Pulmonary Function Impairment in Pneumoconiotic Patients with Progressive Massive Fibrosis

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Background: Progressive massive fibrosis (PMF) is the severe form of coal workers' pneumoconiosis (CWP). Clinical observations have suggested that the components of PMF are inhomogenous. There may be a significant diversity in the magnitude of pulmonary impairment for miners with PMF. This study is intended to investigate the relationship between radiological categories of PMF and pulmonary impairment.

Methods: Eighty-six coal workers with radiological evidence of PMF were enrolled. They were subdivided into 3 categories, i.e., A, B, and C according to the International Labour Office (ILO) classification. Maximal expiratory flow-volume curves and diffusing capacity were measured in each subject.

Results: Our data reveal that forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1) were abnormally low in all categories. However, FVC was only mildly reduced in category A, and then rapidly decreased with the progression of radiological category. The major pattern of impairment for miners with PMF was obstructive, but there was an increasing trend for restrictive impairment for higher radiological categories. A normal spirogram was still observed in 6-11% of subjects in category A and even B. For diffusing capacity (DLCO), there was also a progression of impairment with transition from category A to categories B and C. Smoking miners had even lower FEV_1/FVC and DLCO than did their non-smoking counterparts.

Conclusions: Pulmonary impairment increased with increasing radiological category even in PMF. Assessment of lung function should be individualized and carried out with a combination of tests, i.e., spirometry and DLCO measurement. The loss of lung function cannot be accounted for by different smoking habits.

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Key words: coal workers' pneumoconiosis, progressive massive fibrosis, lung function.

Coal workers' pneumoconiosis (CWP) is the most common inhalational lung disease caused by deposition of respirable coal-mine dust and tissue reaction to its presence.[1,2] Radiographically, CWP is classified into 2 forms, i.e., simple pneumoconiosis and progressive massive fibrosis (PMF).[3] Workers

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with PMF are subject to profound lung functional impairment.[4] In the clinical setting, PMF may progress from simple pneumoconiosis,[5,6] and large opacities may be accidentally resected because they resemble lung cancer. Moreover, cor pulmonale resulting from the malfunctioning lung and recurrent respiratory infection increases the mortality of miners with PMF.[7]

Numerous studies regarding the lung functional changes in CWP have been previously published.[8-10] However, clinical observations have shown that considerable variations in the magnitude of pulmonary impairment exist among miners with PMF. Moreover, pulmonary impairment in PMF assessed according to chest radiographic category and evaluated by principle component analysis[11] have rarely been conducted. In Taiwan, there are no published data on the deleterious effects of CWP in the past 2 decades.[12,13] The purpose of this study was to determine the relationship between radiological category of PMF and pulmonary impairment. The role of cigarette smoking in the progression of functional deterioration in PMF was also investigated.

METHODS

Between October 1998 and February 2000, a total of 1336 working miners and ex-miners visited the medical clinics of 2 teaching hospitals in northern Taiwan. The purpose of their visits to the hospitals was to determine the possibility of their claiming compensation for pneumoconiosis. Their ages ranged from 45 to 76 years. Duration of exposure to coal-mine dust ranged from 2 to 42 years.

Control workers were selected from the almost 600 employees of a local 300-bed hospital and a petroleum company in Keelung where no dust exposure existed. They were healthy professionals, engineers, administration assistants, and service personnel. There were approximately 220 workers aged over 40 who had been requested by their institutions to undergo medical examinations. Nearly 1/2 of them were female. Of the remaining 119 male workers, a final analysis was made on 93 because 21 had cardiovascular disorders, 4 had bronchial asthma or chronic obstructive airway disease, and 1 had tuberculosis.

Each subject underwent a physical examination. Health information such as occupational history, lifetime smoking habits, and past histories regarding hypertension, diabetes, chronic lung and heart diseases, and neuromuscular disorders were obtained from a questionnaire survey modified from those presented in the Epidemiology Standardization Project.[14] We defined smokers as those who had smoked for more than a 1/2 pack-year. Respiratory symptoms such as chronic cough, shortness of breath, chest pain, sputum production, and wheezing were also recorded.

