Airway Function and Respiratory Resistance in Taiwanese Coal Workers with Simple Pneumoconiosis

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Background: Occupational exposure to coalmine dust consisting of coal particles and free silica eventually results in massive lung fibrosis. However, clinical observations of patients with coal workers' pneumoconiosis (CWP) suggest that airway dysfunction may be a predominant feature in the initial development of the disease.

Methods: Forced expirogram, plethysmographic determination of lung volumes, and measurement of respiratory resistance (Rrs) by the forced oscillation technique at 3, 9, and 18 Hz were conducted in a sample of 71 coal miners with simple pneumoconiosis and 36 healthy subjects.

Results: The forced vital capacity (FVC) was well-preserved even in miners with category 2 and 3 CWP. There were no differences in the mean forced expiratory volume in 1 second (FEV1) values between healthy subjects and miners with category 1 disease. However, the level of airflow limitation in these miners increased with the transition from category 1 to category 2 and 3. The FEV1/FVC ratio fell below 70% in miners with category 2 and 3 disease, in both smokers and non-smokers. A consistent increase in the ratio of the residual volume to total lung capacity (RV/TLC) in the miners compared with that of the control workers was found. An abnormally high Rrs at 3 Hz (Rrs3) and frequency dependence in the flow resistance were also demonstrated in these subjects. There was an upward trend in the values of Rrs3 in the higher radiological categories. The correlation between respiratory conductance at this frequency (Grs3) and the RV/TLC ratio was good ($r = -0.763$, $p < 0.001$).

Conclusion: Simple CWP is not associated with a clinically apparent reduction in lung volume. The Rrs3 appears to be a sensitive parameter for detecting airway obstruction in patients with simple CWP associated or not with a reduced FEV1.

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Key words: airway obstruction, coal workers' pneumoconiosis, respiratory resistance, forced oscillation technique

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Coal workers' pneumoconiosis (CWP) is the most common occupational lung disease. It is caused by exposure to inhaled coal dust. Both carbon and silica, the major components of coal mine dust, are capable of inducing cellular reactions and fibrosis in the lung tissue. Indeed, progressive massive fibrosis has been well recognized as the principle disabling (complicated) form of this disorder,[1] despite the fact that it accounts for only 0 – 25% of CWP cases.[2,3] The majority of miners with CWP have simple pneumoconiosis. Although coal dust in itself is fibrogenic and may induce severe restriction of lung volumes,[2,4] coal miners with pneumoconiosis often experience symptoms such as chronic cough, sputum production and episodes of wheezing suggesting the presence of airway dysfunction.

Lung function tests provide objective evidence of respiratory impairment, especially that caused by occupational exposure. Although obstructive ventilatory defect is a common finding in CWP,[2] many miners with pneumoconiosis have normal values for forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1). Thus, the deleterious effects of coal dust inhalation on pulmonary function may not be readily detected by conventional tests,[4] and a more sophisticated approach is required to explore the physiological abnormalities in simple CWP.

Because impedance in the respiratory system varies when airway dysfunction is present,[5,6] measurement of total respiratory resistance (Rrs) has been advocated as a good and sensitive method to detect airway obstruction.[7] However, there are few reports on the extent with which Rrs may deviate from normal in CWP. Moreover, coexisting lung volume changes in miners with pneumoconiosis have not been sufficiently investigated by determination of parameters other than FVC. Since many patients with simple CWP demonstrate a hyperinflated lung on chest roentgenograms,[8] we hypothesize that airflow limitation is the main physiological change in coal workers with initial development of pneumoconiosis, and simple CWP is not associated with significant lung volume reduction. The aim of this study was to examine the functional impairment related to radiological category in a group of miners with simple CWP, and to evaluate the usefulness of various lung function parameters estimated by conventional spirometry, plethysmography and a forced oscillation technique in the assessment of CWP-related airway changes.

METHODS

Subjects

Seventy-one coal miners were selected from a consecutive cohort of 105 workers investigated for compensation benefits in the Pulmonary Function Laboratory of our institution between October 2003 and January 2005. They were referred by the Bureau of Labor Insurance, Taiwan, for assessment of lung functional impairment. All were men and both working and ex-miners were included. Their ages ranged from 48 to 69 years, and the duration of underground work ranged from 12 to 31 years (mean: 22.7 $\pm$ 7.5 years). They also had respiratory complaints such as cough, phlegm, and breathlessness in addition to radiographically confirmed pneumoconiosis.

