

Occupational exposure and idiopathic pulmonary fibrosis: a multicentre case-control study in Korea

J-W. Koo,^{*,†} J-P. Myong,^{*,†} H-K. Yoon,[‡] C. K. Rhee,[§] Y. Kim,[¶] J. S. Kim,[#] B. S. Jo,^{*} Y. Cho,^{*} J. Byun,^{*} M. Choi,^{*} H-R. Kim,^{*,†} E-A. Kim^{**}

^{*}Department of Occupational and Environmental Medicine, and [†]Center for Occupational and Environmental Medicine, Seoul St Mary's Hospital, Catholic University of Korea, Seoul, [‡]Department of Internal Medicine, Yeouido St Mary's Hospital, College of Medicine, Catholic University of Korea, Seoul, [§]Department of Internal Medicine, Seoul St Mary's Hospital, College of Medicine, Catholic University of Korea, Seoul, [¶]Department of Internal Medicine, Bucheon St Mary's Hospital, College of Medicine, Catholic University of Korea, Bucheon, [#]Department of Internal Medicine, Incheon St Mary's Hospital, College of Medicine, Catholic University of Korea, Incheon, ^{**}Occupational Safety and Health Research Institute, Korea Occupational Safety and Health Agency, Ulsan, Republic of Korea

SUMMARY

SETTING: Multicentred hospital-based cases and control subjects in Korea.

OBJECTIVE: To evaluate the association between idiopathic pulmonary fibrosis (IPF) and hazardous materials to which people are occupationally exposed.

DESIGN: A multicentre, hospital-based, matched case-control study was performed. The ratio of IPF cases to controls was 1:1 ($n = 78$ in each group). IPF cases and controls were matched in terms of age group, sex and place of residence. Conditional logistic regression analysis was performed.

RESULTS: In simple logistic regression analysis, exposure to metal dust and any exposure for >1 year in an

occupational setting were significantly associated with IPF (metal dust OR 4.00, 95%CI 1.34–11.97; any exposure OR 3.67, 95%CI 1.02–13.14). After adjustment for environmental and military exposures and smoking history, the OR for metal dust exposure was 4.97 (95%CI 1.36–18.17) in multiple logistic regression analysis.

CONCLUSIONS: Metal dust was associated with incident IPF in Seoul and Gyeonggi Provinces in Korea. This information will be used to support a tailored preventive strategy in specific industries or occupations.

KEY WORDS: IPF; occupational exposure; metals; epidemiology; case-control study

IDIOPATHIC PULMONARY FIBROSIS (IPF), a form of idiopathic interstitial pneumonia, is clinically defined as progressive fibrosing interstitial pneumonia of unknown cause with a chronic clinical course.¹ Previous studies have been aimed at identifying factors associated with IPF, and occupational and environmental causes were considered as attributable risks for IPF. These studies evaluated the associations of silica,^{2–6} wood dust,^{6,7} metals^{2,3,5,7} and chemical fumes² with IPF, and were performed outside Korea, in Sweden, the United Kingdom, the United States, Mexico, Egypt and Japan. The aetiological features of occupational and environmental exposures vary because the composition of industrial materials differs among countries. IPF was associated with wood dust in Sweden⁴ and the United States,⁸ and with metal dust in the United Kingdom⁹ and Japan.¹⁰ These findings show that occupational and environmental exposures may vary according to country.

A recent Korean study has classified risk groups

according to industry or job.¹¹ Although that study attempted to identify an association between occupational exposure and IPF at the nationwide level, the industrial and job classifications used (unemployed, agriculture or fishing, sales or service, clerical or professional, and dust-exposed group) may have been too ambiguous to definitively identify materials such as wood dust, metal dust and chemical exposures as possible risk factors.¹¹

The present multicentre study was performed to evaluate the association between IPF and hazardous materials to which people are occupationally exposed in the Seoul and Gyeonggi Provinces in Korea.

