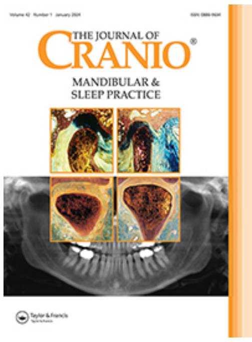

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SLEEP

The relationship between extracellular fluid and obstructive sleep apnea in non-obese patients

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ABSTRACT

Objective: To evaluate the relationship between obstructive sleep apnea syndrome (OSAS) and the fluid change in composition throughout the night.

Methods: The study included 92 non-obese patients who underwent polysomnography because of suspected OSAS. Weight and body composition analyses were applied using a Tanita DC-360 multi-frequency body composition analysis device.

Results: In the correlation analyses between apnea/hypopnea index (AHI) values and independent variables, a positive relationship was determined with extracellular fluid shift (r: 0.381, $p = 0.009$) and change in neck circumference (r: 0.226, $p = 0.031$), and there was a negative relationship between disease severity and an increase in the number of daily steps taken (r: 0.208, $p = 0.047$).

Conclusion: The results of the study clearly showed that movement to the neck area of fluid accumulated in the lower extremities and an increase in extracellular fluid were related to AHI values independent of body mass index (BMI).

KEYWORDS
Obstructive sleep apnea syndrome; body composition analysis; extracellular fluid shift

Introduction

Obstructive sleep apnea syndrome (OSAS), which affects 5–10% of the general population, is a disease that causes severe morbidity [1]. Although previous studies have revealed that it is associated with recurrent collapse of the upper respiratory tract during sleep, and causes such as obesity have been held responsible, the underlying etiology is not yet fully understood [2,3].

Several studies have reported that obesity is the most important risk factor for OSAS, but a community-based study found that only 40% of patients were obese, and OSAS is not seen in all obese individuals [4]. This suggests that factors other than obesity could play a role in the etiology. Recent studies of the etiopathogenesis of OSAS have focused on the change occurring in body fluid composition during sleep, which could cause the disease or play a role in increasing severity [5–7].

That OSAS is seen more in low bodyweight patients with heart and kidney failure than in the general population supports the view that there may be a relationship between fluid involvement or impaired dispersion and OSAS. According to this theory, with the prone position in sleep, the fluid that has accumulated in the lower extremities throughout the day shifts rostrally to the neck and, by accumulating in peripharyngeal soft tissue, causes an increase in upper airway tract resistance [5–9].

Body fluid is known to be in the three basic localizations of intravascular, intracellular, and extracellular areas, and moves dynamically according to various factors [5,10]. Although it has been reported in studies of OSAS patients in the literature that interstitial fluid moves from the legs and trunk to the neck within hours or even minutes of lying down [5,10], in which compartment the basic change occurs (intracellular or intercellular) is a point which has been ignored. To date, there have been no studies on this subject.

To evaluate the intracellular and intercellular fluid composition of the patients in this study, the electrical bioimpedance method was used with measurements taken on a Tanita DC-360 multi-frequency body composition analysis device (Tanita Corporation, Tokyo, Japan). Ritchie et al. [11] showed that the Tanita system was a useful method in the evaluation of body composition and measurement of fluid distribution in adults. It was reported that this system was valid for adults, providing a measurement of body fat percentage and determining interstitial and intracellular fluid measurements non-invasively.

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It has also been shown in the literature that the use of multi-frequency provides basic data about intracellular and extracellular fluid, and in a very short time period, measures many variables from the fat and muscle mass of the patient to basal metabolism rate, levels of visceral fat, phase angle, and intracellular and extracellular body fluid [12].

The aim of this study was to evaluate the relationship between OSAS and the intracellular and extracellular fluid composition and the change in composition throughout the night.

Materials and methods

Study design and participants

Approval for the study was granted by the Local Ethics Committee (decision no: 2019–14/146). All procedures in the study were performed in accordance with the Helsinki Declaration.

