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Clinical characteristics and risk factors in pneumoconiosis patients with asthma

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To investigate the risk factors for pneumoconiosis associated with asthma. A total of 256 pneumoconiosis patients diagnosed by chest X-ray at our hospital were analyzed. Based on pulmonary function tests, pneumoconiosis cases were divided into non-asthma and asthma-complicated groups. Clinical characteristics, clinical manifestations, and laboratory indicators of both groups were collected and compared. Risk factors for asthma in pneumoconiosis patients were identified using univariate and multivariate logistic regression analyses. Among the 256 pneumoconiosis patients, 79 had asthma. The age, BMI, incidence of pneumoconiosis categories II and III, exposure time, IgE levels, FeNO levels, and the incidence of wheezing and dyspnea were all higher in the asthma group compared to the non-asthma group. Conversely, FEV1, FEV1%predicted, FEV1/FVC, and the incidence of cough and expectoration were lower in the asthma group. Multivariate logistic regression analysis revealed that exposure time, low level of FEV1 and FEV1/FVC, high IgE levels, elevated FeNO, and wheezing were independent risk factors for asthma in pneumoconiosis patients. In this study, the prevalence of pneumoconiosis complicated with asthma was 30.9%. High exposure time, elevated IgE levels, increased FeNO levels, incidence of wheezing, low level of FEV1, and FEV1/FVC suggest that pneumoconiosis patients are significantly at increased risk of asthma.

Keywords Pneumoconiosis, Asthma, Clinical features, Risk factors, Odds ratio

Pneumoconiosis is a group of occupational interstitial lung diseases caused by the inhalation of mineral or organic dust, leading to lung dysfunction and an increased risk of developing a range of respiratory diseases, including coal workers' pneumoconiosis, silicosis, dust-related fibrosis, and chronic obstructive pulmonary disease (COPD)[1,2]. The pathological characteristics of this disease include chronic pulmonary inflammation and fibrosis, with inflammation exacerbating the fibrotic process[3]. The destruction of lung parenchyma and upper airway is progressive and irreversible throughout the disease course, ultimately resulting in pneumoconiosis[4,5]. Due to a lack of awareness regarding personal protection, difficulties in early diagnosis, and the absence of effective treatments, pneumoconiosis remains a serious global public health problem.

Pneumoconiosis can lead to numerous complications due to its pathological characteristics. Studies have identified abnormal increases in autoantibodies resulting from overexposure to mineral dust, which can contribute to the development of connective tissue diseases[6,7]. Pneumoconiosis is associated with various complications, including respiratory infections, COPD, pneumothorax, and emphysema[8,9]. Small airway diseases, which are a significant part of the spectrum of respiratory disorders caused by pneumoconiosis, often lead to severe pulmonary dysfunction[10]. Asthma, an allergic airway disease characterized by reversible airflow restriction, is commonly triggered by environmental irritants such as dust mites, dust, and pollen[11,12]. Occupational exposure can cause work-related asthma, which is often more severe and associated with greater levels of dysfunction and disability compared to asthma in the general population[13,14]. Trisnawati et al. found that a history of exposure to volcanic ash can result in silicosis, a condition characterized by the presence of a "high wheezing sound" during lung auscultation, which is a sign of an asthma attack[15]. Studies have shown that long-term, low-level occupational exposure to cleaning chemicals is linked to asthma, and patients with such exposure tend to experience poorer outcomes[16]. Clinically, we have observed that patients with pneumoconiosis

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may not exhibit specific symptoms of asthma, such as "wheezing sound", but asthma can be detected through pulmonary function tests (PFTs). Unfortunately, these patients are often missed or misdiagnosed.

Currently, there are few reports on pneumoconiosis complicated with asthma (pneumoconiosis-asthma), which seriously affects patients' prognosis and quality of life. Therefore, early detection and timely, effective treatment of asthma are crucial for adjusting the diagnosis and treatment of pneumoconiosis and improving patient outcomes. The aim of this study is to investigate the clinical characteristics and associated risk factors of pneumoconiosis complicated with asthma, to guide clinical treatment and enhance prognosis.