Each subject had a full-sized (32¡Ñ 44 cm) posteroanterior chest radiograph. Roentgenologic features were independently interpreted by 2 medically qualified physicians according to the International Labour Office (ILO) classification.[3] Films showing a normal chest or simple pneumoconiosis, i.e., small irregular and/or rounded opacities in the absence of conglomeration, were excluded. Subjects with abnormal roentgenologic findings suggestive of active tuberculosis, bronchiectasis, pulmonary emphysema without pneumoconiosis, or cardiovascular disorders were not enrolled in this study. Large opacities representing progressive massive fibrosis were further classified into 3 categories according to their size.

Category A: Sum of the greatest diameter of 1 or more opacities exceeding 1 cm but less than 5 cm.

Category B: Sum of the greatest diameter of 1 or more opacities exceeding 5 cm , but their combined area not exceeding the equivalent of the right upper lung zone.

Category C: One or more opacities with combined area exceeding the equivalent of the right upper zone.

For lung function measurement, each subject was asked to make at least 3 forced expirations after inspiration to total lung capacity. Subjects were not allowed to take bronchodilators or steroids for at least 12 hours prior to testing. Maximal expiratory flow-volume curves were recorded with an automated plethysmograph (CS-828FC, CHEST, Inc., Japan). FVC, FEV_1, and FEV_1/FVC were reported based upon the best of 3 technically acceptable tests. The values were converted using body temperature, pressure, and saturation (BTPS). Predicted values were calculated using equations of Yang[15] for nor-

mal non-smoking ethnic Chinese.

Single-breath carbon monoxide diffusing capacity (DLCO) was measured in duplicate for each subject who had radiological evidence of PMF. Integrated and automated equipment (CHESTAC-55, CHEST) was used for this purpose. Test procedures were conducted by previously described method.[16] The average of the 2 DLCO and DLCO/VA values (VA = alveolar volume) were compared to the predicted data.

Since miners might have intended to make a submaximal effort to carry out the maneuvers in order to increase their chances of being awarded compensation, quality assurance of the spirometric tests was an important issue in this study. Forced expiratory volume tracings had to be reproducible. The extrapolated volume in the measurement of FEV_1 should be less than 5% of FVC. Spirograms rounded shape the flow-volume graph at the highest point were discarded. Expiratory maneuvers should not contain coughing or show variable flows and early termination. When 3 satisfactory tracings were obtained, we also required that the 3 FVC values agreed with each other within 5%.

For DLCO determination, tests showing a slow inspiration or an inspired volume < 90% of the subject's vital capacity (VC) were rejected. Units for DLCO are milliliters of CO per minute per mmHg, and VA is in liters. To correct the potential effect of CO back pressure in smokers, venous blood was drawn for measurement of carboxyhemoglobin using a CO-oximeter (OSM-3 Hemoximeter, Radiometer, Copenhagen, Denmark). The corrected DLCO values were then calculated according to the following equation:

$$\text{corrected DLCO} = \text{measured DLCO} \times \left(\frac{1 + \text{COHb\%}}{100\%}\right)$$

In order to recognize patterns of functional abnormality that may aid the assessment of pulmonary impairment in PMF, we applied the concept of principle component analysis modified from that of Cowie, et al.[11] The original 3 lung function variables, i.e., FEV_1, FEV_1/FVC, and DLCO were essentially the same except that DLCO was replaced by FVC. Thus, we were able to define 4 mutually exclusive types of functional impairment. Men were considered to have a normal spirometric test if their FVC and FEV_1 values were more than 80% of the predicted values (%p) and FEV_1/FVC was greater than 75%. An obstructive ventilatory defect denoted on FVC of more than 80%p and FEV_1/FVC <75%. A restrictive ventilatory defect was the impression if FVC was less than 80%p, while FEV_1/FVC was greater than 75%. A mixed ventilatory defect indicated that FVC was less than 80 %p, and FEV_1/FVC was less than 75%.

All data were coded, entered into a Cyber DEC-175 computer, and analyzed with Statistical Analysis System (SAS) software. Values are expressed as the mean ± SD. Two-sample *t*-test or ANOVA (analysis of variance) followed by Scheffe's multiple comparison was used for statistical analysis. The significance level was set at 0.05.