This prospective study included 92 patients aged >18 years who were not obese (body mass index (BMI) <30 kg/m^2) and underwent polysomnography (PSG) because of suspected OSAS between January 2019 and November 2019. All the patients in the study were Caucasian. Patients were excluded if they had alcohol abuse, tonsil hypertrophy, congestive heart disease causing body edema, kidney failure, a history of any other chronic disease, or were using prescription drugs. Hypovolemic and cachectic patients were also excluded. It has been shown in previous studies that multi-frequency body composition analysis methods can give false results with increasing age, with 80 years accepted as the upper age limit [5]. Therefore, upper and lower age limits were set in the current study, and the patients included were in the age range of 18–60 years. As there are also studies in the literature showing that the hormonal changes occurring in the menstrual cycle in premenopausal women increase the severity of OSAS [13], the sleep studies of the premenopausal women in the study were applied in the luteal phase. This was ensured by measuring serum progesterone on the 21st day of the cycle and accepting those with a progesterone level of ≥5 ng/ml. All the patients were instructed not to consume alcohol or caffeine or take any sleeping medication for 12 hours before the sleep study.

Sleep studies

Objective evaluation of the sleep status of the patients included in the study was made according to the American Academy of Sleep Medicine (AASM) 2007 criteria using a PSG (Philips Respironics Alice 5, 2016, USA) device in the laboratory. After the patients went to sleep in a specially designed room, they were monitored by a qualified technician, and data were recorded with the standard method. The patients were monitored with the following channels: electroencephalogram (EEG), jaw electromyogram (EMG), electromyogram (EOG), respiratory (nasal/oral thermistor), electron activity, and leg EMG.

Apnea is defined as an interruption of at least 90% of the airflow lasting at least 10 s. Hypopnea is defined as a reduction of ≥50% of the airflow for 10 s or longer, related to ≥3% oxygen desaturation or arousal, which is defined as a sudden shift in EEG frequency lasting at least 3 s. AHI is defined as the number of apnea and hypopnea events throughout sleep, and the severity of OSAS is classified according to the AHI. The patients were separated into four groups according to the severity of OSAS. The groups were defined as follows: Group 1 [n = 23, normal (AHI <5)], Group 2 [n = 26, mild (AHI 5–14.9)], Group 3 [n = 20, moderate (AHI 15–29.9)], and Group 4 [n = 23, severe (AHI ≥30)].

Anthropometric measurements and body composition evaluation

The body weight and body composition analyses were applied using the electrical bioimpedance method with measurements taken on a Tanita DC-360 multi-frequency body composition analysis device (Tanita Corporation, Tokyo, Japan). Body weight and fat percentage (%), fluid ratio (%), extracellular fluid (lt), and intracellular fluid (lt) were recorded. The measurements were taken immediately before going to bed and within the first minute of getting out of bed in the morning. As soon as the patients went to bed, measurements were also taken of the neck at the upper edge of the cricothyroid cartilage and of the chest circumference to include both areola and the thickest part of the calf with a tape measure and recorded in cm. To ensure that measurements were made at the same level before and after sleep, the patient was marked. The measurements were repeated in the morning as soon as the patient woke and before urinating or having anything to eat or drink. The differences in the chest, neck, and calf circumferences after sleep compared to before sleep were calculated as the changes occurring during the night in these variables. The time between these measurements was accepted as the time in bed.

For standardization of factors thought to potentially affect the results, the patients were instructed to remove any jewelry, such as a necklace or wristwatch, and to empty the bladder 5 minutes before the procedures. The environment temperature was maintained at 22.3°C –

27.7°C to avoid any changes, such as sweating or hypothermia, which could cause changes in fluid composition. As anthropometric variables could be affected by the operator, all the measurements were taken by the same operator using the same measurement devices.

The parameters evaluated in the study included age, gender, BMI, nasal and oral airflow (using nasal oral thermal coupling and nasal pressure cannula), mean heart rate (HR), leg movements, and body position. The apnea/hypopnea index (AHI) and oxygen desaturation index (ODI) were scored automatically by the computer software and were then checked manually by the technician. The neck, chest, and calf circumference values within the anthropometric variables measured before sleeping and in the morning were recorded together with the fat percentage (%), fluid ratio (%), intracellular fluid (lt), and extracellular fluid (lt) measured on the Tanita DC-360 multi-frequency body composition analysis device. Finally, the mean number of steps taken per day was recorded according to the results for the previous 7 days on a telephone application downloaded by the patients.

