The survival analyses of 2738 patients with simple pneumoconiosis

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Abstract

Objectives—To explore whether the inhalation of coal mine dust increases the risk of premature death in miners, a survival analysis was conducted in a cohort of 2738 patients with simple pneumoconiosis in the Huai-Bei coal mine, in China.

Methods—Age specific mortalities were calculated by disease severity in terms of pneumoconiotic category with the life table method. The progressions from simple pneumoconiosis to death or progressive massive fibrosis (PMF) were analysed with the Cox's regression model with time as the dependent variable to identify risk factors.

Results—During a follow up period (mean 8 y) 3.2% of patients with simple pneumoconiosis developed PMF. The patients with development of PMF presented higher age specific mortalities than those remaining in a state of simple pneumoconiosis (SMR: 3.42; $P < 0.01$). After adjustment for tuberculosis and duration of work, the relative risk of premature death due to development of PMF was 2.4. Tuberculosis was found to be a main risk factor which not only facilitated premature death (relative risk (RR): 2.0; $P < 0.01$), but was also a strong facilitator for development of PMF (RR: 7.0; $P < 0.01$). Also, a long term of work underground and drilling as a main job were identified as risk factors for development of PMF.

Conclusion—The results imply that patients with simple pneumoconiosis will have altered survival, and premature death among them is related to an increased risk of the development of PMF and the complication of tuberculosis.

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Keywords: pneumoconiosis; progressive massive fibrosis; survival analysis

were conducted to explore the effect of inhalation of coal dust on health in terms of the grades of coal workers' pneumoconiosis (CWP), which is diagnosed on the chest radiographic features of a miner. According to the international classification of pneumoconiosis issued by the International Labour Office (ILO),⁵ based on radiographs, this disease is classified as simple (mild) or complicated (severe); these types are further divided into categories 1, 2, and 3 for the simple disease, and categories A, B, C for the complicated disease. Complicated pneumoconiosis is also named progressive massive fibrosis (PMF).³ Ortmeyer *et al* found that the life expectancy of miners as a whole is the same as that of the general population.⁶ A detailed 20 year follow up study of miners and exminers in South Wales showed that those with simple and category A pneumoconiosis survived as well as those with no evidence of pneumoconiosis.^{7,8} A raised mortality was found only in miners with category B and C pneumoconiosis.⁹

However, Miller and Jacobsen reported a study of 26 363 miners from 20 collieries in England and Wales, and concluded that miners exposed to excessive amounts of inhalable coal dust were at an increased risk of premature death, either from PMF or from chronic bronchitis or emphysema.¹ A recent study conducted by Meijers *et al* in The Netherlands also showed that Dutch miners with CWP had an increased overall mortality risk with a standardised mortality ratio (SMR) of 153 in comparison with the general Dutch male population.² Unfortunately, this analysis could not link each death to any individual coal miner and so it was not possible to investigate the influence of the pneumoconiosis grade on the mortality differences and to make dose-effect computations.

To evaluate the effect of exposure to coal dust on miners' health, Soutar and Hurley also studied pulmonary function.^{10,11} Coal miners had a lower forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC), but no obvious change in FEV₁/FVC. Attfield and Hodous studied the relation between cumulative dust exposure and several variables of pulmonary function in 7139 coal miners in the United States.¹² Their results indicated clear exposure-response relations between various pulmonary functions and estimated cumulative dust exposure even in the absence of radiographically detected pneumoconiosis. This means that coal dust is harmful to workers' health regardless of the pneumoconiosis grade.

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The question, "does the inhalation of coal mine dust increase the risk of premature death in miners?" has been debated for a century from the standpoint of both scientific interest and financial compensation policy.¹⁻³ The earliest observations suggested that coal miners had good health and low death rates and therefore some observers were convinced that working conditions in coal mines were not unhealthy.⁴ Over the past few decades studies