METHODS

Enrolment of cases and controls

Cases were defined as patients newly diagnosed (incident cases) with IPF using chest computed tomography (CT), transbronchial lung biopsy and

Correspondence to: Jun-Pyo Myong, Department of Occupational and Environmental Medicine, College of Medicine, The Catholic University of Korea, 222 Banpo-Daero, Seocho-Gu, Seoul 06591, Republic of Korea. Fax: (+82) 2 2258 6691. e-mail: medical001@catholic.ac.kr

Article submitted 25 February 2016. Final version accepted 16 September 2016.

Table 1 Degree of agreement between occupational physicians in assessing exposure to potentially hazardous materials linked to idiopathic pulmonary fibrosis

Exposures	κ (95%CI)
Occupational exposure	
Silica dust	0.870 (0.782–0.957)
Wood dust	0.944 (0.835–1.000)
Asbestos fibres	0.820 (0.649–0.991)
Metal dust	0.903 (0.820–0.986)
Others*	0.711 (0.569–0.853)
Environmental exposure [†]	0.853 (0.861–0.998)
Military exposure [†]	0.926 (0.825–1.000)

* Fumes, gases, organic solvents, chemicals and cotton dust.

[†] One or more exposure.

CI = confidence interval.

video-assisted thoracoscopic lung biopsy, in line with the official American Thoracic Society (ATS)/European Respiratory Society (ERS)/Japanese Respiratory Society/Latin American Thoracic Association statement.¹ Cases were recruited from in- and out-patient clinics of the departments of respiratory medicine of four teaching hospitals, Seoul St Mary's Hospital (Seoul), Yeouido St Mary's Hospital (Seoul), Bucheon St Mary's Hospital (Bucheon, Gyeonggi Province) and Incheon St Mary's Hospital (Incheon, Gyeonggi) between 1 January and 31 December 2014. To perform a blind interview, the case list was mixed with that of controls and released to the interviewer, who was blinded to the diagnosis. Cases with collagen-vascular disease ($n = 4$), those who refused to participate in the study, those whose history was difficult to evaluate due to admission to an intensive care unit, those whose CT findings made it difficult to distinguish their condition from mycobacterial tuberculosis and/or bacterial infections and those with other types of idiopathic interstitial pneumonia besides IPF ($n = 33$) were excluded. A final total of 78 patients were eligible for inclusion in the study.

Hospital-based controls were enrolled to match each case from these hospitals over the same period of time. Patients with *Mycobacterium tuberculosis* infection, community-acquired bacterial or viral infection, pneumothorax and pleurisy were included. However, among these patients, those with work-related respiratory diseases (e.g., asthma, pneumoconiosis, chronic obstructive lung disease, lung cancer and mesothelioma) were excluded. To avoid information bias by the interviewer, the entire in- and out-patient clinic list from the respiratory physician was given to the chief occupational physician, who randomly selected eligible controls and invited two occupational physicians to perform a blinded in-depth interview. Although 123 controls were enrolled, those aged ≤ 40 years ($n = 3$) were excluded, and 120 controls were selected. After matching cases to controls, a final total of 78 controls was used for the analysis.

The study was approved by the Institutional

Review Board of the Catholic Medical Center, Seoul, Korea (ID: XC14QNNI0035K). Written informed consent was provided by the study participants.

Matching methods

The ratio of IPF cases to controls was 1:1. The age group, sex and place of residence of cases and controls were matched. Age was classified into three groups (<60 , 60–79 and ≥ 80 years), and cases and controls were matched accordingly. The study population was enrolled from two hospitals in Seoul and two hospitals in Gyeonggi Province; the place of residence of cases and controls was also matched. Matching was randomised using the random matching syntax for Statistical Analysis System (Cary, NC, USA).¹²

