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Factors Affecting Pressure Change Requirement in Obstructive Sleep Apnea Patients Under Positive Airway Pressure Therapy

Pozitif Hava Yolu Basıncı Tedavisi Altındaki Obstrüktif Uyku Apnesi Hastalarında Basınç Değişim İhtiyacını Etkileyen Faktörler

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Abstract

Objective: Obstructive sleep apnea syndrome is a chronic disease characterized by recurrent apnea and daytime sleepiness. The effect of weight or symptom change on the ideal positive airway pressure (PAP) change in regular users of PAP therapy is unknown. This study investigated the effect of weight or symptom change on an ideal PAP change in patients with severe obstructive sleep apnea.

Materials and Methods: Fifty-eight patients who were diagnosed with severe obstructive sleep apnea by polysomnography, titration polysomnography determined PAP and PAP treatment was started, and retitrated polysomnography was performed due to weight change or obstructive sleep apnea symptoms while under PAP treatment for at least six months was included in the study. Weight changes, ongoing symptoms, and data from all three polysomnography results were recorded.

Results: There was no difference in the effect of the weight change on ideal PAP. In the persistence of symptoms, PAP change was higher.

Conclusion: Weight gain, loss, or being the same weight did not affect PAP change. However, PAP change was more common in symptom persistence under PAP treatment.

Keywords: Sleep apnea, PAP retitration, weight change, symptom change, oxygen desaturation index, amnesia

Öz

Amaç: Obstrüktif uyku apne sendromu tekrarlayan apneler ve gündüz uyku hali ile karakterize kronik bir hastalıktır. Pozitif havayolu basıncı (PAP) tedavisini düzenli kullananlarda kilo değişimi ya da semptom değişiminin, ideal PAP değişimi üzerine etkisi bilinmemektedir. Bu çalışmanın amacı; düzenli PAP tedavisi kullanan şiddetli obstrüktif uyku apneli hastalarda, kilo değişimi veya semptom değişiminin ideal PAP değişimi üzerindeki etkisini araştırmaktır.

Gereç ve Yöntem: Polisomnografi ile ağır obstrüktif uyku apne tanısı konmuş olan, titrasyon polisomnografiyle PAP belirlenerek tedavisi başlanmış olan, en az 6 ay tedavi altındayken kilo değişimi veya uyku apne semptomları nedeniyle retitrasyon polisomnografisi yapılan 58 hasta çalışmaya dahil edildi. Kilo değişiklikleri, devam eden semptomlar ve her üç polisomnografi sonucundan elde edilen veriler kaydedildi.

Bulgular: Kilo değişiminin ideal PAP üzerine etkisinde anlamlı bir fark bulunmadı. Semptomların devamlılığı halinde ise PAP değişiminin daha fazla olduğu saptandı.

Sonuç: Kilo almanın, vermenin ya da aynı kiloda olmanın PAP değişimi üzerine anlamlı etkisi olmamıştır. Ancak tedavi altında semptom devamlılığında basınç değişimi daha fazla saptanmıştır.

Anahtar Kelimeler: Uyku apne, PAP retitrasyon, kilo değişimi, semptom değişimi, oksijen desatürasyon indeksi, amnezi

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Introduction

Obstructive sleep apnea syndrome (OSAS) is a chronic disease characterized by recurrent apneas and excessive daytime sleepiness (1). These episodes are associated with nocturnal desaturations and arousals, which lead to disruption of the sleep pattern and cognitive deterioration (2). They are known to be some risk factors for OSAS development; obesity is the most critical risk factor; at least 70% of patients are obese (3). It is known that weight gain is an important risk factor for the development of OSAS, but it is not present in every obese patient. In other words, although a clear relationship between OSAS and obesity cannot be demonstrated, there is no doubt that obesity plays a role in the cause or severity of OSAS (4). Various conditions closely related to obesity include oxidative stress, systemic inflammation, visceral fat accumulation, dyslipidemia, and insulin resistance (5). With these multiple mechanisms, obesity increases the prevalence of OSAS, and morbidity and mortality due to OSAS have risen significantly in these patients (6,7).

The diagnosis of OSAS is the combination of symptoms and polysomnography (PSG) findings (8). Positive airway pressure (PAP) is the gold standard in treatment (9). PAP treatment activates the sympathetic system, decreases leptin levels, and improves leptin resistance in patients. It results in a reduction in visceral fat deposition and weight loss. In addition to being a successful method in treating OSAS and related morbidities, weight loss has additional health benefits and should be routinely recommended to most overweight patients (7,10). Although it is possible to lose weight with the improvement of metabolism under PAP treatment, a meta-analysis including 3181 OSAS patients revealed an increase in weight and body mass index (BMI) with PAP treatment (7,11).

PAP retitration is recommended in patients with OSAS who have weight loss after bariatric surgery for obesity (12). As in OSAS patients with weight change under PAP treatment, PAP retitration is recommended for patients whose symptoms continue under treatment (12,13).

PAP retitration is recommended for regular use of PAP therapy, both in weight change and in the presence of symptoms; however, the superiority of these two variables over each other is unknown. This study aims to evaluate the effect of weight change and symptom persistence on the pressure change between PAP titration and retitration and to compare the superiority of these two variables.

Materials and Methods

Study Design and Study Population

The study protocol was designed as a prospective real-life study. Fifty-eight patients who applied to the sleep unit outpatient clinic between January 1, 2016 and January 1, 2017, were chosen to be included in this study.

The İstanbul University-Cerrahpasa, Cerrahpasa Faculty Clinical Research Ethics Committee approved this study (no: E-83045809-604.01.02-2627).

