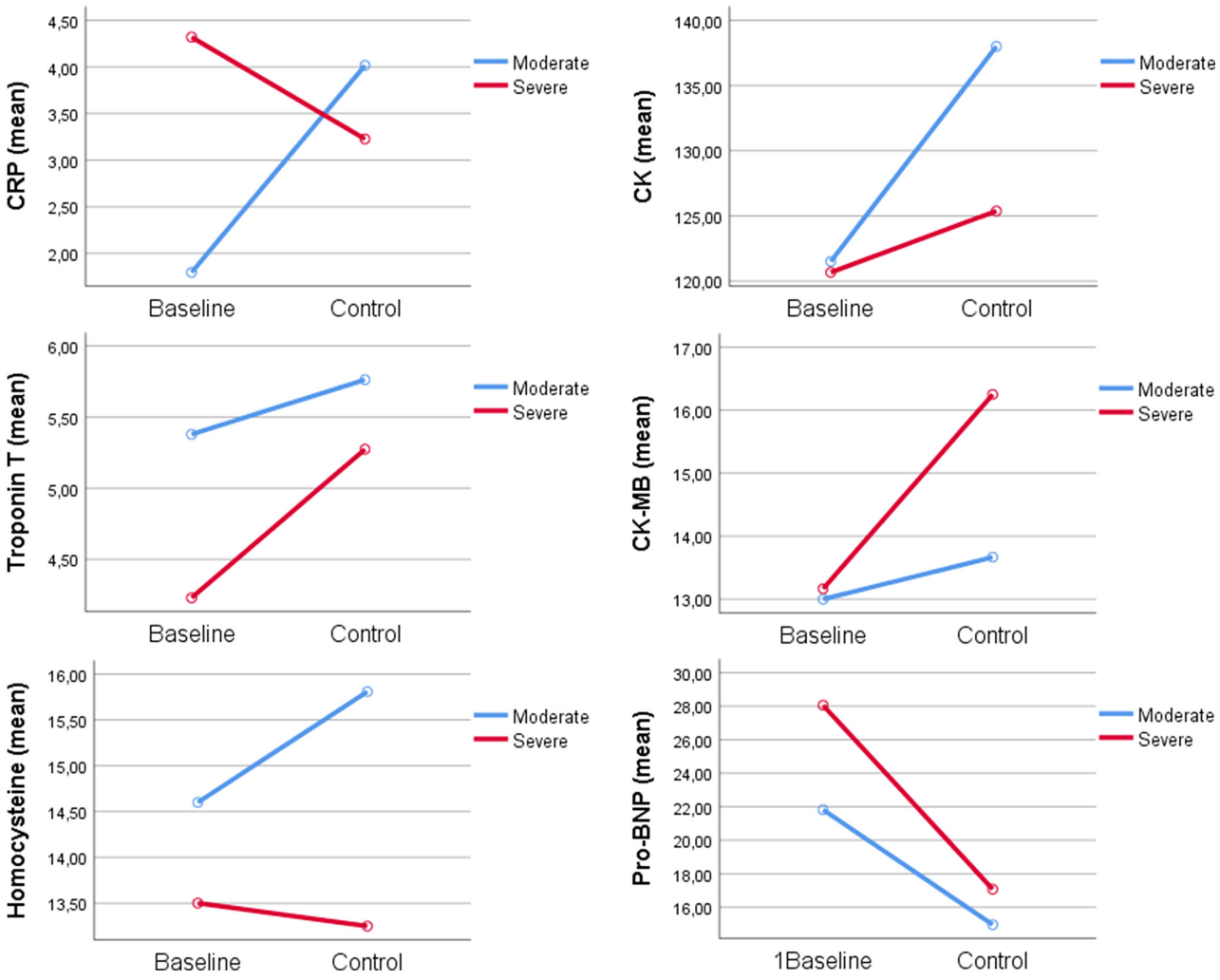

Figure 1. Comparison of baseline and 6-month pro-brain natriuretic peptide, C-reactive protein, homocysteine, and cardiac biomarkers after continuous positive airway pressure treatment by apnea–hypopnea index groups.

with OSA before the occurrence of clinical manifestations, mortality, and morbidity.

