

Diurnal Change of Respiratory Muscle Strength in Patients with Sleep-disordered Breathing

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Background: Obstructive sleep apnea is characterized by repetitive pharyngeal collapse, which increases inspiratory resistive load, and causes intermittent oxygen desaturation and frequent arousals during sleep. This could be damaging to respiratory muscles and result in their weakness. Therefore, we investigated respiratory muscle strength before and after nocturnal sleep in patients with sleep-disordered breathing (SDB).

Methods: Forty eight male patients with SDB undergoing overnight polysomnography were enrolled. Maximal expiratory pressure (MEP) and maximal inspiratory pressure (MIP) were measured before and after the sleep study. Correlation between polysomnographic data and diurnal changes in maximal respiratory pressures were also assessed.

Results: After nocturnal sleep, MEP increased from 94.6 ± 20.8 cm H₂O to 105.9 ± 24.1 cm H₂O ($p < 0.001$) and MIP increased from 72.9 ± 20.2 cm H₂O to 78.3 ± 21.7 cm H₂O ($p = 0.004$). There was no significant correlation between changes in MEP/MIP and apnea-hypopnea index, arousal index, and mean and minimal oxygen saturation.

Conclusion: The respiratory muscle strength of patients with SDB was greater in the morning than at night, which may be contributed to by the restorative effect of nocturnal sleep. This diurnal difference was not correlated to the severity of SDB, which may suggest that respiratory muscles are less impaired by SDB.

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Key words: maximal expiratory pressure, maximal inspiratory pressure, obstructive sleep apnea, respiratory muscle strength, sleep-disordered breathing

Obstructive sleep apnea (OSA) is prevalent in the middle-aged and elderly population, especially in obese male subjects.⁽¹⁾ OSA is characterized by repetitive partial or complete upper airway collapse during sleep with preservation of respiratory effort.

This recurrent upper airway obstruction increases inspiratory resistive load and causes intermittent hypoxemia, as well as frequent arousals from sleep. It has been demonstrated that an inspiratory resistive load applied to the airways may induce diaphragmat-

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ic fatigue.⁽²⁾ Hypoxemia has also been shown to facilitate inspiratory muscle fatigue during inspiratory loading.⁽³⁾ Furthermore, sleep loss has been shown to impair inspiratory muscle endurance, which can be improved by restorative sleep.⁽⁴⁾ Accordingly, patients with OSA may be prone to respiratory muscle fatigue due to upper airway obstruction during sleep. Therefore, non-restorative sleep is likely to decrease respiratory pump muscle strength with rising severity as sleep-disordered breathing (SDB) increases. To test this hypothesis, we measured the diurnal change of respiratory muscle strength in patients with SDB after a nocturnal sleep.

METHODS

Patients

From June to August 2005, 48 male subjects with symptoms related to SDB were consecutively enrolled in this study. Their symptoms included habitual snoring, witnessed apnea during sleep, excessive daytime sleepiness and/or morning headaches. Patients with major cardiovascular, pulmonary and neuromuscular disease that may affect muscle strength were excluded from this study.

Polysomnography

Patients' height, weight and neck circumference were measured prior to overnight polysomnographic study. Subjective sleepiness was assessed simultaneously by means of the Epworth sleepiness scale (ESS), an eight point questionnaire that assesses the subject's tendency to fall asleep during various situations, where a higher score indicates increased sleepiness.^(5,6) A full polysomnography was performed using a standardized commercial suite (Alice 4, Respironics, Marietta, Georgia, U.S.A.).

All subjects completed their polysomnographic study with at least 4 hours of total sleep time as indicated by electroencephalogram. Sleep stage scoring was done at 30-second intervals by experienced technicians according to the standard criteria.⁽⁷⁾ By definition, obstructive apnea was a cessation of airflow for at least 10 seconds with effort to breath during apnea. Obstructive hypopnea was defined as an abnormal respiratory event with at least a 30% reduction in thoraco-abdominal movement or airflow as compared to baseline, lasting at least 10 seconds, with greater than 4% oxygen desaturation.⁽⁸⁾ Apnea-

hypopnea index (AHI) was defined as the total number of apneas and hypopneas per hour of electroencephalographic sleep.

