

# The effect of long-term continuous positive airway pressure treatment on systolic and diastolic function in patients with obstructive sleep apnoea syndrome: A five year observational study

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## ABSTRACT

**Objective:** Evaluation of the long-term effects of continuous positive airway pressure (CPAP) on mean heart rate and left ventricular systolic and diastolic parameters in obstructive sleep apnea syndrome (OSAS) using conventional and tissue Doppler techniques.

**Methods:** This prospective cohort study is designed to evaluate the long-term effects of CPAP treatments in normotensive OSAS patients. Initially 40 patients aged from eighteen to fifty five with documented OSAS syndrome were evaluated within one month of CPAP treatment. All had high self-reported compliance with treatment. From the latter, 21 patients with uninterrupted CPAP therapy (for at least 5 years, 5 hours per day) were included in the study and further evaluated with treatment. The left ventricular systolic function was assessed on apical four-chamber view using modified Simpson method and diastolic function was evaluated with classic transmitral pulsed and tissue Doppler techniques. Paired t test and Wilcoxon signed rank test had been used to compare the clinical and echocardiography data before and after treatment period.

**Results:** A comparison of values assessed after one month and after 5 years of CPAP therapy, revealed a significant increase in the acceleration time(AT) Em/Am ratio and ejection time (ET) (AT:  $p=0.04$ ; Em/Am ratio  $p=0.03$  ET:  $p=0.04$ ) while a significant decrease was observed on deceleration time (DT), isovolumetric relaxation time (IRT), myocardial performance index (MPI), mitral regurgitation (MR) and 24 hour mean heart rate (HR) in all subjects (DT:  $p=0.02$ ; IVRT:  $p=0.04$ ; MPI:  $p=0.01$ ; MR:  $p\leq 0.001$ ; HR:  $p=0.004$ ).

**Conclusion:** We observed a significant improvement in the left ventricular systolic and diastolic function and a significant decrease of 24-hour heart rate and mitral regurgitation with unchanged ejection fraction of the left ventricle with long-term CPAP treatment similar to short-term treatment studies. The long-term maintenance of the beneficial effect of CPAP throughout the 5 year long-term treatment can be one of the pathophysiologic mechanisms that may explain the decrease of cardiovascular mortality observed with long-term CPAP therapy in OSAS patients. (*Anadolu Kardiyol Derg 2014; 14: 265-71*)

**Key words:** obstructive sleep apnoea syndrome, positive continuous airway pressure therapy, systolic and diastolic dysfunction, tissue doppler, echocardiography

## Introduction

Obstructive sleep apnoea is the periodic reduction (hypopnoea) or cessation (apnoea) of breathing due to narrowing and collapse of the upper airways during sleep. The main symptoms are daytime sleepiness, loud snoring, witnessed breathing interruptions, or awakenings due to gasping or choking in the presence of at least 5 obstructive respiratory events per hour of sleep. Epidemiological studies provide evidence that obstructive sleep apnea syndrome (OSAS) is associated with cardiovascular complications such as systemic hypertension, congestive heart failure, and atrial fibrillation (1, 2). The recommended initial

treatment of choice in patients with moderate and severe OSAS is continuous positive airways pressure delivered through a face mask (CPAP) (3, 4). CPAP treatment reduce daytime sleepiness and improve the symptoms and health status in randomised placebo-controlled trials with coincident reductions in systemic hypertension, improvements in left ventricular systolic function, and reductions in sympathetic nervous activity (5, 6).

The combination of increased left ventricular (LV) afterload and increased heart rate (HR) secondary to increased SNA increases myocardial  $O_2$  demand in the face of a reduced myocardial  $O_2$  supply (7, 8). In patients with heart failure and OSA, CPAP improves sympathetic activity, cardiac sympathetic tone, cardiac afterload and systolic function (9).