Exposure assessment

Exposure was assessed by two trained occupational physicians (CYM and CBS) after completion of the qualitative structured questionnaire assessing environmental, occupational and military exposures. The lifetime personal history of each subject's place of residence and occupation and possible exposure to air-borne materials (silica, wood, metal, asbestos, fumes, gases, organic solvents, chemicals and cotton dust) previously linked with IPF or interstitial lung disease (ILD)^{2–7} were recorded. Duration of employment ≥ 6 months and detailed description of the tasks performed since the subject started the first job were described. Subjects exposed to potentially hazardous materials for >1 year were regarded as exposed. Detailed information about work conditions, such as use of respiratory protective equipment, hours worked per day, memory of previous work-related diseases among co-workers or themselves, exposure to hazardous materials via the respiratory tract, etc., were also recorded. Exposure to each potentially hazardous material was assessed by two independent experienced occupational physicians (MJP and CBS). Exposure probability (P) was classified into none ($P = 0\%$), low ($0\% < P \leq 25\%$), moderate ($25\% < P \leq 50\%$) and severe ($50\% < P$); those with moderate or severe exposure were considered occupationally exposed. The degree of agreement in exposure assessment by the two occupational physicians is shown in Table 1.

Environmental and military exposures were assessed using the same procedure. The history of exposure during military service was also taken at the same time as occupational exposure. Korean males undergo mandatory military service in their late teens and early twenties. Military exposures to any potential hazardous materials were recorded as yes or no (Table 1). Environmental and residential history since birth was recorded along with residential information, type of house, use of biological fuels indoors, large-scale demolition for site reconstruc-

Table 2 General and occupational characteristics after matching for age group, sex and place of residence

	Matched		<i>P</i> value
	Cases <i>n</i> (%)	Controls <i>n</i> (%)	
Place of residence			1.0000
Seoul	32 (41.0)	32 (41.0)	
GyeongGi	46 (59.0)	46 (59.0)	
Age, years, mean \pm SD	69.6 \pm 8.8	70.6 \pm 9.5	0.4965
<60	11 (14.1)	12 (15.4)	0.9365
60~79	58 (74.4)	56 (71.8)	
\geq 80	9 (11.5)	10 (12.8)	
Sex			1.0000
Male	55 (70.5)	55 (70.5)	
Female	23 (29.5)	23 (29.5)	
Environmental exposure			0.0090
No	52 (66.7)	66 (84.6)	
Yes	26 (33.4)	12 (15.4)	
Military exposure			0.1595*
No	68 (87.2)	74 (94.9)	
Yes	10 (12.8)	4 (5.1)	
Smoking history			0.1941
Never smoker	26 (33.3)	36 (46.2)	
Ex-smoker	43 (55.1)	32 (41.0)	
Current smoker	9 (11.6)	10 (12.8)	
Pack-years, mean \pm SD	34.5 \pm 25.2	38.4 \pm 22.9	0.4344
Occupational exposure			
Silica			0.3466
No	57 (73.1)	62 (79.5)	
Yes	21 (26.9)	16 (20.5)	
Wood dust			0.4947*
No	75 (92.3)	75 (96.1)	
Yes	6 (7.7)	3 (3.9)	
Metal dust			0.0243*
No	57 (73.1)	69 (88.5)	
Yes	21 (26.9)	9 (11.5)	
Asbestos fibres			1.0000*
No	74 (94.9)	75 (96.1)	
Yes	4 (5.1)	3 (3.9)	
Other [†]			0.4909*
No	69 (88.5)	65 (83.3)	
Yes	9 (11.5)	13 (16.7)	
Any of above			0.2002
No	35 (44.9)	43 (55.1)	
Yes	43 (55.1)	35 (44.9)	
Total	78 (100.0)	78 (100.0)	

* Fisher's exact test.

[†] Fumes, gases, organic solvents, chemicals and cotton dust.

SD = standard deviation.

tions, specific petrochemical factories or asbestos or other dust-generating factories, transporting asbestos products at railway stations, etc. Subjects exposed to hazardous materials such as silica, wood, metal, asbestos, fumes, gases, organic solvents, chemicals and cotton dust within a radius of 500 m of their house for more than 1 year were regarded as exposed.

Statistical analysis

All statistical analyses were performed using SAS 9.4 software (Statistical Analysis System, Cary, NC, USA). The degree of agreement was estimated in κ and 95% confidence intervals (CIs) calculated using the McNemar's test. The χ^2 test was used for categorical variables, and Fisher's exact test was used to calculate *P* values. Student's *t*-test was used for

continuous variables. As this was a matched case-control study, the odds ratio (OR) for any association between IPF and exposure to potentially hazardous materials was estimated using conditional logistic regression. After adjusting for environmental exposure, multiple conditional logistic regression analysis was performed (Model 1). Model 2 was fitted after adjusting for environmental and military exposure. In Model 3, multiple conditional logistic regression analysis was performed after adjusting for environmental, military and smoking exposure.