RESULTS

Of the 1336 coal workers, 451 were found to have radiological evidence of CWP. Of these, 349 were classified as having simple pneumoconiosis and thus were dropped from the study. Among the remaining 102 men who developed PMF, an additional 16 workers were excluded because 2 had pulmonary tuberculosis, 4 had bronchiectasis, and 10 had no acceptable test, thereby reducing the number of subjects in the final analysis to 86.

Table 1 summarizes the physical and spirometric characteristics of the study population. Coal miners with PMF and control workers had similar ages. However, the miners were shorter and thinner ($p < 0.001$) than the control workers. Of the 86 miners with complicated disease, the mean duration of working underground was 28.6 ± 10.3 years. Job categories included 65 rock drillers, 17 who had worked digging coal lodes, while the rest had worked in various jobs in the collieries. Lung function was markedly reduced in those patients compared to that in control workers ($p < 0.001$). For example, FVC was about 41% below predicted values, while FEV_1 was about 43% below predicted values. Observations of the smoking habits of miners who had PMF revealed a much higher prevalence of smoking than for the control workers. Additionally, they consumed more cigarettes than did smokers of the control group in terms of amount and duration of

Table 1. Basic Characteristics of the Study Population

	Coal miners with PMF (N = 86)	Control workers (N = 93)	*p*
Age (years)	57.3 ¡ 6.8	55.8 ¡ 7.2	0.173
Height (cm)	161.6 ¡ 5.2	166.1 ¡ 6.3	< 0.001
Weight (kg)	55.7 ¡ 9.1	63.5 ¡ 8.6	< 0.001
FVC (L)	1.85 ¡ 0.74	3.47 ¡ 0.54	< 0.001
FEV_1 (L)	1.13 ¡ 0.66	2.92 ¡ 0.42	< 0.001
Smoking habits	No. (%)	No. (%)	
Non-smokers	25 (29)	48 (51)	
Ex-smokers	25 (29)	9 (10)	
Current smokers	36 (42)	36 (39)	
Pack-yr	36.4 ¡ 20.1	17.5 ¡ 20.6	< 0.001

Abbreviations: FVC: force vital capacity; FEV_1: forced expiratory volume in one second.

Table 2. Ventilatory Function and Diffusing Capacity of Miners with PMF by Radiological Category

	Control workers	Miners in radiological category			*p**
		A	B	C	
No.	93	45	32	9	
FVC , %p.	98.6 ¡ 12.4	78.6 ¡ 15.5	54.2 ¡ 16.4†	45.1 ¡ 17.3†	< 0.001
FEV_1, %p.	96.0 ¡ 13.5	75.7 ¡ 18.2	50.3 ¡ 16.6†	40.9 ¡ 16.8†	< 0.001
FEV_1/FVC , %	81.5 ¡ 9.0	62.3 ¡ 14.9	65.1 ¡ 11.8	70.4 ¡ 12.7	0.645
DLCO, %p.	100.2 ¡ 15.7	66.2 ¡ 17.3	53.8 ¡ 18.0†	33.5 ¡ 11.2†,‡	< 0.001

Abbreviations: FVC: force vital capacity; FEV_1: forced expiratory volume in one second; DLCO: single-breath carbon monxide diffusing capacity.

*: *p* value was calculated by ANOVA for the significance of difference among miners with various radiological categories of PMF.

†: Values are significantly different from those of category A by Scheffe's multiple comparison, $p < 0.001$.

‡: Values are significantly different from those of category B by Scheffe's multiple comparison, $p < 0.001$.

smoking.

As Table 2 shows, 45 of the 86 subjects (52.3%) with PMF were classified as category A from initial X-ray films, whereas 32 men (37.2%) were classified as category B and 9 (10.5%) as category C. All mean values of spirometric parameters were significantly lower ($p < 0.001$) in men who had complicated disease than in control workers. For FVC and FEV_1, there was a significant progression of impairment with the transition from category A to B. It is of interest to note that FVC and FEV_1 in patients with category A only slightly deviated from their lower normal limits (80%p). However, a remarkable decrease in both parameters was observed with increasing category, thereby leading to a similar FEV_1/FVC among various categories. In addition, when the DLCO of miners who had PMF was plotted against radiological category, there was a constant downward trend in values as the category increased.

