Pulmonary functions and blood biochemical markers for workers with and without coal worker pneumoconiosis☆

Qinghan Jin[1,2], Ailin Liu[1], Qinghai Li[3], Shaohua Xie[1], Enguang Wan[3], Shaohui Zhang[1], Yinfeng Tan[1], Xiaofeng Li[1], Hong Xie[1], Wenqing Lu[1,*]

[1]*Department of Occupational and Environmental Health and the MOE Key Laboratory of Environment and Health*, *School of Public Health*, *Tongji Medical College*, *Huazhong University of Science and Technology*, *Wuhan* 430030, *Hubei*, *China*; [2]*Health Bureau of Jining*, *Jining* 272000, *Shandong*, *China*; [3]*Institute for Labor Hygiene and Occupational Disease*, *Yanzhou Coal Mining Group*, *Yanzhou* 273500, *Shandong*, *China*

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Abstract

Objective. This study aimed to evaluate the feasibility of using pulmonary functions and blood biochemical markers in monitoring coal dust-induced early lung damages and the status of coal worker's pneumoconiosis (CWP). *Methods.* Sixty-four coal workers including tunneling workers, coal hewers, ancillary workers and 45 patients with CWP at different stages were investigated for their pulmonary functions, routine blood biochemical panel and CC16, SOD, CAT and MDA. *Results.* Among coal workers globulin levels were higher in both tunneling workers (27.67 ± 2.45) and hewers (26.71 ± 2.26) than in ancillary workers (25.97 ± 3.39). Compared with coal workers, CWP patients showed decreases in VC, FVC, and FEV1 ($P < 0.01$ for all); those with the stage I and II disease showed lower CAT and higher globulin levels ($P < 0.01$ for both). The decreases of CAT and CC16 levels were associated with the increases of working ages ($P < 0.05$ for both). *Conclusions.* Pulmonary functions and globulin levels may be used as biomarkers to monitor coal dust-induced early lung damages and the CWP progression, respectively. The usefulness of CC16 and CAT levels for these purposes is not determined. [Life Science Journal. 2009; 6(2): 33 – 39] (ISSN: 1097 – 8135).

Keywords: coal worker's pneumoconiosis; pulmonary function; blood biochemical parameters; Clara protein; anti-oxidative response

1 Introduction

Frequent exposure to coal dusts causes serious diseases, mainly the characteristic coal worker pneumoconiosis (CWP); therefore, the effective prevention from the hazardous coal dusts has become a major occupational and public health issue. However, up to date, coal dusts still pose a great threat to the health of coal workers due to the lack of effective monitoring and diagnostic tools for coal dust-induced early lung damages.

The current practice for the CWP prevention is mainly through the routine monitoring of the pulmonary functions[1–3]. Some studies revealed that damages of pulmonary functions existed not only in the patients of CWP but also in many coal workers without an active disease[4–7]. Interestingly, at diagnosis, many CWP patients showed abnormalities of the routine blood biochemical panel[8,9], suggesting that the blood biochemical biomarkers may be used as markers to monitor the coal dust-induced early lung damages and to determine CWP disease progression.

Loss of the oxidation and anti-oxidation balance has been proposed to be a leading cause of the damages to the alveolar macrophages[10,11]. Superoxide dismutase (SOD) and catalase (CAT) are two important enzymes to salvage free radicals and their levels are correlated with the anti-oxidative capacity of the body[12]. On the other hand, malondialdehyde (MDA) is the product of the lipid peroxidation, and its levels are correlated with the

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*Corresponding author. Tel.: 86-27-83610149; Fax: 86-27-83657765; Email: luwq@mails.tjmu.edu.cn

degree of oxidative stress. Therefore, the levels of these molecules may be useful to evaluate the status of oxidation and anti-oxidation, as well as the degree of oxidative damages. Although there have been evidences that CWP patients and coal miners lost the balance of oxidation and anti-oxidation[13–15], whether these molecules are effective markers for the detection of coal dust-induced early lung damages and CWP disease status is still largely unknown.