In the same time period, control subjects were consecutively selected from a group of businessmen and government employees over 45 years old who were having annual health examinations at the hospital at the request of their companies or organizations. Their workplaces were free from dust exposure. Thirty-six healthy men were included in the final analysis.

Study protocol

A medical examination was performed on each subject. All of them completed a self-administered questionnaire modified from those cited in the Epidemiology Standardization Project.[9] The questionnaire included health information such as occupational history, smoking and health history, including hypertension, diabetes, chronic lung and cardiac disease, and neuromuscular disorders.

Each man had a full-sized (32 $\times$ 44 cm) posterioanterior chest radiograph. Two medically-qualified physicians read the radiological appearances, following the criteria of the International Labor Organization classification system.[10] Films showing small irregular and/or round opacities without conglomeration were classified into one of the following three categories of simple pneumoconiosis;

category 1: Few small opacities present. Lung markings are visible.
category 2: Numerous small opacities present. Lung markings are still visible.

category 3: A large number of small opacities present. Lung markings are obscured.

Exclusion criteria included the following: (A) unwilling to take lung function tests, (B) a chest radiograph showing progressive massive fibrosis (the complicated form of CWP), i.e. large opacities with a diameter > 1 cm, or abnormal findings other than pneumoconiosis, (C) clinically apparent or history of cardiovascular disease, or anemia, (D) ingestion of oral corticosteroids during the preceding 2 weeks.

Pulmonary function tests

Spirometric measurements were carried out by having each subject exhale maximally after a full inspiration to total lung capacity (TLC). An automated pressure body plethysmograph CS-828FC (CHEST M.I. Inc., Tokyo, Japan) was used to record the maximal expiratory flow-volume curves. Values for the FVC, FEV1, and FEV1/FVC were reported based on the best of three technically acceptable tests. The body box was then sealed and the subject remained breathing quietly. He was then asked to pant at a rate of no more than two breaths per second. The panting maneuver was continued when the shutter closed automatically at resting expiratory level. The thoracic gas volume was measured to derive the residual volume (RV), TLC, and the RV/TLC ratio.

Measurement of total respiratory resistance (Rrs) was performed with an astograph (TCK-6000, CHEST M.I). The device employs a forced oscillation technique and measures Rrs continuously during tidal breathing. Its principle and clinical application have been previously described.[11,12] Briefly, rapid oscillations of flow at the mouth are produced with a loudspeaker system driven by a low frequency sinewave generator and power amplifier. Pressure oscillations at the frequencies of 3, 9, and 18 Hz are then generated and applied to the mouth. The air flow at the mouth is measured with a Fleish No. 2 pneumotachometer (Hewlett-Parkard, Cupertino, CA, U.S.A.) and the mouth pressure is measured with a differential pressure transducer (MP45-1, Validyne, Northridge, CA, U.S.A.). Spectral analysis of the resulting pressure and flow signals is performed by a computer. It yields calculations of the Rrs and respiratory conductance (Grs), the reciprocal of the Rrs.

Statistical analysis

All data were coded and entered into a computer and then analyzed with the Statistical Analysis System (SAS; SAS Institute, Cary, NC, U.S.A.) software. Lung function parameters, except for the FEV1/FVC ratio, Rrs and RV/TLC%, were expressed as percentages of predicted values (%p) and as mean $\pm$ SD. Predicted values for the FVC, FEV1, and TLC were calculated by equations previously established by Yang & Wu for healthy Chinese.[13,14] The effects of stature and body weight on lung volumes and expiratory flow rates were thus size corrected. Pearson's correlation coefficients were calculated to examine the strength of association between the various airway function parameters, e.g., FEV1 and Rrs. The differences in lung function data between the healthy subjects and miners with different radiological categories of pneumoconiosis were examined with the two-sample t-test. The chi-square test was performed to compare the percentage of smokers between control subjects and miners. The limit of statistical significance was set at $p = 0.05$.

RESULTS

All of the miners had small opacities indicating pneumoconiosis on their chest roentgenograms, and 28 (39%) had category 1 disease, 31 (44%) had category 2 and 12 (17%) had category 3. Because of the small number of subjects in category 3, they were included together with category 2. A representative chest radiograph of a miner with category 2 disease is displayed in Fig. 1. This radiograph shows increased translucency in both lower lung fields and the lung markings are partially obscured by numerous fine nodular depositions.