Participants

Inclusion criteria:

- Patients who applied to the sleep unit outpatient clinic,
- Between the ages of 18 and 85,
- Diagnosed with severe OSAS,
- PSG and PAP titration study,
- Having received regular PAP therapy for six months,
- The PAP retitration study was performed due to persistent symptoms or weight change despite regular PAP therapy,
- Provided signed written consent.

Exclusion criteria:

- Patients with a diagnosis of malignancy, chronic kidney disease, heart, and liver failure,
- Pregnancy,
- Having insufficient sleep time or technically unsuitable for PSG.

Patient Categorisation

Despite regular and appropriate PAP treatment;

- Patients without weight change: No-weight change group: W0,
- Patients with weight change: Weight change group: W1,
- Weight loss: Weight decreased group: W1d,
- Weight gainers: Weight increased group: W1i,
- Patients without symptoms: No-symptom group: S0,
- Patients with persistent symptoms: Symptom group: S1, as separated.

Data Collection

Demographic and anthropometric data of the patients were recorded. The symptoms and weight changes of the patients who were using PAP therapy regularly for 6-36 months with the diagnosis of severe OSAS were recorded, and PAP retitration admissions were performed.

The BMI was calculated by dividing the patient's weight in kg by the square of his/her height in m (kg/m^2). Neck circumference was measured in cm from the level of the cricothyroid membrane.

The Epworth Sleepiness Scale (ESS) was applied to each patient, scored, and the results during 8 hours of monitoring throughout the night were recorded. ESS scores of 10 and above were considered daytime sleepiness. The ESS, which has reliability and validity in Turkish, was used in this study (14).

PSG data: The minimum requirements for PSG are based on the recording protocol from the American Association of Sleep Medicine (AASM) 2007 report (7). Monitorizations were performed using electroencephalography (C3/A2, C4/A1, Fp1/A1, Fp2/A2, O1/A1, O2/A2), electrooculogram (right and left), chin, and 2 legs electromyography, electrocardiogram, nasal cannula, thermistor, tracheal microphone, body position, oximetry, and respiratory effort channels.

PSG recordings were made using the SOMNOscreen plus system (SOMNOmedics GmbH, Randersacker, Germany).

The PSG result of each patient was scored by the same person in accordance with the standards (3). The AASM 2012 scoring criteria were used. The AASM 2013 hypopnea recommended criteria were used for the scoring of hypopneas: required a ≥3%

decline in oxygen saturation accompanied by a ≥30% decline in the amplitude of the nasal airflow.

The AASM has outlined the clinical and sleep testing criteria for OSAS in the third edition of the International Classification of Sleep Disorders (15). The severity of OSAS can be classified according to the number of respiratory events observed per hour, termed the apnea hypopnea index (AHI): mild OSA (AHI 5-14.9/hour), moderate OSA (AHI 15-29.9/hour), and severe OSA (>30/hour) (16).

The respiratory disturbance index (RDI): The number of abnormal breathing events per hour of sleep. It is calculated as the number of apnea events/hour plus the number of hypopnea events/hour plus the number of respiratory-effort-related arousals per hour of sleep.

The oxygen desaturation index (ODI) was calculated as the number of oxygen desaturations per hour during the total sleep time. 3% desaturation was used.

Arousal: It is the sudden transition to lighter sleep or wakefulness during sleep.

Statistical Analysis

All analyses were performed on SPSS v25 (SPSS Inc., Chicago, IL, USA). Q-Q and histogram plots were used to determine whether variables are normally distributed. Data are given as mean ± standard deviation or median (1st quartile-3rd quartile) for continuous variables according to the normality of distribution and as frequency (percentage) for categorical variables. Normally distributed variables were analyzed with the independent samples t-test or one-way analysis of variance (ANOVA) depending on the count of groups. Non-normally distributed variables were analyzed with the Mann-Whitney U test or Kruskal-Wallis test depending on the count of groups. Categorical variables were analyzed with the chi-square tests or Fisher's exact tests. Repeated measurements were analyzed with Friedman's analysis of variance by ranks. Pairwise comparisons were performed with the Bonferroni correction method. Spearman correlation coefficients were calculated to evaluate relationships between continuous variables. P<0.05 values accepted as statistically significant results.

Results

We included 58 patients (21 females and 37 males) in our study, the mean age was 51.83±10.00 (range 30-82). Weight changed (W1) in 41 (70.69%) patients and remained same (W0) in 17 (29.31%) patients. The duration of PAP use was significantly higher in the W1 group than in the W0 group (p=0.029) (Table 1). The ODI at diagnosis was significantly higher in the W0 group than in the W1 group (p=0.026). The RDI at the PAP retitration was significantly higher in the W0 group than in the W1 group (p=0.021) (Table 1). The PAP pressure decreased in 6 (35.29%) patients, remained the same in 6 (35.29%) patients, and increased in 5 (29.41%) patients in the W0 group. The PAP decreased in 19 (46.34%) patients, remained the same in 13 (31.71%) patients, and increased in 9 (21.95%) patients in the W1 group (Figure 1).