Statistical analysis

Data obtained in the study were analyzed statistically using SPSS version 17.0 software (IBM Statistics for Windows version 17, IBM Corporation, Armonk, NY, USA). Conformity of continuous data to normal distribution was assessed with the Kolmogorov–Smirnov test. Quantitative variables were stated as mean ± standard deviation (SD) and median range (minimum-maximum) values. Multiple group comparisons were made with ANOVA and the Tukey HSD test. Categorical data were stated as number (n) and percentage (%). Consecutive measurements showing normal distribution were compared with the paired samples *t*-test, and non-parametric variables were compared with the Wilcoxon signed-rank test. In the evaluation of factors related to AHI, Pearson and Spearman correlation analyses were used. A value of $p < 0.05$ was accepted as statistically significant.

Table 1. Demographic data of patients.

		n = 92
Age (years)		50.6 ± 6.9
Sex (Male)		51 (55.4%)
BMI (kg m^2)		26.12 ± 3.52
OSAS severity	Normal (AHI <5)	23 (25.3%)
	Mild (AHI 5–14.9)	26 (28.6%)
	Moderate (AHI 15–29.9)	20 (22.0%)
	Severe (AHI ≥30)	23 (24.1%)

AHI: Apnea/hypopnea index h-1; BMI: Body mass index; OSAS: Obstructive sleep apnea syndrome

Results

The study included a total of 92 patients. The demographic characteristics of the patients are shown in Table 1. When the patients were grouped according to AHI, no statistically significant differences were determined between the groups in respect to demographic characteristics, such as age and gender, or in PSG data such as total sleep time (TST) (min), time in bed (TIB) (min), and sleep latency (SL) (min) ($p > 0.05$ for all) (Table 2). When the patients were evaluated with respect to anthropometric variables, the differences in Group 3 and Group 4 patients were seen to be greater than in the other groups, but not to a level of statistical significance ($p > 0.05$ for all).

The fat percentage (%), fluid ratio (%), and intracellular fluid (lt) values measured on the Tanita DC-360 multi-frequency body composition analysis device were seen to be higher in Group 4 especially, compared with the control group, but not statistically significant

Table 2. Comparisons between the groups of demographic and polysomnographic variables.

Characteristic	Control (AHI <5) (n = 23)	Mild (AHI 5–15) (n = 20)	Moderate (AHI 15–30) (n = 26)	Severe (AHI >30) (n = 23)	*p*
Age (years)	47.6 ± 9.2	52.0 ± 7.0	49.8 ± 6.0	52.7 ± 4.9	0.066
BMI (kg/m^2)	25.2 ± 4.0	24.6 ± 3.7	27.2 ± 3.0	27.2 ± 2.8	0.232
Gender (F/M)	12/11	11/9	7/19	11/12	0.187
Number of daily steps	9478.9 ± 1899.1	4331.7 ± 1842.3	3250.7 ± 1851.6	1884.0 ± 971.7	0.047
Polysomnographic study results					
TST (min)	329.8 ± 85.1	326.3 ± 158.0	308.4 ± 102.0	364.0 ± 86.5	0.077
TIB (min)	362.9 ± 88.1	369.2 ± 129.3	365.7 ± 88.2	405.5 ± 81.9	0.362
SL (min)	25.7 ± 19.9	24.2 ± 16.5	28.3 ± 19.5	26.7 ± 20.0	0.419
AHI (events/hr TST)	3.2 ± 1.2	10.0 ± 1.9	21.8 ± 4.4	80.1 ± 18.8	0.001
AI (events/hr TST)	1.4 ± 0.7	3.9 ± 3.2	9.6 ± 5.0	51.8 ± 15.6	0.001
ODI	4.3 ± 0.8	7.8 ± 4.5	11.2 ± 6.6	16.5 ± 8.2	0.001

Data are expressed as the mean ± SD or n (%), unless otherwise noted. One-way ANOVA (with Tukey HSD).
AHI: Apnea/hypopnea index h-1; AI: EEG-arousal index; BMI: Body mass index; ODI: Oxygen desaturation index; SL: sleep latency; TIB: time in bed; TST: total sleep time.

($p > 0.05$ for all). In the evaluation of the patients in respect to the change in extracellular fluid, a statistically significant difference was determined in Group 3 and Group 4 compared to the control group ($p = 0.001$, $p = 0.014$) (Figure 1).

In the correlation analysis applied between AHI values and independent variables, a positive relationship was determined between AHI and extracellular fluid shift (r: 0.381, $p = 0.009$) and change in neck circumference (r: 0.226, $p = 0.031$). A negative relationship was determined between AHI and an increase in the number of steps taken per day (r: 0.208, $p = 0.047$) (Table 3Table 4). The relationship between AHI values and extracellular fluid shift is shown in Figure 2. No statistically significant difference was determined in respect to extracellular fluid shift when the patients were evaluated according to gender ($p = 0.833$) (Figure 3).