Patients and methods

Study patients

This study was approved by the Ethics Review Committee of the Second Xiangya Hospital of Central South University (Ethical Code: 2022-025). All patients signed informed consent, and all experiments were conducted in accordance with the Declaration of Helsinki. We included 256 patients diagnosed with pneumoconiosis who were hospitalized at the Second Xiangya Hospital of Central South University between January 2022 and July 2024. The inclusion criteria for patients with pneumoconiosis: (a) Long-term continuous occupational exposure to inhalable dust for more than one year, diagnosis according to China's National Diagnostic Criteria, which is aligned with the 2011 International Labor Organization guidelines on the assessment of opacities in chest radiographs for pneumoconiosis[17]; (b) Completeness of patient data, including patient demographics, clinical data, inhaled dust exposure history, etc. Pneumoconiosis patients were classified into category I, category II, and category III based on the size, density and distribution of chest X-ray opacities[18]. Two experienced radiologists independently evaluate all image findings. Asthma diagnosis was determined according to the 2023 GINA guidelines with bronchodilation forced expiratory volume in 1 s (FEV1) change > 200 ml and 12%[19]. The following patients were excluded from the study: (a) Those with proven pneumothorax, pneumonia, tuberculosis, emphysema, asthma and COPD; (b) Those with cardiac asthma; (c) Those who failed to undergo PFTs. All participants were defined as non-smokers or former smokers with a smoking history of less than 10 pack-years. Figure 1 presents a comprehensive flow diagram illustrating the process of recruiting voluntary participants for the study.

Data collection

After obtaining written informed consent, the study recorded the participants' demographic and clinical information, including body mass index (BMI). Laboratory tests measured immunoglobulin E (IgE) and fractionated exhaled nitric oxide (FeNO) levels. The MasterScreen™ PFT system in Germany was used to measure pulmonary function in accordance with the standards of the American Thoracic Society and the European Respiratory Society[5], including measurements of FEV1, forced vital capacity (FVC), and predicted FEV1%.

Statistical analysis

SPSS 27.0 software (IBM Corp.) was used to perform all statistical analyses. Continuous variables were described as mean ± standard deviation (M ± SD) or median (interquartile range), while categorical variables were expressed as number (percentage). Differences between two groups were assessed using the Student's t-test, Mann-Whitney U-test, and chi-square or Fisher's exact test. Spearman's rank correlation test was used to evaluate correlations between variables. Risk factors were identified through univariate and multivariate logistic regression analyses. Multivariate logistic regression analysis included variables based on univariate analysis $P < 0.05$. A P value < 0.05 indicated a statistically significant difference.

Results

Demographic characteristics of the two groups

Table 1 presents the demographic characteristics of 256 patients with pneumoconiosis. Among these, 79 (30.9%) had pneumoconiosis with asthma, while 117 (69.1%) had pneumoconiosis alone. The majority of patients with pneumoconiosis-asthma were male, comprising 73 (92.4%) of this group.

Compared to the pneumoconiosis-only group, the pneumoconiosis-asthma group showed significantly higher values for age, BMI, incidence of pneumoconiosis categories II and III, exposure time, IgE, FeNO, and incidence of wheezing and dyspnea. Conversely, the pneumoconiosis-asthma group had lower values for FEV1, FEV1%predicted, FEV1/FVC, and incidence of cough and expectoration ($P < 0.05$; Table 1). Details of these patient characteristics are shown in Table 1.

Correlation between pulmonary function and clinical parameters in patients with pneumoconiosis-asthma

In patients with pneumoconiosis-asthma, exposure time was negatively correlated with FEV1 (r=-0.314, $P = 0.005$; Fig. 2A). FEV1/FVC was negatively associated with IgE (r=-0.723, $P < 0.001$; Fig. 2B). No significant correlations were found between FeNO and lung function indicators (Table 2).