Clara cell protein (CC16) is a protein secreted by the Clara cells. This protein has strong immuno-suppressive and anti-inflammatory activities and participates in many pathological and physiological processes. It has been shown that the level of CC16 in the bronchial epithelial lining fluid was associated with the cytotoxicity of silicon dioxide to the epithelium of the airway[16,17]; changes in CC16 levels can lead to the accumulation of fibroblasts and promote pulmonary fibrosis[18,19]. CC16 in the bronchial epithelial lining fluid can enter the blood stream by passive diffusion against the concentration gradient, so serum CC16 level can be used as a sensitive marker for the detection of early changes in the integrity of the Clara cells and the pulmonary capillaries[16,20]. Since the protein is correlated to the degree of pulmonary fibrosis, the decrease in serum CC16 level may also reflex the conditions of early lung damages and pulmonary fibrosis.

In this study, we analyzed the pulmonary functions and a panel of blood biochemical biomarkers for coal workers exposed to different levels of coal dusts, and CWP patients with different disease status. The blood biochemical biomarkers included CC16, SOD, CAT and MDA, in addition to other routine blood biochemical parameters. We hope such study will offer the theoretical basis and a practical method for the monitoring of the coal dust-induced early lung damages and the determination of CWP disease status.

2 Materials and Methods

2.1 Subjects

All subjects were workers in a coal mining factory of Shandong province in China. There were 64 normal coal workers without active CWP, including a high exposure group of 34 tunneling workers, a moderate exposure group of 13 coal hewers, and a control group of 17 ancillary workers who worked on the ground level with very little exposure to concentrated coal dusts. All these workers had been worked in the environments of mixed coal dusts, with the average dust density of 7.04 mg/m^3 for the tunneling working environment, 5.21 mg/m^3 for the hewers' environment, and 0.98 mg/m^3 for the ground level environment of the ancillary workers. In addition, there were 45 workers with CWP including 23 stage 1, 19 stage II and 3 stage III patients, whose diagnosis was made by a group decision from doctors licensed in the nation's first level hospital in the second class with specialty in the pulmonary system according to the "Diagnostic Criteria of Pneumoconiosis" (GBZ 70-2002) (Ministry of Health of the People's Republic of China, 2002). The diagnosis of pneumoconiosis depended fundamentally on evidence of occupational exposure history and radiographic findings; pulmonary function testing results were also considered. All subjects were males without other diseases in the heart, the liver and the kidney by routine physical examinations; they were all asked to complete a questionnaire for weight, height, living habit, professional history, family history and other related information. Blood samples were collected from veins and serum samples were prepared for the study.

2.2 Pulmonary functional tests

AS-PAL Pulmonary Function Testing System (Minato, Japan) was used to analyze all parameters of pulmonary functions including vital capacity (VC), forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and the ratio of forced expiratory volume in one second to forced vital capacity (FEV1/FCV).

2.3 Blood biochemical analysis

Serum samples were collected from blood samples by centrifugation, and all measurements were carried out under the preset conditions. Olympus AU400 Automatic Biochemistry Analyzer was used to measure the routine blood biochemical parameters. Serum CC16 levels were measured by the human CC-16 assay kit from Wuhan USCN Sciences Co., LTD according to the manufactory manual. Serum SOD, CAT and MDA levels were measured by a SOD assay kit, a CAT assay kit, and a MDA assay kit, respectively, all from Nanjing Jiancheng Bioengineering Research Institute according to the manufactory manuals.

2.4 Data analysis and statistics

A database was established by Epidata 3.1 software, and all data were subjected to statistical analysis with SPSS12.0 program. Differences in the routine blood biochemical parameters were analyzed by multivariate analysis of variance; differences in the pulmonary functions and the levels of SOD, CAT and MDA were analyzed by analysis of variance; multi-level comparisons were made by dunnett's t-test and SNK test. Differences

in the serum CC16 levels among groups were analyzed by Kruskal-Wallis nonparametric test. The general linear regression or the nonconditional logistic regression analysis was applied for the multivariate analysis for the influencing factors of the pulmonary functional and the biochemical biomarkers. The correlations of SOD, CAT and MDA with pulmonary functional parameters were analyzed by Spearman rank correlation analysis. The confidence coefficient was set at the level of 0.05.