The female patients were grouped as premenopausal (n = 19) and postmenopausal (n = 22), and the change in extracellular fluid was seen to be lower in premenopausal females compared to the postmenopausal females and the males, but not to a level of statistical significance ($p = 0.091$) (Figure 4).

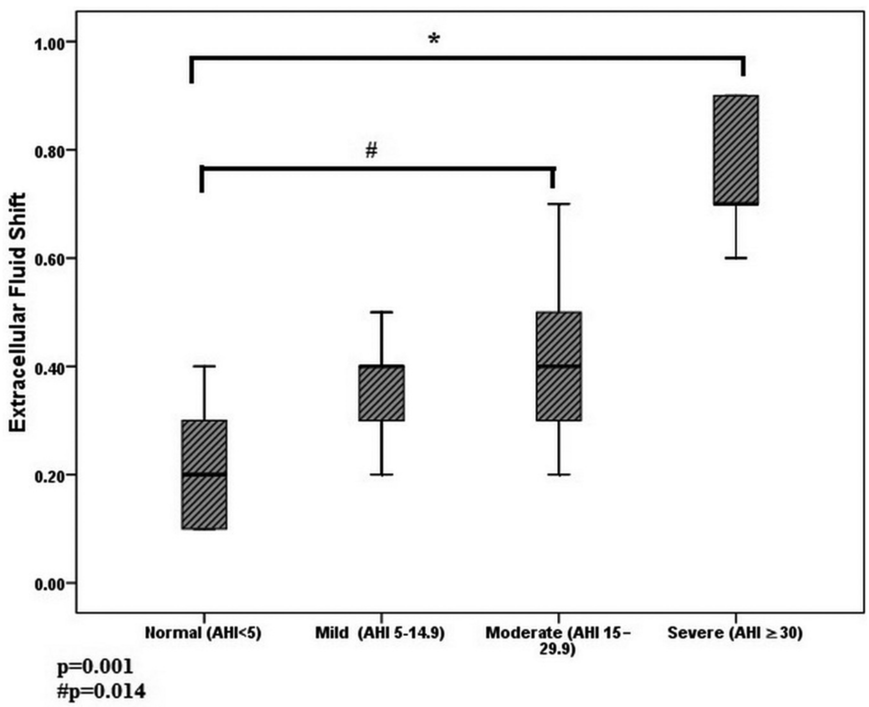

Figure 1. Comparisons between the groups of extracellular fluid shift.

Table 3. Respiratory variables in groups of two consecutive measurements.

	Control (AHI <5) (n = 23)			Mild (AHI 5–15) (n = 26)			Moderate (AHI 15–30) (n = 20)			Severe (AHI >30) (n = 23)		
	Night	Morning	*p*	Night	Morning	*p*	Night	Morning	*p*	Night	Morning	*p*
Neck circumference (cm)	42.4 ± 2.2	42.9 ± 2.2	0.896	42.2 ± 1.8	42.7 ± 1.8	0.897	41.7 ± 1.7	42.3 ± 1.7	0.850	42.5 ± 2.4	43.5 ± 2.5	0.652
Chest circumference (cm)	96.4 ± 12.1	97.1 ± 12.0	0.791	96.5 ± 10.0	97.2 ± 10.0	0.771	97.2 ± 13.1	98.1 ± 13.0	0.696	97.6 ± 13.0	98.6 ± 12.1	0.385
Calf Circumference (cm)	42.6 ± 3.7	42.5 ± 3.7	0.889	43.0 ± 4.0	42.5 ± 3.9	0.866	43.6 ± 4.3	43.0 ± 4.1	0.724	43.7 ± 3.5	42.7 ± 4.1	0.615
Fat rate (%)	29.9 ± 3.5	30.3 ± 3.6	0.723	28.4 ± 3.3	28.4 ± 3.5	0.828	29.0 ± 3.7	29.7 ± 3.4	0.814	29.8 ± 3.3	30.4 ± 3.4	0.504
Liquid ratio (%)	55.9 ± 4.3	55.6 ± 4.3	0.881	55.5 ± 3.3	55.3 ± 3.2	0.859	57.0 ± 2.8	56.4 ± 2.7	0.886	56.4 ± 2.8	55.8 ± 2.8	0. 860
Cell mass (kg)	33.7 ± 7.0	33.9 ± 7.2	0.814	34.5 ± 6.9	34.4 ± 7.0	0.857	32.9 ± 8.1	33.1 ± 10.0	0.759	34.2 ± 7.8	34.3 ± 7.8	0.926
Intracellular fluid (lt)	24.4 ± 5.1	24.2 ± 5.0	0.723	24.6 ± 5.0	24.2 ± 5.0	0.514	24.9 ± 5.0	24.4 ± 4.9	0.318	25.5 ± 5.0	24.7 ± 4.9	0.274
Extracellular fluid (lt)	18.3 ± 4.3	18.5 ± 4.4	0.856	18.6 ± 4.2	19.0 ± 4.2	0.323	18.9 ± 4 .2	19.4 ± 4.1	0.076	19.3 ± 3.8	20.0 ± 3.9	0.041

