ORIGINAL ARTICLE

Awake Respiratory Function in Patients with the Obstructive Sleep Apnoea Syndrome

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Summary

Introduction: The flow-volume curves of patients with obstructive sleep apnoea (OSA) obtained during the awake state are frequently abnormal.

Objective: To determine 1) the relationship between the awake respiratory function and the severity of sleep-disordered breathing in a group of Malaysian patients with the OSA syndrome and 2) the frequency of flow-volume curve abnormality in these patients.

Materials and Methods: A retrospective analysis of the data from respiratory function tests during wakefulness and nocturnal polysomnography was performed on 48 patients with OSA. The severity of OSA was defined by the apnoea-hypopnoea index (AHI) and the lowest oxygen saturation during sleep (SpO_{2nadir}).

Results: AHI had a significant relationship with alveolar-arterial oxygen gradient ($r = 0.34$, $p = 0.046$) and SpO_{2nadir} ($r = -0.49$, $p < 0.001$) but not with any anthropometric parameter or the other awake respiratory function variables measured. SpO_{2nadir} had a significant relationship with body mass index ($r = -0.54$, $p < 0.001$), neck circumference ($r = -0.39$, $p = 0.013$), awake room air PaO_2 ($r = 0.61$, $p < 0.001$), alveolar-arterial oxygen gradient ($r = -0.41$, $p = 0.015$) and baseline supine SpO_2 ($r = 0.53$, $p < 0.001$). There was no correlation between SpO_{2nadir} and any spirometric or static lung volume parameters. The maximum inspiratory and maximum expiratory flow-volume curves of 26 patients (54%) showed a ratio of forced expiratory flow to forced inspiratory flow at mid-vital capacity (FEF_{50}/FIF_{50}) greater than one. In addition, flow oscillations (the "sawtooth" sign) were noted in the inspiratory and/or expiratory flow-volume curves of 21 patients (44%), 9 of whom did not have an $FEF_{50}/FIF_{50} > 1$. Altogether, the maximum flow-volume curves during wakefulness of 35 (73%) of the 48 patients showed variable upper airway obstruction and/or flow oscillations. However, the presence of these two upper airway abnormalities, either occurring alone or together did not have an effect on the severity of OSA as measured by the AHI or SpO_{2nadir}.

Conclusions: Abnormalities of the flow-volume loop consistent with inspiratory flow limitation and/or upper airway instability during wakefulness are common in patients with the OSA syndrome. The degree of oxygen desaturation during sleep in these patients is related to their awake oxygenation status.

Key Words: Flow-volume curves, Respiratory function, Sleep apnoea

Introduction

Patients with obstructive sleep apnoea (OSA) have episodic obstruction of the upper airway during sleep[1]. The flow-volume curves of patients with OSA obtained during the awake state are frequently abnormal and may show two features related to upper airway dysfunction[2-6]. One abnormality of the flow-volume curve described in these patients is "saw-toothing" or flow oscillations occurring at regular intervals on either the inspiratory

and/or expiratory limbs of the flow-volume loop.[2] This sign has been shown to correspond to rapid "fluttering" of redundant pharyngeal tissue visible at endoscopy or loss of tone of the upper airway muscles[2,7]. It is believed that the saw-tooth pattern is related to alteration of the airflow pattern created by intermittent narrowing caused by upper airway tissue vibration[2]. The other abnormality is a ratio of the forced expiratory maximal flow at 50% of vital capacity to forced inspiratory maximal flow at 50% of vital capacity (FEF_{50}/FIF_{50}) greater than one which may indicate variable upper airway obstruction[3].

Little has been published on patients with the OSA syndrome in Malaysia. This study aimed to determine 1) the relationship between the awake respiratory function and the severity of sleep-disordered breathing in a group of Malaysian patients with the OSA syndrome and 2) the frequency of flow-volume curve abnormality in these patients.

Materials and Methods

This is a retrospective study which involved the analysis of data from in-laboratory nocturnal polysomnography and respiratory function tests during wakefulness performed on patients with the OSA syndrome. Patients suspected of having the OSA syndrome based on symptoms of snoring and excessive daytime sleepiness with or without witnessed apnoeas underwent overnight polysomnography in our sleep laboratory. Electroencephalogram, electro-oculogram, chin muscle electromyogram, oronasal airflow, thoracoabdominal movement, finger pulse oximetry and electrocardiogram data were recorded continuously on a Grass polygraph (Model No. 78, Grass Instrument Company, Quincy, Massachusetts). Respiratory movements of the ribcage and abdomen were measured using inductance plethysmography (Respitrace, Ambulatory Monitoring, Ardsley, New York, United States). Oronasal airflow was measured using thermocouples. Oxygen saturation was measured using a Nellcor pulse oximeter with a finger probe.

