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Review Article

Pneumoconiosis and Chronic Diseases: A Narrative Review

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Abstract

Pneumoconiosis, an occupational lung disease that arises from the inhalation of harmful dust, often co-exists with multiple chronic diseases that aggravate its prognosis and complicate treatment. These chronic diseases can include pulmonary and cardiovascular conditions, as well as cerebrovascular, renal, endocrine, and rheumatic comorbidities. The underlying pathogenesis, which involves inflammatory responses, blood vessel damage, and immune system compromise, is rooted in the persistent presence of inhaled dust particles within the pulmonary alveoli and the systemic circulation. Management emphasizes preventive measures, notably through regulatory oversight to reduce exposure, and is coupled with vigilant chronic disease monitoring and lifestyle interventions. This article reviews the mechanisms, research status, and management strategies for pneumoconiosis patients complicated by the aforementioned chronic diseases. We aimed to bridge the gap between understanding the complexities of pneumoconiosis combined with chronic conditions and translating this insight into practical and effective management strategies to enhance patient care.

Keywords: Pneumoconiosis; Chronic diseases; Occupational lung diseases

Introduction

Pneumoconiosis is a diverse group of occupational lung diseases, including silicosis, asbestosis, and coal worker's pneumoconiosis (CWP). These conditions arise from the inhalation of primarily inorganic mineral dust, such as free silica particles, asbestos fibers, and coal mine dust (1). The pathogenesis of pneumoconiosis is multifaceted, involving inhalation of toxic dust particles, subsequent inflammatory responses mediated by macrophages, and eventual pulmonary fibrosis (2). According to recent statistics, pneumoconiosis remains the most common occupational disease globally, with the number of new cases reported worldwide exceeding 600,000 in 2017 (3). As of the end of 2021, the cumulative number of reported pneumoconiosis patients was approximately 951,000 in China (4).

Chronic diseases have placed an escalating and substantial burden on individuals and healthcare systems globally (5). These diseases, such as pul-

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monary disease, cardio-cerebrovascular disease and chronic kidney disease, are responsible for the majority of deaths and serve as primary contributors to disability and healthcare expenditures (6).

Pneumoconiosis has been linked to several chronic diseases, particularly pulmonary and cardiovascular diseases, as well as cerebrovascular, renal, endocrine and rheumatic comorbidities (7). The underlying pathogenesis may be related to the inflammatory response, vascular injury and immunosuppression caused by pneumoconiosis particles deposited in the lungs and circulating vessels (Fig. 1) (8-10). Therefore, it is crucial to elucidate the correlation and impact between pneumoconiosis and chronic diseases in order to enhance clinical diagnosis, treatment, and ultimately improve the prognosis of patients (Table 1).