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Diastolic dysfunction is associated with future occurrence of heart failure, and is a predictor of cardiovascular morbidity and mortality in the general population. Tissue Doppler imaging (TDI) is a newer echocardiographic tool that was suggested to be more sensitive in the early detection of LV diastolic function alterations than traditional Doppler flow methods. In particular, the combination of transmitral flow with TDI-derived diastolic phase parameters provides an estimation of LV diastolic performance that is less dependent on cardiac preload (10). TDI may be used for early non-invasive detection of impaired myocardial function in asymptomatic people with hypertension or diabetes without systolic dysfunction on conventional echocardiography (11).

Several studies addressed the impact of CPAP treatment in OSAS patients using conventional and tissue Doppler techniques. OSAS is associated with RV systolic and diastolic dysfunction, that can be improved by short term CPAP therapy (12). To the best of our knowledge, no study has addressed the long term effects of CPAP therapy ( $\geq 5$  years) on cardiac function using conventional and tissue Doppler imaging techniques. The goal of this study was to investigate whether the reported beneficial cardiac effects of CPAP therapy are sustainable at long term or disappear or worsen as reported in long term follow up of patients with diabetes despite adequate insulin therapy and glycemic control.

## Methods

### Study design and patient population

The study is designed as a prospective cohort study. The study protocol was first submitted to the University hospital Institutional Review board and then approved by the local Ethic Committee. All patients signed written informed consent forms approved by the University hospital Institutional Review board. Patients were ineligible if they had any major ongoing disease other than sleep apnea. Exclusion criteria were pregnancy, diabetes mellitus, chronic obstructive pulmonary disease, coronary or valvular heart disease, or severe kidney or hepatic failure, systolic dysfunction ( $LVEF \leq 40$ ) and hypertension. Only patients whose blood pressure was under 140/90 mm Hg were enrolled in order to prevent the introduction of a bias with antihypertensive medications over the 5 years follow-up period. Forty patients aged from eighteen to fifty-five with OSAS syndrome (documented in sleep laboratory of the University hospital) were evaluated at baseline within one month of the beginning CPAP treatment. As we planned a long term study, the compliance of patients with CPAP therapy was crucial. It was reported that the pattern of adherence is established early, within the first weeks of treatment, and predicts long-term use. Those who skip nights of treatment also use CPAP for shorter nightly durations—on average, 3 hours per night (13). Therefore the patients were reevaluated 2 weeks after the titration and the initiation of CPAP treatment. They were asked to quantify their CPAP use as hours per night. Only patients who had more than 5 hours of CPAP use every night were enrolled in the study. At the end of the follow-

up period, 21 patients with uninterrupted CPAP therapy for at least 5 hours per night during the 5 years period were included in the final study and were further evaluated. Routine transthoracic two-dimensional echocardiography, Doppler, and tissue Doppler imaging studies were performed in the cardiology department outpatient clinic within one month of the initiation of CPAP therapy and after 5 years of CPAP treatment. The mean heart rate was assessed before and after treatment period with a commercial Holter recording and analysis system over 24 hours of data (DMS 300 Holter recorder with Cardioscan 2 DM software). Demographic and clinical baseline data were compared with 5 years late values.

### Polysomnography

Patients included in this study were referred to the neurology department sleep unit due to OSAS related symptoms. They underwent at least one standard overnight PSG at a dedicated sleep laboratory with Smart Sleep System manufactured by Medcare Flaga, Reykjavik, Iceland. The central and occipital electroencephalogram, bilateral electrooculogram, submental electromyogram, bilateral leg electromyogram and electrocardiogram were recorded. The positions of the subject, respiratory airflow (nasal cannula connected to pressure transducer), respiratory efforts (strain gauge) and arterial oxyhaemoglobin saturation ( $SpO_2$ , Ohmeda 3700 pulse oximeter, measured by finger sensor, averaging time 3 s) were measured. Obstructive apnoea was defined as absence of airflow with persistent respiratory effort lasting longer than two baseline breaths, irrespective of  $SpO_2$  changes. Obstructive hypopnoea was defined as reduction of airflow of 50% or more with persistent respiratory effort lasting longer than two baseline breaths and associated with oxygen desaturation of at least 4% and/or arousals. The apnoea–hypopnoea index (AHI) was the total number of obstructive apnoeas or hypopnoeas per hour of sleep. Oxygen desaturation index (ODI) was defined as the total number of dips in arterial oxygen saturation  $\geq 4\%$  per hour of sleep. Arousal was defined as an abrupt shift in electroencephalogram frequency during sleep, which may include theta, alpha and/or frequencies greater than 16 Hz but not spindles, of 3-15 s in duration. In REM sleep, arousals were scored only when accompanied by concurrent increases in submental electromyogram amplitude. Arousal index (Ari) was defined as the number of arousals per hour of sleep. OSA was defined if  $AHI \geq 5$  per hour of sleep (14).