Sleep stages were classified according to the standard described by Rechtschaffen and Kales[8]. Hypopnoeas were defined as drop of tidal volume by at least 50% of its baseline value established during previous breaths, lasting at least 10 seconds and accompanied by an oxygen desaturation of greater than 4%; obstructive apnoea as a cessation of airflow while thoracic and/or abdominal movements persisted; central apnoea a complete cessation of airflow as well as thoracoabdominal movements; and mixed apnoea as a succession of central and obstructive apnoeas. The apnoea/hypopnoea index (AHI) was defined as the number of episodes of apnoea and/or hypopnoea per hour of sleep. The lowest oxygen saturation during sleep (SpO_{2nadir}) was noted. A patient was diagnosed as having sleep apnoea when he/she had an AHI higher than five. The severity of OSA was defined by the AHI and the SpO_{2nadir}.

Routine respiratory function tests which included spirometric measurements, flow-volume loops, static lung volume measurement and single breath carbon monoxide transfer factor (TLCO) were performed using an automated whole body plethysmograph (Sensor Medics 6200 Autobox DL, SensorMedics Corporation, Yorba Linda, California, United States) according to the American Thoracic Society criteria[9] within a week of the sleep study. This computerised plethysmograph measured both the inspired and expired flows at the patient's mouth directly using a mass flow sensor. The mass flow sensor utilised a pair of heated stainless steel wires to measure gas flow. The computer programme integrated these flow signals to obtain volume measurements. The mass flow sensor was linearised through the computer programme. The accuracy of the flow sensor was 0.1 litre/s and the resolution was 30 mL/s.) Maximum flow-volume curves were obtained using a pneumotachograph attached to a microprocessor.

The patients were tested in the sitting position wearing a nose clip. The patient took a full inspiration and exhaled as rapidly, forcefully and completely as possible, and then inhaled in the same manner. The resultant flow-volume curve was discarded if the patient's effort was thought to be submaximal by the laboratory technician who performed the test. At least two reproducible maximum flow-volume curves were obtained. The highest spirometric values and the flow-volume curves with the highest expiratory and inspiratory flows were used for analysis. For each patient, arterial blood gas analysis was performed on

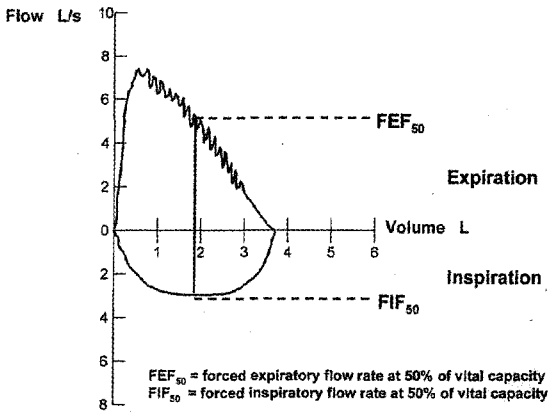

Figure 1: A representative example of a maximum flow-volume loop with an increased FEF_{50} /FIF_{50} ratio and a saw-tooth pattern.

room air taken whilst awake and seated in the mid-morning on the same day respiratory function tests were performed.

The flow volume curves were examined for the presence of two features: 1). the presence of flow oscillations (the "saw-tooth" sign) and 2). the ratio of the expiratory flow during forced expiration at 50% of the vital capacity (FEF_{50}) to the forced inspiratory flow at 50% of the vital capacity (FIF_{50}) greater than one which suggested the presence of variable upper airway obstruction. "Saw-toothing" or flow oscillations were defined as the presence of a reproducible sequence of three or more consecutive peaks and troughs of similar configurations occurring at regular intervals of no greater than 300 mL/s (i.e., accelerations and decelerations of flow) during the middle half of the vital capacity (from 75% to 25% of the vital capacity) in either inspiration, expiration or both[2,7].

