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Ultrasonographic measurement of the diaphragm thickness in patients with obstructive sleep apnea syndrome

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Abstract

Purpose The aim of this study was to evaluate the diaphragm thickness in patients with obstructive sleep apnea syndrome (OSAS).

Methods This prospective study included patients who underwent polysomnography evaluation for the first time with a clinical suspicion of OSAS. All patients underwent polysomnographic evaluation with a 55-channel Alice 6 computerized system (Respironics; Philips, IL). Diaphragm thickness was measured as the distance between the peritoneum and the pleura using electronic calipers with a 7–12-MHz linear probe (PHILIPS EPIQ 5G).

Results A total of 108 patients (67 males, 41 females) were enrolled in the current study. The mean age of the patients was 48.92 ± 11.47 years. The diaphragm thicknesses were significantly higher in OSAS patients both at end-inspirium and end-expirium compared with the normal group ($p < 0.05$). No significant difference was observed regarding the change level and thickening ratio (%) ($p > 0.05$). When the patients were allocated into OSAS subtypes; diaphragm thicknesses at the end of inspirium and expirium on both sides were significantly higher in the severe OSAS group and OSAS+OHS group compared with the other groups of normal, mild OSAS, and moderate OSAS subgroups ($p < 0.05$ for all). There was no significant difference between the groups regarding the thickening ratio ($p > 0.05$ for all). There was a positive correlation between the severity of OSAS and diaphragm thickness.

Conclusion Diaphragm thickness seems to be increased in OSAS patients and the thickness correlates with the severity of OSAS. However, the thickness ratio of OSAS patients does not differ from that of normal subjects.

Keywords Ultrasonography · Ultrasound · Diaphragm thickness · Sleep apnea

Introduction

Obstructive sleep apnea syndrome (OSAS) is the constellation of findings associated with repetitive collapse of the upper airway with recurrent hypoxia and apnea/hypopnea during sleep [1]. The presence/absence and severity of sleep apnea should be ascertained before starting treatment. Diagnostic criteria for OSAS are mainly based on symptoms and clinical findings established during a comprehensive sleep evaluation, physical examination, and findings identified by polysomnography (PSG). Patients suspected of OSAS should undergo an objective sleep testing and PSG is indicated in relevant patients [1, 2]. Apnea is defined as the cessation of airflow (> 10 s) and hypopnea is defined as decreased (3%) oxygen saturation with (at least 50%) decline of airflow (> 10 s). The apnea hypopnea index (AHI) refers to the frequency of obstructive events and OSAS severity is classified using this index [2].

The diaphragm is the main respiratory muscle and there have been few studies in respect of diaphragm function and morphology in OSAS patients. It has been shown that diaphragmatic function is affected acutely during obstructive sleep apnea in an anecdotal rat model. Further, diaphragmatic fatigue due to the inspiratory effort against an occluded airway has been indicated [3]. Diaphragm contractility and increased transdiaphragmatic pressure have also been shown [4, 5].

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Ultrasound (US) is an imaging modality suitable for the evaluation of diaphragm thickness and motion with several advantages such as ease of application, lack of ionizing radiation, providing dynamic imaging, and high spatial resolution. To date, diaphragm thickness has been evaluated by US in respiratory or neuromuscular diseases such as asthma, chronic obstructive pulmonary disease (COPD), and stroke [6–10]. Further, assessment of the diaphragm function using ultrasound imaging can be performed to predict the weaning outcome (from mechanical ventilation) [11]. However, to the best knowledge of the authors, ultrasonographic diaphragm thickness has not been studied before in OSAS. Therefore, the aim of this study was to evaluate diaphragm thickness in patients with OSAS using US.

Methods

Study design and patients

This prospective study included patients who underwent PSG evaluation for the first time with a clinical suspicion of OSAS in a tertiary hospital between December 2018 and March 2019. Exclusion criteria were a history of pulmonary disease (e.g., asthma, COPD), any neurological disorders (cerebrovascular event, multiple sclerosis, spinal cord injury), drug usage for the respiratory system, previous diagnosis of OSAS or continuous airway pressure pump treatment, or any other disorders that might affect diaphragm function/thickness.

Local Ethics Committee approved the study protocol (date 20.11.2018, no. 658) and participants gave informed consent.