Table 1. Summary of patients' characteristics and measurements regarding body weight change

	Weight change			
	No: W0 (n=17)	**Yes: W1 (n=41)**	**Total (n=58)**	**p**
Age	54.94±11.82	50.54±8.99	51.83±10.00	0.128
Gender				
Female	6 (35.29%)	15 (36.59%)	21 (36.21%)	1.000
Male	11 (64.71%)	26 (63.41%)	37 (63.79%)	
Smoking	10 (58.82%)	23 (56.10%)	33 (56.90%)	1.000
Pack-year	5 (0-20)	12 (0-30)	5 (0-23)	0.810
Comorbidities	13 (76.47%)	32 (78.05%)	45 (77.59%)	1.000
Diabetes mellitus	4 (23.53%)	9 (21.95%)	13 (22.41%)	1.000
Hypertension	8 (47.06%)	20 (48.78%)	28 (48.28%)	1.000
Coronary artery disease	4 (23.53%)	6 (14.63%)	10 (17.24%)	0.458
COPD	1 (5.88%)	2 (4.88%)	3 (5.17%)	1.000
Asthma	1 (5.88%)	2 (4.88%)	3 (5.17%)	1.000
Psychiatric disease	0 (0.00%)	3 (7.32%)	3 (5.17%)	0.548
Hypothyroidism	2 (11.76%)	2 (4.88%)	4 (6.90%)	0.573
Other	7 (41.18%)	14 (34.15%)	21 (36.21%)	0.836
Regular use				
No	1 (5.88%)	7 (17.07%)	8 (13.79%)	0.415
Yes	16 (94.12%)	34 (82.93%)	50 (86.21%)	
Symptom, initial	14 (93.33%)	37 (94.87%)	51 (94.44%)	1.000
Snoring	6 (40.00%)	11 (28.21%)	17 (31.48%)	0.516
Apnea	5 (33.33%)	11 (28.21%)	16 (29.63%)	0.747
EDS	10 (66.67%)	33 (84.62%)	43 (79.63%)	0.256
Fatigue	6 (40.00%)	27 (69.23%)	33 (61.11%)	0.097
Headache	3 (20.00%)	14 (35.90%)	17 (31.48%)	0.338
Nocturia	10 (66.67%)	28 (71.79%)	38 (70.37%)	0.747
Amnesia	6 (40.00%)	22 (56.41%)	28 (51.85%)	0.437
Symptom, final	12 (80.00%)	23 (82.14%)	35 (81.40%)	1.000
Snoring	9 (60.00%)	22 (78.57%)	31 (72.09%)	0.287
Apnea	9 (60.00%)	22 (78.57%)	31 (72.09%)	0.287
EDS	11 (73.33%)	22 (78.57%)	33 (76.74%)	0.719
Fatigue	2 (13.33%)	0 (0.00%)	2 (4.65%)	0.116
Headache	0 (0.00%)	0 (0.00%)	0 (0.00%)	N/A
Nocturia	2 (13.33%)	0 (0.00%)	2 (4.65%)	0.116
Amnesia	3 (20.00%)	0 (0.00%)	3 (6.98%)	0.037
Symptom during PAP	12 (70.59%)	16 (39.02%)	28 (48.28%)	0.057
Snoring	6 (35.29%)	7 (17.07%)	13 (22.41%)	0.171
Apnea	6 (35.29%)	7 (17.07%)	13 (22.41%)	0.171
EDS	12 (70.59%)	16 (39.02%)	28 (48.28%)	0.057
Height	164.29±9.60	166.68±10.88	165.98±10.49	0.435
Weight				
Initial	90 (85-105)	96 (86-110)	95 (85-109)	0.241
Final	90 (85-105)	95 (84-112)	94 (84-110)	0.596
Body mass index				
Initial	32.89 (29.67-40.43)	35.27 (32.00-38.74)	34.19 (31.67-39.96)	0.745
Final	32.89 (29.67-40.43)	36.30 (28.89-38.20)	35.53 (29.41-39.44)	0.898