Respiratory muscle strength

Respiratory muscle strength was assessed by measuring maximal expiratory pressure (MEP) and maximal inspiratory pressure (MIP). MEP was the highest positive pressure measured when the subject exhaled with as much force as possible after maximal inspiration, while MIP was determined as the lowest negative pressure when the subject inhaled with maximal effort at their residual volume. Both maneuvers were performed in the sitting position using a flanged mouthpiece attached to a metal tube with a 2 mm air-hole to prevent glottic closure and recruitment of the oro-facial musculature. Both MEP and MIP were assessed the night preceding the polysomnographic study, and the measurements were repeated in the morning immediately after polysomnography.

Data analysis

All data are expressed as a mean \pm standard deviation unless stated otherwise. Differences in maximal respiratory pressures between nighttime and daytime were assessed with paired *t*-test. The relationship between changes in MEP/MIP and AHI, arousal index, mean oxygen saturation and minimal oxygen saturation, as well as other variables, were assessed by Pearson's correlation analysis. Data analysis was performed with a commercial statistical analysis software package (SPSS, version 13.0, Chicago, IL, U.S.A.) and a two-sided *p* value less than 0.05 was considered statistically significant.

RESULTS

The mean age of the subjects was 40.7 ± 6.7 years, with a mean body mass index (BMI) of 26.4 ± 3.8 kg/m². Their anthropometric characteristics and polysomnographic variables are shown in Table 1.

As shown in Fig. 1, after a nocturnal sleep, maximal respiratory pressures increased significantly. MEP increased from 94.6 ± 20.8 cm H₂O to 105.9 ± 24.1 cm H₂O ($p < 0.001$) and MIP also increased from 72.9 ± 20.2 cm H₂O to 78.3 ± 21.7 cm H₂O ($p = 0.004$).

Table 1. Characteristics and Polysomnographic Variables of Subjects

Age (years)	40.7 ± 6.7
Body mass index (kg/m ²)	26.4 ± 3.8
Neck circumference (cm)	40.6 ± 2.8
Epworth sleepiness scale	10.5 ± 5.2
Apnea-hypopnea index (/h)	43.7 ± 27.9
Arousal index (/h)	28.3 ± 16.9
Mean oxygen saturation (%)	88.2 ± 3.5
Minimal oxygen saturation (%)	74.7 ± 13.3

Data represent means ± standard deviation.

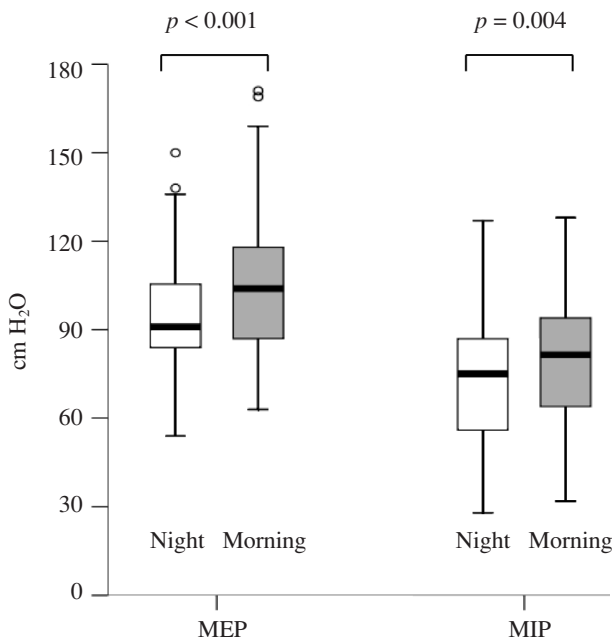


Fig. 1 Differences in morning and nighttime maximal respiratory pressures. Both maximal expiratory pressure (MEP) and maximal inspiratory pressure (MIP) increased significantly after nocturnal sleep.