RESULTS

The characteristics of IPF cases and controls before and after matching are given in Table 2. Before matching, females were predominant in the control group ($P < 0.05$); environmental and military exposure to potentially hazardous materials and smoking history differed significantly between cases and controls. After matching, environmental exposure (cases 33.4% vs. controls 15.4%) and occupational metal exposure (cases 26.9% vs. controls 11.5%) were associated with IPF ($P < 0.05$). Twenty-five cases (vs. 10 controls) were exposed to asbestos from asbestos-containing slate roofing over a one-year period, and one case was environmentally exposed to petrochemical fumes.

The OR and 95% CIs for each hazardous material and IPF are shown in Table 3. In simple logistic regression analysis, exposure to metal dust and any exposure to occupational hazardous materials for >1 year were significantly associated with IPF (metal dust, OR 4.00, 95%CI 1.34–11.97; any exposure, OR 3.67, 95%CI 1.02–13.14). After adjusting for environmental and military exposure and smoking history, the OR for metal dust exposure was 4.97 (95%CI 1.36–18.17) in multiple logistic regression analysis.

DISCUSSION

In this multicentre case-control study conducted in Korea, metal dust was found to be associated with incident IPF. Metal dust has previously been reported to be closely associated with IPF: in a case-control study of the association between metal dust and ILD with 165 cases with cryptogenic fibrosing alveolitis and 408 local Family Health Service Authority controls in the United Kingdom, the OR of questionnaire-reported exposure to metal dust for cryptogenic fibrosing alveolitis was 1.68 (95%CI 1.07–2.65).⁷ The attributable risk for occupational metal dust exposure was estimated to be up to 13.4%. Other epidemiological studies reported ORs of metal dust exposure for IPF ranging from 1.37 to 21.00.^{3–6,9,13} These results are consistent with our findings on metal dust exposure (OR 4.97, 95%CI 1.36–18.17)

Table 3 Associations between occupational exposure and idiopathic interstitial fibrosis as determined by simple and multiple logistic regression analyses

Occupational exposure	Crude	Model 1*	Model 2†	Model 3‡
Silica				
No	Reference	Reference	Reference	Reference
Yes	1.71 (0.67–4.35)	1.62 (0.62–4.18)	1.78 (0.64–4.97)	1.24 (0.41–3.76)
Wood dust				
No	Reference	Reference	Reference	Reference
Yes	2.00 (0.50–8.00)	3.20 (0.67–15.20)	3.26 (0.66–16.02)	2.51 (0.52–12.28)
Metal dust				
No	Reference	Reference	Reference	Reference
Yes	4.00 (1.34–11.97)	3.80 (1.21–11.88)	3.36 (1.06–10.66)	4.97 (1.36–18.17)
Asbestos fibres				
No	Reference	Reference	Reference	Reference
Yes	1.50 (0.25–8.98)	1.50 (0.25–8.98)	1.50 (0.25–8.98)	1.27 (0.17–9.56)
Other				
No	Reference	Reference	Reference	Reference
Yes	0.64 (0.25–1.64)	0.70 (0.27–1.84)	0.89 (0.31–2.54)	0.89 (0.31–2.54)
Any of above				
No	Reference	Reference	Reference	Reference
Yes	3.67 (1.02–13.14)	3.67 (0.94–14.27)	3.40 (0.85–13.53)	2.67 (0.65–10.93)

* Adjusted for environmental exposure.

† Adjusted for Model 1 and military exposure.