There was no difference in the ages between the 2 groups (coal workers mean 55.1 $\pm$ 9.4 years; control subjects mean 52.8 $\pm$ 7.2 years). However, the miners had a much higher prevalence of smoking (77.5%) than the control group (47.2%) ($p = 0.002$). In the miners who smoked, those with category 1 disease had smoked a mean 25.4 $\pm$ 10.8 years and those with category 2 and 3 disease had smoked a mean 27.3 $\pm$ 11.6 years. No significant differences in the duration of smoking were found between these two categories.

The results of oscillographic measurements of total respiratory resistance at different frequencies are shown in Fig. 2. At low oscillation frequencies,

Fig. 1 The chest radiograph of a 57-yr-old coal miner with category 2 CWP. Note the numerous fine nodular (diameter = 2 mm) shadows in both lungs and emphysematous changes in the bilateral lower lung fields. The lung markings are obscured. Results of lung function study showed the following: FVC = 97%p, FEV = 71%p, FEV1/FVC = 68%, TLC = 113%p, RV/TLC = 39%.

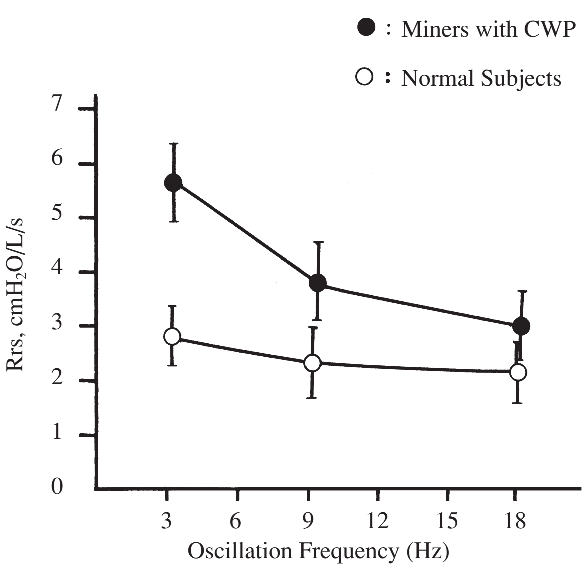

Fig. 2 Values (mean ± SD) of total respiratory resistance at different frequencies in healthy subjects and miners with simple CWP. Note that frequency dependence of Rrs is present only in the miners.

miners with CWP had definitely elevated Rrs values compared with the healthy subjects. In addition, there was a negative frequency dependence of Rrs in miners which was not pronounced in the healthy subjects. Among different oscillation frequencies produced by the sine-wave generator, the highest values of Rrs were found at 3 Hz (Rrs3). Therefore, Rrs3 was used in this study as a sensitive index of airway obstruction and narrowing of the airways.

Observations of airway patency for the miners (Table 1) revealed that they had a significantly lower FEV1/FVC ratio and higher Rrs3 than the healthy subjects. Of more interest is the finding that the FEV1/FVC ratio progressively decreased as the Rrs3 increased with transition from category 1 to category 2 and 3 in both nonsmoking and smoking miners. Clinically obvious airway obstruction was present in category 2 and 3 disease as the FEV1/FVC ratio began to fall below 70%. Although there was a constant trend for the FEV1 to decrease as the radiological category increased, there was no significant difference in the values between miners with category 1 disease and healthy subjects.

As shown in Table 2, the lung volume changes in miners were also consistent with a pattern of obstructive ventilatory defect, regardless of smoking status. The RV/TLC% increased significantly in the miners compared with that in the healthy men. In addition, miners in category 2 and 3 had a well-preserved FVC compared with that in the healthy subjects. Of note, miners with category 1 disease had the largest TLC values among all study subgroups, and there was a trend for TLC to decrease with the increase in radiological category. Similar to the FVC, the TLC remained normal even in category 2 and 3 disease.

Table 3 shows the correlation analysis relating FEV1 (%p) to Rrs3, Grs3, and TLC in both nonsmoking and smoking miners. Although the correlation between FEV1 and Rrs3 was significant, it was not very good (r = −0.453 for nonsmokers and −0.469 for smokers). A better relationship was achieved between the FEV1 and Grs3, i.e., when the respiratory resistance was replaced by respiratory conductance at 3 Hz. In contrast with the healthy subjects, there was a poor correlation between the FEV1 and TLC in the miners group. However, the RV/TLC% and Grs3 correlated well (r = −0.763, $p < 0.001$) in miners in different radiological cate-

Table 1. Level of Airway Obstruction in Miners with Pneumoconiosis by Smoking and Radiological Categories