In regard to the patterns of impairment, all of the control workers were normal except for 5 (5.4%) presenting with an obstructive abnormality. Among these, 4 were heavy smokers. On the other hand, approximately 60% of the men who had complicated disease had an obstructive ventilatory defect (Table 3). However, normal spirometry might still be demonstrated in a small proportion (6-11%) of subjects, even there in category B. It is also noteworthy that the percentage of subjects showing an obstructive defect decreased in category C, resulting in the dominant type of impairment being "restrictive" or "mixed" in this category of patients.

Table 3. Patterns of Functional Abnormality in Coal Miners with PMF by Radiological Category

Category	Patterns of abnormality			
	Normal	Obstructive	Restrictive	Mixed
A (N=45)	5 (11.1)	29 (64.4)	8 (17.8)	3 (6.7)
B (N=32)	2 (6.2)	18 (56.2)	6 (18.8)	6 (18.8)
C (N=9)	0 (0)	4 (44.4)	3 (33.3)	2 (22.2)
Total (N=86)	7 (8.1)	51 (59.3)	17 (19.8)	11 (12.8)

Figures presented are the no. of patients (percentage).

Table 4. Prevalence of Abnormal Diffusing Capacity* in Miners with PMF by Radiological Category

Category	Variable	
	DLCO (ml/min/mmHg)	DLCO/VA (ml/min/mmHg/L)
A (N=45)	39 (86.7)	42 (93.3)
B (N=32)	29 (90.6)	31 (96.9)
C (N=9)	9 (100)	9 (100)
Total (N=86)	77 (89.5)	82 (95.3)

Abbreviation: DLCO: single-breath carbon monxide diffusing capacity.
*: Lower limits of normal for all DLCO variables were defined as 80 % of the predicted.
Figures presented are the no. of patients (percentage).

Table 5. Comparison of Pulmonary Impairment in Non-smoking and Smoking Miners with PMF

	Non-smokers	Smokers	*p*
No.	25	61	
Radiological category	No. (%)	No. (%)	
A	14 (56)	31 (51)	
B + C	11 (44)	30 (49)	
FVC, %p	60.5 ¡ 18.9	57.1 ¡ 17.4	0.462
FEV_1, %p.	55.6 ¡ 17.7	53.6 ¡ 18.1	0.681
FEV_1/FVC, %	64.2 ¡ 16.8	56.3 ¡ 16.5	0.009
DLCO, %p	58.4 ¡ 12.3	50.2 ¡ 14.9	0.002

Abbreviations: FVC: force vital capacity; FEV_1: forced expiratory volume in one second; DLCO: single-breath carbon monxide diffusing capacity.

Mean values for DLCO and DLCO/VA in control workers were 100.2 ¡ 15.7%p and 98.5 ¡ 12.1%p respectively. None of them had an abnormally low (<80%p) DLCO or DLCO/VA. As shown in Table 4, a high prevalence of impaired gas transfer among miners with PMF was found. Only about 10% of subjects in this series had a normal DLCO. Moreover, it is evident that a high prevalence of reduced diffusing capacity was consistently observed with increasing category, and virtually all patients in category C had an abnormal DLCO. The specific pulmonary diffusing capacity (DLCO/VA) seemed able to identify more men with diffusion abnormality than did DLCO.

The lung function of non-smoking and smoking miners with complicated pneumoconiosis is shown in Table 5. Because of the small number of subjects in category C, they were summed into category B, and then compared to those in category A. Smokers included current and ex-smokers. Our results show that there was a comparable percentage of smokers in both groups. It is apparent from this table that both FVC and FEV_1 were obviously reduced irregardless of smoking habits, and that there were no differences in these values between non-smoking and smoking miners. However, smoking subjects had a higher degree of airway obstruction, in terms of FEV_1/FVC, than did non-smoking subjects. In addition, smoking miners also had a significantly lower DLCO than did non-smoking miners.

DISCUSSION

The history of coal mining in Taiwan can be traced back to the late 17th century during the Ching dynasty. However, a booming local coal industry was observed only between 1960 and 1985. In those prosperous years of coal mining, approximately 70,000 workers were employed. Since there were no surface coal mines on the island, most miners had to work underground and were thus inevitably exposed to a considerably high concentration of coal-mine dust.