Univariate and multivariate logistic regression analysis of risk factors for pneumoconiosis complicated with asthma based on sociodemographic characteristics and clinical parameters

Table 3 shows the results of the univariate and multivariate logistic regression analyses of risk factors for asthma in patients with pneumoconiosis, based on clinical parameters and sociodemographic characteristics. The univariate analysis indicated that age, BMI, pneumoconiosis category, exposure time, IgE, FeNO, cough, expectoration, wheezing, dyspnea, and low levels of FEV1, FEV1%predicted, FEV1/FVC were associated with the occurrence of asthma. Multivariate analysis showed that exposure time ($OR = 1.194$, 95%$CI = 1.111–1.282$,

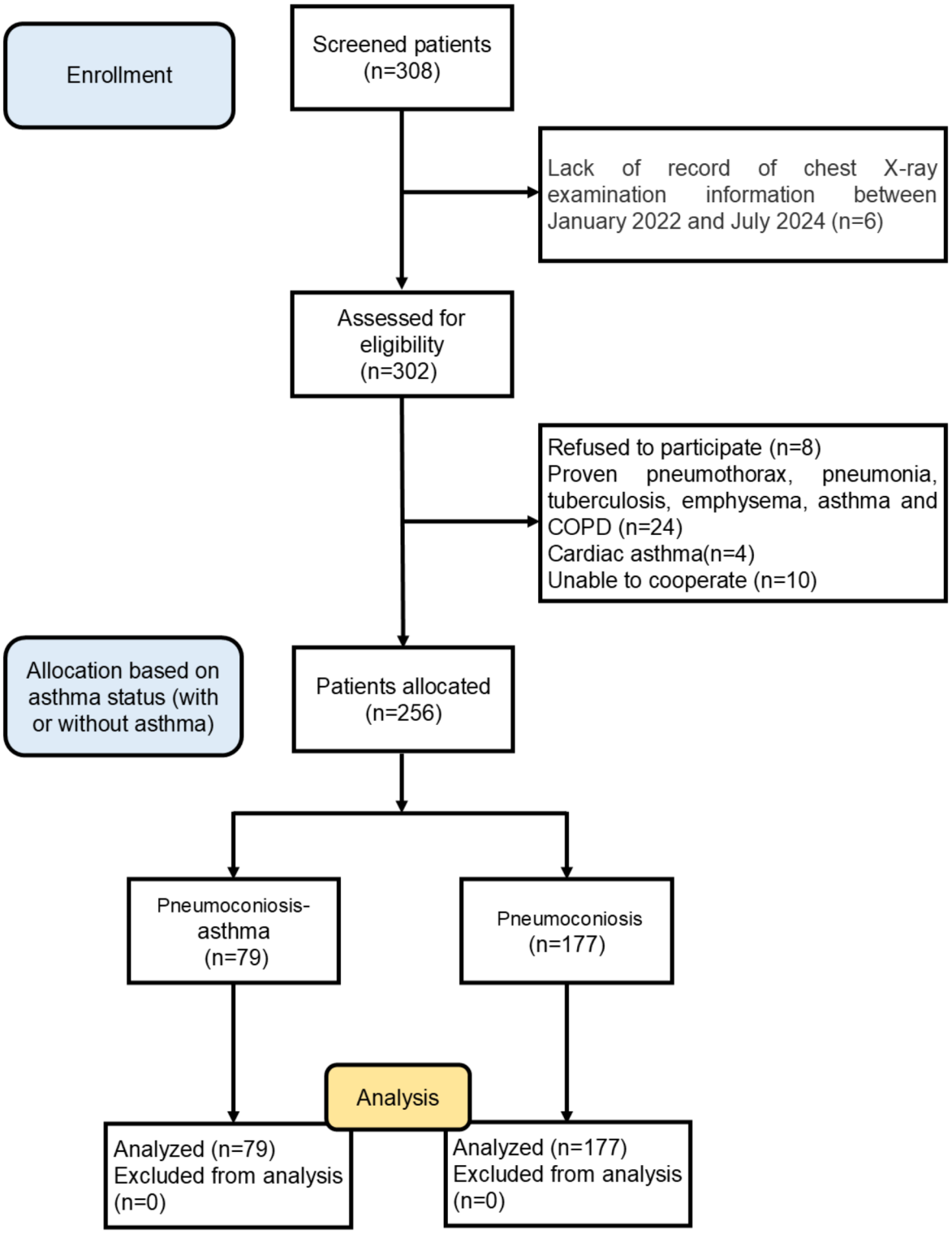

Fig. 1. Flow diagram of the study.