However, whether simple pneumoconiosis increases the risk of premature death—that is, whether a miner's life span will be curtailed because of affected lung function—is still inconclusive. As PMF has been recognised to be a potentially disabling form of CWP, relations between simple pneumoconiosis and PMF have been studied by a few researchers. With data from the pneumoconiosis field research, Hurley *et al* studied the incidence of PMF in relation to earlier simple pneumoconiosis and dust exposure.¹³ This study clearly showed that simple pneumoconiosis predisposed to PMF, with five year attack rates of 13.9%, 12.5%, 4.4%, and 0.2% among men in categories 3, 2, 1, and 0 respectively at the start of the risk periods. Cumulative dust exposure was an important risk factor for development of PMF among miners without pneumoconiosis, but not among miners who had been identified as having pneumoconiosis. A study conducted by Maclaren and Soutar showed that among 172 patients who had developed PMF, 116 had had simple pneumoconiosis at the earlier examination; this study also indicated that simple pneumoconiosis was a strong risk factor for PMF.¹⁴ Therefore, the problem of whether simple pneumoconiosis increases the risk of premature death rationally involves development of PMF among these patients.

The study described here reanalysed a data set collected from a cohort of patients with pneumoconiosis in the Huai-Bei coal mine, China, in 1989. The data set, which included 2906 patients, was analysed in 1990 as an example to illustrate the use of a five state model, and a paper was published in Chinese.¹⁵ We thought that this data set might be informative to help explore the relation between simple pneumoconiosis and PMF, now that a validation study on interpretation of pneumoconiosis between Chinese and American classifications has been published.¹⁶ The validation study allows analysis of the Huai-Bei coal mine data set, based on the ILO classification, and the results can be compared with those from studies performed in other countries. To concentrate this study on simple pneumoconiosis, we studied records of 2738 patients who were classified as having simple pneumoconiosis when the diagnosis of CWP was first established. This paper presents results from analysis of the survival of these patients' with the Cox's regression model with the main variables being time dependent.

Materials and methods

DATA SOURCE

The medical diagnostic records of patients for this study were collected from the occupational hospital in the Huai-Bei coal mine, which is located in the middle of China. This mine was set up before 1949, gradually expanded after 1958, and has been one of the large scale coal mines run by the Chinese government. The first patient with pneumoconiosis was identified in 1963. After that, workers were periodically given medical examinations

to detect incident patients. By the end of 1988, there were 2958 workers diagnosed as having pneumoconiosis. According to a prevention policy on pneumoconiosis issued by the Chinese government in the 1960s,¹⁷ a certified patient would be assigned to a non-dusty position once a diagnosis was made, and a yearly medical examination that included a chest radiograph would be given to monitor progression of disease. As the medical records were the unique evidence for determining the amount of the financial compensation, almost all of the patients' records were kept very well. There were 2906 definite records and 52 lost or incomplete, which is an ascertainment rate of 98.24%.

China uses a radiological classification of pneumoconiosis which differs from the ILO classification.⁵ The Chinese system classifies this disease into categories I, II, and III to refer to light, moderate, and severe disease conditions, respectively. However, a comparison of Chinese and American radiograph readers and pneumoconiosis classifications has shown that a valid correspondence exists between the Chinese and American interpretations.¹⁶ Category I represents simple pneumoconiosis, and category III is an equivalent of complicated pneumoconiosis in categories B and C by the ILO classification. Among the 2906 patients in the cohort, 16 patients were in category III, 152 in category II, and 2738 in category I when the diagnosis was first established. To concentrate the study on the prognosis of patients with simple pneumoconiosis, only the data from the 2738 patients were analysed in this study.

From the medical records, the information includes: age when diagnosis of CWP was first established, age of starting mining work, year of starting mining work, years spent working underground, main job category, whether tuberculosis (TB) existed or not when pneumoconiosis categories I, II, or III were established, year and month when complicated pneumoconiosis was found, and the cause of death if the patient had died. Main job category was defined as that from which a patient got dust exposure responsible for the development of his pneumoconiosis. If a patient had worked on several dusty jobs, the one on which he worked for the longest period or got the greatest amount of dust exposure was referred to as the main job. Among the main job categories, drilling alone usually produced a higher concentration of dust with a higher silica content at the workers' air zone. Therefore, this job was coded as 1 and the others as 0. Table 1 shows the demographic data for the 2738 patients.