	N		FEV1 (%p)	FEV1/FVC (%)	Rrs3 ($cmH_2O/L/s$)
Nonsmokers					
Healthy subjects	19		99.7 ± 9.8*	83.5 ± 6.1*	2.6 ± 0.4†
Miners	16				
category 1		9	95.4 ± 10.6*	76.5 ± 11.3‡	3.5 ± 0.3*
category 2 & 3		7	79.5 ± 11.8	68.0 ± 9.4	5.2 ± 0.5
Smokers					
Healthy subjects	17		97.3 ± 10.5*	82.0 ± 6.9*	3.1 ± 0.4†
Miners	55				
category 1		19	93.8 ± 11.5*	75.8 ± 10.2‡,§	5.0 ± 0.4*
category 2 & 3		36	76.3 ± 10.9	69.7 ± 10.3	6.2 ± 0.5

Abbreviations: FEV1: forced expiratory volume in 1s; FVC: forced vital capacity; Rrs3: respiratory resistance at 3 Hz; %p: percentage of predicted values; *: Values are significantly different from those of miners with category 2 and 3 disease, $p < 0.001$; †: Values are significantly different from those of miners in both radiological categories, $p < 0.001$; ‡: Values are significantly different from those of healthy subjects, $p < 0.05$; §: Values are significantly different from those of miners with category 2 and 3 disease, $p < 0.05$.

Table 2. Lung Volume Changes in Miners with Pneumoconiosis by Smoking and Radiological Categories

	N		FVC (%p)	TLC (%p)	RV/TLC (%)
Nonsmokers					
Healthy subjects	19		100.2 ± 7.3	101.5 ± 6.3*	26.5 ± 6.2*,†
Miners	16				
category 1		9	97.5 ± 9.1	110.8 ± 10.1†	34.2 ± 6.7
category 2 & 3		7	94.3 ± 10.2	94.4 ± 14.3	37.5 ± 9.1
Smokers					
Healthy subjects	17		97.4 ± 7.7	103.3 ± 5.8*	28.1 ± 7.0*,†
Miners	55				
category 1		19	95.7 ± 10.2	112.1 ± 10.5†	34.9 ± 6.4
category 2 & 3		36	94.4 ± 11.0	97.4 ± 13.8	38.3 ± 8.4

Abbreviations: FVC: forced vital capacity; TLC: total lung capacity; RV: residual volume; %p: percentage of predicted values; *: Values are significantly different from those of miners with category 1 disease, $p < 0.01$; †: Values are significantly different from those of miners with category 2 and 3 disease, $p < 0.001$.

gories (Fig. 3).

DISCUSSION

The major components of coalmine dust, i.e., carbon and silica, undergo little degradation in vivo. Deposition of these inhaled particles in the lungs leads to radiological changes.[15] Pathologically the pulmonary lesions of CWP are coal macules and fibrosis. Cellular reactions to the dust particles consist of macrophages and fibroblasts as well as collagen and reticulin fibers.[16,17] These findings give the impression that the main physiological impairment in CWP is that of a restrictive ventilatory defect. Indeed, years of underground coal mining does affect the FVC and TLC, and CWP is generally regarded as an interstitial fibrotic lung disease. Massive fibrosis of the lungs (the disabling form of this disease) inevitably results in volume reduction. On the contrary, simple CWP (the uncomplicated form) is associated with little functional change when assessed by conventional ventilatory tests.[18] Nevertheless, min-

Table 3. Correlation Coefficients between FEV1 and Rrs, Grs, and TLC in Healthy Subjects and Miners with CWP

	Nonsmokers		Smokers	
	Healthy subjects	Miners with CWP	Healthy subjects	Miners with CWP
N	19	16	17	55
Rrs3, $cmH_2O/L/s$	– 0.060	– 0.453*	– 0.071	– 0.469*
Grs3, $L/s/cmH_2O$	0.107	0.582†	0.098	0.624†
TLC, %p	0.566†	0.134	0.553†	0.125

Abbreviations: FEV1: forced expiratory volume in 1s; Rrs3: respiratory resistance at 3 Hz; Grs3: respiratory conductance at 3 Hz; TLC: total lung capacity; CWP: coal workers' pneumoconiosis; %p: percentage of predicted values; *: $p < 0.05$; †: $p < 0.001$.