### Echocardiographic study

All patients underwent transthoracic echocardiographic evaluation including 2-dimensional (2D), M-mode, pulsewave Doppler imaging and TDI according to the recommendations of the American Society of Echocardiography (15) using a commercially available system (Vivid 3, GE Ultrasound system using a 1,7 MHz harmonic transducer). The same machine was used in the initial and 5 year follow-up evaluations. The patients were monitored through a single-lead electrocardiogram and were examined in the left lateral recumbent position using standard

parasternal (short-and long-axis) and apical views (two-chamber, four chamber, and long-axis). Left ventricular end-diastolic diameter mm, LV end-systolic diameter mm, interventricular septum diameter (IVSd; mm) at end-diastole, and posterior wall diameter (PWd; mm) at end-diastole were measured with the M mode echocardiography. RV diameters were detected by two-dimensional echocardiography in apical four -chamber view. Global LV function was assessed by LV ejection fraction using the modified biplane Simpson's rule (15).

#### Left atrium measurements

The left atrial (LA) dimension was measured at end-ventricular systole in the parasternal long-axis view according to ASE recommendations.

#### Mitral regurgitation evaluation

The MR jet was graded as first (<1.5 cm), second (1.5-2.9 cm)-, third (3.4-4 cm) and fourth-degree (>4.5 cm) by color Doppler imaging. The regurgitant jet area within the left atrium was measured by planimetry from the frame with the maximal jet area during systole. The jet area was expressed as an absolute value and as a percentage of the left atrial area (<20%=1. degree, 20-40%=2. degree and >40%=3. degree).

#### Doppler evaluation

The following transmitral Doppler parameters were analyzed: peak early (E) and late (A) transmitral filling velocities, the ratio of early to late peak velocities (E/A) and deceleration time of E wave (DT). The IRT, defined as the time from aortic valve closure to mitral valve opening, was assessed by simultaneous measurement of the flow into the LV outflow tract and mitral inflow by Doppler echocardiography (15). The LV outflow velocity curve was recorded from the apical long-axis view with the Doppler sample volume positioned just below the aortic valve.

Time intervals were also measured from mitral inflow and LV outflow recordings. The time interval "a" from the cessation to the onset of mitral inflow was equal to the sum of ICT, ET, and IRT. Left ventricular ET "b" was the duration of the LV outflow velocity profile. The MPI, which combines parameters of both systolic and diastolic ventricular function, is defined as the sum of isovolumetric contraction time (ICT) and isovolumetric relaxation time (IRT) divided by ejection time (ET), and reflects both systolic and diastolic cardiac function. The MPI was calculated as  $(a - b)/b$  (16).

The sum of ICT and IRT was obtained by subtracting "b" from "a". The ICT was obtained as  $(a-b)-IRT$ .

#### Diastolic function evaluation

LV and RV diastolic indices were assessed from the apical four-chamber view by positioning a sized 2-4 mm sample volume at the tips of mitral and tricuspid leaflets accordingly, during diastole and at end-expiration. The following RV and LV diastolic indices were calculated: peak velocity of E wave, representing early filling; peak velocity of A wave, representing late filling;

ratio of peak early to peak late velocity (E/A); deceleration time of E wave (DTE); and finally filling time (FT). Furthermore, from the apical 5-chamber view and by positioning a sized 2-4 mm sample volume at the LV outflow tract, the LV outflow tract velocity time integral was assessed (LVOT VTI). Isovolumetric relaxation time was obtained from the apical five- chamber view and MPI was measured according to the formula:  $MPI=(IRT+ICT/ET)$ . All Doppler indices were measured at six consecutive beats and averaged.