Polysomnography evaluation

Polysomnographic evaluation was done in a sleep laboratory. All patients underwent overnight PSG with a 55-channel Alice 6 computerized system (Respironics; Philips, IL). American Academy of Sleep Medicine criteria were used as regards the PSG scores and OSAS diagnosis. Apnea was defined as airflow decrease (i.e., ≥ 90%, at least 10 s) on thermistor measurements. Amplitude criteria were also met for at least 90% of the duration. Hypopnea was considered if one of the following criteria was present: (i) a reduction (i.e., ≥ 30%) in the nasal pressure signal as compared with the baseline for at least 10 s, with a simultaneous desaturation of ≥ 4%, (ii) a reduction (i.e., ≥ 50%) in the nasal pressure signal as compared with the baseline for at least 10 s, with a simultaneous desaturation of ≥ 3%. The total number of apnea-hypopnea episodes per hour was taken as the definition of AHI. Regarding the AHI scores, patients were classified as normal (OSAS negative) (AHI < 5), mild OSAS (AHI = 5–14), moderate OSAS (AHI = 15–30), severe OSAS (AHI > 30), and OSAS+OHS (BMI > 30 kg/m^2, chronic daytime hypercapnia (PaCO2 > 45 mmHg), and presence of OSAS in the absence of other hypercapnia causes) [2, 12].

Epworth Sleepiness Scale

The Epworth Sleepiness Scale (ESS) is an 8-item self-reported questionnaire which evaluates sleepiness during eight different activities. Each item is scored from 0 to 3 by the patients and the higher scores represent adverse daytime sleepiness.

Ultrasonographic measurement of diaphragm thickness

Ultrasonographic evaluation of diaphragm is simple, non-invasive, and accurate. Thickness and thickening ratio are the two parameters commonly used in clinical settings and studies. Although electrodiagnostic testing (electrical activity of the diaphragm using a needle electrode) is the gold standard method to quantify the diaphragm function and contractility, it is invasive and challenging to perform [13].

Ultrasonographic measurements were performed by the same physician who was blinded to the PSG results. The ABCDE technique was used for the measurements. This technique has been shown to be a fast, reliable, and simple method in which ultrasound can be used to visualize the diaphragm [14]. A 7–12-MHz linear probe (PHILIPS EPIQ 5G) was used (over the chest wall, in the anterior axillary line) to image the diaphragm which appeared as a hypoechoic structure between two hyperechoic lines. While the upper line corresponded to the pleura, the lower one represented the peritoneum. Diaphragm thickness was measured as the distance between these two white lines with the help of electronic calipers (Fig. 1)—at the end of inspiration and expiration. The following formula was acquired to calculate the level of change (change level = thickness at end-inspirium − thickness at end-expirium). The thickening ratio (i.e., the percentage of

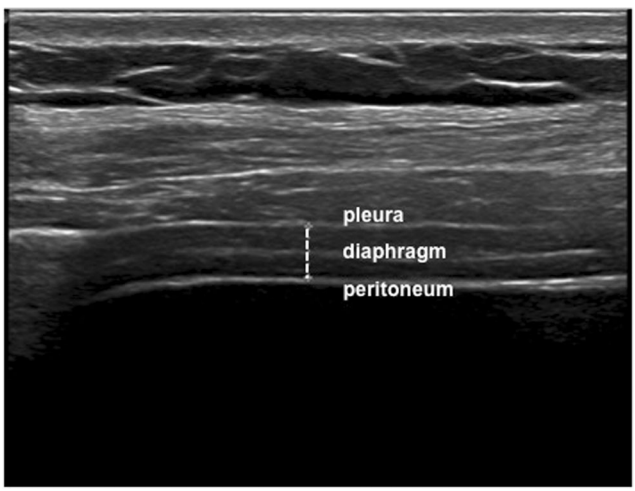

Fig. 1 Ultrasound imaging of the diaphragm

change to the thickness at end-expirium) was also calculated as follows: TR = change level / thickness at end-expirium × 100. Both of the aforementioned parameters have been used to assess diaphragm (dys)function [14–16].

Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL). Descriptive data are given as mean ± standard deviation, median (interquartile rage), number, or percentage (as appropriate). While chi-square test was used to compare categorical variables, Kruskal-Wallis test was used for between-group comparisons. Post hoc analyses were conducted to determine the different groups. Statistical significance was set at $p < 0.05$.