Table 1. Continued				
Neck circumference				
Initial	42.25 (40.25-45)	43 (42-45)	43 (42-45)	0.601
Final	42 (40-43)	42.75 (40.25-44.75)	42 (40-44.5)	0.452
Change	0 (-0.75-0)	0 (-1.5-1)	0 (-1-1)	0.450
Epworth Sleepiness Scale				
Initial	8 (3-11)	7 (5-10)	7 (4-11)	0.738
Final	7 (4-12)	5 (2.5-8)	5 (3- 8.5)	0.212
Change	-2.5 (-5 - -0.5)	-2 (-4 - -1)	-2 (-4 - -1)	0.956
Duration of PAP use, month	8.5 (4-15)	15 (12-24)	14 (7.5-24)	0.029
PAP pressure				
Titration	7 (5-8)	8 (6-9)	8 (5-9)	0.616
Retitration	6 (5-11)	7 (5-8)	6.5 (5-8)	0.877
Change[(1)]	0 (-1-1)	0 (-2-0)	0 (-2-0)	0.459
Decreased	6 (35.29%)	19 (46.34%)	25 (43.10%)	0.717
Same	6 (35.29%)	13 (31.71%)	19 (32.76%)	
Increased	5 (29.41%)	9 (21.95%)	14 (24.14%)	
AHI				
Diagnosis	36 (27.6-42.4)[a]	33.1 (26.4-42.4)[a]	33.4 (27-42.4)[a]	0.709
Titration	4.45 (1.4-9.9)[b]	4.5 (2.9-7.6)[b]	4.5 (2.8-8.3)[b]	0.972
Retitration	4.3 (2.4-5.6)[b]	3.2 (1.3-4.1)[b]	3.2 (1.45-5.1)[b]	0.209
P (within groups)	<0.001	<0.001	<0.001	
Change[(1)]	-0.15 (-0.7-3.45)	-1.3 (-4.4-0)	-0.7 (-3.6-0.3)	0.148
RDI				
Diagnosis	41.8 (30.3-45.1)[a]	38 (30.3-42.9)[a]	39.35 (30.3-43.95)[a]	0.634
Titration	10.75 (5.6-15.2)[b]	8.1 (4.2-15.8)[b]	8.7 (4.2-15.8)[b]	0.585
Retitration	9.2 (4.6-12.6)[b]	4.2 (1.8-7.9)[b]	4.55 (2.75-10.6)[b]	0.021
P (within groups)	<0.001	<0.001	<0.001	
Change[(1)]	-0.75 (-3.15-1.75)	-2.6 (-5.6-1.3)	-0.8 (-4.5-1.7)	0.648
ODI				
Diagnosis	35 (28.4-54.2)[a]	28.4 (9.2-35.9)[a]	29.6 (15.3-41.2)[a]	0.026
Titration	9.8 (6-14.6)[b]	7.9 (3.2-11)[b]	8.3 (3.2-12.8)[b]	0.163
Retitration	6.2 (3.8-12.9)[b]	4.5 (0.4-11.8)[b]	4.7 (1.5-12.35)[b]	0.279
P (within groups)	<0.001	<0.001	<0.001	
Change[(1)]	-1.85 (-4.6-0.4)	-1.2 (-5.8-1.3)	-1.4 (-5-0.9)	0.749
Total sleep duration				
Diagnosis	358 (288-372)	306 (255-366)	349.5 (255-366)	0.274
Titration	362 (329-423)	348.5 (285-368)	351.5 (290-385)	0.220
Retitration	368.5 (273.5-390)	328 (290-379)	343.5 (286-383)	0.513
p (within groups)	0.920	0.962	0.900	
Change[(1)]	-0.5 (-61.25-36.5)	-2 (-52-44)	-2 (-52-44)	0.831
Deep sleep (stage 3) duration				
Diagnosis	50 (25-74.5)	37 (17.5-64)	50 (24-64)	0.377
Titration	36.5 (25.5-80.25)	53.5 (25.5-84)	51 (25.5-84)	0.797
Retitration	43 (28.5-75)	50 (27-73.5)	50 (27-73.5)	0.976
P (within groups)	0.913	0.089	0.118	
Change[(1)]	-3 (-55-62)	-4 (-41.5-14)	-3.5 (-41.5-14)	0.797
REM duration				
Diagnosis	59 (46-83)	46 (12-66)	50 (12.75-66)	0.122
Titration	48 (37.5-76)	58.5 (31-68)	58.25 (36.5-73)	0.798
Retitration	58 (25.5-79.25)	45.5 (35-66)	45.5 (33.5-71.5)	0.670
P (within groups)	0.320	0.656	0.446	
Change[(1)]	6.5 (-4.5-35.5)	0 (-16.5-10.5)	3 (-14-16.5)	0.157

Data are given as mean ± standard deviation or median (1st quartile-3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables. Same letters denote the lack of statistically significant difference between repeated measurements.

[(1)]Difference between retitration and titration. Negative values represent decrease and positive values represent increase in measurements.

The lettering a b b indicates that the first measurement is different from the others, and there is no difference between the second and third measurements. The letters in the tables represent pairwise comparison results.

COPD: Chronic obstructive pulmonary disease, EDS: Excessive daytime sleepiness, ODI: Oxygen desaturation index, REM: Rapid eye movement, RDI: Respiratory disturbance index, AHI: Apnea hypopnea index, PAP: Positive airway pressure

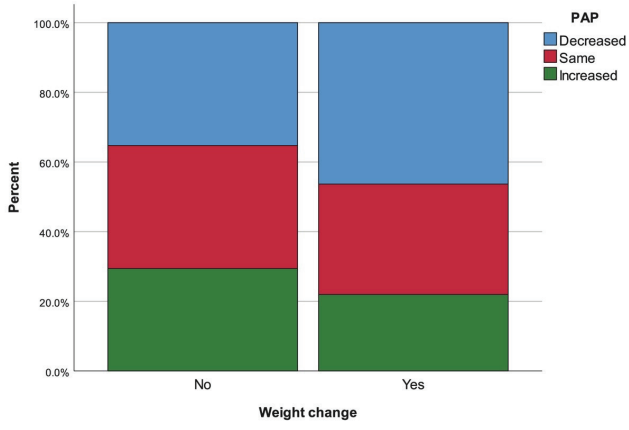

Figure 1. PAP change status regarding presence of weight change
PAP: Positive airway pressure

Weight decreased (W1d) in 19 (32.76%) patients, remained the same (W0) in 17 (29.31%) patients, and increased (W1i) in 22 (37.93%) patients. Regular PAP use percentage was significantly lower in the W1d group than in the other groups (p=0.023). Symptom during PAP use percentage was significantly higher in the W0 group than in the W1d group (p=0.029). When compared according to symptoms, amnesia was significantly higher in the W0 group than in other groups (p=0.049) (Table 2).

We found no significant differences between weight change groups regarding PAP titration, PAP retitration, change in PAP pressure and, changing status (Figure 2).

Twenty eight (48.28%) patients had symptoms (S1) during PAP use and 30 (51.72%) patients had no symptoms (S0) during PAP use. The coronary artery disease percentage was significantly higher in the S1 group than in the S0 group (p=0.038). The decrease in weight percentage was significantly higher in the S0 group than in the S1 group (p=0.029). The final ESS score was significantly higher in the S1 group than in the S0 group. When we evaluated PSG results between symptom groups, RDI at PAP retitration was significantly higher in the S1 group than in the S0 group (p=0.015). The ODI at PAP titration was significantly higher in the S1 group than in the S0 group (p=0.020) (Table 3).