DATA ANALYSIS

Age specific mortalities for patients in different categories were calculated to examine whether the progression from category I to II or from II to III represented a jump in the mortalities. Person-years for different age groups and disease categories were calculated by assuming that each entry, withdrawal, or death occurred at the middle of the age interval to which it

Table 1 Summary statistics for factors involved in this study

Continuous variables (mean (SD)):	
Age CWP first established (y)	47.6 (7.0)
Average follow up period (y)	8.4 (5.2)
Categorised variables (frequency (%)):	
Age at start of mining (y):	
< 20	597 (21.8)
20–29	1737 (63.4)
30–39	379 (13.8)
≥ 40	25 (1.0)
Year at start of mining:	
Before 1949	460 (16.8)
1949–57	656 (24.0)
1955–62	1474 (53.8)
≥ 1963	148 (5.4)
Years spent on mining:	
< 10	124 (4.5)
10–24	1795 (65.6)
≥ 25	819 (29.9)
Job category:	
Drilling	1049 (38.3)
Non-drilling	1689 (61.7)
Tuberculosis at first establishment of pneumoconiosis:	
Yes	343 (12.5)
No	2395 (87.5)
Outcome variables (frequency (%)):	
Death and survival:	
Dead	366 (13.4)
Survival	2372 (86.6)
Complicated pneumoconiosis (PMF):	
Yes	87 (3.2)
No	2651 (96.8)

belonged.¹⁸ The SMRs were calculated by taking category I as a control group; the hypothesis was tested with the Poisson distribution. This examination showed that the progression from category I to category II did not imply an increase in death risk, but the progression from category I or II to III implied a notable increase in the risk of premature death (table 2).

Therefore, Cox's regression analysis was applied in two strategies. Firstly, we did a general survival analysis to identify risk factors which facilitate premature death. The survival time was defined as the time period from the first establishment of the diagnosis of CWP to death or end of the follow up at the end of 1988. Progressions from category I to categories II or III were defined as dichotomous time dependent variables; the age when the diagnosis was first established and its squared term were added into the model in a form of continuous variables; and the other factors were categorised into several dummy variables (table 1). The time dependency of TB and age were also checked by creating their interaction terms with the survival time. Ties were

Disease progression model: where, T is a rate of the transition from category I to III; P_I and P_{III} are death rates for the patients in category I and III; t_I and t_{III} are the times at which patients arrive in categories, I and III respectively; and X is the vector of covariates.

handled with the Breslow method.¹⁹

Thereafter, a three state model²⁰ was defined based on the disease categories I and III (figure), and Cox's regression analysis was then applied to each transition path. This multistate analysis was expected to provide more detailed information on the effect of the risk factors on premature death and especially on the progression from category I to III—that is, development of PMF. In these analyses, the survival time, failure, and censoring were differently defined for each transition. When the transition from category I to death was analysed, the progression to category III was defined as censoring, only death without the progression as failure, and the survival time was the duration in category I (and II). When the transition from category I to category III was analysed, death before the progression was defined as censoring, and only the progression into category III as failure. The effect of progression from category I to II on the transitions was analysed by defining a dichotomous time dependent variable as in the general survival analysis. The transition from category III to death was analysed only on 87 patients who reached category III before death or the end of 1988. In this analysis, the survival time was measured from the time when the diagnosis of category III was made. To explore the effect of the existence of TB on survival or progression, only information at the start of the interval analysed was used. For example, when the transition from category I to category III or death was analysed, only patients who were found to have TB when their pneumoconiosis was first diagnosed were referred to as TB positive and the others were TB negative.

Table 2 Age specific mortalities for patients with pneumoconiosis by category*

Age	Category I			Category II			Category III		
	Person-years	Death	Death rate	Person-years	Death	Death rate	Person-years	Death	Death rate
< 30	10.0	1	0.100	0.0	0	0.000	0.0	0	0.0
30–	130.0	3	0.023	5.0	0	0.000	0.0	0	0.0
35–	867.5	9	0.010	35.0	0	0.000	0.0	0	0.0
40–	2667.5	28	0.011	200.0	1	0.005	17.5	0	0.0
45–	4462.5	43	0.010	592.5	6	0.010	82.5	4	0.048
50–	4567.5	61	0.013	747.5	9	0.012	137.5	4	0.029
55–	3162.5	63	0.020	587.5	14	0.024	95.0	6	0.063
60–	1650.0	38	0.023	415.0	7	0.017	37.5	2	0.053
65–	687.5	26	0.038	230.0	10	0.044	25.0	5	0.200
≥ 70	180.0	14	0.078	77.5	8	0.103	10.0	4	0.400

*Pneumoconiosis was classified into three categories in China. Category I represents simple pneumoconiosis and category III represents complicated pneumoconiosis of ILO categories B and C. Category II was between them.