There was no significant correlation between change in MEP and AHI, arousal index, mean oxygen saturation and minimal oxygen saturation ($p = 0.413, 0.826, 0.761$ and 0.922 , respectively; Fig. 2). In addition, no significant correlation between change in MIP and AHI, arousal index, mean oxygen saturation and minimal oxygen saturation was revealed ($p = 0.275, 0.263, 0.995$ and 0.460 , respec-

tively; Fig. 3). Similarly, the correlations between changes in MEP/MIP and age, BMI, neck circumference and ESS were insignificant (change in MEP: $p = 0.383, 0.615, 0.091$ and 0.197 , respectively; change in MIP: $p = 0.845, 0.471, 0.705$ and 0.335 , respectively).

DISCUSSION

In this study, we demonstrated that the maximal respiratory strength of patients with SDB improves after nocturnal sleep, and this increment was not correlated to the severity of SDB. This suggests that nocturnal sleep has a restorative effect on respiratory muscles regardless of the severity of sleep impairment by SDB. It also indicates that respiratory muscles are relatively resistant to increased load and intermittent hypoxia during nocturnal obstructive respiratory events.

Few studies have been conducted on the respiratory pump muscles of patients with SDB. Therefore, it remains unclear whether SDB causes adverse effects on respiratory muscle strength. OSA has an insidious onset, marked by repetitive upper airway collapse during sleep. Increased upper airway resistance, associated with a reduced upper airway cross-sectional area, has been shown to be closely related to the severity of OSA.^(9,10) Thus, the respiratory resistive load of OSA patients during both sleep and wakefulness is likely to be greater when compared to normal subjects. The resistive load experienced by subjects should correlate with the severity of SDB. Bellemare and colleagues showed that inspiratory resistive load applied to the airways causes possible diaphragmatic fatigue.⁽²⁾ Intermittent hypoxemia has also been shown to facilitate inspiratory muscle fatigue during inspiratory loading.⁽³⁾ Furthermore, sleep deprivation or fragmentation may cause respiratory muscle weakness since sleep loss impairs inspiratory muscle endurance.⁽⁴⁾ Therefore, it is reasonable to presume that patients with OSA have a certain level of respiratory muscle weakness.

There is little supporting evidence for the hypothesis of weaker respiratory muscles in subjects with SDB. In patients with OSA, impaired inspiratory muscle contractility has been documented by Griggs *et al.*⁽¹¹⁾ SDB was also shown to be correlated to respiratory muscle weakness in patients with amyotrophic lateral sclerosis without significant bulbar