The difference between PAP retitration and titration pressure was significantly lower in the S0 group than in the S1 group (p=0.043). We found no significant difference between symptom groups regarding PAP titration, PAP retitration, or changing status (Figure 3).

We found a negative correlation between PAP pressure change and change in sleep stage N3 duration (r=-0.334, p=0.040). We found a positive correlation between PAP change and change in rapid eye movement (REM) duration (r=0.429, p=0.007) (Table 4).

In the study, there were 5 (8.62%) patients with no weight change and no symptoms during PAP use. PAP decreased in three of them, PAP remained the same in one of them and PAP increased in one of them (Table 5).

Discussion

In this study, investigating the effect of weight change and symptom change with regular PAP treatment on PAP pressure, it was observed that weight gain, loss, or being at the same weight did not significantly affect the pressure change. However, PAP pressure change was more significant in the persistence of symptoms. While the persistence of symptoms was less in those who lost weight, the persistence of symptoms was more frequent in those without weight change, and primarily amnesia was found to be significantly more frequent. Weight change was little, and symptom persistence was more frequent in those with high ODI at diagnosis. The incidence of coronary artery disease was found to be higher in patients with ongoing symptoms. It was determined that as the PAP pressure difference between titration and retitration increased, the duration of deep sleep decreased, while REM sleep increased.

Table 2. Summary of patients' characteristics and measurements regarding body weight change

	Weight			
	W1d: decreased (n=19)	**W0: same (n=17)**	**W1i: increased (n=22)**	**p**
Age	49.11±6.85	54.94±11.82	51.77±10.50	0.220
Gender				
Female	6 (31.58%)	6 (35.29%)	9 (40.91%)	0.822
Male	13 (68.42%)	11 (64.71%)	13 (59.09%)	
Smoking	13 (68.42%)	10 (58.82%)	10 (45.45%)	0.328
Pack-year	15 (0-30)	5 (0-20)	0 (0-30)	0.645
Comorbidities	14 (73.68%)	13 (76.47%)	18 (81.82%)	0.817
Diabetes mellitus	3 (15.79%)	4 (23.53%)	6 (27.27%)	0.674
Hypertension	8 (42.11%)	8 (47.06%)	12 (54.55%)	0.724
Coronary artery disease	1 (5.26%)	4 (23.53%)	5 (22.73%)	0.241
COPD	0 (0.00%)	1 (5.88%)	2 (9.09%)	0.418
Asthma	0 (0.00%)	1 (5.88%)	2 (9.09%)	0.418
Psychiatric disease	2 (10.53%)	0 (0.00%)	1 (4.55%)	0.358
Hypothyroidism	1 (5.26%)	2 (11.76%)	1 (4.55%)	0.639
Other	6 (31.58%)	7 (41.18%)	8 (36.36%)	0.836
Regular use				
No	6 (31.58%)	1 (5.88%)	1 (4.55%)	0.023
Yes	13 (68.42%)	16 (94.12%)	21 (95.45%)	
Symptom, initial	16 (94.12%)	14 (93.33%)	21 (95.45%)	0.960
Snoring	5 (29.41%)	6 (40.00%)	6 (27.27%)	0.698
Apnea	4 (23.53%)	5 (33.33%)	7 (31.82%)	0.797
EDS	15 (88.24%)	10 (66.67%)	18 (81.82%)	0.302
Fatigue	11 (64.71%)	6 (40.00%)	16 (72.73%)	0.125
Headache	6 (35.29%)	3 (20.00%)	8 (36.36%)	0.529
Nocturia	10 (58.82%)	10 (66.67%)	18 (81.82%)	0.277
Amnesia	12 (70.59%)	6 (40.00%)	10 (45.45%)	0.166
Symptom, final	9 (81.82%)	12 (80.00%)	14 (82.35%)	0.985
Snoring	9 (81.82%)	9 (60.00%)	13 (76.47%)	0.413
Apnea	9 (81.82%)	9 (60.00%)	13 (76.47%)	0.413
EDS	9 (81.82%)	11 (73.33%)	13 (76.47%)	0.879
Fatigue	0 (0.00%)	2 (13.33%)	0 (0.00%)	0.141
Headache	0 (0.00%)	0 (0.00%)	0 (0.00%)	N/A
Nocturia	0 (0.00%)	2 (13.33%)	0 (0.00%)	0.141
Amnesia	0 (0.00%)	3 (20.00%)	0 (0.00%)	0.049
Initial	7 (5-11)	8 (3-11)	7 (4-9)	0.848
Final	5 (2-10)	7 (4-12)	5 (4-7)	0.445
Change	-3 (-4- -1)	-2.5 (-5- -0.5)	-2 (-4-0)	0.626
Duration of PAP, month	15 (7-24)	8.5 (4-15)	15 (12-24)	0.089
PAP				
Titration	8 (6-10)	7 (5-8)	7 (5-8)	0.247
Retitration	7 (5-8)	6 (5-11)	6 (5-8)	0.912
Change[1]	-1 (-2-0)	0 (-1-1)	0 (-1-0)	0.457
Decreased	11 (57.89%)	6 (35.29%)	8 (36.36%)	0.558
Same	4 (21.05%)	6 (35.29%)	9 (40.91%)	
Increased	4 (21.05%)	5 (29.41%)	5 (22.73%)	