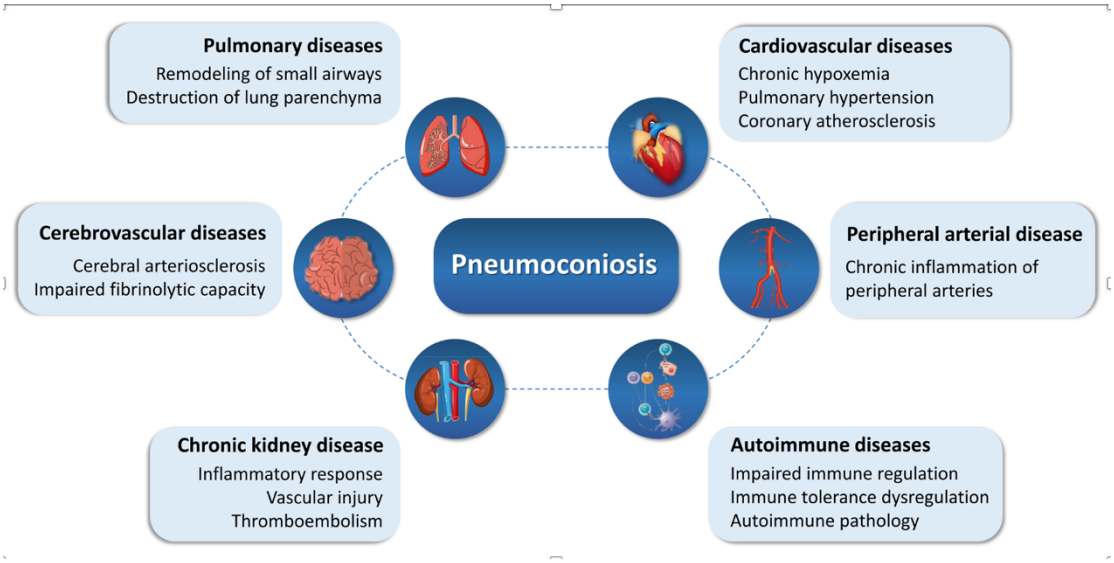

Fig. 1: Pathogenesis of pneumoconiosis-related chronic diseases

Table 1: Pneumoconiosis-related chronic diseases and references

Pneumoconiosis-related chronic diseases	References
Pulmonary diseases	(4), (9), (10), (11), (12), (13), (14)
Cardiovascular diseases	(15), (16), (17), (18), (19), (20)
Cerebrovascular diseases	(8), (21), (22), (23), (24), (25)
Peripheral arterial disease	(26), (27)
Chronic kidney disease	(7), (26), (28), (29), (30)
Autoimmune diseases	(31), (32), (33), (34), (35), (36), (37), (38), (39)

The occurrence and development of pneumoconiosis

Pneumoconiosis is a group of interstitial occupational lung diseases caused by the inhalation of mineral dust, primarily in various occupational settings (1). The condition leads to chronic inflammation and progressive fibrosis in the lungs, which can result in significant respiratory impairment and even death (11).

Silicosis results from inhaling silica dust, commonly found in mining and construction, while asbestosis is caused by asbestos fibers, which are prevalent in industries such as shipbuilding and construction. Moreover, CWP, which results from inhaling coal dust and is often observed in

miners, can manifest either as simple pneumoconiosis, involving minimal symptoms, or as complicated pneumoconiosis, known as progressive massive fibrosis (PMF), characterized by larger fibrotic masses and significant respiratory symptoms.

Upon inhalation, mineral dust particles become trapped in the lungs, where alveolar macrophages attempt to engulf them, leading to cell death and the activation of inflammatory pathways; this process, in turn, promotes fibrosis as fibroblasts proliferate and deposit collagen around the trapped particles, ultimately resulting in scarring and a loss of lung function (12).

Pneumoconiosis and different chronic diseases

1. Pulmonary diseases

Pneumoconiosis may play an important role in the development of various pulmonary diseases, including chronic obstructive pulmonary disease (COPD), asthma, pulmonary tuberculosis (TB) and lung cancer. Inhaled silica and coal dust are mainly deposited in the bronchioles and engulfed by alveolar macrophages, causing chronic inflammation, remodeling of small airways and destruction of lung parenchyma (13). The accumulation of dust particles in the lungs can stimulate the production of reactive oxygen species (ROS) and proinflammatory cytokines, resulting in tissue damage and scarring, ultimately leading to COPD (14, 15). Pneumoconiosis can also lead to asthma in certain individuals sensitive to the dust particles responsible for the disease, with the asthma often stemming from the inflammation or fibrosis that these particles induce in the lungs (16). Furthermore, the long-term course of pneumoconiosis causes immune dysfunction in patients, leading to increased risk of pulmonary tuberculosis and lung cancer (17, 18).