Our data indicate that 22.6% of the men with CWP presented the complicated form of this disorder. This figure is quite close to that (23.7%) reported by Morgan et al.[17] for eastern Pennsylvania anthracite miners of the US. However, the prevalence of pneumoconiosis category 2 or 3 or PMF was reported to be 2.9 % among working British coal miners.[5] Because cumulative dust exposure, category of simple pneumoconiosis, and age of miners were each found to affect the probability of developing PMF,[5] regional differences in prevalence may be

explained in part by the fact that we included ex-miners in the sample. In general, ex-miners were older and had a longer duration of exposure to respirable dust than did working miners. Besides, it should be emphasized that virtually all miners on this island had worked with little or no respiratory protection, and there were no government-enforced dust control programs until the 1990s. All of these factors account for the high prevalence of PMF in Taiwanese coal miners.

The current minimal requirement applicable to Taiwan miners for claiming disability compensation, in terms of lung function impairment, is 1 of the following: (i) FVC < 80%p, (ii) FEV_1 < 80%p, (iii) FEV_1/FVC < 75%, and/or (iv) DLCO < 80%p. Therefore, a man with radiological evidence of PMF but who was spirometrically normal would encounter difficulty in claiming compensation for respiratory impairment unless he also had an abnormal DLCO.

In Taiwan, the effect of coal dust exposure on lung function of miners has not been adequately studied. In a series of 142 silicotic patients, Wu[13] reported that 41.8% of them had the restrictive pattern of functional impairment, while obstructive ventilatory defect was found in only 7.8% of the sample. Hsieh et al.[12] noted that there was hyperinflation of the lungs of coal miners. Their ventilatory capacity progressively decreased with increasing radiological category. However, patients with different categories of PMF were lumped together and regarded as a whole while making comparisons with others.

Results of this study show that the components of PMF are inhomogenous from a functional point of view. There is extensive diversity in the level of respiratory impairment among patients with this clinical entity. Therefore, to consider that all miners with PMF have a high magnitude of functional abnormalities may be misleading. Assessment of pulmonary function of workers even with this severe form of pneumoconiosis should be individualized. This is especially true in the management of claimants for disability compensation.

The present study shows that the conventional spirogram was normal in a few miners with category A and even B PMF. Among them, however, 3 with category A and 2 with category B still had an abnormally low DLCO. The finding that profound diffusion impairment might be present in subjects with PMF and who had a normal FVC and FEV_1 is very important to both miners and the Bureau of Labor Insurance, the 2 main parties concerned in the process of disability determination.

Abnormal lung function in pneumoconiosis is usually assessed by individual spirometric parameters. It is certain that analysis using a set of linear combinations of variables will select more men with abnormal lung function than will the conventional method. This approach may also provide insight into the various functional patterns of abnormalities which the lung may express. Although complicated pneumoconiosis may be accompanied by obstructive, restrictive, and mixed patterns of ventilatory impairment, a detailed distribution of abnormal patterns according to radiological category has not been well documented. In 1974, Morgan et al.[18] noted that the onset of PMF is associated with a remarkable and substantial decline in FEV_1 and FEV_1/FVC, while only minor changes were observed for FVC. Our data indicate that obstructive ventilatory defect is a prominent feature in all categories of PMF. However, increased prevalence of restrictive and mixed impairment become obvious as the disease progresses.

The pathogenesis of CWP[19,20] may be closely related to functional abnormalities seen in PMF. In simple pneumoconiosis, coal macules center around the walls of respiratory bronchioles. At this stage, reduction in airflow[21] can be detected. As the disease progresses, macules increase in size and may converge and coalesce. As a result, lung tissues are stretched and lung volumes are reduced. Therefore, our finding that there is a trend from obstructive to restrictive or mixed ventilatory defect with increasing category of PMF can be well explained by the sequential histological changes observed in CWP.