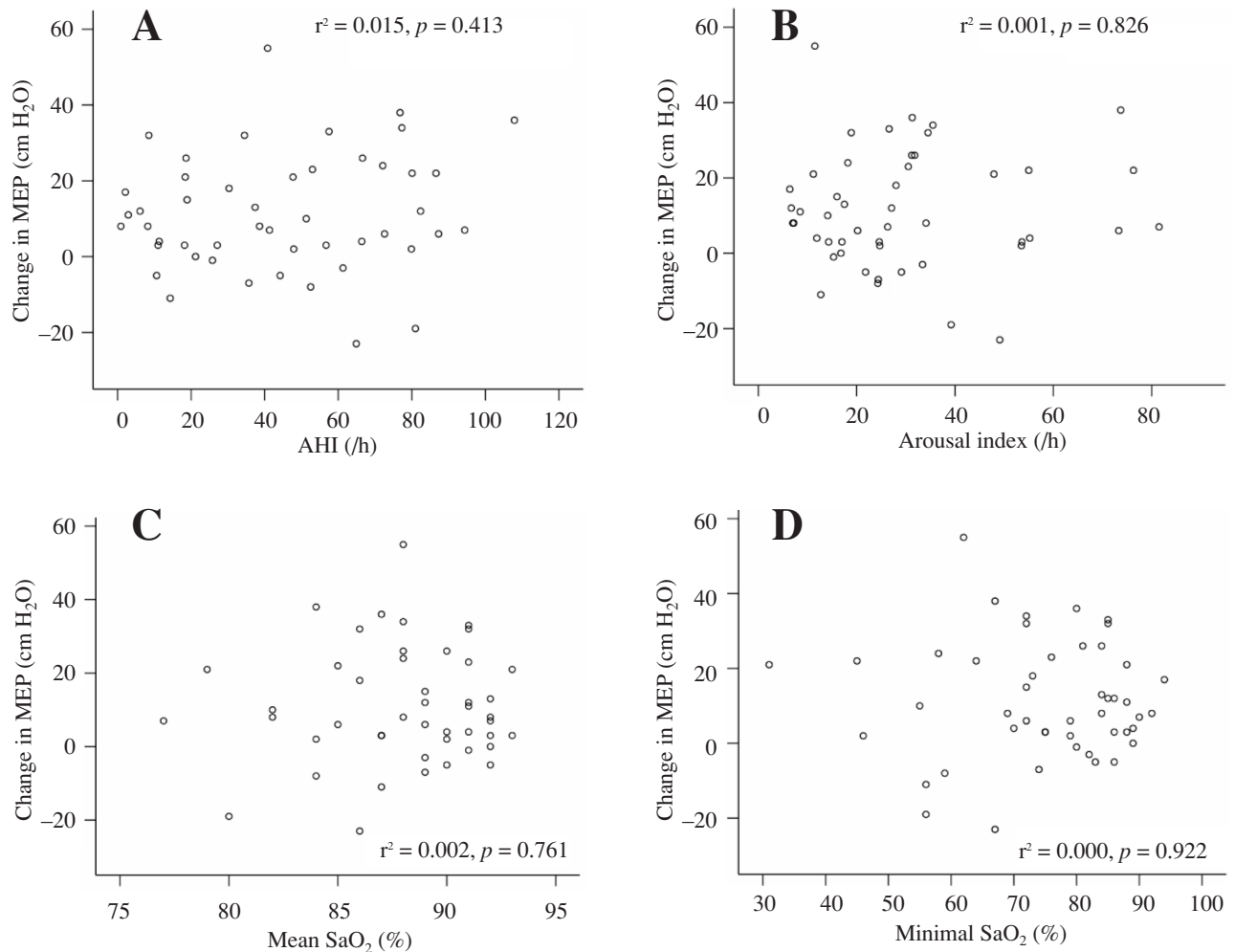


Fig. 2 Correlation between change in maximal expiratory pressure (MEP) and apnea-hypopnea index (AHI) (A), arousal index (B), mean oxygen saturation (C), and minimal oxygen saturation (D). There is no significant correlation between the change in MEP and these polysomnographic variables.

involvement.⁽¹²⁾ Nevertheless, Cibella and colleagues used diaphragmatic pressure time index testing on obese OSA patients and showed no evidence of diaphragmatic fatigue or impaired diaphragmatic contraction during sleep.⁽¹³⁾ These observations, as well as our findings, suggest that SDB per se does not cause respiratory pump muscle weakness. Rather, SDB may aggravate preexisting respiratory muscle weakness caused by other comorbid conditions.

Patients with weak respiratory muscles appear to generate insufficient intra-thoracic pressure, which results in hypoventilation and decreased lung volume. A decreased end-expiratory lung volume leads to a smaller and more collapsible pharyngeal air-

way,⁽¹⁴⁾ thereby increasing the inspiratory resistive load. Thus, the respiratory muscle strength of a patient with heart failure or neuromuscular disorders, such as amyotrophic lateral sclerosis, could be further impaired by SDB. Such respiratory muscle weakness could be corrected by medical treatment. Patients with congestive heart failure have signs of respiratory muscle weakness,⁽¹⁵⁾ and treating heart failure with an angiotensin-converting enzyme inhibitor would improve respiratory muscle strength and decrease the degree of dyspnea.⁽¹⁶⁾ Also, nasal continuous positive pressure treatment can abolish sleep apnea and alleviate respiratory load leading to an increase in inspiratory muscle strength in patients