Results

A total of 108 patients (67 males, 41 females) were enrolled in the current study. The mean age of the patients was 48.92 ± 11.47 years. The demographical and clinical characteristics are given in Table 1. The diaphragm thickness significantly increased with inspiration on both sides ($p < 0.01$). The median change level was 0.79 mm (33.62%) and 0.71 mm (38.3%) on the right and left sides, respectively. When the participants were allocated into two groups in terms of OSAS occurrence, the diaphragm thicknesses were significantly higher in OSAS patients compared with those in the normal group both at end-inspirium and end-expirium ($p < 0.05$). No significant difference was determined regarding the change level and thickening ratio (%) ($p > 0.05$ for both) (Table 2). When the patients were allocated into OSAS subtypes, diaphragm thicknesses at the end of inspirium and expirium on both sides were significantly higher in the severe OSAS group and OSAS+OHS group compared with those in the normal, mild OSAS, and moderate OSAS subgroups ($p < 0.05$ for all) (Fig. 2). There was no significant difference between the groups regarding the thickening ratio ($p > 0.05$ for all). There was a positive and moderate correlation between AHI and diaphragm thickness and a positive and weak correlation between AHI and change level in diaphragm thickness. There was no significant correlation between thickening ratio and AHI (Table 3).

Discussion

As far as we know, this is the first study to have explored diaphragm thickness and thickening ratio in patients with OSAS. Two results emerged from this study. First, diaphragm thickness was significantly higher in OSAS patients (particularly in severe OSAS and OSAS+OHS patients) compared

Table 1 Clinical and demographic features

Variables	Data ($N = 108$)
Age (years)	48.92 ± 11.4
Gender	
Male	67 (62)
Female	41 (38)
Body mass index (kg/m^2)	31.33 ± 5.6
Polysomnography results	
Normal	23 (21.3)
Mild OSAS	21 (19.4)
Moderate OSAS	22 (20.4)
Severe OSAS	28 (25.9)
Obesity+hypoventilation syndrome	14 (13.0)
Epworth Score	9.0 ± 4.6
Apnea hypopnea index	18.30 (6.4–48.27)
Desaturation index	19.55 (5.32–41.67)
Diaphragm thickness at end-expiration (mm)	
Right	2.30 ± 0.7
Left	2.20 ± 0.7
Diaphragm thickness at end-inspiration (mm)	
Right	3.28 ± 1.1
Left	3.12 ± 1.1
Change in diaphragm thickness (mm)	
Right	0.79(0.41–1.31)
Left	0.71 (0.33–1.34)
Diaphragm thickening ratio (%)	
Right	33.62 (19.75–69.0)
Left	38.30 (14.19–58.51)

The data are shown as mean ± standard deviation, median (25–75%), or *n*, (%)

Table 2 Diaphragm thickness of the patients according to the polysomnography results

Variables	Normal ($N = 23$)	OSAS ($N = 85$)	*p* value
Diaphragm thickness at end-expiration (mm)			
Right	1.87 (1.59–2.23)	2.21 (1.72–2.90)	*0.024*
Left	1.75 (1.56–2.15)	2.07 (1.77–2.76)	*0.006*
Diaphragm thickness at end-inspiration (mm)			
Right	2.59 (2.11–3.30)	3.31 (2.58–4.03)	*0.009*
Left	2.59 (1.87–3.01)	3.01 (2.38–4.13)	*0.009*
Change in diaphragm thickness (mm)			
Right	0.44 (0.20–1.14)	0.82 (0.48–1.34)	0.130
Left	0.61 (0.17–1.33)	0.79 (0.37–1.36)	0.246
Diaphragm thickening ratio (%)			
Right	28.67 (12.5–55.97)	33.69 (21.33–71.05)	0.336
Left	40.71 (6.8–71.05)	38.25 (14.94–58.29)	0.663