‡ Adjusted for Model 2 and smoking history.

in multiple logistic regression analysis. Aluminum,¹⁴ cadmium¹⁵ and zinc¹⁶ may be related to pulmonary fibrosis. The underlying mechanism is unknown; however, in vitro and in vivo studies suggest that inorganic dusts and metals are related to inflammatory and fibrotic responses.¹⁷ In a study on aluminium silicates and lung fibrosis among potroom workers, aluminium particles were predominantly detected in fibrosing lung specimens.¹⁴ Another study detected aluminium dust levels 1000-fold higher than background levels among workers with diffuse interstitial fibrosis.¹⁸ In the present study, there were several incident cases with definite aluminium exposure among aluminium potroom workers, workers at a foundry for aluminium-containing materials and workers manufacturing aluminium pipes.

Wood dust and job-related exposure to birds are associated with IPF in countries other than Korea.^{2–4,7} Differences in industrial and environmental distribution as well as exposure might underlie differences among countries. In a study on occupational exposure and pulmonary fibrosis using data derived from the Swedish Oxygen Register, hardwood dust was related to pulmonary fibrosis in Swedish men (OR 2.10, 95%CI 1.22–3.75).⁴ The authors of the Swedish study suggest that wood dust exposure might be more frequent in Sweden than in other countries.⁴ In addition, a multicentre study of occupational and environmental exposure in Egypt reported that exposure to wood dust (males, OR 2.71, 95%CI 1.01–7.37) and birds (males, OR 3.49, 95%CI 1.49–8.19; females, OR 3.86, 95%CI 1.95–7.62) was associated with incident IPF cases.² Because the poultry industry, including poultry farms, has grown rapidly in Egypt, the authors concluded that a lack of appropriate

hygiene during poultry farming contributed to these results.² There are several industrial clusters related to the manufacturing of precision machinery and the electrical and electricity industry in Seoul, Incheon and Bucheon, the cities included in our study,¹⁹ and differences in baseline industrial or environmental exposure should be carefully considered.

The OR for each exposure for incidental or prevalent pulmonary fibrosis or IPF might differ according to study design and the source of cases and controls (Table 4). In a study using a factory-based registry with individual employment records, the OR for metal exposure in pulmonary fibrosis was 21.0.⁹ However, the ORs for IPF were much lower in hospital-based case-control studies.^{3,4,7,13} The probability of meeting a possibly exposed person may be higher among factory-based subjects than among the general population and hospital-based subjects. Another reason for these discordant results is the study design. Most studies on IPF used a case-control design, which is the most appropriate approach for evaluating rare diseases. However, selection bias might arise due to the low prevalence of such diseases. To overcome this problem, a multicentre case-control study^{2,3,7,10} or a national registry may be recommended.⁴ According to Table 4 and a meta-analysis,²⁰ selection bias is less likely in such cases. A multicentre study design was therefore used here to reduce selection bias. However, as there are differences in the distribution of industries among regions, studies in other regions of Korea are needed.

Exposure assessment is an important factor for introducing discordance in study results and the statistical significance of study results. Structural questionnaires are generally adapted to assess expo-

Table 4 Previous epidemiological studies of the association between occupational exposure and idiopathic pulmonary disease

Author, year, country, reference	Study design	Source of controls and cases	Matching	Adjustment	Exposure assessment	Statistically significant result
Iwai, 1994, Japan ¹³	Case-control study	Hospital controls; healthy controls	Age, sex, region		Questionnaire	Metal exposure Hospital controls, OR 1.37 (95%CI 1.08–1.73) Healthy controls, OR 1.34 (95%CI 1.14–1.59)
Hubbard, 1996, UK ⁷	Case-control study	Multicentre hospital (cases); community-based (controls)	Age, sex, region		Self-reported questionnaire (cases); telephone interview (controls)	Metal dust, OR 1.68 (95%CI 1.07–2.65) Wood dust, OR 1.71 (95%CI 1.01–2.92)
Mullen, 1998, USA ⁶	Case-control study	Hospital (cases and controls)	Age, sex		Self-reported questionnaire	Silica dust, OR 11.0 (95%CI 1.05–11.1)
Baumgartner, 2000, USA ³	Case-control study	Multicentre hospital (cases and controls)	Age, sex, region	Age, smoking	Telephone interview	Metal dust, OR 2.0 (95%CI 1.0–4.0) Birds, OR 4.7 (95%CI 1.6–14.1) Silica dust, OR 3.9 (95%CI 1.2–12.7) Vegetable or animal dust, OR 4.7 (95%CI 2.1–10.4)
Hubbard, 2000, UK ⁹	Case-control study	Rolls-Royce Plc. workers (cases and controls)			Individual employment record	Sheet-metal workers, OR 21.0 (95%CI 3.47–141.9)
Miyake, 2005, Japan ¹⁰	Case-control study	Multicentre hospital (cases); hospital (controls)	Age, sex, region	Smoking	Doctor interview; telephone interview	Metal dust, OR 9.55 (95%CI 1.68–181.12) Smoking, OR 3.23 (95%CI 1.01–10.84)
Gustafson, 2007, Sweden ⁴	Case-control study	Registry-based (cases and controls); Swedish Oxygen Register	Age, sex	Smoking	Swedish Oxygen Register data; questionnaire	Organic dust, OR 1.7 (95%CI 1.06–2.80) Wood dust, OR 2.1 (95%CI 1.22–3.75) Males
Awadalla, 2012, Egypt ²	Case-control study	Multicentre hospital (cases and controls)			Questionnaire	Wood dust, OR 2.56 (95%CI 1.02–7.01)

