Spirometry and flow-volume curve in patients with obstructive sleep apnea

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ABSTRACT

الأهداف: نتائج الدراسات التي بحثت علاقة منحنى جريان الهواء التنفسي وقياس السعات الحيوية للرئة عند المرضى المصابين بتوقف التنفس الإنسدادي أثناء النوم أظهرت نتائج متباينة. لذلك قمنا بهذا البحث لدراسة مدى شيوع اضطرابات قياس السعات الحيوية للرئة عند المرضى المصابين بتوقف التنفس الانسدادي أثناء النوم ومدى فائدة هذا الاختبار في تشخيص حالات توقف التنفس أثناء النوم.

الطريقة: أجريت هذا الدراسة في مستشفى الملك خالد الجامعي بين مارس ٢٠٠٦ ومارس ٢٠٠٧. وتم خلال الدراسة قياس كل مؤشرات اختبار قياس السعات الحيوية للرئة مثل السعة الحيوية في الثانية الأولى من الزفير(FEV1) والسعة الحيوية للرئة (FVC) والجريان الزفيري الأعظم٥٠ (FEF_{50}) والجريان الشهيقي الأعظم٥٠ (FIF_{50}). كما تم قياس منحنيات جريان الهواء الزفيرية والشهيقية وتم تحديد وجود علامة أسنان المنشار. وتم مقارنة المرضى الذين لديهم هذه التغيرات بالذين لم توجد عندهم التغيرات.

النتائج: وجدت علامة أسنان المنشار عند ١٢٫٣٪ من المرضى وكانت نسبة FEF_{50}/FIF_{50} >1 عند ٢٦٫١٪. لم تظهر الدراسة أي اختلافات بين مرضى توقف التنفس أثناء النوم الذين أظهروا هذه العلامات والذين لم يظهروها على مستوى العمر، مؤشر كتلة الجسم، مؤشر تناقص الأكسجين أثناء النوم، والقياسات الأخرى لاختبار قياس السعات الحيوية للرئة. كما لم تظهر أي علاقة بين شدة توقف التنفس أثناء النوم وعلامة أسنان المنشار أو نسبة FEF_{50}/FIF_{50} >1.

خاتمة: اضطرابات اختبار قياس السعات الحيوية للرئة غير شائعة عند مرضى توقف التنفس الذين لا توجد لديهم أمراض مزمنة في الرئة. كما أنه لا يمكن الاعتماد عليها في اكتشاف حالات توقف التنفس أثناء النوم.

Objectives: To assess the prevalence of spirometric abnormalities in obstructive sleep apnea (OSA) patients and its clinical utility in diagnosing OSA.

Methods: We conducted an observational study between March 2006 and March 2007 at King Khalid University Hospital on consecutive patients presenting with suspected OSA. Spirometric indices of forced expiratory volume in 1 second (FEV_1)/forced expiratory volume (FVC), maximum mid-expiratory flow $(MMEF)_{75/25}$, peak expiratory flow (PEF), forced expiratory flow $(FEF)_{50}$, and forced inspiratory flow $(FIF)_{50}$ were analyzed for 138 patients with OSA. Expiratory and inspiratory flow volume curves were examined for the presence of fluttering of the upper airway (saw-tooth sign) and signs of upper airway obstruction defined as a FEF_{50}/FIF_{50} >1. Patients with flow-volume curve abnormalities were compared with patients who did not show any abnormalities.

Results: Saw-tooth sign was present in 12.3% and the ratio of FEF_{50}/FIF_{50} >1 was found in 26.1% of OSA patients. Obstructive sleep apnea patients who had these abnormalities did not differ from patients who did not have them with regard to age, body mass index, apnea-hypopnea index (AHI), desaturation index and other spirometric indices. The presence of saw-tooth sign and FEF_{50}/FIF_{50} >1 was not related to the severity of AHI.

Conclusion: Spirometric abnormalities are not common in OSA patients not known to have underlying chronic lung diseases. Saw-tooth sign and FEF_{50}/FIF_{50} >1 are not useful in predicting OSA.