The data are shown as median (25–75%). Italicized *p* values denote significance

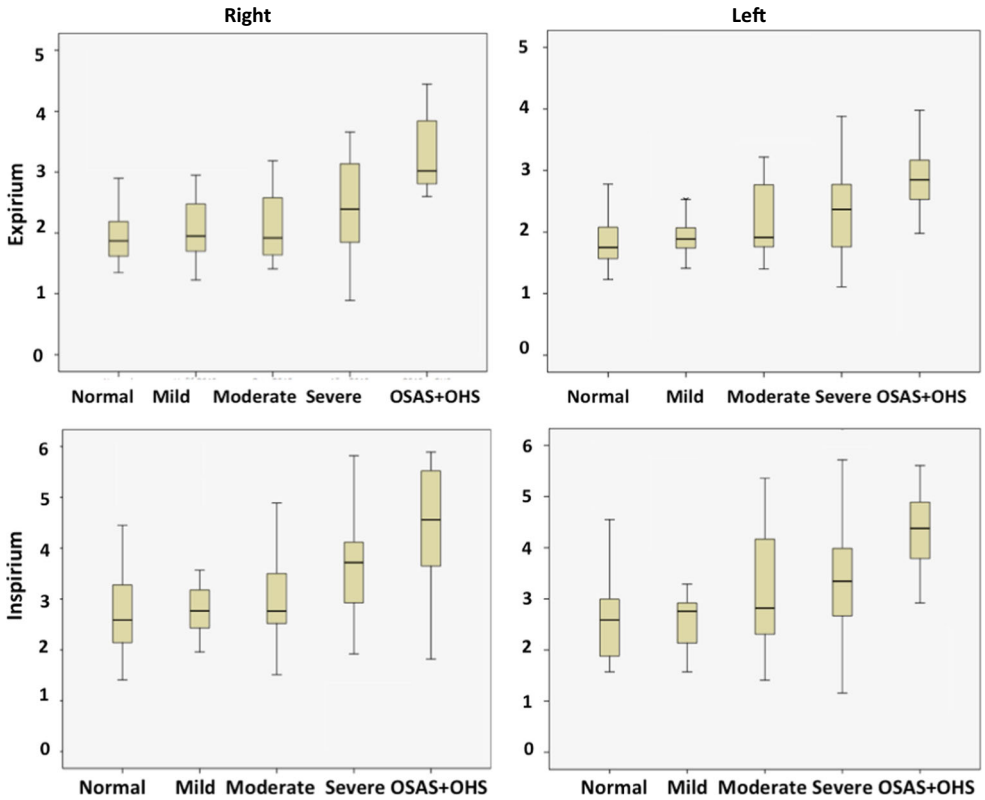

Fig. 2 Comparison of the diaphragm thickness at end-expirium and end-inspirium according to the apnea subtype. Bold *p* values denote significance. End-expirium (right/left). Normal vs. mild OSAS: $p = 0.681/p = 0.353$. Normal vs. moderate OSAS: $p = 0.699/p = 0.086$. Normal vs. severe OSAS: $p = 0.032/\mathbf{p = 0.012}$. Normal vs. OSAS+OHS: $\mathbf{p < 0.001/p < 0.001}$. Mild vs. moderate OSAS: $p = 0.971/p = 0.543$. Mild OSAS vs. severe OAS: $p = 0.110/p = 0.071$. Mild OSAS vs. OSAS+OHS: $\mathbf{p < 0.001/p = 0.001}$. Moderate OSAS vs. severe OSAS: $p = 0.069/p = 0.358$. Moderate OSAS vs. OSAS+OHS: $\mathbf{p < 0.001/p = 0.013}$. Severe OSAS vs. OSAS+OHS: $\mathbf{p = 0.010/p = 0.023}$. End-inspirium (right/left). Normal vs. mild OSAS: $p = 0.549/p = 0.638$. Normal vs. moderate OSAS: $p = 0.388/p = 0.117$. Normal vs. severe OSAS: $\mathbf{p = 0.002/p = 0.005}$. Normal vs. OSAS+OHS: $\mathbf{p < 0.001/p < 0.001}$. Mild OSAS vs. moderate OSAS: $p = 0.771/p = 0.259$. Mild OSAS vs. severe OAS: $\mathbf{p = 0.003/p = 0.009}$. Mild OSAS vs. OSAS+OHS: $\mathbf{p < 0.001/p < 0.001}$. Moderate OSAS vs. severe OSAS: $\mathbf{p = 0.026}/p = 0.278$. Moderate OSAS vs. OSAS+OHS: $\mathbf{p < 0.001/p = 0.004}$ Severe OSAS vs. OSAS+OHS: $p = 0.063/\mathbf{p = 0.025}$

with that in the normal group. Second, the thickening ratio of OSAS patients was similar to that of normal subjects.