Table 2. Continued				
AHI				
Diagnosis	33.7 (31.2-42.4)[a]	36 (27.6-42.4)[a]	32.75 (26.2-41.95)[a]	0.877
Titration	4.25 (2.85-7.9)[b]	4.45 (1.4-9.9)[b]	5.2 (3.2-7.6)[b]	0.999
Retitration	1.9 (1.3-3.2)[b]	4.3 (2.4-5.6)[b]	3.95 (2.1-4.8)[b]	0.211
P (within groups)	<0.001	<0.001	<0.001	
Change[(1)]	-2.7 (-5.8-0)	-0.15 (-0.7-3.45)	-0.6 (-3.6-0.3)	0.166
RDI				
Diagnosis	39.7 (31.2-42.9)[a]	41.8 (30.3-45.1)[a]	34.2 (29.65-42.65)[a]	0.781
Titration	4.45 (4.1-9.75)[b]	10.75 (5.6-15.2)[b]	8.8 (5.2-22)[b]	0.253
Retitration	3.8 (1.8-6.5)[b]	9.2 (4.6-12.6)[b]	4.25 (2.3-10.1)[b]	0.052
P (within groups)	<0.001	<0.001	<0.001	
Change[(1)]	-3 (-3.4-0.3)	-0.75 (-3.15-1.75)	-1.6 (-6.6-1.3)	0.867
ODI				
Diagnosis	28.4 (8.4-34.7)[a]	35 (28.4-54.2)[a]	24.75 (9.2-38.3)[a]	0.082
Titration	3.95 (2.75-12.4)[b]	9.8 (6-14.6)[b]	8.3 (3.2-11)[b]	0.377
Retitration	3.2 (0.9-11.6)[b]	6.2 (3.8-12.9)[b]	4.95 (0.4-13.7)[b]	0.508
P (within groups)	0.001	<0.001	0.003	
Change[(1)]	-0.1 (-3.6-0.9)	-1.85 (-4.6- 0.4)	-1.75 (-5.8-1.3)	0.893
Total sleep duration				
Diagnosis	294 (254-366)	358 (288-372)	325.5 (275-364)	0.536
Titration	323.75 (248.75-355.5)	362 (329-423)	362 (305-402)	0.062
Retitration	336 (294-358)	368.5 (273.5-390)	320 (248-382)	0.807
P (within groups)	0.232	0.920	0.232	
Change[(1)]	27.5 (-12-44.5)	-0.5 (-61.25-36.5)	-28 (-82-14)	0.214
Level 3 duration				
Diagnosis	35.5 (24-54)	50 (25-74.5)	45.5 (12-69)	0.625
Titration	50 (28.5-81.75)	36.5 (25.5-80.25)	54 (21-95)	0.921
Retitration	50 (36.3-73.5)	43 (28.5-75)	51.75 (16.5-73)	0.949
P (within groups)	0.232	0.913	0.368	
Change[(1)]	1.5 (-34-18.5)	-3 (-55-62)	-4 (-41.5-9)	0.745

Table 2. Continued				
REM duration				
Diagnosis	46 (12-66)	59 (46-83)	44.5 (12.25-62)	0.302
Titration	43.75 (27.75-64.25)	48 (37.5-76)	62 (47.5-76.8)	0.574
Retitration	45.5 (33.5-66)	58 (25.5-79.25)	44.5 (39.5-62)	0.886
P (within groups)	0.926	0.320	0.538	
Change[(1)]	2.5 (-12-10.5)	6.5 (-4.5-35.5)	-1 (-27.5-8)	0.325

Data are given as mean ± standard deviation or median (1st quartile-3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables. Same letters denote the lack of statistically significant difference between repeated measurements.

[(1)]Difference between retitration and titration. Negative values represent decrease and positive values represent increase in measurements.

The letters in the tables represent pairwise comparison results. The lettering a b b indicates that the first measurement is different from the others, and there is no difference between the second and third measurements.

COPD: Chronic obstructive pulmonary disease, EDS: Excessive daytime sleepiness, ODI: Oxygen desaturation index, REM: Rapid eye movement, RDI: Respiratory disturbance index, AHI: Apnea hypopnea index, PAP: Positive airway pressure

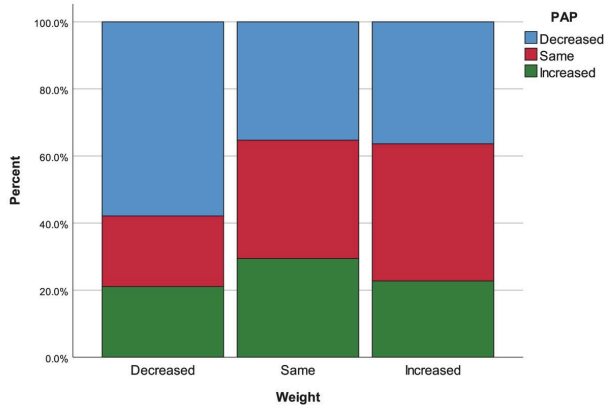

Figure 2. PAP change status regarding weight change groups
PAP: Positive airway pressure

A study on patients with severe OSAS showed that PAP treatment prevents weight gain and facilitates weight loss (17). Another study that included 86 OSAS patients diagnosed with metabolic syndrome found a significant decrease in BMI after three months of regular PAP treatment (18). On the other hand, in another study investigating the change in BMI in the first year after regular PAP treatment, no significant difference was found in BMI, and it was emphasized that some patients had weight gain (19). Contrary to these, in our study, the effect of weight and symptom change on PAP pressure was investigated, and it was observed that a negative or positive weight change did not cause a significant change in PAP pressure, while PAP pressure change was found to be more in symptom persistence.

