Association between increased small airway obstruction and asbestos exposure in patients with asbestosis

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Abstract

Background: Asbestos exposure may cause asbestos-related lung diseases including asbestosis, pleural abnormalities and malignancies. The role of asbestos exposure in the development of small airway obstruction remains controversial. Anatomic and physiologic small airway abnormalities may develop as part of the pathophysiologic process of asbestosis. We hypothesized that inhalation of asbestos may induce small airway defects in addition to asbestosis and pleural abnormalities.

Methods: In total, 281 patients with newly diagnosed asbestosis were evaluated. Clinical data were collected from the patients’ medical charts. The patients were classified into various stages according to their chest X-ray findings using the International Labour Organization classification. Pulmonary function was evaluated by plethysmography and the forced oscillation technique.

Results: Expiratory flow, including the predicted values of the maximum expiratory flow between 25% and 50% of the forced vital capacity (MEF25–50), was significantly lower in the different stages of asbestosis. Accordingly, the predicted percentage of $R_{5–20}$ was significantly higher with increasing stages of asbestosis. Furthermore, the duration of exposure to asbestos was significantly associated with the forced expiratory volume in the first second (FEV1)/forced vital capacity (FVC) ratio and the predicted percentage of MEF25 or MEF50 according to the regression analysis in non-smoking patients with asbestosis. The predicted percentage of FEV1 or the FEV1/FVC ratio was significantly lower and the predicted percentage of $R_{5–20}$ was significantly higher in smokers than non-smokers.

Conclusions: The patients with asbestosis have small airway obstructive defects that are significantly associated with asbestos exposure.

Keywords
asbestosis, asbestos, forced oscillation technique, plethysmography, pulmonary function, small airway

1 INTRODUCTION

Asbestos is a general term for a heterogeneous group of hydrated magnesium silicate minerals that can be separated into fibres. Asbestos is inhaled and displaced to lung tissue by various means. This may result in the development of asbestos-related lung disease (ARD), which is a common clinical problem and major health concern worldwide. Epidemiologic studies have established that exposure to asbestos fibres causes pulmonary fibrosis (asbestosis), pleural abnormalities (thickening, plaques and effusion) and malignancies (eg, bronchogenic carcinoma and mesothelioma).
Although the use of asbestos has been banned or strongly restricted in Western and Northern Europe, North America and Australia, the annual production and global use of asbestos has remained high at >2 million metric tons.\(^3\) China is currently one of the largest producers of asbestos.\(^4\) Generally, ARDs can be diagnosed by their quite long latency periods of 10 to 50 years or more after exposure.\(^1,2\) Countries continuing to use asbestos will shoulder the burden of ARDs in proportion to their prior levels of asbestos use.\(^5\) Countries in which asbestos has been banned or greatly limited invariably exhibit a sustained epidemic of ARDs.\(^6\)

Asbestos exposure has traditionally been considered to cause predominantly restrictive physiologic abnormalities. The role of asbestos as a cause of airway obstruction has been debated. Anatomic and physiologic airway abnormalities may develop as part of the pathophysiologic process of asbestosis. Histologically, the mildest form of asbestosis involves the alveolated walls of respiratory bronchioles and alveolar ducts.\(^7\) Asbestos bodies are commonly seen in the walls of the respiratory bronchioles and/or adjacent alveoli.\(^7\) Epidemiologic findings have also shown a significant association between asbestos exposure or the radiographically defined asbestosis category and a reduction in the forced expiratory volume in the first second (FEV\(_1\)), the FEV\(_1/\text{forced vital capacity (FVC)}\) ratio and mid-expiratory flow rates.\(^8,9,10\)

However, the role of asbestos exposure in inducing airway obstruction remains controversial. Previous studies have been unable to support the hypothesis that asbestos exposure may induce significant airway obstruction.\(^10,11,12\) One study involving 3660 workers in the absence of confirmed asbestosis failed to demonstrate a relationship between estimated cumulative occupational exposure to asbestos and lung function parameters.\(^10\) The findings did not support a causal link between asbestos exposure and the pathogenesis of airway obstruction.