#### Tissue Doppler evaluation

Doppler tissue myocardial velocities were measured in the apical 4-chamber view sampling the lateral mitral annulus, as septal Ea velocities are slightly lower than lateral Ea velocities because of intrinsic differences in myocardial fiber orientation. Peak systolic myocardial wave Sm is measured as a good estimate of left ventricular systolic function. Early and late diastolic peak myocardial velocities (Em and Am), as well as their ratio (Em/Am), were recorded in order to evaluate diastolic relaxation of the left ventricle with tissue Doppler technique. The combination of early transmitral inflow velocity and mitral annular tissue Doppler imaging (E/Em ratio) was also calculated as it was widely applied to noninvasively estimate LV filling pressures. Several cardiac cycles were evaluated and the best 3 consecutive ones were analyzed and averaged.

#### Statistical analyses

As the number of patients enrolled in the final study was limited to 21 individuals after drop-outs, the Kolmogorov-Smirnov test was performed for testing the assumption of normality of echocardiography data. The test revealed that the data belongs to Gaussian distribution. Therefore, for paired comparisons of continuous variables, a paired sample T test was performed for statistical analysis of study data. The non parametric Wilcoxon signed-rank test was used to evaluate the rate of occurrence of the mitral regurgitation; blood pressure and heart rate before and after treatment. All analyses were performed using a SPSS 13.0 packet program (SPSS Inc., Chicago, IL, USA). Descriptive statistics were provided for the numeric and categorical variables using mean, standard deviation, and per cent distributions where necessary. A p value of <0.05 was used as the cutoff for statistical significance. In subsample multiple analysis of data as comparing males to females, a Bonferoni adjustment had been used as suggested by Perneger et al. (17) for multiple test adjustments.

## Results

#### General results

The demographic characteristics of patients are summarized in Table 1. There was no significant difference between body mass index (BMI) of patients compared to the beginning and the end of the 5 years period. Initially 40 OSAS patients receiving CPAP treatment for one month were enrolled for long term cardiologic follow-up of CPAP treatment with Doppler echocardiog-

**Table 1. The demographic characteristics of patients with 5 year uninterrupted CPAP treatment**

	N	BMI Before	BMI After	BMI P value	Age
Female	9	29.8±5.4	29.9±4.8	NS	54.1±8.2
Male	12	30.3±3.4	30.3±3.8	NS	58.9±9.1
Total	21	30.1±4.2	30.1±3.1	NS	56.9±8.8

Data are presented as mean±standart deviation.  
BMI - body mass index

**Table 2. Comparison of clinical variables at the beginning and the end of the 5 year period**

	Initial data Mean±SD	5 years later Mean±SD	P value (p<0.05)
Heart rate (beats per minute)	77±2	71±4	0,004
Systolic blood pressure, mm Hg	130±6	125±7	NS
Diastolic blood pressure, mm Hg	84±5	81±4	NS

Data are presented as mean±standart deviation. Wilcoxon signed-rank test had been used to compare clinical data before and after CPAP treatment

raphy. The dropout rate was high as many people migrate to bigger cities in order to improve their financial situation. After dropouts for various reasons over the 5 year period, 21 remaining patients, (9 women 12 men) completed the uninterrupted 5 year CPAP treatment. The mean age was 56.9±8.8 and mean body mass index (BMI) was 30.1±4.2 (Table 1). These patients were followed regularly by the neurology department sleep unit throughout the 5 year period for regular control of their compliance to CPAP treatment. They claimed to use the CPAP treatment for at least 5 hours every night. They were free of OSAS symptoms as daytime sleepiness, loud snoring, witnessed breathing interruptions, or awakenings in the night at the time of cardiac evaluation. The apnea-hypopnea index (AHI) is an index of severity that combines apneas and hypopneas. The male patients had significantly more AHI compared to female patients (Males AHI: 27.9±14.4 Females AHI: 10.5±9.1 p=0.03). Even though there was a trend to decrease on blood pressure after the 5 year treatment period, the difference was not significant. The mean heart rate assessed by 24-hour Holter recordings was significantly lower after the treatment period (p=0.004) (Table 2).