Although publications show that OSAS may develop memory impairment and cause amnesia, its etiology is still unknown (20). In this study, amnesia was found to be more common in

Table 3. Summary of patients' characteristics and measurements with regard to symptom			
	Symptom during PAP		
	No (n=30)=S0	**Yes (n=28)=S1**	**p**
Age	50.90±9.85	52.82±10.25	0.470
Gender			
Female	14 (46.67%)	7 (25.00%)	0.149
Male	16 (53.33%)	21 (75.00%)	
Smoking	17 (56.67%)	16 (57.14%)	1.000
Pack-year	8.5 (0-20)	3.5 (0-26.5)	0.808
Comorbidities	25 (83.33%)	20 (71.43%)	0.440
Diabetes mellitus	7 (23.33%)	6 (21.43%)	1.000
Hypertension	14 (46.67%)	14 (50.00%)	1.000
Coronary artery disease	2 (6.67%)	8 (28.57%)	0.038
COPD	3 (10.00%)	0 (0.00%)	0.238
Asthma	1 (3.33%)	2 (7.14%)	0.605
Psychiatric disease	3 (10.00%)	0 (0.00%)	0.238
Hypothyroidism	2 (6.67%)	2 (7.14%)	1.000
Other	13 (43.33%)	8 (28.57%)	0.370
Regular use			
No	4 (13.33%)	4 (14.29%)	1.000
Yes	26 (86.67%)	24 (85.71%)	
Height	165.47±10.61	166.54±10.53	0.702
Weight			
Initial	95 (86-109)	95 (84-109)	1.000
Final	90 (84-106)	95 (85-110)	0.523
Body mass index			
Initial	33.60 (32.05-37.89)	35.48 (30.62-40.81)	0.950
Final	35.28 (28.39-38.05)	36.11 (29.54-40.67)	0.465
Body weight change			
Decreased	14 (46.67%)	5 (17.86%)	0.029
Same	5 (16.67%)	12 (42.86%)	
Increased	11 (36.67%)	11 (39.29%)	
Neck circumference			
Initial	42.5 (42-45)	43 (40.5-47)	0.312
Final	42.25 (40.5-44.5)	42 (40-45)	0.974
Change	0 (-1-1)	0 (-1-0.5)	0.668
Symptom, initial	26 (92.86%)	25 (96.15%)	1.000
Snoring	7 (25.00%)	10 (38.46%)	0.441
Apnea	8 (28.57%)	8 (30.77%)	1.000
EDS	22 (78.57%)	21 (80.77%)	1.000
Fatigue	19 (67.86%)	14 (53.85%)	0.438
Headache	8 (28.57%)	9 (34.62%)	0.854
Nocturia	19 (67.86%)	19 (73.08%)	0.903
Amnesia	17 (60.71%)	11 (42.31%)	0.280
Symptom, final	16 (76.19%)	19 (86.36%)	0.457
Snoring	15 (71.43%)	16 (72.73%)	1.000
Apnea	15 (71.43%)	16 (72.73%)	1.000
EDS	15 (71.43%)	18 (81.82%)	0.488

Table 3. Continued			
Fatigue	0 (0.00%)	2 (9.09%)	0.488
Headache	0 (0.00%)	0 (0.00%)	N/A
Nocturia	0 (0.00%)	2 (9.09%)	0.488
Amnesia	0 (0.00%)	3 (13.64%)	0.233
Epworth Sleepiness Scale			
Initial	7 (4-8)	8.5 (4-12.5)	0.232
Final	4 (3-7)	7 (3-12)	0.040
Change	-2 (-4-0)	-3 (-4 - -1)	0.609
Duration of PAP, month	15 (12-24)	13 (4-23)	0.119
PAP			
Titration	8 (6-9)	7.5 (5-8.5)	0.648
Retitration	6 (5-8)	7 (5-9.5)	0.494
Change[1]	-1 (-2-0)	0 (-1-1.5)	0.043
Decreased	17 (56.67%)	8 (28.57%)	0.092
Same	7 (23.33%)	12 (42.86%)	
Increased	6 (20.00%)	8 (28.57%)	
AHI			
Diagnosis	31.65 (26.2-39.2)[a]	38.7 (31.8-43.9)[a]	0.101
Titration	3.95 (1.6-7.3)[b]	7.6 (3.3-9.9)[b]	0.076
Retitration	2.55 (0.9-4.5)[b]	3.95 (2.8-7.1)[b]	0.077
P (within groups)	<0.001	<0.001	
Change[1]	-1.4 (-3.6-0)	-0.5 (-0.7-1.9)	0.444
RDI			
Diagnosis	33.7 (28.65-41.6)[a]	41.05 (34.2-45.05)[a]	0.081
Titration	7.15 (4-14.9)[b]	10.4 (5.6-16.4)[b]	0.167
Retitration	4.05 (1-6.5)[b]	8.4 (4.2-13.2)[b]	0.015
P (within groups)	<0.001	<0.001	
Change[1]	-3 (-6.6-0)	0.3 (-2.6-1.7)	0.157
ODI			
Diagnosis	29 (9.2-39.15)[a]	29.8 (20.85-41.2)[a]	0.472
Titration	3.75 (1.2-10.5)[b]	9.1 (7.5-13.6)[b]	0.020
Retitration	3.6 (0.9-6.7)[b]	8.15 (2.5-13.7)[b]	0.276
P (within groups)	<0.001	<0.001	
Change[1]	-1.05 (-3.6-0.9)	-3.1 (-5-0.6)	0.461
Total sleep duration			
Diagnosis	302.5 (255-365)	358 (291.5-370)	0.262
Titration	352 (295-385)	349 (285-367)	0.763
Retitration	320 (294-380)	357.5 (264-390)	0.640
P (within groups)	0.385	0.444	
Change[1]	-5.5 (-52-34)	2 (-47-53)	0.734
Level 3 duration			
Diagnosis	54 (25-64)	35.25 (15.5-59.5)	0.212
Titration	53.5 (25.5-74.5)	49 (23.5-94.5)	0.568
Retitration	51.75 (34-73.5)	38.5 (27-73)	0.955
P (within groups)	0.293	0.344	
Change[1]	1.25 (-34-14)	-4.25 (-47.85-13.75)	0.647