3 Results

3.1 Subject statistics

The 64 study subjects had an average age of 36.2 ± 8.2 years, specifically an average of 38.3 ± 7.3 years for the tunneling workers, 34.5 ± 9.0 years for the coal hewers, and 33.3 ± 8.4 years for the ancillary workers. The averaged age of the tunneling workers was significantly higher than those of the other two groups ($P < 0.05$). In this study, there were no significant differences in the average working age (14.7 ± 8.8 years), the body weight, and cigarette and alcohol consumptions among different groups of workers. The average ages of the CWP patients were 64.2 ± 6.3 years for patients with stage I disease, 68.7 ± 8.6 years for the stage II patients and 67.0 ± 9.0 years for the stage III patients, which were all significantly older than those of coal workers without the disease ($P < 0.01$). The average working ages of the CWP patients were 22.3 ± 9.0 years for the stage I patients, 24.8 ± 10.4 years for the stage II patients, and 16.7 ± 10.0 years for the stage III patients, which were also significantly older than the average working age of the general coal workers ($P < 0.01$). The percentages of smokers and alcohol consumers for the CWP patients were actually significantly lower than those of the general coal workers ($P < 0.01$ and $P < 0.05$, respectively, for the smokers and the alcohol consumers).

3.2 Pulmonary functions and the associated factors

Table 1 shows that there was no significantly differences in all the pulmonary functional parameters among different groups of coal workers without CWP. However, the CWP patients of all stages displayed significantly lower values of VC, FVC and FEV1 than the non-CWP coal workers ($P < 0.01$). The stage I CWP patients had significant lower values of FEV1/FVC than all other coal workers ($P < 0.05$) but these values were not significantly different between the stage II and III patients and all other coal workers ($P > 0.05$).

From Table 1, for the general linear regression analysis to determine the factors associated with or affecting the pulmonary functions, each of the pulmonary functional parameters was used as the dependent variable, and surveyed factors such as age, working age, weight, smoking status, alcohol consumption, job type, CWP disease stage were used as the independent variables. All variables belonging to multiple classifications were transformed to the dummy variables.

As shown in Table 2, compared with the coal workers without the disease, patients with stage I CWP had lower values of VC, FEV1 and FEV1/FVC, the stage II patients had lower values of VC and FEV1, and the stage III patients had lower values of FEV1. Values of VC and FCV decreased with increase of age, and FEV1 decreased with increase of the working age.

3.3 Routine blood biochemical parameters and associated factors

Table 3 shows that both the tunneling workers and the hewers had higher alanine aminotransferase-aspartate transaminase ratio (ALT/AST ratio) and blood glucose levels, the tunneling workers had the lower blood sodium level and the hewers had the higher urea nitrogen than the ancillary workers. Compared with the coal workers without CWP, the CWP patients of all stages showed higher total bilirubin and indirect bilirubin levels, lower albumin levels, higher globulin levels, lower Albumin/Globulin ratios, higher ALT/AST ratios and glucose levels, as well as lower urea nitrogen and blood sodium

Table 1. Pulmonary functional status of coal workers and CWP patients

Biomarkers	Without CWP				CWP patients			
	Tunneling workers	Hewers	Ancillary workers	All groups	Stage I	Stage II	Stage III	All groups
VC (L)	3.22 ± 0.12	3.70 ± 0.15	3.46 ± 0.19	3.38 ± 0.71	1.90 ± 0.65**	1.60 ± 0.64**	1.76 ± 0.29**	1.76 ± 0.64
FVC (L)	3.05 ± 0.10	3.46 ± 0.23	3.42 ± 022	3.23 ± 0.74	1.74 ± 0.67**	1.49 ± 0.86**	1.70 ± 0.30**	1.63 ± 0.74
FEV1 (L)	2.53 ± 0.98	2.61 ± 0.18	2.66 ± 0.17	2.58 ± 0.62	1.15 ± 0.59**	1.09 ± 0.56**	1.28 ± 0.25**	1.13 ± 0.55
FEV1/FVC (%)	83.19 ± 1.83	76.54 ± 3.70	78.01 ± 3.22	80.46 ± 12.13	65.58 ± 20.96*	74.87 ± 20.14	74.90 ± 2.26	70.12 ± 20.19

Data were presented as χ^2 ± SD. *P* values were calculated in comparison with the coal workers; *: $P < 0.05$, **: $P < 0.01$.

levels.