AHI: Apnea hypopnea index.

Table 4. Correlations between Apnea-Hypopnea Index (AHI) values and independent variables.

Variable	r	p
Age	0.220*	0.035
Body mass index (kg/m^2)	0.198	0.062
Change in neck circumference	0.226*	0.031
Change in calf circumference	0.113	0.286
Change in chest circumference	0. 201	0.056
Body fat rate	0.153	0.189
Extracellular fluid shift	0.381**	0.009
Number of daily steps	−0.208*	0.047

*Correlation is significant at the 0.05 level (2-tailed).
**Correlation is significant at the 0.01 level (2-tailed).

Discussion

The aim of this study was not to question the place and importance of obesity in OSAS etiology but to evaluate the underlying mechanisms in patients of normal weight. Thus, it is a study opening new horizons for new treatment modalities to be developed for OSAS. The present study is the first study to have evaluated the relationship between OSAS etiology and changes in intracellular and extracellular fluid. Although the results only showed a weak relationship, another point considered important was that an increase in daily activity (number of steps walked, taken as reference in this study) was significant in development of the disease or in reducing weight.

Several studies in the literature have reported a relationship between OSAS and age [5,14,15]. One of the basic reasons for this may be the decrease in physical performance together with advancing age, and there may be an increase in interstitial fluid associated with failure occurring in the valve mechanism of the leg veins or defects in the cardiac compliance mechanisms [5]. Although no significant difference was seen between the groups in the current study when they were evaluated in respect to age, there was determined to be a significant positive correlation between AHI and increased age (r: 0.220, p = 0.035). These results were seen to be consistent with findings in the literature.

When the current study patients were evaluated in respect to gender, no significant difference was determined between the groups in respect to extracellular fluid change (p = 0.833) (Figure 3). The premenopausal females in this study were all in the luteal phase of the menstrual cycle. Driver et al. [13] reported that upper airway resistance was significantly decreased during sleep in the luteal phase of the cycle compared to the follicular phase. This was attributed to the stimulating effect of progesterone on the upper respiratory tract muscle system. It was also emphasized that clinicians should take the menstrual cycle into account in the diagnosis and treatment protocols for females of child-bearing age. In a recent study of non-obese OSAS patients, females were excluded from the study to avoid the potential effects of this situation [5]. An interesting result in the current study was that, although the difference was small, the extracellular fluid shift in the female patients in the luteal phase was different from