Statistical analysis

Results are expressed as mean (SD) and range. The correlation between two continuous variables was tested with the Pearson's correlation coefficient. Categorical variables were compared using the chi-square test with Yates' correction or Fisher's exact test. To compare continuous variables, the Student's *t* test was used. A *p* value of less than 0.05 for a two-tailed test was considered statistically significant. All statistical analyses were performed using Kwikstat statistical software (Kwikstat 4.1. Cedar Hill, Texas: TexaSoft, 1995).

Results

Among the sleep apnoea patients who were evaluated and confirmed to have OSA by full nocturnal polysomnography at our medical centre, 48 patients (45 males and 3 females) also underwent routine respiratory function tests. The patients' anthropometric, respiratory function test and polysomnography data are shown in Table I. The patient's BMI had a significant correlation with the awake baseline supine SpO_2 ($r = -0.37$, $p = 0.01$) but not with the awake PaO_2 ($r = 0.17$, $p = 0.241$). There was also significant correlation between the neck circumference and the awake baseline supine SpO_2 ($r = 0.33$, $p = 0.021$) but not between neck circumference and awake PaO2 ($r = -0.04$, $p = 0.768$). The AHI had a significant relationship with alveolar-arterial oxygen gradient ($r = 0.34$, $p = 0.046$) and SpO_{2nadir} ($r = -0.49$, $p < 0.001$) but not with any anthropometric parameter or the other awake respiratory function variables measured (Table II). SpO_{2nadir} had a significant relationship with body mass index (BMI) ($r = -0.54$, $p < 0.001$), neck circumference ($r = -0.39$, $p = 0.013$), awake room air arterial oxygen tension (PaO_2) ($r = 0.61$, $p < 0.001$), alveolar-arterial oxygen gradient ($r = -0.41$, $p = 0.015$) and baseline supine SpO_2 ($r = 0.53$, $p < 0.001$). There was no correlation between SpO_{2nadir} and any spirometric or static lung volume parameters.

The maximum inspiratory and maximum expiratory flow-volume curves of 26 patients (54%) showed a mid-vital capacity expiratory to inspiratory flow ratio (FEF_{50}/FIF_{50}) greater than one. In addition, flow oscillations (the "saw-tooth" sign) were noted in the inspiratory and/or expiratory flow-volume curves of 21 patients (44%). Eighteen patients had a saw-tooth pattern only in the inspiratory curve, two patients had it only in the expiratory curve and one patient had it in both curves. A representative example of a maximum flow-volume loop with an increased FEF_{50}/FIF_{50} ratio and a saw-tooth pattern is shown in Figure 1.

Table I
Anthropometric, respiratory function and polysomnography data of patients with the obstructive sleep apnoea syndrome

	Mean	(SD)	Range
Age, year	46.2	(10.7)	32 - 72
Body mass index, kg/m^2	30.8	(5.9)	22.6 - 48.2
Neck circumference, cm	42.8	(3.6)	34.0 - 49.5
Forced expiratory volume in 1 second (FEV_1), % predicted	80.0	(18.1)	37 - 131
Vital capacity (VC), % predicted	71.7	(14.8)	41 - 119
FEV_1/VC, %	84.6	(8.8)	52 - 97
FEF_{50}/FIF_{50} ratio	1.10	(0.62)	0.27 - 4.13
Residual volume (RV), % predicted	104.0	(42.1)	18 - 237
Total lung capacity (TLC), % predicted	87.6	(14.6)	49 - 121
RV/TLC, %	36.5	(12.4)	11 - 77
Carbon monoxide diffusing capacity,% predicted	135.7	(31.3)	88 - 237
PaO_2, kPa	10.9	(2.4)	5.5 - 14.3
$PaCO_2$, kPa	5.6	(1.2)	3.9 - 10.0
Alveolar-arterial oxygen gradient, kPa	2.1	(1.4	0.5 - 5.2
Baseline supine SpO_2, %	96	(4)	82 - 100
Apnoea/hypopnoea index, per hour	55.4	(30.9)	6 - 123
Lowest SpO_2 during sleep (SpO_{2nadir}), %	66	(20)	6 - 91

FEF_{50}/FIF_{50} = mid-vital capacity flow ratio, PaO_2 = arterial oxygen tension, $PaCO_2$ = arterial carbon dioxide tension, SpO_2 = oxygen saturation by pulse oximetry