OR = odds ratio; CI = confidence interval.

sure. There are two principal factors, interviewer training and estimation of possible exposure, i.e., metal or wood dust, for ensuring proper assessment of exposure. As IPF is a rare disease, differential bias may arise in estimations of ORs without proper exposure assessment, which should be performed by trained, experienced occupational physicians. As the degree of agreement between occupational physicians in exposure assessment is high (Table 1), differential information bias may have been reduced.

According to the ATS/ERS statement, the most important criterion for defining IPF is the exclusion of other known causes of ILD, such as domestic, occupational, environmental and connective disorders.¹ However, as the association between occupational exposure and IPF has been widely reported (Table 4), it may be difficult to identify any specific material as the definitive cause of IPF even in IPF patients with a history of exposure to hazardous materials. It may also be difficult to make a differential diagnosis between IPF without any exposure and ILD due to specific exposure. An operational definition, and not a definite diagnosis, is therefore necessary to diagnose specific exposure-induced ILD. Definite causes of IPF have not been previously identified, and various possible candidates for IPF have been suggested. To validate the differential diagnosis, subjects with silicosis and asbestosis were excluded from the present study. However, our results indicate that occupational exposure may be associated with IPF. This suggests that clinicians should ensure that the history of occupational and environmental exposure is systematically recorded to avoid classifying these diseases as idiopathic.²¹

There are several limitations to the present study. First, the dose-response relationship was not assessed. Baumgartner et al. reported that duration of exposure to metal dust for ≥ 5 years was significantly associated with IPF.³ The authors had estimated the proper appropriate numbers of study participants with and without specific exposure for a matched case-control study. The duration of exposure was therefore not classified in the present study. More participants should be enrolled to show the dose-response relationship in future studies. Second, the location of the participating hospitals was restricted to Seoul and Gyeonggi Provinces. Selection bias due to the restricted location also existed in previous studies with a hospital-based case-control design (Table 4). To reduce information or selection bias during enrolment of IPF cases from a single centre study, a multicentre design was adopted. Third, differential misclassification may have occurred in assessing occupational exposure. In the absence of individual employment records, this misclassification is inevitable due to recall bias.⁹ Individual employment records including the frequency of exposure

intensity (i.e., an hour per day, or 8 hours/day, etc.) was not assessed as this was a hospital-based case-control study. These limitations were overcome by history of exposure and occupational exposure being recorded by two experienced occupational physicians, and showing the degree of agreement between them. Fourth, the elimination of the possible impact of excluding patients with possible occupational exposure may have resulted in selection bias. In terms of epidemiological research, if diseases such as lung cancer, chronic obstructive pulmonary disease and asthma-related occupational exposure had been included in the control group, the strength of the association between hazardous material exposure and IPF may have been underestimated. In addition, the design of the present study did not include the exploration of possible associations, as in an ecological study. The exclusion of possible occupational lung disease and the matched case-control design may have reduced potential selection bias in the study.