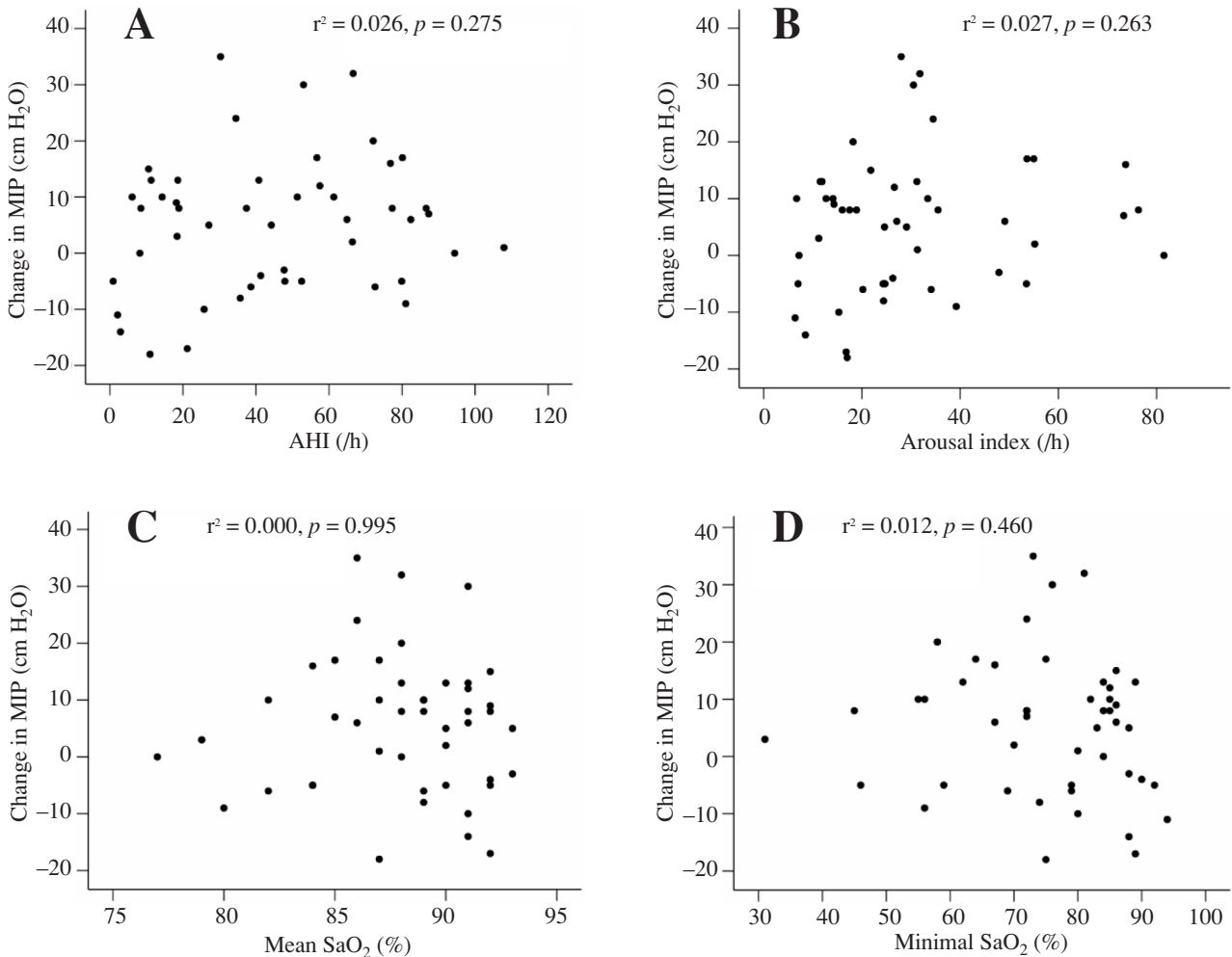


Fig. 3 Correlation between change in maximal inspiratory pressure (MIP) and apnea-hypopnea index (AHI) (A), arousal index (B), mean oxygen saturation (C), and minimal oxygen saturation (D). There is also no significant correlation between the change in MIP and these polysomnographic variables.