Table 2. General linear regression analysis for the affecting factors on pulmonary functions

Pulmonary functional biomarkers	Factors	Estimated regression coefficient	t	P	95% CI	
					Upper limit	Lower limit
VC (L)	CWP stage I	– 0.75	– 2.37	< 0.05	– 1.37	0.12
	CWP stage II	– 0.86	– 2.51	< 0.05	– 1.54	– 0.18
	Age (year)	– 0.03	– 1.42	< 0.05	– 0.05	– 0.01
FVC (L)	Age (year)	– 0.03	– 2.60	< 0.05	– 0.06	– 0.01
FEV1 (L)	CWP stage I	– 1.15	– 3.88	< 0.01	– 1.74	– 0.56
	CWP stage II	– 1.09	– 3.38	< 0.01	– 1.73	– 0.45
	CWP stage III	– 1.00	– 2.04	< 0.05	– 1.96	– 0.03
	Work age (year)	– 0.02	– 2.00	< 0.05	– 0.03	– 0.00
FEV1/ FVC (%)	CWP stage I	– 30.78	– 2.43	< 0.05	– 46.66	– 14.89

To determine the factors associated with or affecting the blood biochemical parameters, a general linear regression analysis was performed with each of the parameter as a dependent variable, and factors such as age, working age, body weight, smoking status, alcohol consumption, job type, and CWP stage as the independent variables. Results showed that the ratios of AST/ALT decreased with the increase of body weights ($P < 0.05$), total bilirubin and indirect bilirubin levels increased with the increase of age and amount of alcohol consumption (both had $P < 0.05$). Levels of blood albumin decreased with the increase of age. Smokers showed lower globulin levels ($P < 0.05$). The tunneling workers and the hewers had higher globulin levels than the ancillary workers ($P < 0.05$). The CWP patients also showed higher globulin levels than the non-CWP workers ($P < 0.05$). All the analyzed factors showed no significant associations with the levels of blood glucose, sodium, and urea nitrogen.

3.4 Serum CC16 levels and associated factors

As shown in Table 4, Kruskal-Wallis nonparametric test revealed that there was no statistically significant difference in serum CC16 levels between the CWP patients and the non-CWP coal workers ($x^2 = 2.94$, $v = 3$, $P = 0.40$), nor among the coal workers from different groups ($P = 0.20$, $v = 2$, $P = 0.90$).

Based on the mean value of serum CC16 levels, the subjects were divided into two groups: a high CC16 group with at least 100 pg/ml serum CC16 and a low CC16 group with CC16 levels below 100 pg/ml. CC16 was used as the dependent variable and the factors listed in the subject questionnaire were used as the independent variables for a non-conditional logistic regression analysis. After a series of selections and medical considerations, the independent variables were determined to be the smoking status, alcohol consumption, job type, age, working age and the CWP stage. Results showed that increase of the working age was significantly associated with the decrease in the serum CC16 levels ($P < 0.05$, OR = 0.900, 95%CI = 0.823 – 0.985). Other factors were not significantly correlated with the serum CC16 levels.

3.5 Serum SOD, CAT MDA levels associated factors and correlations with pulmonary functions

As shown in Table 5, there were no significant differences in the levels of SOD, CAT and MDA among different groups of coal workers without CWP. However, patients with stage I CWP had significantly lower serum CAT levels than coal workers without CWP ($P < 0.01$); patients with the stage II CWP showed lower levels of both serum SOD and CAT than the workers without the disease (both with $P < 0.01$). The levels of MDA were not significantly different among all study groups.