### Echocardiogram and Doppler results

The Doppler parameters of the patients at the beginning and at the end of the 5 years period are given on Table 3. Classical Doppler parameters, AT and ET increased while DT, IVRT and MPI values decreased in a statistically significant way after 5 year treatment with CPAP. The tissue Doppler measurements Sm values were similar at the beginning and the end of the treatment. Similary the E/Em ratio widely used to estimate the filling pressure of the left ventricle was also reduced after 5 years of treatment but the difference was not statistically significant. The value of Em also increased with long term treatment but the increase did not reach statistical significance. The Em/Am ratio

was increased after long term CPAP treatment and was the only tissue Doppler parameter that differ statistically (Table 3).

The left ventricle posterior wall thickness in male and female patients decreased but the difference was not significant after Bonferoni correction for multiple group comparison over the 5 year period of CPAP treatment (Table 4, 5).

On color Doppler 66% of OSAS patients had grade 1 mitral regurgitation while 9.5% had grade 2 MR after a month of CPAP treatment. After 5 years of uninterrupted CPAP treatment only 14.3% of the patients had grade 1 MR (Fig. 1). There was a significant decrease on the mitral regurgitation occurrence in patients at the beginning and the end of 5 year treatment period (p<0.001).

### Discussion

Doppler studies investigating OSAS patients with short time CPAP treatment revealed the beneficial effect of CPAP treatment on cardiac function. The 6 month CPAP treatment follow-up study by Bayram et al. (18) suggest a significant increase in LV septal and lateral wall Em velocity and Em/Am ratio and a decrease in IVRT and DT. Arias et al. (19) reported an increase in E/A ratio and a decrease in DT and IVRT among the diastolic parameters with a 12 week CPAP therapy in 27 patients with OSAS. The study of Dursunoğlu et al. (20) suggest a significant decrease of MPI and decrease of left ventricular wall thickness after 6 months of CPAP therapy.

To the best of our knowledge our study is the first long term (≥5 years) follow-up study of the cardiac effects of CPAP treatment evaluated by conventional and tissue Doppler echocardiography. The present study was designed to determine whether the beneficial cardiac effects of short term CPAP therapy reported by prior studies were still maintained after 5 years of treatment or offset by other factors such as ageing. The most important finding of our study was the maintained improvement of diastolic parameters IVRT, DT, MPI and Em/Am ratio after 5 years of treatment as suggested in previous studies evaluating the short term effects of CPAP treatment.

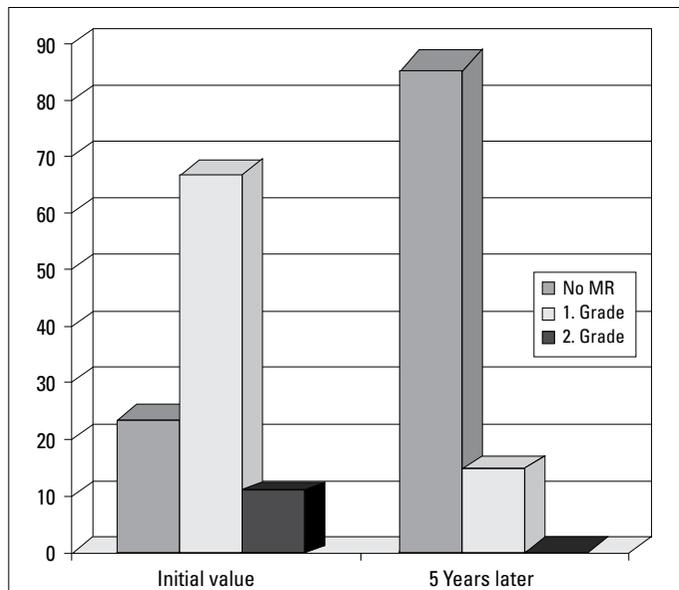
The Doppler-derived myocardial performance index (MPI, also denoted the Tei-Doppler index), evaluating the combined systolic and diastolic function, is defined as the sum of isovolumetric contraction time and isovolumetric relaxation time divided by the ejection time. In the presence of ventricular global dysfunction, MPI increases in contrast to normal ejection fraction (EF) of the left ventricle. MPI is a reproducible and simple non-invasive method for the estimation of ventricular global function. It is observed to increase in OSAS patients and to correlate with the apnoe-hypopnea index. It was reported to decrease significantly even with very short term CPAP treatment of one three and six months (21).