with heart failure.⁽¹⁵⁾

Patients with SDB without severe medical comorbidities have no obvious symptoms of respiratory muscle fatigue. In the present study, we showed that the MIP and MEP of patients with SDB improved after nocturnal sleep. This change in maximal respiratory muscle strength may have resulted from the restorative effect of nocturnal sleep or be due to circadian variation. However, the change in respiratory muscle strength had no correlation with the severity of SDB. This suggests that respiratory pump muscles may be resistant to long-term inspiratory resistive loading. One of the possible mechanisms is the inhibition of the central neural drive of

the inspiratory pump muscles when the upper airway is occluded.⁽¹⁷⁾ Sustained hypoxia also suppresses the sensory processing of respiratory resistive loads.⁽¹⁸⁾ In healthy individuals, the responses to hypoxia are also markedly attenuated during sleep, consistent with a sleep-related reduction in respiratory chemosensitivity due to increases in upper airway resistance.⁽¹⁹⁾ These inhibitory reflexes prevent excessive negative intrathoracic pressure and probably protect respiratory muscles from fatigue.

There were several limitations in this study. The first limitation was the lack of female subjects. Low numbers of female subjects with suspected SDB visiting our sleep clinic makes it unlikely that we can

give an accurate estimation of the female population. However, the prevalence of SDB is much higher in the male population.⁽²⁰⁾ Whether gender differences would alter the results requires further investigation. The second limitation of this study was the lack of a more sophisticated method to determine respiratory muscle strength, such as a diaphragmatic electromyogram, sniff test or trans-diaphragmatic pressure measurement. Such tests may be more sensitive in detecting muscular weakness but would be more complicated and not easily incorporated into the polysomnographic study. However, respiratory muscle strength can be approximated non-invasively from maximal mouth pressures. This maximal voluntary ventilation test is the only simple index of ventilatory or respiratory muscle endurance.⁽²¹⁾

In conclusion, we revealed a diurnal difference in respiratory muscle strength in patients with SDB in this study. The change in respiratory muscle strength was not correlated to the severity of SDB, indicating that the respiratory muscle strength of patients with SDB can be restored by nocturnal sleep, even if sleep is fragmented. Further studies are required to explore the protective mechanisms of respiratory muscles from SDB.

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睡眠呼吸障礙病患呼吸肌肉強度之晝夜變化

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背景：阻塞性睡眠呼吸中止症病患夜間睡眠時，其反覆上呼吸道阻塞與氧合濃度降低以及頻繁的覺醒可能導致呼吸肌肉耗弱，因此我們研究睡眠呼吸障礙病患夜間睡眠前、後呼吸肌肉強度的變化，並加以探討其可能原因。

方法：本研究收集了48位接受標準整夜多頻道睡眠檢查 (polysomnography) 之男性睡眠呼吸障礙病患，於睡眠前後測量患者最大呼氣壓力 (maximal expiratory pressure, MEP) 以及最大吸氣壓力 (maximal inspiratory pressure, MIP)，並比較 MIP 和 MEP 等之呼吸肌肉強度晝夜差異以及多頻道睡眠檢查數據之間的關聯性。

結果：在一個夜晚的睡眠之後，睡眠呼吸障礙病患之 MEP 和 MIP 均有增加的現象。MEP 從 94.6 ± 20.8 cm H₂O 增加至 105.9 ± 24.1 cm H₂O ($p < 0.01$)，而 MIP 則從 72.9 ± 20.2 cm H₂O 增加至 78.3 ± 21.7 cm H₂O ($p = 0.004$)。然而 MEP/MIP 之晝夜變化程度則與窒息指數 (apnea-hypopnea index)、覺醒指數 (arousal index)、最低以及平均氧合濃度 (mean and minimal oxygen saturation) 等數據之間並無顯著之關聯性。

結論：睡眠呼吸障礙病患早上的呼吸肌肉強度大於夜晚，這可能歸因於夜間睡眠的恢復作用。此呼吸肌肉強度的晝夜變化與睡眠呼吸障礙之嚴重度並無明顯關聯，這暗示著呼吸肌肉可能因某種保護機制而不易被睡眠呼吸中止症影響。
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關鍵詞：最大呼氣壓力，最大吸氣壓力，阻塞性睡眠呼吸中止症，呼吸肌肉強度，睡眠呼吸障礙