In a study by Shamsuzzaman et al.[20] CRP levels were found to be significantly higher in patients with OSA compared to the healthy control group; CRP level was significantly correlated with the severity of OSA, and significantly lower CRP levels were observed after effective CPAP treatment. Yokoe et al[8] demonstrated that CRP levels were associated with both AHI and BMI and decreased after 1 month of CPAP treatment. Improvement in AHI with CPAP treatment was found to be associated with a decrease in CRP. In our study, we observed that there was an average 0.43 unit decrease in CRP levels at the 6-month follow-up, but this decrease was not statistically significant. Köktürk et al[21]investigated CRP levels and increased risk of CVD in OSAS patients and found that CRP levels were significantly higher in the group that had both OSAS and CVD compared to the other 2 groups; there was no significant difference between the OSAS group without CVD and the group that only had CVD in terms of CRP.[21] In a study by Chu et al.[22] it was observed that CRP was significantly higher in the OSA group than in the control group, and after 6 months of CPAP treatment, CRP levels were significantly lower than baseline.[22] In another study by Wang et al.[23] it was observed that the level of CRP was significantly lower after CPAP treatment. In a study by Panoutsopoulos et al.[24] it was observed that CRP significantly decreased after 3 months of CPAP treatment in OSA patients,[24] whereas in our study, as well as in some other studies,[25-27] no significant decrease was found in CRP levels after CPAP treatment. Conflicting results regarding CRP may be attributed to population differences; some studies have included participants with more comorbid diseases or have not reported data regarding comorbid diseases or smoking/alcohol use, whereas it is known that CRP levels are affected by age, smoking, gender, and presence of atherosclerotic diseases.[28]

In a study by Can et al.[11] OSA patients with CAD were found to have higher homocysteine levels compared to OSAS patients without CAD; however, in our study, no comment can be made since no CAD patients were included. Kokturk et al[29] found that homocysteine levels were significantly higher in both OSA patients with and without CVD compared to patients with only CVD and reported that the severity of OSA was associated with homocysteine levels. Svatikova et al[30] compared patients newly diagnosed with moderate and severe OSA to a healthy control group matched in terms of age and BMI without OSA and did not find a significant difference between the groups in terms of homocysteine levels. Li et al[31] found that changes in homocysteine levels in different OSA patient groups were not proportional to disease