$P=0.021$), IgE ($OR=1.007$, 95%$CI=1.001–1.012$, $P=0.018$), FeNO ($OR=1.048$, 95%$CI=1.013–1.085$, $P=0.007$), wheezing ($OR=4.179$, 95%$CI=1.716–10.177$, $P=0.002$) and low levels of FEV1 ($OR=0.383$, 95%$CI=0.220–0.665$, $P<0.001$) and FEV1/FVC ($OR=0.779$, 95%$CI=0.712–0.852$, $P<0.001$) were identified as independent risk factors for asthma.

Items	Total	Pneumoconiosis ($n=177$)	Pneumoconiosis-asthma ($n=79$)	P value
Subjects, n (%)	256	117 (69.1)	79 (30.9)	
Age (y), median (IQR)	53.0 (47.0–61.0)	51.0 (46.0–56.0)	61.0 (49.0–67.0)	< 0.001
< 45, n (%)	39 (15.2)	28 (15.8)	11 (13.9)	< 0.001
45–60	150 (58.6)	122 (68.9)	28 (35.4)	
≥ 60	67 (26.2)	27 (15.3)	40 (50.6)	
Sex, n (%)				0.210
Male	226 (88.3)	153 (86.4)	73 (92.4)	
Female	30 (11.7)	24 (13.6)	6 (7.6)	
Smoking history, n (%)				0.082
Never-smoker	196 (76.6)	130 (73.4)	66 (83.5)	
Ex-smoker	60 (23.4)	47 (26.6)	13 (16.5)	
BMI (kg/m^2)		23.34 ± 2.54	24.08 ± 2.44	0.029
Pneumoconiosis category, n (%)				
I	203 (79.3)	164 (92.7)	21 (26.6)	< 0.001
II	27 (10.5)	6 (3.4)	26 (32.9)	
III	26 (10.2)	7 (4.0)	32 (40.5)	
Exposure type				0.748
Silicosis dust	58 (22.7)	39 (22.0)	19 (24.1)	
Coal dust	198 (77.3)	138 (78.0)	60 (75.9)	
Exposure time (y)	12.0 (9.0–15.0)	11.0 (8.0–13.0)	16.0 (13.0–23.0)	< 0.001
Lung function indexes, median (IQR)				
FEV_1 (L)	2.38 (1.79–2.81)	2.5 (2.1–3.4)	2.1 (1.3–2.4)	< 0.001
FEV_1%predicted (%)	72.1 (63.4–84.6)	73.8 (68.4–91.1)	63.2 (55.1–71.4)	< 0.001
FEV_1/FVC (%)	79.3 (73.4–82.5)	81.2 (77.1–83.5)	73.0 (71.4–78.2)	0.008
Biochemical indexes, median (IQR)				
IgE (mg/L)	123.5 (89.5–186.2)	121.0 (85.8–160.2)	148.3 (108.2–230.5)	0.011
FeNO (ppb)	27.5 (20.0–36.0)	25.0 (18.5–34.0)	35.0 (23.0–45.0)	< 0.001
Clinical manifestations, n (%)				
Cough	120 (46.9)	67 (37.9)	53 (67.1)	< 0.001
Expectoration	107 (41.8)	59 (33.3)	48 (60.8)	< 0.001
Wheezing	75 (29.3)	31 (17.5)	44 (55.7)	< 0.001
Chest distress	56 (21.9)	35 (19.8)	21 (26.6)	0.253
Dyspnea	24 (9.4)	9 (5.1)	15 (19.0)	< 0.001
Shortness of breath	60 (23.4)	42 (23.7)	18 (22.8)	1.000