Table 3. Continued			
REM duration			
Diagnosis	44.5 (12.25-66)	50.5 (26.5-72)	0.333
Titration	52.75 (31-70.5)	59.75 (39.25-74.5)	0.723
Retitration	44.5 (35-66)	52 (31-73.5)	0.610
P (within groups)	0.422	0.813	
Change[(1)]	1 (-12-7.5)	7.25 (-25.75-20.75)	0.574

Data are given as mean ± standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables. Same letters denote the lack of statistically significant difference between repeated measurements.

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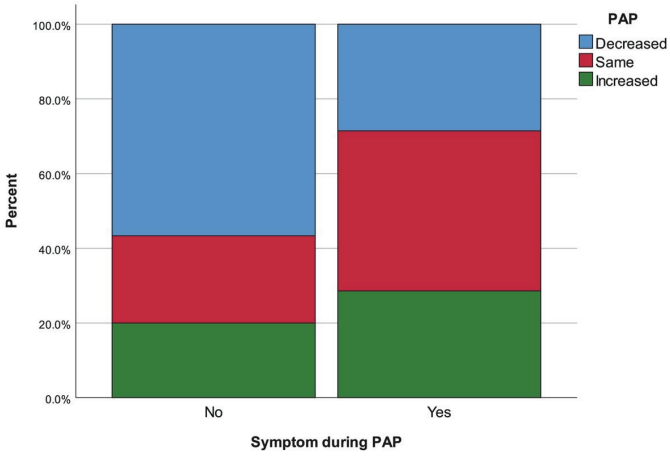

Figure 3. PAP change status regarding presence of symptoms during PAP use
PAP: Positive airway pressure

Table 4. Correlations between PAP change and other variables					
Age	r	0.233	Change in AHI	r	0.106
	p	0.079		p	0.522
Smoking pack-year	r	-0.125	Change in RDI	r	0.076
	p	0.349		p	0.645
Change in weight	r	0.088	Change in ODI	r	0.058
	p	0.511		p	0.728
Change in body mass index	r	0.091	Change in total sleep duration	r	0.024
	p	0.497		p	0.883
Change in neck circumference	r	0.033	Change in level 3 duration	r	**-0.334**
	p	0.814		p	**0.040**
Change in Epworth Sleepiness Scale score	r	0.032	Change in REM duration	r	**0.429**
	p	0.817		p	**0.007**

r: Spearman correlation coefficient, REM: Rapid eye movement, RDI: Respiratory disturbance index, AHI: Apnea hypopnea index, PAP: Positive airway pressure, ODI: Oxygen desaturation index

Table 5. Summary of PAP change regarding body weight change and symptom status					
	No weight change & no symptom (n=5)	**No weight change & symptom (n=12)**	**Weight change & no symptom (n=25)**	**Weight change & symptom (n=16)**	**p**
PAP change					
Decreased	3 (60.00%)	3 (25.00%)	14 (56.00%)	5 (31.25%)	0.533
Same	1 (20.00%)	5 (41.67%)	6 (24.00%)	7 (43.75%)	
Increased	1 (20.00%)	4 (33.33%)	5 (20.00%)	4 (25.00%)	

Data are given as frequency (percentage), PAP: Positive airway pressure

patients with elevated ODI, whose symptoms persisted during PAP treatment, and in patients with persistent symptoms and no weight change. More studies are needed regarding the relationship between hypoxia and amnesia in OSAS.

A study investigating OSAS in men with coronary artery disease emphasized that ODI was higher, and hypoxemia was more frequent in them (21). In our study, symptom persistence under treatment was more common in patients with high ODI. The incidence of coronary artery disease was higher in these patients whose symptoms continued under treatment.

Studies have shown that apneas last longer and hypoxemia deepens in REM sleep (22). However, it has been shown that improvement in RDI with PAP treatment is correlated with REM sleep duration (23). This study showed that as the PAP pressure requirement increases, our study's strength is that it is the first study to investigate and compare the effects of weight and symptom change on PAP pressure changes as the REM time increases.

The strength of our study is that it is the first study to investigate and compare the effects of weight and symptom change on PAP pressure change.

The limitations of our study are that the number of patients included in the study was limited, as sleep service hospitalizations were delayed due to the Coronavirus-2019 pandemic.

Conclusion

Weight gain, loss, or being the same weight did not significantly affect PAP pressure change. However, PAP pressure change was more common in symptom persistence under PAP treatment. More studies are needed on conditions that affect PAP pressure.

Ethics

Ethics Committee Approval: The İstanbul University-Cerrahpasa, Cerrahpasa Faculty Clinical Research Ethics Committee approved this study (no: E-83045809-604.01.02-2627).
Informed Consent: Informed consent was obtained from all individual participants included in the study.
Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.A., A.G., B.Ç.Ö., Concept: E.A., Design: E.A., B.Ç.Ö., Data Collection or Processing: A.G., Analysis or Interpretation: E.A., A.G., B.Ç.Ö., Literature Search: A.G., Writing: A.G.
Conflict of Interest: No conflict of interest was declared by the authors.
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