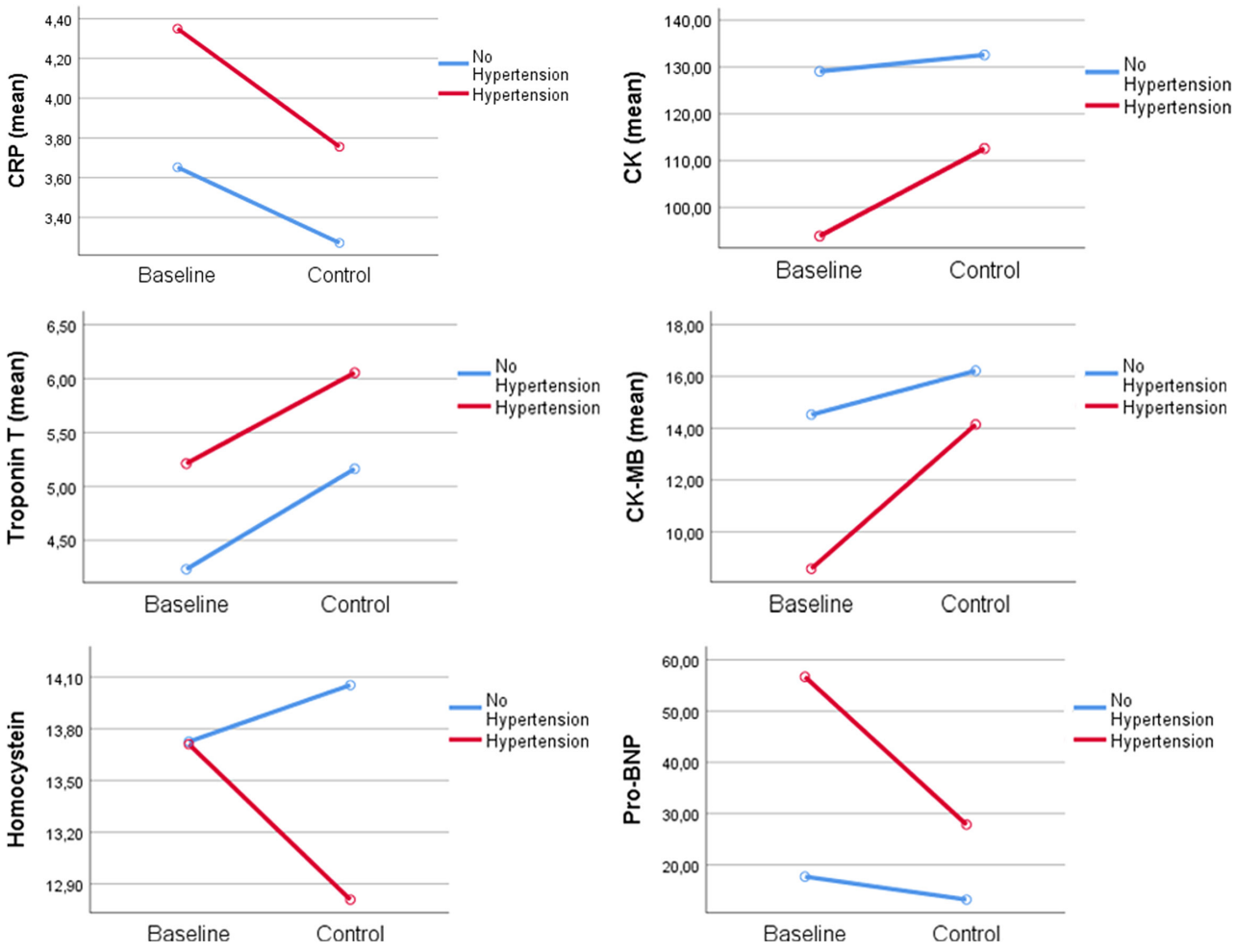

Figure 2. Comparison of baseline and 6-month pro-brain natriuretic peptide, C-reactive protein, homocysteine, and cardiac biomarkers after continuous positive airway pressure treatment by the presence of hypertension.

severity and CPAP treatment did not affect homocysteine levels. Kumor et al[32] did not observe a significant change in homocysteine and leptin levels in OSAS patients after 3 months of CPAP treatment but found a significant decrease in lipid levels in OSA patients without ischemic heart disease. In terms of homocysteine, the results of the aforementioned study were consistent with our results. In our study, the 0.1 unit increase in homocysteine levels at 6 months compared to baseline homocysteine levels was not statistically significant, and this finding is consistent with studies by Svatikova et al and Kumor et al. The fact that the homocysteine level is affected by many nonstandardized factors and the insufficient number of cases may have led to varying results regarding homocysteine in studies.

Gami et al[33] found that nocturnal hypoxia that occurred in OSA patients caused myocyte damage which increased troponin levels in the blood. They also reported that troponin levels in the blood in the morning and at night did not increase in patients with moderate and severe OSA who also had CAD. Cifçi et al[7] reported that serum CK-MB and troponin I levels did not change after 6 months of CPAP treatment and were not associated with the severity of OSA. Colish et al[12] conducted a prospective study on 47 OSA patients and did not find a significant change in troponin T levels after CPAP treatment compared to baseline. Strehmel et al[34] found that CPAP treatment had no effect on high-sensitive troponin T (hs-Trop T) levels. In our study, we observed a significant increase in troponin T and CK-MB levels after treatment. Chang et al[13] reported that CPAP therapy had no significant effect on hs-Trop T levels. Randby et al[35] found that OSA severity increased as troponin T levels increased. In contrast, Barceló et al[36] observed a significant increase in high-sensitive cardiac troponin T (hs-cTnT) levels after effective CPAP, which was consistent with our findings. It also indicates that treatment with CPAP is followed by a rise in hs-cTnT concentrations. It is reasonable to suggest that CPAP therapy may induce a potential degree of cardiac stress, resulting in detrimental consequences for the heart. Zhang et al[37] observed elevated hs-cTnT levels in patients with severe OSA and that CPAP treatment had no effect on these levels. In the present study, a statistically significant difference was found in CK-MB and troponin T values, except for CK after 6 months of CPAP treatment, compared to baseline values.

The limitations of our study were the low number of patients in our study group, the subjective evaluation of patient compliance to CPAP, and the lack of a healthy control group.

The strength of our study is important in terms of showing the effect of CPAP therapy on cardiac biomarkers in OSA patients without heart failure.

CONCLUSION

While there was no statistically significant change in CRP, homocysteine, and CK levels, there was a significant change in pro-BNP, troponin T, and CK-MB levels after 6 months of CPAP therapy in patients with moderate and severe OSAS without heart failure. A more significant decrease in pro-BNP levels was observed in hypertension patients. This finding suggests that pro-BNP may be used as an early indicator of cardiac dysfunction in OSA patients without any heart diseases except for hypertension.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of the Cerrahpaşa Faculty of Medicine at İstanbul University University (Approval No: 20908).

Informed Consent: Written informed consent was obtained from all patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – N.G., Ş.B.; Design – N.G., Ş.B.; Supervision – Ş.B., B.M.; Materials – N.G., Ş.B., H.C.Ç., E.C., F.A., B.M.; Data Collection and/or Processing – N.G., Ş.B, H.C.Ç., E.C., F.A., B.M.; Analysis and/or Interpretation – H.C.Ç.; Literature Review – N.G., Ş.B.; Writing – N.G.; Critical Review – N.G., Ş.B., B.M.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: This study received no funding.

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