The neck circumference [42.8 (3.6) cm] and BMI [29.9 (4.9) kg/m^2] of patients with an FEF_{50}/FIF_{50} >1 were not significantly different from that [42.8 (3.6) cm and 31.8 (6.8) kg/m^2, respectively] of patients with an FEF50/FIF50 <1 (p = 0.960 and p = 0.251, respectively). Similarly, the neck circumference [42.6 (3.6) cm] and BMI [31.4 (6.8) kg/m^2] of patients with the saw-tooth pattern were not significantly different from that [42.9 (3.6) cm and 30.3 (5.1) kg/m^2, respectively] of patients without the saw-tooth pattern (p = 0.749 and p = 0.509, respectively). Nine patients with the saw-tooth pattern did not have an FEF_{50}/FIF_{50} >1. Altogether, the maximum flow-volume curves of 35 (73%) of the 48 patients showed a variable upper airway obstruction pattern and/or flow oscillations. However, the presence of these two upper airway abnormalities, either alone or together did not have an effect on the severity of OSA as measured by the AHI or SpO_{2nadir} (Table III).

Discussion

To our knowledge, this is the first publication on the anthropometric and respiratory function data of patients with the OSA syndrome in Malaysia. This study showed a significant correlation of the nadir of oxygen saturation during sleep with the BMI, neck circumference and also with the awake PaO_2 and awake baseline supine SpO_2 of OSA patients. The nadir oxygen saturation during an obstructive apnoea is determined by the apnoea duration and the rate of fall of oxygen saturation. The longer the

Table II
Correlation between respiratory function variables and sleep apnoea severity

Sleep apnoea severity	Anthropometric and respiratory function variable	Correlation coefficient (r)	P value
Apnoea/ hypopnoea index (AHI)	Body mass index-0.17	0.286	
	Neck circumference	0.26	0.099
	Forced expiratory volume in 1 second	-0.04	0.776
	Vital capacity	-0.07	0.653
	FEF_{50}/FIF_{50} ratio0.20	0.190	
	Residual volume (RV)	0.07	0.641
	Total lung capacity (TLC)	0.03	0.866
	RV/TLC	0.15	0.327
	Carbon monoxide diffusing capacity	-0.01	0.937
	PaO_2	-0.22	0.201
	$PaCO_2$	-0.21	0.227
	Alveolar-arterial oxygen gradient	0.34	0.046
	Baseline supine SpO_2	-0.27	0.113
	Lowest SpO_2 during sleep (SpO_{2nadir})	-0.49	<0.001
Lowest SpO_2 during sleep (SpO_{2nadir})	Body mass index	-0.54	<0.001
	Neck circumference	-0.39	0.013
	Forced expiratory volume in 1 second	0.19	0.215
	Vital capacity	0.09	0.566
	FEF_{50}/FIF_{50}	0.09	0.576
	Residual volume (RV)	-0.05	0.764
	Total lung capacity (TLC)	0.09	0.572
	RV/TLC	-0.10	0.529
	Carbon monoxide diffusing capacity	-0.17	0.286
	PaO_2	0.61	<0.001
	$PaCO_2$	0.06	0.713
	Alveolar-arterial oxygen gradient	-0.41	0.015
	Baseline supine SpO_2	0.53	<0.001

apnoea or the steeper the rate of fall of oxygen saturation, the lower the resulting nadir oxygen saturation[1,10]. The rate of fall in oxygen saturation during an apnoea depends on the patient's position on the oxyhaemoglobin dissociation curve which in turn is determined by his baseline oxygen saturation. Patients with low resting arterial oxygen tension during wakefulness are likely to show more rapid falls in oxygen saturation for a given duration of apnoea. The significant negative correlation between the nadir SpO_2 and BMI and neck circumference is explained by the significant negative correlation between BMI and neck circumference with the awake supine baseline SpO_2.

Table III
Effect of flow-volume loop abnormality on apnoea/hypopnoea index (AHI) and lowest oxygen saturation during sleep (SpO_{2nadir})

Flow-volume loop abnormality	n	Mean AHI (SD) (per hour)	P value	Mean SpO_{2nadir} (%)	P value
Saw-tooth pattern					
Present	21	54.5 (38.2)	0.866	61.5 (22.3)	0.163
Absent	27	56.1 (24.5)		69.8 (17.1)	
FEF_{50}/FIF_{50} >1	26	59.8 (28.8)	0.291	70.3 (15.4)	0.140
FEF_{50}/FIF_{50} <1	22	50.2 (33.1)		61.3 (24.3)	
Sawtooth pattern and/or FEF_{50}/FIF_{50} >1					
Present	35	57.9 (36.7)	0.365	66.0 (21.4)	0.939
Absent	13	48.7 (25.4)		66.5 (17.4)	