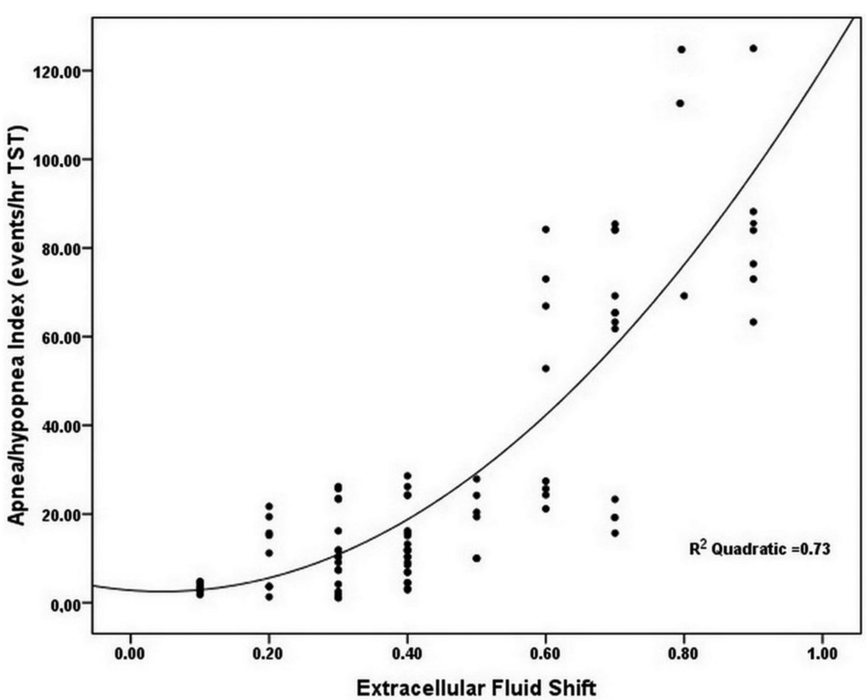

Figure 2. The relationship between rostral extracellular fluid shift and apnea-hypopnea index (AHI).

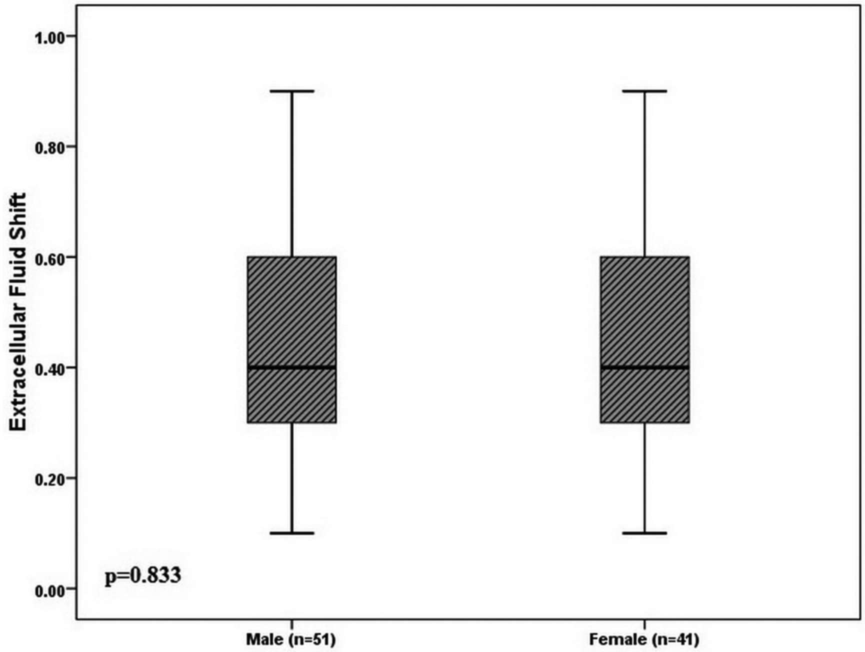

Figure 3. Rostral extracellular fluid shift in patients grouped according to gender.

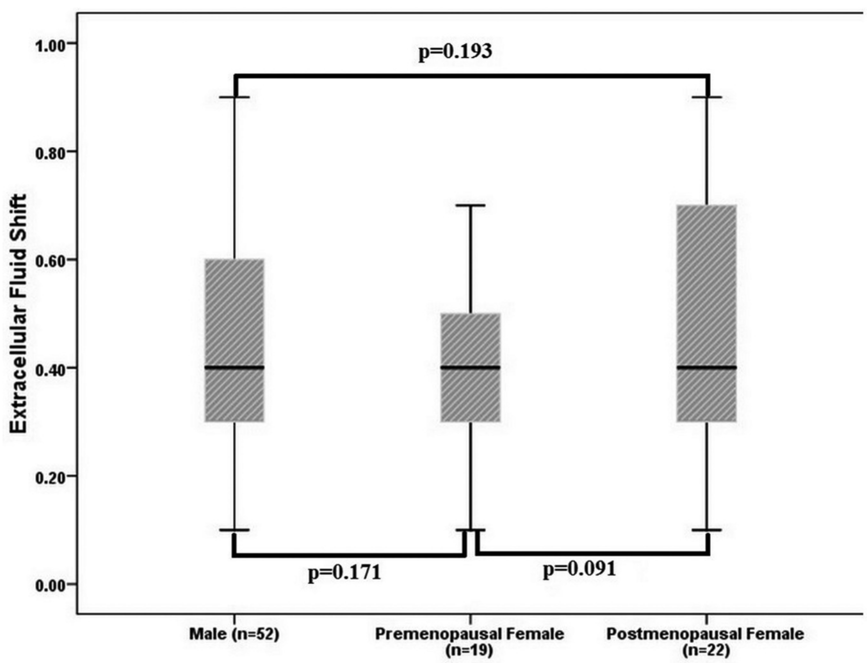

Figure 4. Rostral extracellular fluid shift in premenopausal, postmenopausal, and male patients.