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Obstructive sleep apnea (OSA) is an important health problem and is associated with complications such as hypertension, ischemic heart disease, pulmonary hypertension, cardiac arrhythmias, stroke and sudden death.[1] Patients with OSA have various structural and functional abnormalities of the upper airway during sleep, which may reflect on their pulmonary function tests.[2] Spirometry and flow-volume loop are simple and commonly used tests in patients with respiratory symptoms. Abnormalities in the flow volume curves and other spirometric indices have been reported to be present and related to OSA.[3-5] These abnormalities include (i) saw-tooth sign which consists of regular oscillations occurring on constant intervals at forced expiratory and inspiratory flow volume curves,[6] and (ii) increased the ratio of forced expiratory flow to forced inspiratory flow at 50% of vital capacity (FEF_{50}/FIF_{50}) >1.[3] The results of the earlier studies that explored the utility of these tests have been inconsistent. While some studies demonstrated some specificity for the flow-volume curve in OSA patients, others failed to replicate those results.[4,6-8] Whereas Shore and Millman showed that the presence of saw-tooth sign had a high specificity of 92% for the diagnosis of OSA,[7] Krieger et al[8] showed contradictory results with regard to the usefulness of flow volume curves in diagnosing OSA and demonstrated that saw-tooth sign was present in 61% of patients with OSA and in 46% of the patients without OSA. Additionally, the sign of extra thoracic upper airway obstruction (FEF_{50}/FIF_{50}>1) was present in 67% of patients with OSA and 71% of patients without OSA.[8] It seems from the above that there is no consensus yet on the diagnostic role of flow-volume curve and spirometry in patients with OSA. Additionally, most of the published studies are relatively old, included small number of patients, and did not directly address the differences between OSA patients with saw-tooth sign and OSA patients without this sign. Therefore, we designed this study to assess the prevalence of spirometric abnormalities in OSA patients and the differences between OSA patients with flow-volume curves and other spirometric abnormalities and those without.

Methods. This study was conducted in the Sleep Disorders Center (SDC) at King Khalid University Hospital, a tertiary care University Hospital in the Kingdom of Saudi Arabia. The local ethics committee approved the study and informed consent was obtained from all participants. Consecutive patients presenting to the SDC with suspected OSA between March 2006 and March 2007 underwent polysomnography (PSG) after completing a detailed questionnaire on sleep disorders. All patients who were diagnosed with OSA were enrolled in the study. Current smokers and patients with Chronic Obstructive Pulmonary Disease (COPD) or other chronic lung diseases, neurological disorders, congestive heart failure and those who did not complete the pulmonary function tests were excluded from the study. For polysomnography, Alice-4 and 5 diagnostic equipment from Respironics, Inc, Murrysville, Pennsylvania, USA were used for data acquisition. The procedure consisted of continuously recording of the following parameters: 4 electro-encephalography (EEG) (C1-A4, C2-A3, O1-A4, O2-A3), chin electromyography (EMG), electro-oculography (EOG) (eye movement), leg EMG, electro-cardiography (ECG), oxygen saturation, chest, and abdominal wall movements, 2 air flow signals (nasal prong pressure and thermistor), sleep position, and microphone for snoring. Standard definitions were used to classify central, obstructive apneas and hypopneas and central hypoventilation.[9] Apnea was defined as the cessation of airflow ≥10 seconds, and hypopnea as a recognizable, transient reduction of airflow (>50%) for ≥10 seconds using nasal prong pressure flow signal resulting in a 4% decrease in oxygen saturation or an arousal. Obstructive sleep apnea was defined according to the International Classification of Sleep Disorders (ICSD 2005): 1) apnea-hypopnea index (AHI), ≥5 events/hour with evidence of respiratory effort during all or portion of the event associated with one of the following: excessive daytime sleepiness or unrefreshing sleep, gasping, or choking during sleep, or witnessed apnea or loud snoring or 2) AHI ≥15 events/hour with evidence of respiratory effort during all or portion of the event.[9] After PSG, all patients underwent spirometry according to the standards of American Thoracic Society (ATS).[10] Expiratory and inspiratory flow volume curves and the spirometric indices of forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), FEVI/FVC%, peak expiratory flow (PEF), FEF_{50}, $FIFF_{50}$, and maximum mid-expiratory flow $(MMEF)_{75/25}$ of vital capacities were obtained from each patient using master screen, Jaeger, Germany. At least 3 curves were obtained for each patient and the one with highest flow was used for analysis. The flow-volume curves were examined for the presence of saw-tooth sign and extra thoracic airway obstruction. Saw-tooth sign was considered to be present when there were ≥3 peaks and troughs of not >300 ml during the middle of 80% inspiratory and/or expiratory flow volume curves (**Figure 1**).[4] Extrathoracic upper airway obstruction was considered present when the FEF_{50}/FIF_{50} ratio was >1.[3] Patients who showed saw-tooth pattern were compared to patients who did not show this sign (patients with a negative saw-tooth sign were taken as controls). Similarly, patients who had a FEF_{50}/FIF_{50} >1 were compared to patients who had