Table 1. Demographic characteristics of the two groups. Comparisons were determined using the Student's t-test, Mann-Whitney U-test, and chi-square test or Fisher's exact test between the two groups. $P < 0.05$ was considered statistically significant. BMI, body mass index; FeNO, fractionated exhaled nitric oxide; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; IgE, immune globulin E; IQR, interquartile range; M ± SD, mean ± standard deviation; ppb, parts per billion.

Discussion

Pneumoconiosis, due to its pathological characteristics, frequently leads to various complications, including respiratory diseases. Patients with pneumoconiosis-asthma often present with symptoms such as wheezing, chest pain, and dry cough, significantly impacting their prognosis and quality of life[15]. It has been reported that occupational asthma, which constitutes about 25% of adult asthma, can result from sensitization to irritants at the workplace[16]. The mechanism behind irritant-induced asthma is believed to involve the disruption of the lung epithelial barrier caused by prolonged exposure to irritants[20]. However, the diagnosis of occupational asthma can be challenging, and the early prevalence of pneumoconiosis-asthma may be underestimated due to the absence of clear clinical signs in the early stages. Therefore, studying the prevalence of pneumoconiosis-asthma and its risk factors holds significant clinical importance. In this study, asthma was diagnosed in 79 (30.9%) out of 256 patients with pneumoconiosis using PFTs. The prevalence of chronic bronchitis among former coal miners in Ukraine is reported to be 18.1%[21]. This is the first report of 79 cases of pneumoconiosis-asthma, compared to previously reported cases in medical records. This finding may be related to sample source, sample size, extensive pulmonary function testing among pneumoconiosis patients, and clinicians' efforts to improve asthma diagnosis sensitivity.

In this study, we observed a high prevalence of asthma was associated with older adults and pneumoconiosis categories. Advanced age is recognized as a risk factor for the development and progression of asthma[22], and our findings align with this, showing an increase in asthma prevalence with advancing age, particularly among