OSAS is a syndrome, resulting in hypoxia, reoxygenation, and arousals during sleep that is characterized by repetitive partial or full upper airway obstruction [1]. The highly complex pathophysiology and the roles of contributing factors vary among individuals with OSAS. People who have decreased muscle tone and soft tissue around the airway and structural characteristics resulting in a narrowed airway are at high risk for sleep apnea. The cyclic breathing pattern in which the patient is released between obstructive respiratory events (sleep) and arousal (wakefulness) is a typical feature of OSAS and information on the role of respiratory control instability in the pathogenesis of OSAS is increasing [17].

The main inspiratory pump muscle is the diaphragm and for the maintenance of airway patency, this functions together with the pharyngeal respiratory muscles [18]. Skeletal muscle is known to be the tissue that is highly adaptable and malleable, changing its phenotype as a response to several environmental, physiological, and pathological conditions [19]. Changes in diaphragm physiology during apnea have also been reported. El-Kabir et al. [4] mentioned the inspiratory efforts made against an occluded airway and diaphragm fatigue in untreated OSAS patients. Wilcox et al. [5] focused on

Table 3 Correlation analyses

Variables		Thickness (end-expirium)	Thickness (end-inspirium)	Change level	Thickening ratio
Apnea hypopnea index	*r*	0.405	0.452	0.256	0.091
	p	< 0.001*	< 0.001*	0.008*	0.351

*Correlation is significant at the 0.01 level

the diaphragm as the major inspiratory muscle and reported an increase in gastric pressure and repetitive inspiratory effort against an obstructed airway during apnea.

According to current literature, although there has been no study exploring diaphragm thickness in patients with sleep apnea using US, this issue has been examined in some diseases such as COPD, amyotrophic lateral sclerosis, and mechanically ventilated patients. Noda et al. [20] found an excellent correlation between vital capacity and diaphragm thickness in a study comprising 37 patients with neuropathies, myopathies, and amyotrophic lateral sclerosis. Overall, the diaphragm thickness in patients' neurological conditions was less than that of the normal control group. This result is usually due to the paralysis in neurological conditions or mobility restriction [10]. Furthermore, a reduction in thickening ratio (< 20%) was consistent with diaphragmatic paralysis and this can be used to differentiate diaphragm paralysis from a healthy diaphragm [21]. De Bruin et al. [22] reported increased diaphragmatic thickness at the end of expiration, due to possible pseudohypertrophy, using US in children with Duchenne muscular dystrophy. In the current study, OSAS patients were found to have a significantly thicker diaphragm compared with the normal patients. Furthermore, diaphragm thickness was determined to be significantly correlated with AHI. On the basis of the relevant literature, it can be considered that the diaphragm contracts more strongly to open the obstruction and hypertrophy develops due to excessive functioning over time.

Limitations

There are some important drawbacks to this study. First, although the total sample size was acceptable, the small sample size for the subgroup analyses and the lack of a power analysis should be stated as limitations. Second, the whole sample was described as patients and "normal" according to the PSG scores. However, as they were selected from patients referred for PSG evaluation, selection bias should be stated as a limitation. Electrodiagnostic methods comprising phrenic nerve stimulation and surface or esophageal recording of the electrical activity of the diaphragm are the gold standard method to quantify the function of the diaphragm [13]. Therefore, the lack of evaluation with electrodiagnostic testing and pulmonary function tests can be considered another limitation.

Conclusion

In the light of these first, preliminary results, diaphragm thickness seems to be increased in patients with sleep apnea and the thickness correlates with the severity of OSAS. However, the thickening ratio of OSAS patients was not observed to be different from that of normal subjects. This study provides an insight into the diaphragm morphology and OSAS pathophysiology. Increased diaphragm thickness may indicate diaphragm hypertrophy due to excessive contractility and inspiratory effort of the diaphragm against an occluded airway [3, 16]. As for the clinical use of the diaphragm thickness, this US finding may be useful in identifying high-risk OSAS patients. In this purpose, cutoff values can be determined for OSAS patients in larger sample groups. Further studies comparing US findings with electromyography findings and pulmonary function tests are awaited.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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