With each of the oxidative response biomarker as the dependent variable, and using age, working age, body weight, smoking status, alcohol consumption, job type, and CWP stage as the independent variables, general linear regression analysis was used to determine the factors associated with the oxidative response capacity. CWP patients of stages I and II had CAT levels lower than the non-CWP workers. The serum CAT levels decreased with the increase of working ages ($P < 0.05$), and SOD levels decreased along with increase of ages ($P < 0.05$). All other factors showed no significant associations with serum MDA levels. Spearman rank correlation analysis showed positive correlations of VC, FVC, and FEV1 with serum SOD and CAT levels. The correlation coefficients of VC with SOD and CAT were 0.225 and 0.195, respectively ($P < 0.05$ for both); the correlation coefficients of FVC with SOD and CAT were 0.216 and 0.207, respectively ($P < 0.05$ for both); the correlation coefficients for FEV1 with SOD and CAT were 0.210 and 0.298, respectively ($P < 0.05$, $P < 0.01$).

4 Discussion

Table 3. Biochemical biomarkers in coal workers without CWP and CWP patients

Biomarkers	Without CWP				CWP patients			
	Tunneling workers	Hewers	Ancillary workers	All groups	Stage I	Stage II	Stage III	All groups
Total bilirubin (μmol/L)	14.45 ± 5.88	11.94 ± 4.18	15.21 ± 8.37	14.14 ± 6.37	18.03 ± 7.50	18.59 ± 8.64$^{\#}$	20.40 ± 3.25	18.40 ± 7.71
Direct bilirubin (μmol/L)	4.28 ± 1.60	3.75 ± 1.03	4.46 ± 2.04	4.22 ± 1.64	5.04 ± 1.83	5.03 ± 2.21	4.60 ± 1.23	5.00 ± 1.93
Indirect bilirubin (μmol/L)	10.17 ± 4.43	8.19 ± 3.23	10.75 ± 6.38	9.92 ± 4.84	12.99 ± 5.74	13.56 ± 6.49$^{\#}$	15.80 ± 2.34	13.40 ± 5.87
Total protein (g/L)	74.84 ± 3.08	73.98 ± 3.88	72.61 ± 5.47	74.08 ± 4.04	72.87 ± 4.46	74.01 ± 4.12	79.77 ± 0.72	73.80 ± 4.45
Albumin (g/L)	44.18 ± 1.81	47.27 ± 2.28	46.65 ± 2.92	47.06 ± 2.22	44.32 ± 1.92$^{\#\#}$	44.28 ± 2.03$^{\#\#}$	46.40 ± 2.08	44.40 ± 2.00
Globulin (g/L)	27.67 ± 2.45	26.71 ± 2.26	25.97 ± 3.39	27.02 ± 2.75	28.57 ± 3.43	29.73 ± 3.15$^{\#\#}$	33.37 ± 1.36$^{\#\#}$	29.40 ± 3.39
Albumin/globulin ratio	1.72 ± 0.16	1.79 ± 0.13	1.83 ± 0.19	1.76 ± 0.17	1.56 ± 0.18$^{\#\#}$	1.51 ± 0.17$^{\#\#}$	1.37 ± 0.12$^{\#\#}$	1.50 ± 0.18
ALT (U/L)	26.46 ± 11.62	23.78 ± 15.23	33.80 ± 18.40	28.50 ± 15.90	22.52 ± 7.82	18.78 ± 6.56	18.23 ± 6.19	20.70 ± 7.33
AST (U/L)	28.77 ± 8.95	25.00 ± 5.97	29.71 ± 14.75	28.25 ± 10.34	26.14 ± 5.68	26.00 ± 5.47	30.33 ± 7.64	26.40 ± 5.67
AST/ALT	1.21 ± 0.39*	1.31 ± 0.61**	0.90 ± 0.40	1.20 ± 0.50	1.25 ± 0.36	1.52 ± 0.52$^{\#\#}$	1.73 ± 0.32$^{\#}$	1.40 ± 0.45
Alkaline phosphatase (U/L)	99.50 ± 22.9	99.00 ± 23.53	97.29 ± 26.87	98.80 ± 23.70	105.26 ± 29.23	98.53 ± 18.13	108.67 ± 33.32	102.60 ± 25.01
γ-glutamyl transpeptidase (U/L)	30.60 ± 14.20	31.20 ± 22.22	35.42 ± 14.94	32.00 ± 16.10	32.60 ± 18.90	22.64 ± 7.02	17.77 ± 4.48	27.40 ± 4.48
Urea nitrogen (mmol/L)	5.97 ± 1.20	6.79 ± 1.19*	5.27 ± 1.23	5.95 ± 1.30	5.19 ± 1.12$^{\#}$	5.06 ± 0.97$^{\#}$	5.37 ± 0.95	5.10 ± 1.03
Creatinine (μmo/L)	68.74 ± 9.36	68.88 ± 7.18	70.09 ± 8.53	69.13 ± 8.63	69.29 ± 7.93	70.00 ± 8.28	75.10 ± 4.61	70.00 ± 7.90
Glucose (mmol/L)	5.19 ± 0.43*	5.33 ± 0.62*	4.80 ± 0.54	5.12 ± 0.53	5.81 ± 1.07$^{\#\#}$	5.87 ± 1.51$^{\#\#}$	5.00 ± 0.83	5.80 ± 1.26
Potassium (mmol/L)	4.37 ± 0.33	4.28 ± 0.33	4.31 ± 0.42	4.33 ± 0.35	4.40 ± 0.35	4.22 ± 0.35	4.45 ± 0.46	4.30 ± 0.36
Sodium (mmol/L)	143.85 ± 1.57**	145.02 ± 1.75	145.29 ± 1.23	144.47 ± 1.65	142.00 ± 3.40$^{\#\#}$	140.52 ± 4.48$^{\#\#}$	143.53 ± 1.10	141.5 ± 3.85
Chloride (mmol/L)	101.90 ± 1.83	103.05 ± 2.61	102.56 ± 1.83	102.31 ± 2.03	102.87 ± 2.13	102.10 ± 2.23	102.32 ± 2.10	102.30 ± 2.22
Calcium (mmol/L)	2.42 ± 0.07	2.41 ± 0.05	2.36 ± 0.20	2.41 ± 0.12	2.35 ± 0.06	2.35 ± 0.08	2.44 ± 0.05	2.40 ± 0.07
CO2 combining power (mmol/L)	23.40 ± 1.91	23.50 ± 1.79	23.18 ± 1.76	23.36 ± 1.82	23.97 ± 1.75	24.03 ± 2.26	22.93 ± 0.31	23.90 ± 1.93