Table 3 Correlation coefficients between any pair of factors

	TB	JOB	YSU	ASM	YSM
AGE	0.05051*	-0.2256**	0.5054**	0.3528**	-0.4550**
TB		0.0218	-0.0062	0.0327	-0.1663*
JOB			-0.2779**	0.1017**	0.1738**
YSU				-0.4174*	-0.6585**
ASM					0.3989**

*P < 0.05; **P < 0.01.

AGE = age at which pneumoconiosis category I was established; JOB = drilling as the main job; YSU = years spent working underground; ASM = age at start of mining; YSM = year at start of mining.

As many explanatory variables are correlated with each other (table 3), univariate analysis was not used as a primary step. For the above analyses of each transition, two regression models were created. One was the complete model and the other was the condensed model. In the condensed model, year of starting mining work and age of starting mining work were dropped, and only years spent working underground, which is highly correlated with the year of starting mining work and age of starting mining work, was

Table 4 Results from the stepwise Cox's regression analysis of the general survival process

Variable	Simple model		Complete model	
	Coefficient (SE)	RR	Coefficient (SE)	RR
Age at which CWP was first diagnosed (AGE)	-0.062 (0.062)	0.940	-0.037 (0.065)	0.963
AGE ²	0.001 (7E-5)	1.001**	0.001 (0.001)	1.001
Progression from category I to II	0.108 (0.164)	1.115	0.097 (0.164)	1.101
Progression from category I to III	0.859 (0.245)	2.363**	0.859 (0.246)	2.360**
Tuberculosis	0.688 (0.119)	1.989**	0.666 (0.122)	1.946**
Drilling operation	-0.053 (0.116)	0.949	-0.032 (0.118)	0.968
Years at start of mining:				
< 1949	NA		0.000	1.000
1949-57			-0.069 (0.183)	0.934
1958-62			-0.282 (0.208)	0.754
≥ 1963			0.356 (0.363)	1.428
Years spent working underground:				
< 10	0.000	1.000	0.000	1.000
10-24	-0.474 (0.233)	0.622*	-0.472 (0.240)	0.624*
≥ 25	-0.217 (0.248)	0.805	-0.386 (0.295)	0.680
Age at start of mining:				
< 20	NA		0.000	1.000
20-29			-0.141 (0.146)	0.868
30-39			-0.167 (0.219)	0.846
≥ 40			0.080 (0.424)	1.084

*P value < 0.05; **P value < 0.01.

NA = not applicable.

Table 5 Relative risk (RR) from the Cox's regression analysis of the transitions from category I to death

Variable	Simple model		Complete model	
	Coefficient (SE)	RR	Coefficient (SE)	RR
Age at which CWP was first diagnosed (AGE)	-0.098 (0.063)	0.907	0.069 (0.067)	0.933
AGE ²	0.001 (0.001)	1.002*	0.001 (0.001)	1.001
Progression from category I to II	0.290 (0.171)	1.336	0.271 (0.172)	1.312
Tuberculosis	0.741 (0.123)	2.099**	0.709 (0.126)	2.032**
Drilling	0.085 (0.122)	0.919	-0.049 (0.122)	0.952
Years at start of mining:				
< 1949	NA		0.000	1.000
1949-57			-0.055 (0.188)	0.947
1958-62			-0.300 (0.214)	0.741
≥ 1963			0.330 (0.368)	1.391
Years spent working underground:				
< 10	0.000		0.000	1.000
10-24	-0.472 (0.239)	0.624*	-0.465 (0.247)	0.628
≥ 25	-0.168 (0.255)	0.845	-0.341 (0.302)	0.711
Age at start of mining:				
< 20	NA		0.000	1.000
20-29			-0.168 (0.149)	0.845
30-39			-0.200 (0.227)	0.819
≥ 40			0.167 (0.427)	1.183

*P < 0.05; **P < 0.01.