A cross-sectional study in China found that the prevalence of COPD among pneumoconiosis patients was 18.65%, and patients with combined COPD and pneumoconiosis had higher silica or coal dust exposure and more severe airflow limitation compared with those with pneumoconiosis alone (19, 20). Pneumoconiosis was found to be a factor of severity in acute exacerbation of COPD (AECOPD), and inpatients with AECOPD combined with pneumoconiosis were prone to prolonged hospital stays, increased expenditures, and higher incidence of infections (19, 21). Furthermore, individuals with pneumoconiosis were found to have a higher incidence of TB compared with the general population, and TB infection served as a prognostic marker for poor clinical outcomes, even when potent antimicrobial therapies were used (17). The TB incidence in pneumoconiosis patients was 15.82%, with varying rates depending on the stage of pneumoconiosis: 14.82% for stage I, 14.74% for stage II, and 34.60% for stage III (22). In terms of lung cancer, a cohort study conducted on 3335 hospitalized male pneumoconiosis patients in Japan found a significantly high observed/expected ratio (O/E ratio) of 4.80 for lung cancer mortality (23). This study also found a more than 2-fold increase in lung cancer risk among those who had never smoked, indicating that pneumoconiosis itself may be a risk factor for lung cancer independent of smoking (23).

2. Cardiovascular diseases

Pneumoconiosis can lead to a range of cardiovascular diseases, believed to be associated with various factors, including chronic inflammatory responses, chronic hypoxemia, and pulmonary fibrosis (24). The scarring and inflammation in the lungs caused by pneumoconiosis may result in decreased lung function and reduced oxygen levels in the blood, which can, in turn, contribute to the development of pulmonary hypertension (25). Over time, as the pulmonary arteries become stiff, narrowed, or damaged, the pressure within these vessels increases, placing a greater workload on the right ventricle of the heart, which can lead to the enlargement and weakening of the right ventricle, and eventually result in right heart failure (25). Additionally, pulmonary cytokines and relevant mediators may activate inflammatory cascades in vessel walls, potentially contributing to the development of atherosclerosis (26). In terms of blood pressure, patients with pneumoconiosis experience increased blood

pressure variability and disrupted day-night rhythm due to prolonged nocturnal and chronic hypoxia (27).

Yen et al. have reported a higher risk of congestive heart failure (CHF) in patients with pneumoconiosis, particularly in cases with coexisting coronary artery disease, hypertension, and chronic obstructive pulmonary disease. The overall incidence of CHF was higher in the pneumoconiosis cohort than in the non-pneumoconiosis cohort (15.7 vs. 11.2 per 1000 person-years, HR 1.40, $P<0.001$) (28). Additionally, a retrospective cohort study showed that pneumoconiosis has been linked to an increased risk of acute myocardial infarction (AMI), the overall incidence of AMI was 1.34-fold higher in the pneumoconiosis cohort than in the comparison cohort (4.33 vs. 3.23 per 1000 person-years, respectively, $P<0.05$) (25). Pneumoconiosis was associated with a significantly higher risk of cardiovascular events than that of the non-pneumoconiosis cohort (log-rank test $P<0.001$) (10). Pneumoconiosis was also related to increased risk of incident atrial fibrillation (AF), and the risk of AF in pneumoconiosis patients was 1.30-fold higher than that of controls (95% CI=1.17-1.44) (29). These findings illustrated a significant correlation between pneumoconiosis and cardiovascular disease, highlighting the importance of monitoring and managing the cardiovascular health of patients with this condition.

3. Cerebrovascular diseases

Clinical evidence has demonstrated an increased risk of cerebrovascular diseases, particularly ischemic stroke, in patients with pneumoconiosis, suggesting a possible pathophysiological link between these two conditions (10, 30). Pneumoconiosis induces chronic inflammation, which can alter the hemodynamic status of the brain and trigger cerebral angiopathy, potentially explaining the increased risk of ischemic stroke in these patients (10). According to foundational research, prolonged exposure to dust was shown to result in shortened clotting times and accelerated arterial thrombosis formation, and the underlying mechanism involves decreased bleeding time, reduced prothrombin and partial thromboplastin times, elevated fibrinogen levels, and enhanced activities of factors II, VIII, and X (10, 31). Moreover, exposure to dust particulates has been associated with an amplified expression of plasminogen activator inhibitor-1 and a concomitant reduction in plasma tissue plasminogen activator levels, factors that collectively contribute to an impaired fibrinolytic capacity (32).