In the present study, we evaluated small airway function in a cohort of patients with asbestosis during an 8-year period in a single centre for occupational diseases. The aim of the study was to determine whether small airway obstruction is related to asbestos exposure after controlling for smoking factors that impact lung function.

2 | MATERIALS AND METHODS

2.1 | Patients

In total, 341 outpatients with newly diagnosed asbestosis were sequentially recruited from the Department of Occupational Medicine and Toxicology, Beijing Chao-Yang Hospital, during a 9-year period (January 2007 to December 2015). The diagnosis of asbestosis was based on the following modified criteria\(^1:\) (1) a history of occupational asbestos exposure, (2) the presence of interstitial abnormalities on HRCT with or without benign pleural thickening and plaques or pleural effusion in patients who did not undergo surgical lung biopsy and (3) exclusion of other known causes of interstitial lung disease. The presence of collagen vascular diseases was excluded in all patients using a detailed history, clinical examination and serum tests for anti-neutrophil cytoplasmic antibody, extractable nuclear antigens, antinuclear antibodies, anti-mitochondrion antibodies, anti-DNA antibodies, rheumatoid factor and immunoglobulins. Drug toxicities and other environmental exposures were excluded in all patients.

Pleural abnormalities were diagnosed according to their presence on chest radiographs and computed tomography scans and included calcified and non-calcified circumscribed pleural thickening and pleural effusion.

Of the 341 originally recruited patients with asbestosis, 60 (17.6%) were excluded for the presence of lung cancer or mesothelioma (n = 50) and incomplete pulmonary function testing (n = 10). No patients had a history of asthma or bronchiectasis.

The smoking status of all patients was carefully collected, and they were categorized as non-smokers, ex-smokers (had quit smoking ≥12 months previously) and smokers (currently smoking or had quit smoking <12 months previously). Cigarette smoking is shown by pack-years.

All investigations were conducted in accordance with the ethical standards of Beijing Chao-Yang Hospital and the World Medical Association Declaration of Helsinki.

2.2 | Asbestos exposure

All patients completed a standardized questionnaire to collect information on work history. All jobs within each participant’s working life were taken into account. Our hospital is the largest centre for occupational diseases in the city and is located 20 km away from the asbestos product plants that were open from the 1950s to 1970s. Because of the absence of atmospheric measurements and the lack of detailed information regarding the frequency of exposure for each job suspected to be associated with asbestos exposure, the duration of asbestos exposure (number of years) was determined.

2.3 | Plethysmography

Pulmonary function tests were performed according to the guidelines of the hospital physiology laboratory. Parameters used for analysis of the flow–volume curve were the FVC, FEV\(_1\), FEV\(_1/\text{FVC ratio, peak expiratory flow and maximal expiratory flow between 25%, 50% and 75% of FVC (MEF}_{25}, \text{ MEF}_{50} \text{ and MEF}_{75}). For each patient, the residual volume (RV), total lung capacity (TLC) and diffusing capacity of the lung for carbon monoxide (DLCO) (single-breath method, with the values corrected for the present
haemoglobin concentration) were tested as well. The results are expressed as percentages of the predicted values on the basis of age, height and sex using equations established by the European Respiratory Society. The forced expiratory maneuvers were repeated until 3 sequential measurements were obtained. The indices were obtained from the best curve, which was associated with the highest value of FEV\textsubscript{1} plus FVC. Quality control measures for spirometry were provided by the American Thoracic Society criteria, with software used to detect unacceptable maneuvers.

2.4 | Forced oscillation technique

The forced oscillation technique (FOT) has been previously described in detail and meets the international standards. We used a standard multifrequency FOT test system that operated within the most commonly used frequency range. To perform the FOT analysis, the subject remained in a sitting position, maintaining the head in a normal position and breathing at functional reserve capacity through a mouth-piece. During the measurements, the subject wore a nose clip and firmly supported his or her cheeks and mouth floor using both hands. A minimal coherence function of 0.9 was considered adequate.

