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Association Between Occupational Dust Exposure and Prognosis of Idiopathic Pulmonary Fibrosis

A Korean National Survey

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BACKGROUND: Previous studies have investigated the relationship between occupational and environmental agents and idiopathic pulmonary fibrosis (IPF). However, there have been few studies regarding the prognosis of patients with IPF according to patient occupation.

METHODS: We investigated whether occupational dust exposure was associated with clinically decreased lung function and poor prognosis. The Korean Interstitial Lung Disease Research Group conducted a national survey to evaluate the clinical, physiologic, radiologic, and survival characteristics of patients with IPF. A total of 1,311 patients with IPF were stratified into five groups according to their occupation: (1) unemployed or homemakers (n = 628); (2) farmers, fishers, or ranchers (n = 230); (3) sales or service personnel (n = 131); (4) clerical or professional personnel (n = 151); and (5) specific dust-exposed workers (n = 171).

RESULTS: The mean age of subjects at diagnosis, was 67.5 ± 9.7 years. Current smokers were 336 patients, 435 were exsmokers, and 456 were never smokers. Dust-exposed workers showed early onset of IPF (61.3 ± 8.6 years; $P < .001$) and a longer duration of symptoms at diagnosis (17.0 ± 28.2 months; $P = .004$). Aging ($P = .001$; hazard ratio [HR], 1.034; 95% CI, 1.014-1.054), FVC % predicted at diagnosis ($P = .004$; HR, 0.984; 95% CI, 0.974-0.995), and dust-exposure occupation ($P = .033$; HR, 1.813; 95% CI, 1.049-3.133) were associated with mortality.

CONCLUSIONS: These findings indicate that occupational dust may be an aggravating factor associated with a poor prognosis in IPF. CHEST 2015; 147(2):465-474

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ABBREVIATIONS: DLCO = diffusing capacity of the lung for carbon monoxide; HR = hazard ratio; HRCT = high-resolution CT; ILD = interstitial lung disease; IPF = idiopathic pulmonary fibrosis; PFT = pulmonary function test; RR = relative risk; TLC = total lung capacity

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Idiopathic pulmonary fibrosis (IPF) is a chronic and diffuse progressive lung disease that usually results in a fatal outcome. The disease manifests histologically as usual interstitial pneumonia of unknown etiology. Further, it is associated with irreversible, worsening pulmonary function tests (PFTs), increasing respiratory symptoms, and eventually, considerable morbidity and mortality.[1] Although the clinical course is unpredictable and highly variable, the prognosis is very poor, with respiratory failure being the primary cause of death.[2]

Previous studies have suggested that occupational and environmental agents may contribute to the etiology of the disease or play a role in the its manifestations. These agents include cigarette smoke[3]; agriculture/farming[4]; stone, sand, or metal dust[5]; diesel exhaust particles[6]; chemical fumes[7]; and wood dust.[8] In addition, microbial agents,[9] gastroesophageal reflux,[10] and genetic factors[11,12] have been suggested to be involved in IPF. This information may also be helpful for planning individualized therapeutic strategies and predicting individual prognoses. Some case-control studies[4,6,8,13] have examined the occupational and environmental risk factors associated with IPF; however, the clinical features and prognostic factors related to the patients' occupations have not been well studied to date.

The Korean Interstitial Lung Disease (ILD) Research Group carried out a national, multicenter survey to evaluate the clinical, physiologic, and radiologic aspects. In this study, we evaluated the clinical features and prognostic factors of 1,311 Korean patients with IPF, according to their occupation.

Materials and Methods

Study Subjects

The Korean ILD Research Group, comprising 54 universities and teaching hospitals with pulmonary specialists (n = 82), enrolled patients newly diagnosed with IPF from January 1, 2003, to December 31, 2007. The diagnosis of IPF was established based on pulmonologic, radiologic, and pathologic evaluations, according to the 2002 criteria of the American Thoracic Society/European Respiratory Society.[14] Additionally, the Scientific Committee of the Korean Academy of Tuberculosis and Respiratory Diseases reviewed all enrolled patients.

Patients with collagen-vascular disease or a history of ingesting drugs or agents known to cause pulmonary fibrosis were excluded from the study. Silicosis and coal-worker pneumoconiosis were excluded for individuals who had a history of exposure to either silica or coal dust, with a finding of nodular or reticulonodular opacities without evidence of pulmonary fibrosis on high-resolution CT (HRCT) scan. The patients' medical records were entered into the Korean ILD web-based registry (www.ild.or.kr). In total, 2,186 patients were registered, but some patients were excluded if they had other idiopathic interstitial pneumonias according to the American Thoracic Society/European Respiratory Society guidelines.[14] Additionally, 374 patents with incomplete data related to their occupational history were excluded. Consequently, 1,311 medical records of patients with IPF were included in this study (Fig 1).

Occupational history was investigated by patients' self-report. A total of 145 job activities were investigated. The mean number of years worked was 23.9 ± 11.4. These collected occupational data were coded using the International Standard Classification of Occupation and the Korean Standard Classification of Occupation.[15,16] We initially stratified the coded data into 10 major groups (managers; professionals; technicians and associate professionals; clerical support workers; services and sales workers; skilled agriculture, forestry and fishery workers; craft and related trades workers; plant and machine operators and assemblers; elementary occupations; armed forces occupations). To further simplify these classifications, we subcategorized the groups into the following five groups, considering occupation previously proven to be related to IPF: (1) unemployed or homemakers; (2) farmers, fishers, or ranchers; (3) sales or service personnel; (4) clerical or professional personnel; and (5) workers exposed to specific types of dust (wood, metal, sand, stone, diesel, or chemical). For each patient, age, sex, smoking status and amount smoked, symptom duration, diagnostic method, initial PFT results, arterial blood gas analysis, comorbidities, HRCT scan findings, survival, and occupation were examined. The average follow-up duration was 17.7 ± 15.8 months.

Statistical Analysis

Continuous variables were analyzed using analysis of variance, and categorical variables were analyzed using the Pearson χ^2 test. Data are shown as mean ± SD for continuous variables and number for categorical variables. The effects of clinical, physiologic, radiologic, and occupational features on survival were assessed using the Cox proportional hazard models. The duration of survival after diagnosis was used for survival analysis. The results were expressed as the relative hazard ratio (HR) for death; the estimated survival curves were stratified by occupational group. An adjusted P value $< .05$ was considered statistically significant. All statistical analyses were carried out using SPSS, version 18 (IBM Corp).

Ethics Statement

This study protocol was reviewed and approved by the Institutional Review Board of Yonsei University Health Service, Severance Hospital (IRB approval number: 4-2009-0372), which deemed that informed consent was unnecessary.

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