Investigations have demonstrated that patients with pneumoconiosis exhibited a significantly higher incidence of ischemic stroke (HR 1.14, 95% CI 1.07-1.22, $P<0.01$); while a higher incidence of hemorrhagic stroke was also noted, but not significant (HR 1.20, 95% CI 0.99-1.46) (10). An additional cohort analysis revealed that 19.6% of pneumoconiosis patients and 15.8% of non-pneumoconiosis patients developed stroke, and the hazard ratio for stroke development was 1.36 times higher in patients with pneumoconiosis compared to those without it (30). Furthermore, pneumoconiosis is often accompanied by various comorbidities such as hypertension and diabetes mellitus, recognized as salient risk factors in the pathogenesis of cerebrovascular disease (33). In terms of cognitive function, data showed that diminished circadian activity rhythms (CARs) in male workers with pneumoconiosis are correlated with exacerbations in cognitive decline (34). Therefore, it is important for healthcare professionals to be aware of the potential elevated risk of cerebrovascular disease in patients with pneumoconiosis and to consider preventive measures accordingly.

4. Peripheral arterial disease

Patients with pneumoconiosis exhibit chronic inflammation in peripheral blood vessels, a condition that, in conjunction with direct oxidative damage and the activation of alveolar macrophages, plays a pivotal role in vascular injury and the pathogenesis of peripheral arterial disease (PAD) (35). A nationwide population-based retrospective cohort study showed that the incidence of PAD was 1.25 times greater in the pneumoconiosis group than in the non-pneumoconiosis group. After adjusting for sex, age, and comorbidities, the adjusted HRs of PAD

for the pneumoconiosis group were 1.30 (95% CI=1.08-1.57) compared with the non-pneumoconiosis group (35). The concurrent presence of pneumoconiosis along with other medical conditions, including COPD, coronary artery disease, hypertension, hypercholesterolemia, and diabetes mellitus could potentially heighten the risk of developing PAD (35, 36). This association suggests that clinicians should be vigilant in monitoring for signs of PAD in patients with pneumoconiosis and underscores the need for comprehensive management strategies that address both pulmonary and vascular health in these patients.

5. Chronic kidney disease

Chronic kidney disease (CKD) is a chronic disease characterized by gradual loss of renal function over time, and its risk has been confirmed to be elevated in pneumoconiosis patients. Pneumoconiosis-related inflammatory responses, vascular injury, and thromboembolic processes may all play a role in the development of CKD (35). Furthermore, previous studies on silicosis and CKD suggested that either a direct toxic action of inhaled dust or other autoimmune processes could lead to chronic kidney injury (9, 37).

A retrospective cohort study revealed that the overall incidence of CKD was 1.69-fold higher in the pneumoconiosis cohort than in the comparison cohort, with an adjusted hazard ratio of 1.83. The study controlled for age, gender, and comorbidity, and the association between pneumoconiosis and CKD risk remained significant across different age groups, genders, and comorbidity statuses (38). Additionally, a case report and literature review depicted a rare case of a CWP patient who developed tubulointerstitial nephritis as a consequence of IgG 4-related disease, which subsequently led to progressive kidney disease (39). These findings suggest a potential link between pneumoconiosis and chronic kidney disease, highlighting the importance of monitoring kidney health in individuals with pneumoconiosis.