Three measurements were obtained, and the result is expressed as the mean of these 3 measurements. A linear regression analysis over the frequency range of 5 to 35 Hz was performed to interpret the resistance results. The total mechanical load of the respiratory system, including the resistive and elastic effects, was estimated using the absolute value of respiratory impedance at 5 Hz ($Z_{5\text{Hz}}$). $R_5$ reflected the total respiratory resistance measured based on 5 Hz. $R_{20}$ reflected the central airway resistance measured based on 20 Hz. $R_5-R_{20}$ reflected the peripheral airway resistance, which was the difference between these 2 values. The reactive properties are described by the following 2 parameters: resonance frequency, defined as the frequency at which $X_{rs}$ equals zero; the reactance ($X_5$), which is a property that is usually related to respiratory system non-homogeneity and is calculated based on 5 Hz. $X_5$ reflects the dynamic compliance, including the compliances of the lung and bronchial walls, the chest wall/abdominal compartment, the upper airways and thoracic gas compression.

2.5 | Imaging

Conventional chest radiographs were performed in each patient, and 2 occupational medicine experts independently evaluated the images according to the International Labour Organization classification. High-resolution computed tomography (HRCT) was also performed with 1-mm sections, a 1-second scan time and 10-mm interval in the apex-base scans, with inclusion of both lungs in the field of view.

2.6 | Statistical methods

Values are presented as mean ± standard deviation or as frequency counts and percentages. Comparisons between groups were made using the t-test, $\chi^2$ test or Fisher’s exact test, as appropriate. Multiple regression techniques were utilized to analyse the relationships of age or exposure with pulmonary function values. All analyses were performed with SPSS statistical software (version 17.0; SPSS Inc., Chicago, IL, USA). All comparisons were two-sided, and a $P$ value of <.05 was considered significant.

3 | RESULTS

3.1 | Demographics

Of all 281 patients with asbestosis, 169 (60.1%) were women and 96 (34.2%) were smokers (Table 1). The mean duration of asbestos exposure was 16.3 ± 12.2 years. The duration of asbestos exposure increased from asbestosis stage I to III. All patients with asbestosis showed interstitial abnormalities, and 272 (96.8%) patients showed various pleural abnormalities including local or diffuse pleural thickening, pleural plaques or pleural effusion on HRCT. A total of 29 (10.3%) patients had combined limited emphysema and asbestosis. All patients were local residents who had been exposed to chrysotile dust or fibres, including 235 (83.6%) working in the manufacture of asbestos textiles or asbestos-based products and 46 (16.4%) who had been exposed to asbestos products in a working atmosphere (eg, heat insulation workers and boiler maintenance workers).

3.2 | Lung function profiles in various stages of asbestosis

Lung volume parameters including FVC, FEV\textsubscript{1} and TLC decreased significantly with increasing stages of asbestosis (all $P<.05$ or $P<.01$) (Table 2). Meanwhile, the DLCO also decreased significantly with increasing stages of asbestosis ($P<.01$). The decrease in DLCO preceded the decrease in lung volume in patients with asbestosis. The FEV\textsubscript{1}/FVC ratio in all patients with asbestosis showed a mild obstructive defect that did not reach the criterion for chronic obstructive pulmonary disease. Neither the FEV\textsubscript{1}/FVC ratio nor the forced expiratory volume in the third second (FEV\textsubscript{3}/FVC) ratio differed among the stages of asbestosis.

3.3 | Small airway function values in patients with asbestosis

The flow–volume curve showed that the expiratory flow, including the predicted values of MEF\textsubscript{25} and MEF\textsubscript{50}, were
significantly lower in the different stages of asbestosis showing small airway dysfunction (Table 3).

Using the FOT, the predicted percentage of $R_5$ or $R_{20}$ was within the normal range, showing that the total respiratory resistance or central airway resistance was within the normal range (Table 4). However, the predicted percentage of $R_5$–$R_{20}$ was significantly higher with increasing stages of asbestosis ($P < .05$), showing obviously elevated peripheral airway resistance. Both $X_5$ and the resonance frequency were elevated in patients with asbestosis, indicating a significant increased dynamic compliance of the chest in line with the changes in lung volume parameters. The predicted percentage of FVC was positively correlated with $X_5$ ($r = .344, P < .01$) (Figure 1).