NA = not applicable.

kept in the model (table 3). All these analyses were performed on the main frame computer with SAS software.

Results

AGE SPECIFIC MORTALITIES

Table 2 lists a comparison of age specific mortalities among patients in three pneumoconiosis categories. Apparently, patients in category III had much higher mortalities than those in categories I or II; there was no difference between categories I and II. Taking category I as a control, the expected numbers of deaths for patients in categories II and III were 54.6 and 7.3, respectively, and the observed numbers of deaths were 55 and 25, and SMRs were 0.99 and 3.42 (P < 0.01), respectively.

GENERAL SURVIVAL ANALYSIS

Table 4 lists results from the Cox's regression analysis to show the main effects of the factors studied. After adjustment for age when CWP was first established and working duration underground, TB, and progression from category I to III were identified as risk factors for premature death. The relative risk (RR) estimates imply that a patient with TB would have a double risk of death (1.9) over a patient without TB, and a patient in category III would have a 2.4-fold risk of death over a patient in category I. Between 10 and 24 years spent working underground was found to be significant with a negative coefficient, indicating that the patients with a longer exposure (≥ 25 years spent working underground) or shorter exposure (< 10 years spent working underground) would have a higher risk of death. The group with < 10 years spent working underground may reflect a special subgroup of miners who could not work underground for a longer time period. The group with ≥ 25 years spent working underground is directly related to higher exposure. The interaction terms of TB and age at which pneumoconiosis was first established with the survival time were not significant. No significant relation between the risk of death and the interaction term of TB and age at which pneumoconiosis was first established was detected.

MULTISTATE MODEL ANALYSIS

Tables 5 and 6 list the results from the Cox's regression analyses on transitions from category I to death and category I to III. They show that TB facilitates both premature death (relative risk: RR = 2.0) and progression to category III (RR = 5.9), and that the second effect is stronger than the first. Age at which pneumoconiosis was first established has different coefficients for the two transitions, which indicates that younger patients have more chance of progression to category III and older patients are more likely to die without progression. Duration of time spent working underground had different coefficients too. The patients who worked underground between 10 and 24 years might have had a lower premature death risk before progression to category III, but they also had a high chance

Table 6 Relative risk (RR) from the Cox's regression analysis of the transitions from category I to category III

Variable	Final model		Complete model	
	Coefficient (SE)	RR	Coefficient (SE)	RR
Age at which CWP was first diagnosed (AGE)	-0.269 (0.144)	0.764	-0.350 (0.157)	0.705*
AGE ²	0.002 (0.002)	1.002	0.003 (0.002)	1.003
Progression from category I to II	0.426 (0.242)	1.531	0.384 (0.251)	1.469
Tuberculosis	1.943 (0.223)	6.837**	1.868 (0.232)	6.477**
Drilling	0.795 (0.248)	2.214**	0.854 (0.253)	2.348**
Years at start of mining:				
< 1949	NA		0.000	1.000
1949-57			-0.572 (0.356)	0.564
1958-62			-0.990 (0.383)	0.372
≥ 1963			Drop†	
Years spent working underground:				
< 10	0.000	1.000	0.000	1.000
10-24	1.363 (0.616)	3.906*	1.803 (0.666)	6.074**
≥ 25	1.373 (0.692)	3.946*	2.074 (0.836)	7.958**
Age at start of mining:				
< 20	NA		0.000	1.000
20-29			0.890 (0.318)	2.436**
30-39			1.416 (0.530)	4.120**
≥ 40			2.945 (1.217)	19.011*

*P < 0.05; **P < 0.01.

†Drop due to a huge (SE) and a huge P value.

NA = not applicable.