FEF_{50}/FIF_{50} ≤1 (patients with FEF50/FIF50 ≤1 were taken as controls).

Statistical analyses. The data were entered into MS Excel and analyzed using the Statistical Package for Social Sciences Version 11.0. Descriptive statistics (mean ± SD) were calculated for all the continuous variables. Student's t-test for independent samples was used to compare the mean values of study variables in relation to the 2 categories of saw-tooth sign and FEF_{50}/FIF_{50}. A probability value of <0.05 was considered as statistically significant. The spirometric indices of FEV_1, FVC, FEV_1/FVC%, $MMEF_{75/25}$, PEF, FEF_{50} and FIF_{50} were reported as percentages of the predicted based on age, height, and gender.

Results. The study group (138 patients) comprised 104 males and 34 females. The demographics and spirometric indices of these patients are shown in **Table 1**. The saw-tooth sign was present in 17 (12.3%). The demographics and spirometric indices of these patients are shown in **Table 2**. The mean body mass index (BMI) of these 17 patients was 35.6 kg/m^2. When compared with 121 patients (control group) with a negative saw-tooth sign, there was no significant difference between the 2 groups with regard to age, AHI, BMI, desaturation index and other spirometric indices. Saw-tooth sign was not associated with a higher AHI. The spirometric indices of FEV_1, FVC, FEV_1/FVC%, $MMEF_{75/25}$, PEF, FEF_{50} and FIF_{50} of all patients (with and without saw-tooth sign) were within normal. The difference in the ratio of FEF_{50}/FIF_{50} between patients with saw-tooth sign and controls was not statistically significant (0.94 versus 0.85). A FEF_{50}/FIF_{50} ratio greater than one (a sign of extrathoracic upper airway obstruction) was

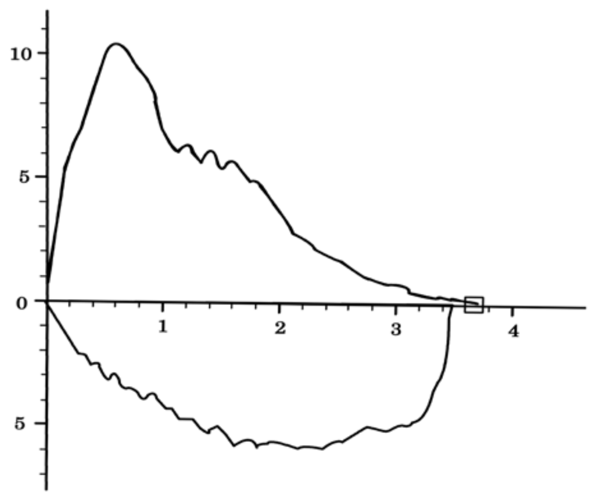

Figure 1 - Flow-volume loop of a patient with saw-tooth pattern.

Table 1 - Characteristics of all patients (n=138).