### 3.4 Relationships between independent factors and small airway obstruction

We further analysed the effect of smoking on lung function values in our group of patients with asbestosis (Table 5). Among the patients with asbestosis, the predicted percentage of FEV$_1$ and the FEV$_3$/FVC ratio were significantly lower in smokers than non-smokers ($P < .05$). Additionally, the predicted percentage of $R_5$–$R_{20}$ was significantly higher in

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**Table 1** Demographics of the study patients with asbestosis

|                          | All asbestosis | Stage I  | Stage II | Stage III | $P^*$ |
|--------------------------|----------------|----------|----------|-----------|-------|
| Subjects (n)             | 281            | 196      | 67       | 18        |       |
| Age (yr)                 | 65.0 ± 9.1     | 64.8 ± 10.6 | 66.8 ± 10.1 | 67.1 ± 9.4 | .066  |
| Female/male (n)          | 169/112        | 118/78   | 40/27    | 11/7      | .994  |
| Smokers (n, %)           | 96 (34.2)      | 66 (27.5) | 21 (30.4) | 9 (50.0)  | .126  |
| Exsmokers (n, %)         | 38 (13.5)      | 20 (8.3)  | 12 (17.4) | 6 (33.3)  | .001  |
| Smoking (pack-yr)        | 5.5 ± 12.0     | 5.6 ± 12.5 | 4.7 ± 10.4 | 6.4 ± 10.7 | .034  |
| Duration of exposure (yr)| 16.3 ± 12.2    | 9.7 ± 9.1 | 16.3 ± 13.7 | 17.2 ± 12.0 | .039  |
| Latency (yr)             | 46.9 ± 10.8    | 46.0 ± 10.9 | 49.6 ± 9.7 | 48.9 ± 10.6 | .035  |
| PaO$_2$ (mm Hg)          | 80.5 ± 12.2    | 84.8 ± 13.1 | 75.1 ± 14.7 | 69.9 ± 13.0 | .000  |
| Emphysema (n, %)         | 29 (10.3)      | 14 (7.1)  | 3 (4.4)  | 4 (2.2)   | .087  |

Data are presented as means ± SD or n (%).

*P*-value denotes statistical differences among 3 groups of stage I, stage II and stage III. Ever smoker means quitting smoking ≥ 12 months. Cigarette smoking was shown by pack-year. Pack-yr means package of cigarettes per day × duration of smoking.

**Table 2** Lung function profiles in various stages of asbestosis

|                          | All asbestosis | Stage I  | Stage II | Stage III | $P^*$ |
|--------------------------|----------------|----------|----------|-----------|-------|
| Subjects (n)             | 281            | 196      | 67       | 18        |       |
| FVC (% predicted)        | 76.7 ± 21.2    | 81.3 ± 19.6 | 64.6 ± 17.3 | 63.8 ± 21.8 | .000  |
| FEV$_1$ (% predicted)    | 72.5 ± 22.3    | 77.7 ± 20.5 | 60.7 ± 18.0 | 61.5 ± 23.4 | .000  |
| FEV$_1$/FVC (%)          | 77.5 ± 10.3    | 77.5 ± 9.1 | 76.9 ± 12.3 | 78.1 ± 10.7 | .879  |
| FEV$_3$/FVC (%)          | 94.4 ± 5.05    | 94.8 ± 3.7 | 93.1 ± 7.3 | 94.7 ± 7.3 | .270  |
| RV/TLC (%)               | 44.8 ± 9.2     | 40.0 ± 7.6 | 45.9 ± 10.2 | 47.3 ± 13.0 | .404  |
| TLC (% predicted)        | 81.9 ± 20.9    | 84.3 ± 16.5 | 75.1 ± 28.6 | 58.7 ± 23.9 | .000  |
| DLCO (% predicted)       | 59.9 ± 23.5    | 66.6 ± 22.2 | 45.2 ± 23.9 | 35.4 ± 15.1 | .000  |

Abbreviations: DLCO, diffusing capacity of the lung for carbon monoxide; FEV$_1$, forced expiratory volume in the first second; FEV$_3$, forced expiratory volume in the third second; FVC, forced vital capacity; TLC, total lung capacity.

Data are presented as means ± SD.