6. Autoimmune diseases

Prolonged inhalation of airborne contaminants, such as inorganic dust, in patients with pneumoconiosis, is implicated in elevating the risk for specific autoimmune diseases, notably rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), psoriasis, and type 1 diabetes mellitus (T1DM) (40). Region-specific epidemiological data indicate that 13.8% of Chinese pneumoconiosis patients concurrently present with connective tissue disease (CTD), moreover, women and stage II or III pneumoconiosis are independent risk factors for CTD (41). In many reports of pneumoconiosis with autoimmune diseases from Japan, several pneumoconiosis patients with scleroderma had a past history of silica exposure (42). Dust particles stimulate T cells, which not only promotes their prolonged survival and chronic activation but may also lead to the generation of self-recognizing clones that have the potential to trigger autoimmune diseases (43). Concurrently, some studies suggest that alterations occur in the regulation of autoimmunity among pneumoconiosis patients (43). For instance, fas-mediated apoptosis in lymphocytes from silicosis patients is more pronounced than in healthy individuals, signifying an altered immune function (44). Furthermore, the presence of inflammatory factors and chemokines initiates chemotaxis, attracting fibrocytes that exacerbate the immune response (44). This chain of events culminates in the excess production of fibronectin and collagen, leading to scar formation and tissue remodeling (45). Additionally, genetic predisposition plays a role, rendering certain individuals more prone to developing autoimmune diseases upon dust exposure (45).

Silica exposure, a well-recognized etiological factor for pneumoconiosis, has been linked to immune tolerance dysregulation and subsequent autoimmune pathology in affected patients, which significantly exacerbates the prevalence including systemic sclerosis (43, 46). There is immune hyperactivity that is sparked by silica in which monocytes and macrophages release cytokines such as interleukin-1 and granulocyte-

macrophage-colony-stimulating factor and tumor necrosis factor-alpha (47). Another notable example is Kaplan syndrome, characterized by the co-occurrence of RA and pneumoconiosis, which manifests as intrapulmonary nodules detectable on a chest X-ray. (48). There is a certain association between pneumoconiosis and various autoimmune diseases, however, the exact pathogenetic link between exposure to dust, pneumoconiosis, and autoimmune diseases has not been conclusively clarified (48).

Management strategies for pneumoconiosis with chronic diseases

The cornerstone of pneumoconiosis management should be prevention, necessitating government-led enhancements in regulatory oversight at critical sites to mitigate exposure to harmful dust and thereby decrease the incidence of pneumoconiosis. According to Japan's regular pneumoconiosis health examination report, with the introduction and supervision of relevant laws, the prevalence of pneumoconiosis decreased from 17.4% in 1982 to 1% in 2013 (49). In patients diagnosed with pneumoconiosis, there should be an increased level of vigilance for respiratory conditions and chronic disorders such as cardiovascular and cerebrovascular diseases, with an emphasis on maintaining a healthy lifestyle regimen, abstaining from smoking, limiting alcohol intake, and routinely undergoing specific medical screenings (10, 24, 50). It is crucial to exclude the coexistence of active TB in patients with pneumoconiosis through TB testing, as this impacts treatment and prognosis (51).

Upon confirmation of such chronic conditions, it is imperative for patients to seek prompt specialist consultation to obtain clinical advice and multisystem interventions. The lung damage due to pneumoconiosis cannot be reversed, and treatments aim to limit further damage to the lungs and relieve symptoms, and may include inhalers, pulmonary rehabilitation, and oxygen therapy. Concurrently, persons afflicted with pneumoconiosis must sustain an optimal nutritional status to support physiological functionality and immunocompetence, in conjunction with proactive rehabilitation training (52). Additionally, pneumoconiosis patients may encounter psychological and social adversities, including depression and social isolation, highlighting the necessity for tailored psychological support interventions (53).

Conclusion

Pneumoconiosis is closely associated with various chronic diseases, predisposing to an increased risk of chronic diseases, the underlying mechanisms of which require further investigation. Clinical physicians should enhance their awareness of prevention and management of chronic diseases in these patients, adopting a multisystem approach that encompasses pulmonary, cardiac, cerebral, and autoimmune aspects for a comprehensive diagnosis and treatment. Pneumoconiosis remains a global threat, necessitating collaborative efforts from all societal sectors to further research and develop new models for the management of pneumoconiosis and its associated chronic conditions, as well as to discover new and effective pharmaceutical interventions against pneumoconiosis and chronic diseases, thereby improving the prognosis for patients worldwide.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interests.

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