Demographics and spirometric indices (% of predicted) of all patients	Mean ±SD
Age	44.5 ± 12.6
Body mass index (kg/m^2)	35.2 ± 7.8
Apnea hypopnea index	56.1 ± 35.4
Desaturation index	31.7 ± 29.4
FEV_1 (%)	92.7 ±19.5
FVC (%)	95.6 ± 16.5
FEV_1/FVC%	102.9 ± 8.5
$MMEF_{75/25}$ (%)	96.8 ± 34.3
FEF_{50} (%)	99 ± 34.2
FIF_{50} (%)	101.4 ± 32.3
PEF (%)	103.9 ± 24.4

FEV_1 - forced expiratory volume in 1 second; FVC - forced vital capacity; $MMEF_{75/25}$ - maximum mid expiratory flow between 75 and 25% of vital capacity; FEF_{50} - forced expiratory flow at 50% of vital capacity; FIF_{50}=forced inspiratory flow at 50% of vital capacity; PEF=peak expiratory flow. FEV_1, FVC, $MMEF_{75/25}$, FEF_{50}, PEF and FIF_{50} are expressed as percentage of predicted

Table 2 - Characteristics of obstructive sleep apnea patients with saw-tooth sign positive and negative.

Demographics and spirometric indices of patients (% of predicted)	Saw-tooth sign positive n=17	Saw-tooth sign negative n=121	*P* -value
Age	45.3 ± 13.3	44.4 ±12.6	NS
BMI (kg/m^2)	35.6 ± 6.2	35.1 ± 8	NS
AHI	71.3 ± 37.7	59.9 ± 34.9	NS
Desaturation index	41.9 ± 33.7	30.2 ± 28.6	NS
FEV_1 (%)	95.1 ± 17	92.3 ± 19.8	NS
FVC (%)	93 ± 18	96 ± 20	NS
FEV_1/FVC%	103.6 ± 8	102.8 ± 8.5	NS
$MMEF_{75/25}$ (%)	95.8 ± 34	103.7± 30	NS
FEF_{50} (%)	98.4 ± 35	103 ± 28	NS
FIF_{50} (%)	105.7 ± 24	107 ± 32	NS
PEF (%)	105.8 ± 23	103.7 ± 24.6	NS

BMI - body mass index; AHI - apnea hypopnea index; FEV_1 - forced expiratory volume in 1 second; FVC - forced vital capacity; $MMEF_{75/25}$ - maximum mid expiratory flow between 75 and 25 % of vital capacity; FEF_{50} - forced expiratory flow at 50% of vital capacity; FIF_{50} - forced inspiratory flow at 50% of vital capacity; PEF - peak expiratory flow; NS=not significant. FEV_1, FVC, $MMEF_{75/25}$, FEF_{50}, PEF and FIF_{50} are expressed as percentage of predicted

Table 3 - Characteristics of OSA patients with FEF_{50}/FIF_{50} > 1 and controls ($FEF_{50}/FIF_{50} \leq 1$).

Demographics and spirometric indices of patients (% of predicted)	FEF_{50}/FIF_{50} >1 n=36	FEF_{50}/FIF_{50} ≤1 n=102	*P*-value
Age	45 ± 12.1	44.3 ± 12.9	NS
Body mass index (kg/m^2)	34.9 ±7.2	35.3 ± 8.1	NS
Apnea hypopnea index	62.1 ± 32.6	54 ± 36.5	NS
Desaturation index	36.8 ± 31.2	29.8 ± 28.6	NS
FEV_1 (%)	91.9 ± 20	94.7± 17	NS
FVC (%)	89 ± 17.1	98 ± 22.2	NS
FEVI/FVC %	101.2 ± 8.7	104.6 ± 6.9	NS
$MMEF_{75/25}$ (%)	94.8 ± 31.7	88.7 ± 31.5	NS
FEF_{50} (%)	97.3 ± 30.9	99.6 ± 27.9	NS
FIF_{50} (%)	96.9 ± 21.1	101.4 ± 24.5	NS
PEF (%)	108.7± 24.5	102.3 ± 24.3	NS

FEV_1 - forced expiratory volume in 1 second; FVC - forced vital capacity; $MMEF_{75/25}$ - maximum mid expiratory flow between 75 and 25 % of vital capacity; FEF_{50} - forced expiratory flow at 50% of vital capacity; FIF_{50} - forced inspiratory flow at 50% of vital capacity; PEF - peak expiratory flow; NS - not significant. FEV_1, FVC, $MMEF_{75/25}$, FEF_{50}, PEF and FIF_{50} are expressed as percentage of predicted.