*P*-value denotes statistical differences among 3 groups.
TABLE 3  Expiratory flow by the flow–volume curve in various stages of asbestosis

|                | All asbestosis | Stage I | Stage II | Stage III |
|----------------|----------------|---------|----------|-----------|
| Subjects (n)   | 281            | 196     | 67       | 18        |
| PEF (% predicted) | 78.1 ± 28.5    | 83.5 ± 26.5 | 68.4 ± 26.9 | 69.5 ± 28.8 | .001 |
| MEF25 (% predicted) | 48.3 ± 26.4   | 51.0 ± 26.0 | 37.8 ± 22.5 | 46.3 ± 24.4 | .004 |
| MEF50 (% predicted) | 56.3 ± 28.5    | 60.1 ± 28.5 | 44.2 ± 23.6 | 55.2 ± 24.2 | .001 |
| MEF75 (% predicted) | 72.7 ± 35.8    | 75.4 ± 33.6 | 64.9 ± 31.3 | 63.5 ± 34.5 | .067 |

Abbreviations: MEF25–75, maxima expiratory flow between 25%, 50% and 75% of forced vital capacity. Data are presented as means ± SD. *P-value denotes statistical differences among 3 groups.

smokers than in non-smokers (P < .05). However, both the predicted percentages of MEF25 and MEF50 were low in smokers and nonsmokers and showed no significant difference between the 2 groups (P > .05).

After accounting for age, the regression analysis showed that the duration of exposure to asbestos was significantly associated with the FEV1/FVC ratio and the predicted percentage of MEF25 or MEF50 in non-smokers with asbestosis (Table 6).

In addition, the predicted percentages of $R_{5–R_{20}}$ were significantly negatively correlated with the predicted percentages of MEF25, MEF50 and MEF75, (Figure 2).

4 | DISCUSSION

In this study of patients with asbestosis, small airway obstruction was associated with the duration of asbestos exposure. Expiratory flow, including the predicted values of MEF25 and MEF50 by the flow–volume curve, was significantly lower in the different stages of asbestosis showing small airway dysfunction. Accordingly, the predicted percentage of $R_{5–R_{20}}$ was significantly higher with increasing stages of asbestosis, showing obviously elevated peripheral airway resistance. Furthermore, the predicted percentage of $R_{5–R_{20}}$ was significantly negatively correlated with the predicted percentages of MEF25, MEF50 and/or MEF75.

Asbestosis is a slowly progressive and persistent interstitial fibrosis of the lung. It is associated with the inhalation of asbestos dust and characterized by the appearance of large numbers of asbestos fibres and bodies within the lung tissue.1,2 Pleural abnormalities associated with asbestos exposure are caused by collagen deposition, which results in subpleural thickening that may subsequently calcify; additionally, the visceral pleura may exhibit parenchymal fibrosis in adjacent subpleural alveoli.1,2 Pleural thickening as a marker of asbestos exposure may be induced by relatively low exposure levels in comparison with asbestosis.16–18 In our cohort of patients with asbestosis, 88% of patients also had pleural abnormalities. A recent systematic review

TABLE 4  Respiratory impedance by the forced oscillation technique in asbestosis

|                | All asbestosis | Stage I | Stage II | Stage III |
|----------------|----------------|---------|----------|-----------|
| Subjects (n)   | 281            | 196     | 67       | 18        |
| $R_{5}$ (% pred) | 146.4 ± 63.6   | 143.9 ± 65.6 | 157.0 ± 57.5 | 138.4 ± 60.3 | .384 |
| $R_{20}$ (% pred) | 115.7 ± 38.6   | 118.7 ± 38.8 | 113.0 ± 38.3 | 104.2 ± 30.8 | .068 |
| $R_{35}$ (% pred) | 153.5 ± 54.1   | 163.6 ± 51.3 | 136.6 ± 57.7 | 127.3 ± 59.8 | .001 |
| $R_{5–R_{20}}$, % pred | 298.9 ± 183.7 | 222.2 ± 167.3 | 368.2 ± 193.1 | 383.1 ± 236.1 | .013 |
| $Z_{5Hz}$ (%pred) | 167.2 ± 73.7   | 150.9 ± 71.0 | 179.6 ± 70.5 | 176.9 ± 56.1 | .054 |
| $X_{5}$ (kPa·L⁻¹·s⁻¹) | −0.3 ± 0.09    | −0.2 ± 0.08 | −0.3 ± 0.1 | −0.3 ± 0.08 | .001 |
| Fres (L·s⁻¹)    | 18.3(6.4,390.2) | 16.6(7.7,390.4) | 21.3(6.4,312.5) | 20.3(12.5,274.3) | .000 |