(RR = 4.3) of progression to category III. The patients with ≥ 25 years spent working underground had a higher chance of progression to category III and also had a higher death risk than those with 10-24 years spent working underground. Those miners who could not work underground for more than 10 years were more likely to die before progression to category III. Drilling was a risk factor that facilitated progression into category III (RR = 2.0), but would not cause patients in category I an earlier death. The time dependent variable of progression to category II has a marginally significant effect on death risk and development of PMF with P values of 0.09 and 0.08, respectively. The positive sign of their coefficient implied that patients with progression to category II may have had a higher risk of death and a higher chance of developing PMF.

We also analysed the transition from category III to death, but no factor was found to be significant except for age when the patient arrived at category III. The general survival analysis has shown that after adjustment for a time dependent variable, progression from category I to III, TB was still a significant risk factor. Therefore, the inability to identify subgroups in this analysis may be caused by the small number of subjects as only 87 patients in category III were followed up in the study.

Discussion

This study used medical diagnostic records preserved during the past 25 years, so some misclassification bias is likely. However, the following facts give us some confidence that the bias would not be substantial. Pneumoconiosis was designated in China as an occupational disease. Therefore, each diagnosis (including progression) had to be made by a series of discussions by a medical panel. Besides, China conducted a national epidemiological survey of pneumoconiosis in 1987. During this survey, the medical records for

every patient were carefully checked to correct potential mistakes in the classification of pneumoconiosis, diagnosis of the complication TB, and dates when diagnoses were made. The records before 1987 for our study had been checked carefully before we started data collection and the new patients identified in 1988 were diagnosed by the same panel members who were responsible for checking previous records. Therefore, misdiagnosis should be minimal.

One drawback of this study was that information about cigarette smoking habits for these patients was not available. However, as the results were based on internal comparisons, all patients being male workers and working in the same mine, it is expected that the prevalence of smoking among workers with different durations of work underground would not have differed greatly. The current smoking habit of a patient (or a miner) is usually influenced by severity of his respiratory disease or the condition of his lung function. A patient who has worked underground longer is expected to have lower lung function and he will be more likely to reduce or stop smoking. Similarly, a patient with TB is also more likely to give up smoking than one without TB. Therefore, the potential confounding from smoking would have resulted in an underestimate of risk due to TB or duration of work underground; controlling for smoking would be expected to strengthen the present conclusion from this analysis, not weaken it.

This study used Cox's regression analysis, which has the following advantages. The most important one is that the healthy worker effect has been excluded as Cox's regression analysis is an internal comparison. Coal workers are usually stronger and healthier than the general population and therefore would have lower mortalities. Taking the general population as a reference will lead to an underestimate of the effect of a risk factor. Another advantage due to internal comparison may result from the fact that this disease has a long survival period and any change in medical or health care may influence the patients' chance of having other diseases. A patient with pneumoconiosis is definitely provided with more medical service than another worker or the general population and he will also pay more attention to his health problems. As a result, these patients compared with other workers will receive medical examinations more frequently and their disease can be detected and given treatment earlier. Furthermore, they will no longer be engaged in an occupation requiring strenuous labour. Obviously, an internal comparison will yield a less biased conclusion for these reasons. The Cox's regression analysis also provides other advantages, such as the use of continuous variables, and the ability to analyse the time dependent variable and check the time dependency of a risk factor. In our analysis, age was used as a continuous variable so that the effect of the risk factor on the survival time could be evaluated more accurately than would be possible by dividing the patients into several age groups.

Analysis of age specific mortality shows that patients in category III had a notable increase in death risk over patients in category II or I (table 2). Different rates of TB (12.5% for patients at category I and 56.3% for patients at category III) indicated that TB also contributed to this jump in increase. However, after adjustment for TB (table 4), progression to category III still very significantly increased the risk of premature death. This result further confirmed the valid correlation between the Chinese and American interpretations of pneumoconiosis classification,¹⁶ as previous studies found that only the patients with categories B or C pneumoconiosis had increased mortalities.^{7,8} The transition from category I to category III then represented a transition from simple pneumoconiosis to category B and C pneumoconiosis by ILO classification. In terms of analysing patients' prognoses, grouping categories B and C should be more meaningful than grouping categories A, B, and C together. Hence, the analysis described in this paper should yield more meaningful results than an analysis with categories A, B, and C together. On the other hand, perhaps the present results would not be essentially different from those if the analysis had used categories A, B, and C together because categories A, B, and C are in the same direction in the course of disease progression.