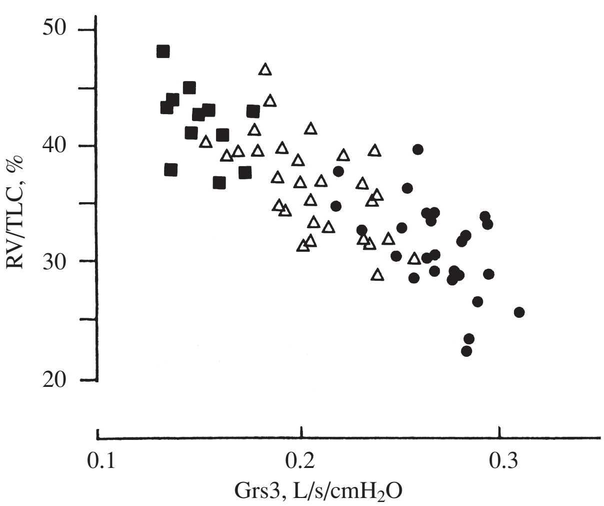

Fig. 3 Relationship between the RV/TLC ratio and respiratory conductance at 3 Hz in miners with simple CWP; r = – 0.763. $p < 0.001$. Closed circles = radiological category 1; triangles = category 2; closed squares = category 3.

ers with simple pneumoconiosis often complain of bronchitic symptoms characterized by cough and sputum production with or without airway obstruction.[19] Since the reticular nodulation pattern of simple pneumoconiosis on chest radiographs represents the initial stage of dust deposition, it is reasonable to postulate that the predominant physiological abnormality in simple CWP is airway obstruction, and pulmonary parenchymal fibrosis causes little change in lung volume during the early development of CWP.

In expiratory spirograms, the FVC and FEV1 are the two most important parameters assessing lung volume and airway obstruction, respectively. However, our study demonstrated that the FVC was normal in uncomplicated CWP, and slightly decreased measurements of the FEV1 (79.5%p) were only observed in miners with category 2 and 3 disease. This is not a surprising finding. Cooper and Johnson[20] found that in a population of 690 miners applying for disability compensation, only 111 (16.1%) had a FEV1 <70%. Unfortunately, the RV and TLC were not measured in their study. In a series of 65 patients with simple CWP, Zhicheng[21] reported 48 (74%) had normal values for the FVC and FEV1. Radiological classification, however, was not taken into account. Hsieh et al.[22] noted hyperinflation of the lungs in coal miners. Their ventilatory capacity progressively decreased with increasing radiological category. However, the analysis did not control for a smoking history. Therefore, the effect of coal dust exposure on lung function has not been sufficiently studied. The statement that airway obstruction is a predominant feature in simple CWP, in terms of physiological impairment, is inconclusive based upon measurements of the FVC and FEV1.[15,23]

The present results show that additional functional parameters including the FEV1/FVC and RV/TLC ratios were significantly impaired in simple CWP. It is of note that measurements of the FEV1, after correction for the FVC, should be more sensitive than the FEV1 alone in detecting airflow limitation. In fact, the FEV1/FVC ratio has been reported to be a good spirometric indicator of abnormality in obstructive lung disease.[24] In addition, Sterk and coworkers[25] found that the RV/TLC was a better index than the closing volume in detecting early emphysema in smokers. Therefore, it would be reasonable to demonstrate abnormal FEV1/FVC and RV/TLC ratios in miners with pneumoconiosis in this study. The lack of correlation between the FEV1 and TLC in miners may reflect an early sign of shrinkage in lung volume during progression from simple CWP to progressive massive fibrosis.

The application of forced oscillation during tidal breathing has been employed to measure the impedance of the respiratory system.[26,27] This method is generally accepted to evaluate airway obstruction. Dellacà and associates[6] compared a sample of healthy subjects and patients with COPD, and found that the latter had larger Rrs values. Data concerning impedance in patients with CWP are very limited at the present time. In our study the Rrs was already abnormally elevated in category 1 disease and there was a decrease in resistance with frequency. The frequency dependence of flow resistance is demonstrable in many instances including asthma, pulmonary emphysema, and chronic bronchitis.[5] It often coexists with the frequency dependence of compliance. The frequency dependence of resistance and compliance are thought to be an effect of uneven distribution of mechanical properties in the lungs, e.g., uneven time constant in different regions of the lungs.[6] The frequency dependence of resistance in healthy subjects is of small and insignificant magnitude.