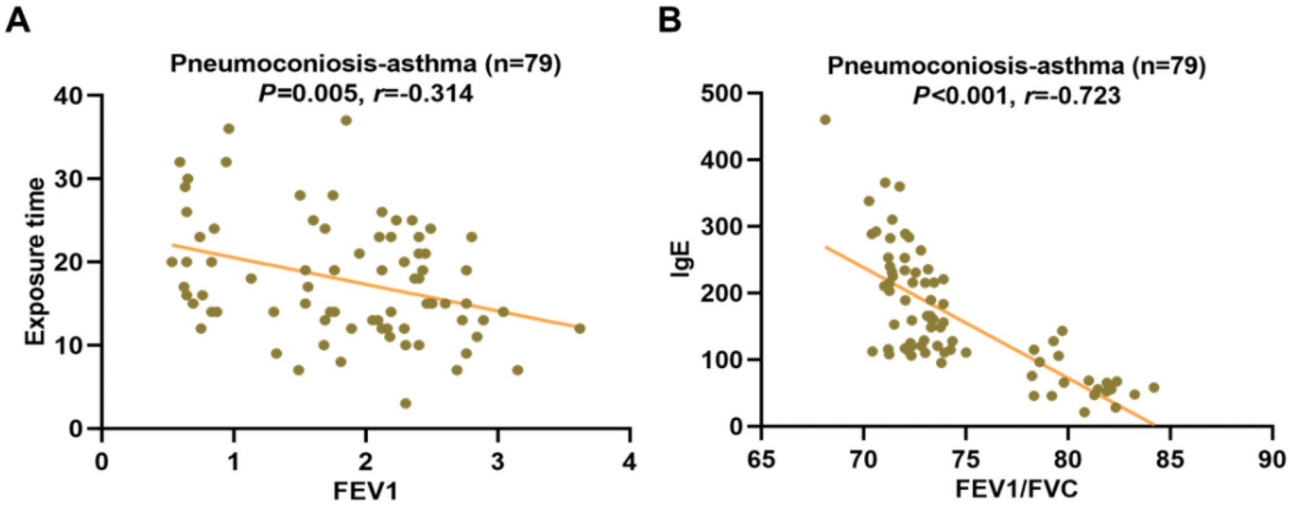

Fig. 2. Pulmonary function in patients with pneumoconiosis-asthma is correlated with exposure time and IgE. (**A**) The correlation between FEV1 and exposure time. (**B**) The correlation between FEV1/FVC and IgE. Correlations were determined by Spearman's rank correlation test. $P < 0.05$ was considered statistically significant. FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; IgE, immune globulin E.

Items	FEV_1		FEV_1%predicted		FEV_1/FVC	
	r	*P* value	r	*P* value	r	*P* value
Exposure time	−0.314	0.005**	−0.192	0.090	0.006	0.959
IgE	−0.008	0.945	−0.087	0.447	−0.723	< 0.001***
FeNO	−0.053	0.645	−0.078	0.492	−0.084	0.461

Table 2. Correlation between pulmonary function and clinical parameters in patients with pneumoconiosis-asthma. FeNO, fractionated exhaled nitric oxide; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; IgE, immune globulin E. Correlations were determined by Spearman's rank correlation test. $P < 0.05$ was considered statistically significant. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

those over 60 years. However, it remains uncertain whether this age-related trend is a direct reflection of cumulative dust exposure over time. In addition, we noted the highest asthma prevalence among patients in pneumoconiosis category III. The classification of pneumoconiosis is diagnosed by chest X-ray findings, and imaging abnormalities are strongly linked to lung function in workers exposed to occupational dust[23]. In coal miners, decreases in lung function measures such as FEV1, FEV1%predicted, and FEV1/FVC are associated with an increase in small-opacity profusion[23]. However, multiple logistic regression analysis revealed no association between age, pneumoconiosis category, and asthma risk. One study has found that pneumoconiosis categories II and III are risk factors for small airway dysfunction[24].

BMI is a risk factor for asthma development, and IgE and FeNO are markers of airway inflammation related to asthma attacks[25,26]. In this study, BMI, IgE and FeNO were higher in the asthma group compared to the non-asthma group. Studies have reported that BMI in pneumoconiosis patients is significantly associated with an increased risk of small airway dysfunction[24]. In pneumoconiosis-asthma, lung function is closely linked to exposure time and IgE. Prolonged, low-level occupational exposure can lead to sensitization in pneumoconiosis patients; however, IgE and FeNO tests lack specificity because exposed workers without symptoms can also test positive, so these tests need to be interpreted in conjunction with the patient's exposure history[27]. We found that the exposure time to pneumoconiosis-asthma was significantly longer in the asthma group compared to the non-asthma group. Prolonged occupational exposure causes a variety of symptoms and decreases lung function simultaneously. TenHarmsel et al. found that among surface miners who had worked for 15 years or longer, PFTs revealed that the majority had possible work-related asthma[28]. Persistent occupational exposure leads to small airway damage, with macrophages engulfing inhalable particles that enter the small airways and alveoli. This increases macrophage activity, which induces airway repair and regeneration processes by upregulating pro-inflammatory and pro-fibrotic pathways, leading to airway remodeling and potentially inducing or aggravating asthma[29].

Measures of lung function in this study were significantly reduced in patients with pneumoconiosis-asthma. Both pneumoconiosis and asthma may present with similar symptoms, including cough, phlegm, chest tightness, wheezing, and dyspnea. However, in this study, only wheezing and dyspnea symptoms were more prevalent in the pneumoconiosis-asthma group compared to the non-asthma group. This suggests that PFTs are essential for the early screening of pneumoconiosis with asthma, in addition to assessing clinical manifestations.