Abd El Rahim et al. (22) found a high sensitivity and specificity of the Tei index for the detection of patients with elevated left ventricular (LV) filling pressure and a correlation (p<.0001) between the Tei index and pulmonary capillary wedge pressure

**Table 3. Comparison of diastolic ve systolic Doppler parameters at the beginning and at the end of the 5 year period**

	Initial data n=21 Mean±SD	5 years later n=21 Mean±SD	P value (p<0.05)
E-Vel, cm/sn	71.57±27.47	69.29±14.70	0.72
A-Vel, cm/sn	77.05±11.61	77.76±13.56	0.79
E/A	0.92±.27	0.88±0.21	0.60
AT, msec	108.14±25.62	129.82±33.93	0.04
DT, msec	221.24±29.53	214.86±27.41	0.02
IVRT, msec	96.33±11.11	91.19±8.52	0.04
IVCT, msec	69.95±13.93	70.29±11.27	0.89
ET, msec	277.43±39.76	285.48±33.53	0.04
MPI, %	0.60±0.09	0.56±0.06	0.01
Sm, cm/sec	9.32±1.38	9.39±1.31	0.16
Em, cm/sec	9.11±1.59	9.42±1.54	0.12
Am, cm/sec	10.34±1.72	10.02±1.57	0.19
Em/Am	0.92±0.26	0.96±0.26	0.03
E/Em	6.63±1.55	7.61±2.35	0.11

Data are presented as mean ± standard deviation. Paired t test is used to assess the evolution of parameters before and after CPAP treatment.  
Am - late diastolic myocardial peak velocity; A Vel- velocity of the A wave;  
AT - acceleration time; DT - deceleration time; Em - rarly diastolic myocardial peak velocity; E-Vel - Velocity of the E wave; ET - ejection time; IVRT - isovolumetric relaxation time; IVCT - isovolumetric contraction time; MPI - myocardial performance index (Tei index); Sm- systolic myocardial velocity



**Figure 1. Percentage distribution of patients with mitral regurgitation in patients before and after 5 year uninterrupted CPAP treatment period (PCWP). Myocardial performance index was suggested as a predictor for cardiovascular mortality, independent of other measurements of cardiac function and of traditional cardiovascular risk factors in a cohort study of Årnlöv et al. (23) on 583 seventy-year-old men free from coronary heart disease with a mean follow-up time of 6.8 years. The same authors suggested**

**Table 4. Comparison of echocardiographic parameters before and at the end of the 5 year period in male patients**

	Initial data n=12 Mean±SD	5 years later n=12 Mean±SD	P value (p<0.05)
LV mass, g	189.75±46.94	194.83±45.46	0.61
PW, cm	1.14±0.08	1.09±0.12	0.08
IVS, cm	1.14±0.12	1.16±0.11	0.54
PABS, mm Hg	16.33±8.01	17.00±5.64	0.85
LV EF, %	62.42±3.65	62.83±3.21	0.80

IVS - interventricular septum; LA - left atrium; LVEF - left ventricular ejection fraction;  
LV mass - left ventricular mass index; PABS - pulmonary arthey systolic pressure;  
PW - posterior wall

**Table 5. Comparison of echocardiographic parameters before and at the end of the 5 year period in female patients**

	Initial data n=9 Mean±SD	5 years later n=9 Mean±SD	P value (p<0.05)
LV mass, g	154.22±37.88	162.00±36.26	0.60
PW, cm	1.01±0.09	0.9667±0.18	0.48
IVS, cm	1.03±0.11	1.08±0.20	0.45
PABS, mm Hg	19.11±10.04	19.11±9.99	1.00
LV EF, %	63.56±2.01	62.44±4.13	0.47