The finding of an increased impedance of the respiratory system in combination with abnormal changes in the spirometric parameters and chest radiographs made us consider that the predominant pattern of functional abnormality in simple CWP is airway obstruction, and the fibrogenic effects of coal dust on lung parenchyma play a minor role in functional impairment at this stage. Our explanation of this phenomenon is that deposition of coal particles in the airway occurs earlier and faster than in the alveoli. These formed coal macules center around the walls of terminal bronchioles and obstruct their lumen.[28] There is inflammatory and fibrotic narrowing of the peripheral airways. Moreover, anthracosis and deformity of large airways also occurs.[17,29] The pathology of this condition thus leads to a reduction in airflow. However, our study was limited by the small number of miners with category 3 disease. Whether an obstructive ventilatory defect remains a major physiological abnormality in this subgroup of simple CWP needs further investigation.

A large proportion of the miners in this study were smokers. It is now well known that cigarette smoking can cause a considerable loss of lung function. Although the mechanisms of the adverse effects of smoking are, to a large extent, unknown, the contribution of inhaled particles, other than the toxic substances in question, to the impairment of function should be taken into account.[30] It has been shown that cigarette smoking induces serious lung functional changes in miners, and the effects of smoking are much more prominent than those of coalmine dust.[1,28] On the contrary, the results of other studies show that all miners with CWP are subject to a decrease in ventilatory function, even if they don't smoke.[4,19] Miners with pneumoconiosis who are cigarette smokers have a significantly lower FVC, FEV1, and FVC/FEV1 ratio than non-smokers. There is also no apparent relationship between smoking and radiological progression, and thus between smoking and the functional deterioration of CWP.[1] In this study, we were able to demonstrate that nonsmoking miners did have a higher degree of airflow limitation than their normal counterparts. Thus, it is possible that exposure to coal dust alone is capable of inducing functional changes in the respiratory system.

In conclusion, simple CWP is not associated with an appreciable decline in lung volume. In contrast, pronounced bronchial obstruction can be detected early by discriminative lung functional parameters such as the FVC/FEV1 and RV/TLC ratios and more extensive analysis such as forced oscillation indices. Reduction in expiratory airflow can cause hyperinflation of the lungs and an increase in dead space, and this may be the explanation for the respiratory symptoms and exercise limitation experienced by miners with simple CWP.

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罹患單純塵肺症之台灣煤礦工人的氣道功能與呼吸阻力

楊錫欽 林鈺芳

背 景：煤礦塵是由碳粒與二氧化矽 (矽子) 所組成，其職業性暴露終將導致重度肺纖維化。然而臨床上對於罹患煤礦工人塵肺症之患者所作的觀察卻顯示本病在發展的初期，呼吸道功能之異常才是一個主要的表徵。因此，罹患單純煤礦工人塵肺症時的生理異常需要更精密的檢查方法來加以測定。

方 法：為要探討因暴露於煤礦塵而導致的氣道變化，我們針對 71 位罹患單純煤礦工人塵肺症之患者與 36 位正常健康者實施多項肺功能檢查包括用力呼氣圖形、全肺容積測定與呼吸阻力的評估；其中全肺容積是以體箱計測定，而呼吸阻力則是以強制振盪法在 3, 9, 及 18Hz 的頻率下加以評估。

結 果：數據顯示罹患單純煤礦工人塵肺症之患者，其用力肺活量仍然正常且保存良好。而具塵肺症 X 光第一等級之礦工其 FEV1 與正常健康者相較並無差異。另一方面，煤礦工人組的氣道流速卻異常受阻，此表現於 FEV1 與／或 FEV1/FVC 之異常低下，且受阻的程度隨著塵肺症胸部 X 光的等級而增加。無論有無吸菸，罹患塵肺症 X 光第二，三等級之礦工其 FEV1/FVC 比值均低於 70%。全肺容積測定則發現這些患者的殘氣量／全肺量之比值升高，代表他們的肺臟處於過度充氣的狀態；呼吸阻力的評估結果則顯示礦工組在 3 周波時有異常上升，且上升的幅度隨著周波數的增加而遞減。此在 3 周波時的呼吸阻力亦隨著 X 光等級之增加而有上揚的趨勢，而其殘氣量／全肺量之比值與在此頻率下的呼吸傳導度 (Grs3) 則有顯著的負相關 ($r = -0.763$, $p < 0.001$)。

結 論：罹患單純煤礦工人塵肺症之患者其呼吸功能上主要的變化是氣道阻塞，至於其肺容積則並無異常減少。所以在罹患單純煤礦工人塵肺症之患者，不論其 FEV1 是否下降，呼吸阻力都可作為偵測氣道阻塞上的一種敏感指標。

(長庚醫誌 2009;32:438-46)

關鍵詞：氣道阻塞，煤礦工人塵肺症，呼吸阻力，強制振盪法

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