The relation between simple and complicated pneumoconiosis is very clear from this study. During the past 25 years only 16 out of all the workers who had ever worked in this mine before 1988 were diagnosed to be in category III, (category B and C pneumoconiosis by ILO classification) without an earlier diagnosis of category I, whereas 87 patients were diagnosed to be in category III against a background of category I diagnosed in an earlier examination. This indicates that a history of simple pneumoconiosis is a very strong risk factor for the development of complicated pneumoconiosis. If a patient has at the same time TB, long term exposure, and drilling as a main job he will have a high chance of developing PMF, and so have a shorter life expectancy. These results may be useful in identifying a high risk group among the patients who currently have simple pneumoconiosis, and thus allow them to receive intensive medical attention.

The role of TB in the development of PMF from simple pneumoconiosis deserves discussion. At one time, TB was considered to be an important factor in the development of PMF in the lungs of coal miners. In 1954, James found evidence of TB in the PMF tissue in 99 cases out of 245 (40%).²¹ Rivers *et al* in 1957 cultured tubercle bacilli from 35% of 118 PMF lesions.²² However, the study conducted by Cochrane in 1962 indicated that the attack rate of PMF was not influenced by TB.²³ Pearson *et al* in 1982 also said that they did not find evidence to support this hypothesis.²⁴ Leibowitz and Goldstein in 1987 found histologically one active case of TB out of nine cases of PMF although the incidence of TB in the population was 0.2% in the study area.²⁵

They thought that TB could be an important cause of localising quartz laden macrophages in the interstitial tissues. A case-control study in China indicated that TB was a risk factor for PMF.²⁶ Our study showed a strong influence of TB on the development of PMF. As TB has been well controlled in some developed countries,²⁶ it seems necessary to answer this question with information from countries where TB still is a highly prevalent disease in the general population. Obviously, with the elimination of tubercle bacilli from the working environment, TB cannot definitely play any part in the progression of disease. But this does not mean that TB is not able to facilitate development of PMF if the environment has this bacillus or the patient has this disease. The final conclusion awaits more information from a variety of countries.

To answer the question whether inhalation of coal dust increases the risk of premature death involves a logical judgment. Age specific mortalities indicated that patients in category III will have a decreased life expectancy. The general survival analysis clearly shows that progression to PMF is a risk factor for premature death (RR = 2.4). As patients with simple pneumoconiosis have a high chance of developing PMF, we cannot say that simple pneumoconiosis did not increase the risk of premature death. Regression analyses also indicate that either premature death or development of PMF is related to working underground, drilling, or progression from category I to II. All these variables are associated with inhalation of coal dust. Obviously, without exposure to coal dust, a worker will not develop simple pneumoconiosis. The results from the above analyses also indicate that TB is a risk factor for premature death with and without development of PMF. Numerous clinical and epidemiological studies have documented the frequent occurrence of TB among miners, especially those with silicosis.²⁸⁻³⁰ If there is a higher incidence of TB among coal miners than among the general population and no other risk factors can be identified, we cannot say that TB does not have any association with the inhalation of coal dust. Therefore, the effect of TB on premature death also can be attributed to the inhalation of coal dust.

To decrease the harm of inhalation of coal dust on coal miners, a commonly used strategy is to end exposure before severe lung damage occurs as was practiced in China. The criterion for ending exposure usually is simple pneumoconiosis. However, this study implies that this strategy may not be effective enough to keep miners as healthy as the general population. Premature death is still possible. This fact tells us that, as Hurley *et al* said, the only safe strategy is to continue to minimise and maintain strict control of dust concentrations underground.¹³

In summary, this study proved that patients in category III (with complicated pneumoconiosis category B and C, or PMF) have a shorter life span after adjustment by age. Applying the Cox's regression model with

time dependent variables on to the general survival process and different transition paths, we explored the effect of investigated factors on different stages in detail, especially effects of a progression from category I to II or III on the development of PMF or premature death. The study provides some evidence to support the opinion that inhalation of coal dust increases the risk of premature death.

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