AHI = *apnoea/hypopnoea index*
SpO_{2nadir} = *lowest oxygen saturation during sleep*
FEF_{50}/FIF_{50} = *mid-vital capacity flow ratio*

The "saw-tooth" sign on maximum flow volume curves first described by Sanders et al[2] has been examined in several studies with highly divergent results. These studies have shown its sensitivity and specificity for the diagnosis of OSA range from less than 10% to 61%[4,6,11,12] and from 38% to 100%,[2,4,11,12] respectively. Flow oscillations during inspiration or expiration may be caused by functional instability of the upper airway due to lack of support[7]. Flow oscillations, however, are not specific for OSA and can occur spuriously when generated by sound production cough or glottic closure[7]. Flow oscillations have also been described in neuromuscular disorders involving the upper airway muscles[13,14].

Studies on the effect of flow oscillations in patients with OSA on the severity of the disease as judged by the AHI and the lowest oxygen saturation during sleep have also shown inconsistent results. Some investigators have reported the absence of an association between the presence of flow oscillations and the severity of sleep apnoea as defined by AHI[4,11]. However, patients with combined inspiratory and expiratory flow oscillations have been found to have higher AHI than patients without flow oscillations in one study[11]. While one study[4] shows that OSA patients whose flow-volume curves demonstrated saw-toothing have a significantly greater fall in oxygen saturation during sleep than in those without saw-toothing, another study[5] has shown that the presence of saw-toothing does not have an effect on the degree of oxygen desaturation.

Some authors[11,14] do not define the amplitude of the flow oscillations while others have variously defined the accelerations and decelerations to be not greater than 300 mL/s[2,6] and not greater than 500 mL/s[15]. While the majority of published reports do not define the maximum width of the oscillations, some investigators have variously defined the width to be of no more than 10% of the forced vital capacity[15] and no more than 300 mL[16]. Only saw-toothing in the middle 50% of the vital

capacity is considered physiologically significant because artifacts created by muscle activity as a result of effort may occur at the extremes of the forced vital capacity[2]. At greater than 75% of the vital capacity, forced expiration is effort dependent and at lower lung volumes, i.e., less than 25% of the vital capacity, a subject may tend to strain during a forced expiratory manoeuvre. Even though inspiration is dependent on effort throughout the vital capacity, muscle tremors are not a problem at either end of the vital capacity[2].

Vincken and Cosio[7] stressed that "most flow-volume loops digitally generated do not have sufficient flow or volume resolution; as a result, computer-steered flow-volume loop recording may underestimate the frequency content and flow oscillations may go unrecognized." Furthermore, computer-sampling algorithms in most computerised equipment may smooth the flow-volume curves to minimize the variability of the derived forced expiratory flow rates[7].

A mid-vital capacity flow ratio (FEF_{50}/FIF_{50}) greater than one due to inspiratory flow limitation is suggestive of variable extrathoracic upper airway obstruction[3]. We have found that 53% of our OSA patients had a mid-vital capacity flow ratio exceeding one. This is within the range of 31% to 67% reported in the literature[2,4,12,17]. The specificity of this sign for OSA has been reported to range from 29% to 92%[12,17].

Seventy-one percent of our OSA patients had either an FEF_{50}/FIF_{50} ratio greater than one or the presence of a saw-tooth pattern or both on their maximal flow-volume curves[4]. Various studies have found the sensitivity of the combination of these two signs for the diagnosis of OSA to range from 50% to 86%[6,12,18] and its specificity to range from 13% to 80%[6,12,18]. However, because of the low sensitivity and low specificity, flow-volume curve abnormalities are not useful as screening parameters for OSA[16,19,20]. We did not find an association between decreased inspiratory flow rates and sleep apnoea severity as measured by the AHI or SpO_{2nadir}. Other workers have also reported no correlation between the mid-vital capacity flow ratio and the AHI or lowest oxygen saturation during sleep[11].

In conclusion, the degree of desaturation during sleep in patients with OSA is related to their daytime oxygenation as well as their baseline supine SpO_2 before sleep. Abnormalities of the maximal flow-volume loop consistent with inspiratory flow limitation and/or upper airway instability as evidenced by flow oscillations during wakefulness are common in patients with OSA. However, the presence of these two upper airway abnormalities, either occurring alone or together, do not have an effect on the severity of OSA as measured by the AHI or SpO_{2nadir}.

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