The reduction in diffusing capacity in subjects with PMF can be explained by a loss of lung volume or excessive airflow obstruction, or both.[22] As discussed previously, emphysema and lung fibrosis may be concomitantly present in complicated pneumoconiosis. Pulmonary emphysema is associated with alveolar destruction and increased dead space, whereas lung fibrosis results in volume reduction and thickening of alveolar membrane. However, the question of whether emphysema occurs as a complication of CWP or as a consequence of cigarette smoking has been raised.

The role of cigarette smoking in the pathophysi-

ologic consequences of CWP is still a matter of debate. Gross et al.[23] pointed out that cigarette smoking induces serious lung functional changes in coal miners, and the effects of smoking are much more prominent than those of coal-mine dust. Morgan et al.[17] also conceded that cigarette smoking is preeminent in the pathogenesis of obstructive airway disease in coal workers. In contrast, there are a number of studies that have shown that smoking habits are unrelated to lung functional changes in CWP.[12,24] Moreover, autopsy data on miners from the study of Lyons and colleagues[25] indicated that the amounts of emphysema in smokers and non-smokers were similar.

Our results indicate that the ventilatory function of non-smoking miners with PMF is already significantly impaired. This serves as supporting evidence of the viewpoint that inhalation of respirable coal-mine dust itself is capable of inducing the functional changes in the lung. Of course, the interaction between the effects of cigarette smoking and the effects of occupational exposure is difficult to resolve with epidemiologic studies. But this is relatively unimportant for disability compensation if we can be sure that the pulmonary impairment did not result from cigarette smoking alone.

In summary, assessment of the functional status of coal workers with PMF is still inconclusive when only a simple ventilatory test is applied. Measurement of diffusing capacity may be able to identify additional subjects with pulmonary impairment. Furthermore, the functional abnormalities observed in PMF cannot be totally explained by cigarette smoking, although the latter possibly exerts significant influences on the former. This information may be of help to those individuals and institutions involved in the management of disability compensation for PMF.

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進行性重度肺纖維化之肺功能不全

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背 景： 進行性重度肺纖維化是煤礦工塵肺症中較爲嚴重的一型，但臨床經驗顯示即使同屬重度肺纖維化之礦工群，彼此間在肺功能損害的程度上仍然有很大的差異。過去甚少對此型患者再詳加分類，以觀察其群內呼吸功能低下之演變情況。然而事關我國勞工安全衛生制度及塵肺症殘廢標準之建立，實需多加以關心。本研究之目的乃在探討進行性重度肺纖維化時X光等級與肺功能損害之間的關係，並觀察吸菸與否在此等功能演變上所扮演的角色。

方 法： 本研究針對86位罹患進行性重度肺纖維化之煤礦工進行觀察分析。他們的胸部X光表現依國際勞工組織的分類法分爲A , B , C三個等級。每位礦工均接受用力吐氣流速—容積圖形與肺瀰散量測定；其職業工作史、過去病史、呼吸症狀之有無與吸菸習慣等則以問卷的方式加以調查。

結 果： 與對照組勞工相比，罹患進行性重度肺纖維化之礦工，不論其X光等級爲何，FVC與FEV1均有異常低下的現象。FVC之異常且隨著X光等級而加重。但FVC在A等級之進行性重度肺纖維化只有輕度減少，隨X光片級數即快速下降。故就整體罹患進行性重度肺纖維化之礦工的通氣障礙類型而言，是以阻塞型爲主。但隨著X光等級的升高，則拘限型的出現率會增加。有6-11%之A , B等級的患者其FVC及FEV_1仍爲正常。肺瀰散功能在進行性重度肺纖維化時之損害亦相當明顯，有89.5% (77/86)之患者其DLCO有異常低下。又吸菸者其FEV_1/FVC及DLCO均比不吸菸者爲更低。

結 論： 煤礦工塵肺症即使進行到重度肺纖維化，其肺功能損害的內涵仍非均勻一致。雖然一般而言，肺功能惡化的程度隨著X光等級的加重而增大，但在殘障鑑定上仍需針對個人作主要考量，並合併通氣功能與肺瀰散量之檢測結果，方能獲致正確的答案。又吸菸並非導致此種損害之唯一因素。

(長庚醫誌 2002;25:72-80)

關鍵字： 煤礦工塵肺症，進行性重度肺纖維化，肺功能。

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