IVS - interventricular septum; LA - left atrium; LVEF - left ventricular ejection fraction;  
LV mass - left ventricular mass index; PABS- pulmonary arthey systolic pressure;  
PW - posterior wall

MPI provides important prognostic information for the risk of future CHF, beyond other measurements of cardiac function and traditional heart failure risk factors in elderly men (24). Patients with diabetes have higher MPI values compared to normal people (25). In stable coronary disease patients with normal ejection fraction the MPI value was impaired in proportion to the severity of CAD (26). Weight loss suggested a decrease of MPI index (27). The decrease of MPI with long term CPAP treatment may account for another beneficial effect of long term treatment.

The rate of occurrence of mitral regurgitation observed in our study was significantly reduced after 5 years treatment. We can speculate that the reduction of the afterload with CPAP treatment may be responsible for this finding. The mainstay of medical treatment in most other cases of mitral regurgitation is afterload reduction. Afterload reduction decreases the impedance to left ventricular ejection and, as a result, decreases the regurgitant volume.

Our patients had significantly lower heart rates after long term treatment suggesting a decrease of sympathetic system activity. Studies suggest that severe OSA is independently associated with pulmonary hypertension in direct relationship with disease severity and application of CPAP reduces pulmonary systolic pressure levels (28). The E/Em ratio described as a predictor of left atrial pressure was also found to be reduced in our study however, the observed difference was not statistically significant.

Our study did not confirm the significant increase of Em velocity and decrease of E/Em ratio suggested with prior studies even though The absence of a significant decrease in the Em may be related to the low number of the subjects in our study or the absence of additional benefit of long term treatment. Even in the latter case scenario, the maintenance of unchanged cardiac function as evaluated by tissue Doppler with long term 5 year treatment can still be considered beneficial. A recent 5 year follow up study by Vintila et al. (29) suggested a significant decrease of systolic and early diastolic myocardial velocities by 13% and 20%, respectively despite improved glycemic control in diabetic patients - a systemic disease affecting diastolic function as sleep apnoea syndrome.

Several studies reported the occurrence of left ventricular hypertrophy in OSAS patients and the severity of LV hypertrophy may be related to the degree of severity of OSAS (30). Treatment with CPAP is reported to decrease the left ventricular hypertrophy even after 6 month treatment in hypertensive OSAS patients (12). Five years treatment with CPAP decreased the posterior free wall thickness mostly in men in our study but the difference did not reach statistical significance after Bonferoni correction. It can be speculated that the exclusion of hypertensive patients from the study may explain the absence of significant reduction of wall thickness with long term CPAP treatment. Similarly the blood pressure of patients did not differ significantly with CPAP treatment even though a trend to decrease was observed in systolic and diastolic blood pressure values after treatment.

### Study limitations

One potential limitation of the study is the limited number of patients evaluated after a 5 year treatment period. 40 patients were initially planned for the study but many patients could not be reached by telephone while some refused to submit to a cardiologic evaluation as they moved away of Manisa city.

Initially a two year midway follow-up evaluation was planned but could not be done as only a very few patients agreed to come for echocardiographic evaluation at this time.

As we were planning a long term study only patients who were evaluated as compliant to CPAP therapy within two weeks of the initiation of CPAP therapy were enrolled in the study. Therefore we did not have the echocardiography Doppler data of patients before the initiation of CPAP treatment to be compared to our initial results obtained within one month of CPAP therapy.

### Conclusion

The results of this study confirm the ongoing beneficial cardiovascular effects of short term CPAP therapy in OSAS patients with a 5 year long term treatment. Our results support the necessity of providing the OSAS patients with CPAP treatment on a long term basis. The decrease of MPI index may predict improvement of cardiac function and also the decrease of the

risk of the development of heart failure and cardiac death in OSAS patients with long term CPAP treatment. MPI index and Doppler evaluation may also be used to monitor the efficacy of CPAP therapy in OSAS patients during long term follow-up.

**Conflict of interest:** None declared.

**Peer-review:** Externally peer-reviewed.

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