Variable	Univariate analysis		Multivariate analysis	
	P value	OR (95% CI)	*P* value	OR (95% CI)
Age	< 0.001	1.079 (1.047–1.112)	0.180	NA
BMI	0.031	1.128 (1.011–1.257)	0.214	NA
Pneumoconiosis category				
I	Reference		Reference	
II	< 0.001	14.718 (5.567–38.909)	0.689	NA
III	< 0.001	11.414 (4.484–29.053)	0.353	NA
Exposure time	< 0.001	1.192 (1.129–1.259)	0.021	1.194 (1.111–1.282)
FEV_1	< 0.001	0.311 (0.211–0.459)	< 0.001	0.383 (0.220–0.665)
FEV_1%predicted	< 0.001	0.934 (0.913–0.956)	0.181	NA
FEV_1/FVC	< 0.001	0.763 (0.710–0.820)	< 0.001	0.779 (0.712–0.852)
IgE	0.003	1.005 (1.002–1.009)	0.018	1.007 (1.001–1.012)
FeNO	< 0.001	1.061 (1.037–1.086)	0.007	1.048 (1.013–1.085)
Cough	< 0.001	3.347 (1.914–5.853)	0.788	NA
Expectoration	< 0.001	3.097 (1.788–5.363)	0.681	NA
Wheezing	< 0.001	5.921 (3.284–10.674	0.002	4.179 (1.716–10.177)
Dyspnea	< 0.001	4.375 (1.824–10.496)	0.829	NA

Table 3. Univariate and multivariate logistic regression analysis of risk factors for pneumoconiosis complicated with asthma based on sociodemographic characteristics and clinical parameters. BMI, body mass index; FeNO, fractionated exhaled nitric oxide; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; IgE, immune globulin E. Values were expressed as odds ratio (OR) and 95% confidence interval (CI). Factors associated with smoking cessation were determined by univariate and multivariate logistic regression analysis. Multivariate analysis was adjusted for age, sex, BMI.

Multivariate logistic regression analysis showed that exposure time, low levels of FEV1 and FEV1/FVC, IgE, FeNO and wheezing were independent risk factors for asthma in pneumoconiosis patients. When patients with pneumoconiosis experience wheezing due to long-term environmental exposure, the possibility of concurrent asthma should be considered. PFTs, along with tests for asthma-related IgE and FeNO levels, should be conducted in a timely manner to facilitate early detection and intervention.

There were some limitations of this study: (a) At baseline, the median age of patients with pneumoconiosis-asthma was 10 years older than those with pneumoconiosis alone. This is because concurrent asthma was not diagnosed in time, resulting in older age at diagnosis. (b) This is a cross-sectional descriptive study; therefore, no conclusions can be drawn about the direction of causality. The results of this study can only provide data related to smoking cessation, but not on predictive factors or causes of disease occurrence. (c) The mechanism of asthma associated with pneumoconiosis remains unexplained and requires further investigation.

Conclusion

At present, the treatment options for pneumoconiosis are still limited, and slowing its progression remains the primary approach. This is the first study to report the prevalence of pneumoconiosis-asthma and investigate its associated risk factors. In this study, the prevalence of pneumoconiosis-asthma was higher (30.9%). Factors such as exposure time, low levels of FEV1 and FEV1/FVC, IgE, FeNO, and wheezing suggested a significantly increased risk of asthma in pneumoconiosis patients. Clinical diagnosis and treatment should pay particular attention to pneumoconiosis patients with these risk factors.

Data availability

The data used and analyzed in this study are available from the corresponding author on reasonable request; E-mail: xudongxiang@csu.edu.cn.

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Author contributions

Conceptualization and design: Z.C., S.G.; Methodology and data management: Z.C., Y.S., B.W.; Statistical analysis and interpretation: Z.C., X.X.; All authors contributed to drafting the original manuscript of important intellectual content and final approval of the manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics approval

This study was approved by the Ethics Review Committee of the Second Xiangya Hospital of Central South University (Ethical Code: 2022-025). All participants signed an informed consent.

Additional information

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