that of males and postmenopausal females (p = 0.091). The basic reason for the lower fluid shift in premenopausal females was that the mean age of the patients in this group was lower than that of the other two groups. The extracellular fluid shift in postmenopausal patients was observed to have developed in a wider range. When the data were re-examined, this was not seen to have been caused by outlier values, but the main reason was that despite the strict exclusion criteria, the fluid shift that could develop could be increased by age. When the premenopausal women were evaluated within the group with male patients, the level of significance between the groups was seen to be lower (p = 0.171).

There are many studies in the literature, especially within the last 10 years, on OSAS etiology in both obese and non-obese patients, which have shown that fluid accumulated in the legs with the effect of gravity throughout the day shifts to the thorax and, especially, the neck region, and this is directly related to the disease and the severity of the disease [5–9]. In a study by Redolfi et al. [10], it was reported that after the application of lower body positive pressure to non-obese individuals, approximately 160–190 ml of fluid in each leg shifted to the upper trunk and neck region, and this reduced upper airway tract caliber and increased resistance [10]. In another more recent study by Redolfi et al. [5], there was found to be a spontaneous shift of this fluid from the legs to the neck during sleep, and this was reported to be strongly and independently related to AHI. In the current study, although there was determined to be an increase in the neck and chest measurements and a decrease in the calf measurements in the morning, the difference from the previous measurements taken before sleep was not statistically significant.

However, the basic aim of this study was to evaluate from which compartment the fluid shift occurred. When the results were evaluated in this respect, the fluid shift was seen to occur in the interstitial space. This was correlated with AHI values and suggested that more fluid pooled in the interstitial area in patients with high AHI values and could contribute to the pathogenesis of OSAS even in non-obese patients.

It is not possible to link the underlying pathophysiological mechanism of OSAS to a single condition. However, in previous studies of this subject, a consensus has been reached that a sedentary lifestyle is an important factor [5,16–18]. It has been reported that high capillary hydrostatic pressure that occurs especially when sitting or standing without moving for long periods causes fluid leakage into the interstitial areas. However, the reduction in venous pressure that occurs with muscle movement prevents fluid leakage. In two separate studies by Peppard [19] and Quan [20], performing exercises was seen to have an effect on reducing the severity of OSAS. In a recent study by Redolfi et al. [5], it was also shown that there was a positive correlation between the time spent sitting during the day and OSAS severity and that exercise had a reducing effect. No special studies were requested of the patients in the current study, and the authors aimed to evaluate whether or not there was an association between the amount of daily walking and OSAS severity. Therefore, the patients were requested to download a pedometer application onto their cell phones, and evaluation was made of the relationship between AHI and the mean number of steps taken in a week. Even though the patients made no extra effort for exercise, the severity of OSAS was seen to be reduced in patients with a higher number of daily steps.

The most important limitation of this study was that, for technical reasons, the extracellular fluid shift could not be specifically evaluated in the neck region, and evaluations were only able to be made for the chest and neck. Nevertheless, this study can be considered to be of value and guidance for further studies of this type. Another limitation of the study was that the change in airway associated with a change in head position was not evaluated. For example, there may be changes in the airway with a change of head position toward the anterior or posterior. Although this was not evaluated in this study, the association between head position and airway is an important point that should be evaluated in future studies.

Conclusion

There are still several points to be clarified in the etiopathogenesis of OSAS, especially in non-obese patients. When examined from this perspective, the results of this study clearly show that there is a relationship between AHI values and the shift of fluid accumulated in the lower extremities to the neck region and the increase in fluid in extracellular areas, irrespective of BMI. Despite the focus of previous studies, another result obtained from the current study was that increased exercise throughout the day reduced extracellular fluid leakage, suggesting that this could be used effectively in protection against the disease or in the treatment process. Finally, it was also seen that PSG procedures can be applied safely in the luteal phase of premenopausal females.

Disclosure statement

The authors have no conflict of interest to declare.