The present study also has several strengths. First, incident IPF cases were enrolled to follow the premise of a case-control study. Second, occupational exposure was evaluated by two occupational physicians, and the degree of agreement between them was assessed. Third, to avoid bias in the matching method for age group, sex and place of residence, a random computerised method was used.¹² Fourth, history of environmental, military and smoking exposure was adjusted for in multiple analysis.

CONCLUSIONS

Exposure to metal dust is associated with incident IPF in Seoul and Gyeonggi Provinces, Korea. There are several types of industry in Korea. A pooled analysis of IPF and occupational exposure should therefore be performed to evaluate the association between specific exposures and IPF. Such studies can be used to create preventive strategies tailored to specific industries or occupations. In future, further studies are needed of ILD or IPF induced by different occupational exposures to evaluate whether they have a different prognosis.

Acknowledgements

The study was supported by the Korean Occupational Safety and Health Agency, Ulsan, Korea.

Conflicts of interest: none declared.

Reference

- Raghu G, Collard H R, Egan J J, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med* 2011; 183: 788–824.
- Awadalla N J, Hegazy A, Elmetwally R A, Wahby I. Occupational and environmental risk factors for idiopathic pulmonary fibrosis in Egypt: a multicenter case-control study. *Int J Occup Environ Med* 2012; 3: 107–116.
- Baumgartner K B, Samet J M, Coultas D B, et al. Occupational and environmental risk factors for idiopathic pulmonary fibrosis: a multicenter case-control study. Collaborating Centers. *Am J Epidemiol* 2000; 152: 307–315.
- Gustafson T, Dahlman-Hoglund A, Nilsson K, et al. Occupational exposure and severe pulmonary fibrosis. *Respir Med* 2007; 101: 2207–2212.
- Miyake Y, Sasaki S, Yokoyama T, et al. Case-control study of medical history and idiopathic pulmonary fibrosis in Japan. *Respirology* 2005; 10: 504–509.
- Mullen J, Hodgson M J, DeGraff C A, Godar T. Case-control study of idiopathic pulmonary fibrosis and environmental exposures. *J Occup Environ Med* 1998; 40: 363–367.
- Hubbard R, Lewis S, Richards K, Johnston I, Britton J. Occupational exposure to metal or wood dust and aetiology of cryptogenic fibrosing alveolitis. *Lancet* 1996; 347: 284–289.
- Pinheiro G A, Antao V C, Wood J M, Wassell J T. Occupational risks for idiopathic pulmonary fibrosis mortality in the United States. *Int J Occup Environ Health* 2008; 14: 117–123.
- Hubbard R, Cooper M, Antoniak M, et al. Risk of cryptogenic fibrosing alveolitis in metal workers. *Lancet* 2000; 355: 466–467.
- Miyake Y, Sasaki S, Yokoyama T, et al. Occupational and environmental factors and idiopathic pulmonary fibrosis in Japan. *Ann Occup Hyg* 2005; 49: 259–265.
- Lee S H, Kim D S, Kim Y W, et al. Association between occupational dust exposure and prognosis of idiopathic pulmonary fibrosis: a Korean national survey. *Chest* 2015; 147: 465–474.
- Kawabata H, Tran M, Hines P. Using SAS to match cases for case control studies. Cary, NC, USA: Statistical Analysis System. <http://www2.sas.com/proceedings/sugi29/173-29.pdf>. Accessed September 2016.
- Iwai K, Mori T, Yamada N, Yamaguchi M, Hosoda Y. Idiopathic pulmonary fibrosis. Epidemiologic approaches to occupational exposure. *Am J Respir Crit Care Med* 1994; 150: 670–675.
- Jederlinic P J, Abraham J L, Churg A, et al. Pulmonary fibrosis in aluminum oxide workers. Investigation of nine workers, with pathologic examination and microanalysis in three of them. *Am Rev Respir Dis* 1990; 142: 1179–1184.
- Yates D H, Goldman K P. Acute cadmium poisoning in a foreman plater welder. *Br J Ind Med* 1990; 47: 429–431.
- Bartter T, Irwin R S, Abraham J L, et al. Zirconium compound-induced pulmonary fibrosis. *Arch Intern Med* 1991; 151: 1197–1201.
- Huax F, Lasfargues G, Lauwerys R, Lison D. Lung toxicity of hard metal particles and production of interleukin-1, tumor necrosis factor-alpha, fibronectin, and cystatin-c by lung phagocytes. *Toxicol Appl Pharmacol* 1995; 132: 53–62.
- Gilks B, Churg A. Aluminum-induced pulmonary fibrosis: do fibers play a role? *Am Rev Respir Dis* 1987; 136: 176–179.
- Korea Industrial Complex Corporation. Year book of Korea Industrial Complex Corporation. Daegu, Korea: Korea Industrial Complex Corporation, 2016. <http://www.kicco.or.kr/ebook/ecatalog59.html>. Accessed September 2016.
- Taskar V S, Coultas D B. Is idiopathic pulmonary fibrosis an environmental disease? *Proc Am Thorac Soc* 2006; 3: 293–298.
- Gribbin J, Hubbard R B, Le Jeune I, et al. Incidence and mortality of idiopathic pulmonary fibrosis and sarcoidosis in the UK. *Thorax* 2006; 61: 980–985.