found in 36 (26.1%) patients. One hundred and two patients with a FEF_{50}/FIF_{50} ratio of less than one were taken as controls. There was no significant difference between the patients and the control group in relation to age, BMI, AHI, and desaturation index. When the spirometric indices of FVC, FEV_1, FEV_1/FVC%, $MMEF_{75/25}$, PEF, FEF_{50}, FIF_{50} were compared, no significant difference was found between the 2 groups (**Table 3**). These indices were also found to be in the normal range predicted for these patients. Among OSA patients with positive saw-tooth sign (n=17), FEF_{50}/FIF_{50} was found to be greater than one in 6 patients only. The age, BMI, AHI, desaturation index and other spirometric indices of these 6 patients were not different from that of patients with none of either signs (saw-tooth and FEF_{50}/FIF_{50} >1).

Discussion. Several studies have shown alterations in upper airway mechanics in OSA patients.[2,11] Some of the older studies have reported some abnormalities in spirometry of patients with OSA and raised the possibility that spirometry may serve as a useful screening test in the diagnosis of OSA.[4,7,12] Sanders et al[4] demonstrated saw-tooth sign in 85% of the patients with OSA and in none of the subjects without OSA with a sensitivity of 85% and specificity of 100% for OSA. Haponik et al[3] reported a FEF_{50}/FIF_{50} >1 in 44% of patients with OSA and in only 8% of the patients without OSA. In our study, the prevalence of the abnormalities in spirometry and flow volume curves as FEF_{50}/FIF_{50} >1 and saw-tooth sign was low. Patients who showed those abnormalities did not differ with regard to age, BMI, AHI, desaturation index and other spirometric indices from those patients who do not have these abnormalities, which raise doubts on the diagnostic roles of these spirometric signs in detecting patients with OSA. Our results concurred with recent studies that showed a low prevalence and specificity of saw-tooth sign and other spirometric parameters in detecting OSA. Hoffstein et al[13] reported FEF_{50}/FIF_{50} >1 in 12% in OSA patients compared to 14% in non apneic patients. Katz et al[14] demonstrated that flow-volume curves are not a useful test for the diagnosis of OSA in snoring patients. Additionally, Rauscher et al[15] reported that FEF_{50}/FIF_{50} ratio and saw-tooth sign were of limited value for predicting OSA. Amado et al[16] analyzed the flow-volume curves and spirometric indices of FEV_1, FVC, FEV_1/FVC%, FEF_{50}, FIF_{50} and PEF in snoring patients with and without OSA. They found no significant difference in these parameters between patients and controls. More recently, Campbell et al[17] demonstrated no differences in patients with OSA and healthy controls when they compared flow-volume curve abnormalities and other spirometric indices. Hoffstein and Oliver[18] studied pulmonary function tests in OSA patients (without lung disease) referred for evaluation of OSA. They compared flow-volume curves, body plethysmography and single breath diffusing capacity for carbon monoxide in different groups of OSA patients who were grouped according to severity of AHI. They found no differences between OSA patients with varying degrees of AHI severity.[18] Vincken and

Cosio[19] reviewed 2800 flow-volume curves performed in their pulmonary function laboratory. They identified saw-tooth pattern in 40 (1.4%) patients. Thirty-one of these 40 patients (77%) did not have OSA. In 16 of those 31 patients (52%), a structural disorder of upper airway or neurologic disease involving the upper airway was found. The discrepancy between different studies is due to several reasons including; the small number of patients with OSA included in earlier studies, the handling of confounders such as the presence of underlying lung diseases, the measurement techniques used, and the saw-tooth sign diagnostic criteria. Based on the above, it appears that spirometric changes are not good indicators of the presence of OSA. Relying on these signs may result in significant under-detection of patients with sleep apnea and unnecessary delay in the diagnosis. The current study has a limitation that needs to be addressed. Due to study design, the investigators who interpret the spirometric parameters were not blinded to the clinical diagnosis of the patients, which might result in some bias.

In summary, spirometric abnormalities are not common in OSA patients not known to have underlying chronic lung diseases. Patients who showed spirometric abnormalities did not differ from those without abnormalities with regard to age, BMI, AHI, and desaturation index. It thus appears that saw-tooth sign and FEF_{50}/FIF_{50} >1 are not useful in predicting OSA.

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