*: $P < 0.05$, and **: $P < 0.01$ for the ancillary workers in comparison with the tunneling workers and the hewers. $^{\#}$: $P < 0.05$, and $^{\#\#}$: $P < 0.01$ for workers without CWP in comparison with the CWP patients.

Coal worker's pneumoconiosis is one of the most serious occupational diseases, which can be pathologically characterized by the silicotic nodule formation and the wide-spread diffuse interstitial pulmonary fibrosis. Although great progress has been made from many studies in recent years, our knowledge on its pathogenesis is still limited, and there is still no effective cure for the disease. Therefore, seeking sensitive biomarkers to monitor the coal dust-induced early lung damages and to determine the CWP progression is critical to the prevention and treatment of this disease. In this study we explored the possibility of using pulmonary functional and the blood

Table 4. Serum CC16 (pg/ml) levels in coal workers without CWP and CWP patients

Group		No. (*n*)	Mean ± SD	Median values (range)
CWP stages	None	64	110.18 ± 142.14	20.73 (9.45 – 399.26)
	Stage I	23	62.57 ± 114.92	17.19 (8.76 – 412.47)
	Stage II	19	76.89 ± 104.55	37.76 (11.58 – 386.62)
	Stage III	3	84.67 ± 122.24	15.46 (12.73 – 255.81)
Work types	Tunneling workers	34	108.11 ± 147.84	20.73 (9.45 – 399.26)
	Hewers	13	99.84 ± 137.67	22.80 (11.06 – 388.57)
	Ancillary workers	17	122.23 ± 141.45	20.25 (10.79 – 343.96)