Abbreviations: Fres, resonant frequency; $R_{5}$, resistance; $X_{5}$, the reactance calculated based on 5 Hz; $Z_{5Hz}$, the total mechanical load of the respiratory system estimated at 5 Hz. Data are presented as means ± SD or median (min, max). *P-value denotes statistical differences among 3 groups.
showed that the presence of pleural plaques is associated with a small but statistically meaningful decrease in the FVC and FEV₁ compared with asbestos-exposed individuals without plaques or other abnormalities. Previous studies have indicated that the pattern of spirometric impairment associated with asbestos exposure is primarily restrictive, with a reduced FEV₁ and FVC and a relatively preserved FEV₁/FVC ratio. In the present study, the normal pattern on spirometry was 34.5%, and a restrictive, obstructive and mixed pattern of spirometric impairment was present in 28.8%, 19.6% and 17.1% of patients with asbestosis respectively. The various pulmonary function patterns that were found in our cohort are in line with those in a previous study, although they showed a different constituent ratio. In the present study, the percentage of FEV₁/FVC indicated a mild obstructive defect that did not reach the criterion for COPD, and the RV/TLC was mildly elevated. X₅ was elevated and positively correlated with FVC, indicating significantly increased dynamic compliance of the chest in line with the changes in the lung volume parameters. All patients with asbestosis had a decreased diffusing capacity that preceded the reduction in lung volume, suggesting parenchymal and interstitial lesions.

Inhaled asbestos dusts or fibres are able to reach the distal part of the lung, resulting in small airway lesions and interstitial fibrosis. The histological process of inhalation of asbestos dust is probably the basis of small airway lesions in patients with asbestosis. Small airways are defined as bronchioles of <2 mm in diameter, including all bronchioles and terminal bronchioles. The small airway lumens are slender, have no cartilage and are characterized by slow air flow. Previous studies have suggested that a component of airway obstruction, particularly small airway obstruction, can also be present in workers exposed to asbestos. Chrysotile-exposed workers have been found to develop abnormal MEF₂₅–₇₅ and nitrogen washout curves. Abnormalities in maximal expiratory flow volume curves were also seen in workers with industrial exposure to asbestos with normal spirometry and TLC, suggesting air flow dysfunction in small airways. Spirometry showed that small airway obstruction in asbestos-exposed workers was related to dust exposure and not to alveolar inflammation or fibre retention. Spirometry also revealed an obstructive pattern in chrysotile-exposed workers and in those with an increase in RV/TLC. However, the results of a Delphi study by the American College of Chest Physicians suggested that a decline in small airway flow rates in nonsmokers cannot be reliably attributed to asbestos exposure. In the present study, small airway obstruction was detected in patients with various severities of asbestosis with decreased MEF₂₅ and MEF₅₀ by the flow–volume curve, and elevated R₅–R₂₀ was detected by the FOT. Furthermore, after accounting for age, the regression analysis showed that the duration of exposure to asbestos was significantly associated with the FEV₁/FVC ratio and the percentage of MEF₂₅ or MEF₅₀ in non-smokers with asbestosis.

Smoking cigarettes is one of the most common risk factors for airway obstruction. A cross-sectional analysis of data from approximately 3400 Copenhagen men confirmed associations between chronic bronchitis and smoking [odds ratio (OR), 2.4], occupational smoke inhalation (OR, 1.7) and long-term dust exposure (OR, 1.5). In 2611 long-term...
insulators, including 511 non-smokers, a prolonged \( \text{FEF}_{25\%-75\%} \) as an indicator of small airway dysfunction was seen in 33% of non-smokers and 67% of smokers.\(^{27}\) The 35.0% of patients with a reduced \( \text{FEV}_1/\text{FVC} \) among smoking insulators was higher than the proportion of 21.5% for smokers in the general population.\(^{28}\) The fact that a reduced FVC and \( \text{FEV}_1/\text{FVC} \) are more frequent in insulators who have smoked indicates the presence of an interaction between asbestos and smoking in the development of both of these physiologic abnormalities. In the present study of patients with asbestosis, there were significantly more patients with obstruction in the smoking than non-smoking group. The predicted percentages of \( \text{MEF}_{25} \) and \( \text{MEF}_{50} \) according to the flow–volume curve were lower in both smokers and non-smokers and showed no significant difference between the 2 groups. The findings of airway obstruction are more common in asbestos-exposed smokers than in smokers in the general population or non-smoking insulators, which is consistent with the augmented effect of exposure to smoking and asbestos.