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References

[1] Punjabi NM. The epidemiology of adult obstructive sleep apnea. Proc Am Thorac Soc. 2008 Feb 15;5 (2):136–143. DOI:10.1513/pats.200709-155MG.

[2] Kosacka M, Porębska I, Jankowska R. Decreased sL-selectin serum levels in sleep apnea syndrome patients with cardiovascular diseases. Adv Clin Exp Med. 2017 May-Jun;26(3):449–453. DOI:10.17219/acem/62215.

[3] Boyacı H, Gacar K, Barış SA, et al. Positive airway pressure device compliance of the patients with obstructive sleep apnea syndrome. Adv Clin Exp Med. 2013 Nov-Dec;22(6):809–815.

[4] Young T, Shahar E, Nieto FJ, et al. Sleep heart health study research group. Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. Arch Intern Med. 2002;162:893–900.

[5] Redolfi S, Yumino D, Ruttanaumpawan P, et al. Relationship between overnight rostral fluid shift and obstructive sleep apnea in nonobese men. Am J Respir Crit Care Med. 2009 1;179(3):241–246. DOI:10.1164/rccm.200807-1076OC.

[6] White LH, Bradley TD. Role of nocturnal rostral fluid shift in the pathogenesis of obstructive and central sleep apnoea. J Physiol. 2013 1;591(5):1179–1193. DOI:10.1113/jphysiol.2012.245159

[7] Perger E, Jutant EM, Redolfi S. Targeting volume overload and overnight rostral fluid shift: a new perspective to treat sleep apnea. Sleep Med Rev. 2018 Dec;42:160–170. DOI:10.1016/j.smrv.2018.07.008

[8] Carlisle T, Ward NR, Atalla A, et al. Investigation of the link between fluid shift and airway collapsibility as a mechanism for obstructive sleep apnea in congestive heart failure. Physiol Rep. 2017;5(1):pii: e12956.

[9] Ogna A, Forni Ogna V, Mihalache A, et al. Obstructive sleep apnea severity and overnight body fluid shift before and after hemodialysis. Clin J Am Soc Nephrol. 2015 5;10(6):1002–1010. DOI:10.2215/CJN.08760914.

[10] Redolfi S, Yumino D, Ruttanaumpawan P, et al. Association between overnight fluid shift and obstructive sleep apnea. Am J Respir Crit Care Med. 2008;177:A484.

[11] Ritchie JD, Miller CK, Smiciklas-Wright H. Tanita foot-to-foot bioelectrical impedance analysis system validated in older adults. J Am Diet Assoc. 2005;105(10):1617–1619.

[12] Vasold KL, Parks AC, Phelan DML, et al. Reliability and validity of commercially available low-cost bioelectrical impedance analysis. Int J Sport Nutr Exerc Metab. 2019 Jul 1;29(4):406–410. DOI:10.1123/ijsnem.2018-0283.

[13] Driver HS, McLean H, Kumar DV, et al. The influence of the menstrual cycle on upper airway resistance and breathing during sleep. Sleep. 2005 Apr;28(4):449–456. DOI:10.1093/sleep/28.4.449.

[14] Young T, Palta M, Dempsey J, et al. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med. 1993;328:1230–1235.

[15] Kawashima S, Ueda K, Shinohara M, et al. Relationship between growth of facial morphology and chronologic age in preschool children with obstructive sleep apnea. J Oral Biol Craniofac Res. 2012 Jan-Apr;2(1):20–24. DOI:10.1016/S2212-4268(12)60006-2.

[16] Andrade FM, Pedrosa RP. The role of physical exercise in obstructive sleep apnea. J Bras Pneumol. 2016 Nov-Dec;42(6):457–464. DOI:10.1590/S1806-37562016000000156.

[17] Van Offenwert E, Vrijsen B, Belge C, et al. Physical activity and exercise in obstructive sleep apnea. Acta Clin Belg. 2019;74(2):92–101.

[18] Jean RE, Duttuluri M, Gibson CD, et al. Improvement in physical activity in persons with obstructive sleep apnea treated with continuous positive airway pressure. J Phys Act Health. 2017;14(3):176–182.

[19] Peppard PE, Young T. Exercise and sleep-disordered breathing: an association independent of body habitus. Sleep. 2004;27:480–484.

[20] Quan SF, O'Connor GT, Quan JS, et al. Association of physical activity with sleep-disordered breathing. Sleep Breath. 2007;11:149–157.