Table 5. Serum SOD, CAT and MDA levels of coal workers and CWP patients

Biomarkers	Without CWP				CWP Patients			
	Tunneling workers	Hewers	Ancillary corkers	All groups	Stage I	Stage II	Stage III	All groups
SOD (U/ml)	36.94 ± 21.91	36.16 ± 24.40	42.64 ± 11.42	41.35 ± 18.33	38.94 ± 29.64	20.11±16.74**	24.72 ± 15.02	29.66 ± 22.12
CAT (U/ml)	4.24 ± 4.96	3.48 ± 4.46	7.13 ± 10.89	4.87 ± 7.01	2.09 ± 2.76**	1.29 ± 0.97**	1.89 ± 0.83	1.77 ± 2.03
MDA (U/ml)	8.56 ± 12.74	9.42 ± 9.17	6.60 ± 4.49	8.19 ± 10.31	6.83 ± 5.95	6.89 ± 6.37	4.06 ± 1.58	6.89 ± 5.73

Data were presented as χ^2 ± s. *P* values were calculated in comparison with the coal workers; **: $P < 0.01$.

biochemical biomarkers as such markers.

The lung damage caused by coal dusts is a leading cause of the labor force decrease in the coal mining industry. Our study showed that all CWP patients had significantly damages of the pulmonary functions, which was worsened in the stage II patients. General linear regression analysis revealed that the pulmonary functions were correlated with the stages of CWP, suggesting that the pulmonary functional parameters may be used as the markers for CWP staging.

Our results did not show any significant differences in these markers among coal workers with different levels of coal dust exposure. This may be due to the strong functional compensation of the lung, which does not display signs of abnormality unless the damages are accumulated to certain high levels. Therefore, the pulmonary functional parameters may not be sensitive enough for the detection of early lung damages before the disease onset.

The damages in the bronchioles and other pulmonary tissues may affect the exchange of air between the body and the outside, ultimately resulting in a chronic hypoxic state of the body. This condition may in turn lead to the degeneration and necrosis of cardiac myocytes, hepatic cells, renal glomerular and tubular cells, and then further change the blood biochemical parameters. In this study, general linear regression analysis showed that levels of globulin varied among all groups of coal workers with or without CWP, and it increased with the increase of exposure level to coal dusts and the stage of CWP in the CWP patients; therefore, globulin may offer a sensitive marker for the detection of the coal dust-induced early lung damages and the CWP disease progression.

Recent studies have shown that CC16 is a sensitive marker for the early detection of the acute or chronic changes in Clara cells and the alveolar membrane structures[21,22]. In this study, levels of serum CC16 decreased with the longer exposure to coal dusts; it may be because that Clara cells are the stem cells for the renewal of the epithelial cells in the bronchioles, the cell number and CC16 secretion may decrease as the result of the damages in the pulmonary epithelial cells by coal dusts[23]. On the other hand, CC16 is passively transported to the blood stream across the lung-blood barrier[10,22]. The lung damages may decrease the permeability of the barrier then decrease the CC16 levels in the peripheral blood. However, we did not observe any significant differences of serum CC16 levels among all study groups with different exposure levels to coal dusts or with different CWP stages; therefore, the use of serum CC16 as marker for the detection of the coal dust-induced early lung damages and CWP disease progression still needs to be further studied.

The generation of reactive oxygen species (ROS) and the response to such oxidative stress play important roles in the pathogenesis of lung damages induced by external toxic particulate matters[24,25], which are also the key factors causing pulmonary fibrosis and decrease in the pulmonary functions. Our results showed that although there were no significant differences in the anti-oxidative capacity among non-CWP coal workers from three groups of different job types, there was a significant difference in the CAT values between the non-CWP workers and the CWP patients. In addition, CAT and SOD levels were shown to be positively correlated with the pulmonary functional parameters, and CAT values decreased with the increase of the working ages. Therefore, levels of CAT and SOD may offer complementary or reference values for the detection of coal dust-induced early lung damages and CWP disease progression. Whether they can be also used as true markers for the detection of coal dust-induced early lung damages is still a question.

We also observed that serum CAT levels decreased along with the disease progression in CWP patients. This may be the result of the enzyme consumption by the large amount of free radicals released from the alveolar macrophages while uptaking the coal dusts in the lung[26]. This process may activate the reactions of free radicals to cause the oxidation of the alveolar macrophage membrane and increase the fatty acid perioxidation, therefore ultimately leading to the release of a large amount of free radicals.

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