### Table 6

|                      | \( \text{FEV}_1/\text{FVC} \% \) | \( \text{MEF}_{25} \text{ pred}\% \) | \( \text{MEF}_{50} \text{ pred}\% \) | \( R_5 \text{ pred}\% \) | \( R_5-R_{20} \text{ pred}\% \) |
|----------------------|---------------------------------|----------------------------------|---------------------------------|-----------------|-----------------|
| Age                  | 0.20 (0.07)*                    | 0.64 (0.20)                      | −0.44 (0.22)                    | −0.40 (0.55)    | −2.86 (2.28)    |
| Exposure time        | −0.14 (0.09)*                   | −0.24 (0.25)*                    | −0.40 (0.28)*                   | −0.01 (0.70)    | 3.04 (2.92)     |

Abbreviations: \( \text{FEV}_1 \), forced expiratory volume in the first second; \( \text{FVC} \), forced vital capacity; \( R \), resistance; \( \text{MEF}_{25–50} \), maxima expiratory flow between 25% and 50% of forced vital capacity.

Data are presented as coefficient (SE).

\(*P < .05.\)

### Figure 2

The predicted percentages of \( \text{MEF}_{25} \) (A), \( \text{MEF}_{50} \) (B) or \( \text{MEF}_{75} \) (C) negatively correlated with \( R_5-R_{20} \) respectively (\( r = -.341, P = .000 \); \( r = -.443, P = .000 \); \( r = -.383, P = .000 \))

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**TABLE 6** Relationships of lung function values and age or exposure time of asbestos in non-smokers in asbestosis by linear-regression analysis (n = 185)
One limitation of this study is that asbestosis was diagnosed without histological examination of the lung tissue. The diagnosis was based on the exposure history, clinical features of interstitial fibrosis and radiographic studies. A recent histological study suggested that the radiologic diagnosis of mild asbestosis (eg, close to the recommended International Labour Organization profusion cut-off of $\geq 1/0$) has significant overlap with smoking-associated fibrosis in the face of a concomitant history of heavy cigarette smoking.$^{29}$ A histological assessment for asbestosis will be helpful when the clinical and radiological features are atypical or nondiagnostic. A lung biopsy that shows microscopic asbestos fibres in the lung tissue is the most reliable sign with which to confirm asbestos-related abnormalities.$^{2}$ Another limitation is that smoking-induced emphysema and pulmonary fibrosis have different physiologic effects on asbestosis. In one cohort of patients with idiopathic pulmonary fibrosis, the pathologic changes of coexisting emphysema and fibrosis resulted in normal or near normal spirometry values and lung volumes with severely diminished DLCO.$^{29}$ The reliance on spirometry parameters may lead to underestimation in patients with combined fibrosis and emphysema.

5 | CONCLUSIONS

The patients with asbestosis had small airway obstructive defects, although the magnitude of the airway obstruction was relatively small according to spirometric parameters. The additive effects of smoking and asbestos may increase the risk of clinically significant small airway obstruction. A long-term study is warranted to explore the decline in airflow over time in patients with asbestos exposure and those with asbestosis.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

AUTHOR CONTRIBUTIONS

All authors read and approved the final version of the manuscript.

Study design: Qiao Ye

Performed experiments: Yongji Yan, Changjiang Xue, Xuqin Du, Qiao Ye

Data analysis: Xiaoli Yang, Yongji Yan, Changjiang Xue

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Obtained financial support:

ETHICS

This work was conducted at Beijing Chao-Yang Hospital, Capital Medical University. Informed consent was documented in writing.

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