R E S U M E

CONTEXTE : Etude cas témoins multicentrique en hôpital.

OBJECTIF : Evaluer l'association entre fibrose pulmonaire idiopathique (IPF) et matériaux auxquels sont exposées les personnes dans leur travail dans un endroit bien précis de Corée.

SCHEMA : Une étude multicentrique cas-témoins appariés, basée dans des hôpitaux, a été réalisée. Le ratio de cas d'IPF aux témoins était de 1:1 ($n=78$ dans chaque groupe). Les cas d'IPF et les témoins ont été appariés sur la tranche d'âge, le sexe et le lieu de résidence. Une analyse de régression logistique conditionnelle a été réalisée.

RÉSULTATS : En analyse de régression logistique simple, l'exposition à la poussière de métal et toute

exposition durant plus d'une année sur les lieux de travail ont été significativement associées à l'IPF (poussière de métal, OR 4,00 ; IC95% 1,34–11,97) ; toute forme d'exposition (OR 3,67 ; IC95% 1,02–13,14). Après ajustement sur les expositions environnementales et militaires et les antécédents de consommation de tabac, l'OR pour la poussière de métal a été de 4,97 (IC95% 1,36–18,17) en analyse de régression logistique multiple.

CONCLUSION : La poussière de métal a été associée aux cas d'IPF dans les provinces de Séoul et Gyeonggi en Corée. Cette information sera utilisée pour étayer une stratégie de prévention adaptée dans des industries ou des postes de travail spécifiques.

R E S U M E N

MARCO DE REFERENCIA: Un estudio hospitalario multicéntrico de casos y testigos.

OBJETIVO: Evaluar la asociación entre la fibrosis pulmonar idiopática (IPF) y los materiales responsables de exposición laboral en las personas de una región específica de Corea.

MÉTODO: Fue este un estudio hospitalario multicéntrico de casos y testigos emparejados. La proporción de casos de IPF y testigos fue 1:1 ($n=78$ en cada grupo). Los casos y los testigos se emparejaron con respecto al grupo de edad, el sexo y la residencia. Se llevó a cabo un análisis de regresión logística condicional.

RESULTADOS: En el análisis sencillo de regresión logística se observó que la exposición al polvo metálico

y cualquier exposición en el entorno laboral durante más de 1 año se asociaba de manera significativa con la IPF (OR 4,00; IC95% 1,34–11,97) y con cualquier exposición (OR 3,67; IC95% 1,02–13,14). Tras ajustar con respecto a la exposición ambiental y militar y el antecedente de tabaquismo, la exposición al polvo de metal exhibieron un OR de 4,97 (IC95% 1,36–18,17) en el análisis de regresión logística múltiple.

CONCLUSIÓN: La exposición al polvo de metal se asoció con la aparición de casos IPF en Seúl y la provincia de Gyeonggi en Corea. Esta información se utilizará con el fin de fundamentar la elaboración de una estrategia preventiva dirigida específicamente a las industrias y las ocupaciones.