RESPIRATORY INVESTIGATION 53 (2015) 51–59

Contents lists available at ScienceDirect

Respiratory Investigation

journal homepage: www.elsevier.com/locate/resinv

Original article

A prospective survey of idiopathic interstitial pneumonias in a web registry in Japan ☆

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ARTICLE INFO

Article history:
Received 11 July 2014
Received in revised form
14 October 2014
Accepted 6 November 2014
Available online 4 December 2014

Keywords:
Idiopathic interstitial pneumonias
Idiopathic pulmonary fibrosis
Prospective multicenter
epidemiological study
Web registration

ABSTRACT

Background: There have been no prospective large-scale multicenter epidemiological studies on the clinical course and treatment from the time of diagnosis of idiopathic interstitial pneumonias (IIPs) in Japan. The purpose of this study was to clarify the current clinical situation of IIP in Japan.

Methods: This study was supported by a grant from the Ministry of Health, Labour and Welfare to the Diffuse Lung Diseases Research Group. Data including clinical findings, course, and treatment of IIP from a web database created by a collaborative effort of medical institutions across Japan that specialize in the care of interstitial pneumonias were collected and analyzed.

Results: A total of 436 IIP patients from 19 institutions were newly registered during a 5-year period. Idiopathic pulmonary fibrosis (IPF) was the most frequently encountered IIP, and 28% of the IPF cases were initially diagnosed by abnormal chest X-ray or CT in asymptomatic patients. Until the 2008 fiscal year, no treatment was given for most cases of IPF. After the end of 2008, when pirfenidone was approved for manufacture, the number of patients for whom no treatment was recommended declined, and pirfenidone therapy was initiated in 32.9% of cases in 2009. The median survival times for IPF from the onset symptoms and from the initial visit were 105 months and 69 months, respectively.

Conclusions: This study should provide valuable information for understanding the current state of IIP in Japan.

http://dx.doi.org/10.1016/j.resinv.2014.11.001
2212-5345/

1. Introduction

Idiopathic pulmonary fibrosis (IPF) is a lung disease of unknown etiology with a poor prognosis that follows a chronic and progressive course resulting in severe fibrosis and formation of irreversible honeycomb lung [1,2]. The natural course and prognosis of IPF varies for each patient, and is difficult to predict. Determination of the need for intervention and the development of effective treatment strategies depend on a multifaceted evaluation of the clinical course and the risk factors for poor prognosis [2,3].

IPF is categorized as an idiopathic interstitial pneumonia (IIP). To date, there have not been a large-scale prospective epidemiological study of the clinical course and treatment of IIP from the time of diagnosis in patients in Japan. We analyzed data on diagnoses, clinical findings, treatments, and disease course from an integrated internet database of IIP patients that was created with the participation of medical institutions across Japan that specialize in IIPs. This study was aimed at describing the current state of IIP in Japan and examining diagnostic findings and standards of care. This prospective survey on diffuse lung diseases that was conducted within the framework of a research project supported by the Ministry of Health, Labour and Welfare Grant-in-Aid for Scientific Research.

2. Materials and methods

2.1. Patients and data collection

A research project for overcoming intractable diseases, the Clinical Research Group on Groundbreaking Treatment for IIPs, supported by the Ministry of Health, Labour and Welfare, embarked on the registration system in the 2003 fiscal year (FY). In FY 2005, the system of web registration of clinical details of IIP patients of the Diffuse Lung Diseases Research Group, which existed at that time as the project leader, was completed. These details included: IIP type; patient characteristics at initial visit (gender, age, age of onset, family history, smoking history, complications); clinical findings (initial symptoms, form of onset, main symptoms, presence or absence of clubbed fingers); serological findings (including presence or absence of elevated Krebs von den Lungen-6 factor [KL-6] and surfactant protein [SP] A and D [SP-A and SP-D]); pulmonary function parameters (including % predicted vital capacity [%VC], % predicted diffusing capacity for carbon monoxide [%DLco], partial pressure of arterial oxygen [PaO_2] at rest, and lowest oxygen saturation by pulse oximetry [SpO_2] during 6 min walking); diagnostic imaging results (shadow distribution, presence or absence of honeycomb lung and traction bronchiectasis, presence or absence of ground glass opacity and infiltration); disease severity; treatment (no treatment, pirfenidone, inhaled N-acetylcysteine [NAC], steroids, immunosuppressive drugs, and others); clinical course; and cause of death. The severity grade of IPF was determined according to the severity classification of the Japanese Respiratory Society criteria [1]. Acute exacerbations were also assessed according to established criteria in Japan [4]. This study was approved by the Institutional Review Board of the Tohoku University (Approval date: January 17, 2005; Approved #: 2004-331). Informed consent was obtained from patients.

2.2. Statistical analysis

Time-to-event distribution for overall survival was estimated using the Kaplan–Meier method and survival rate between groups was compared by log-rank test.

3. Results

3.1. Web registry and patient follow-up

As shown in Table 1, 436 patients from 19 institutions were newly registered in the database during FY 2006–2010 (321 IPF, 82 non-specific interstitial pneumonia [NSIP], 15 other, and 18 not entered). Of the 436 patients, 261 remained in the registry at one year after the registration period, and the number of follow-up cases continued to decrease over time to 74 cases in the fifth year after the initial registration period.

3.2. Characteristic of the registered patients

Table 2 shows patient characteristics by diagnosis at the initial visit (gender, age, age of onset, family history of interstitial pneumonia, smoking history, and complications). IPF was the most frequent diagnosis, and accounted for 321 cases (73.6%). Among the IPF patients, 78.8% were male, ~80% were older than 60 years, and 6.2% were those whose age of onset was younger than 50 years. Surgical lung biopsy was performed in 131 (40.8%) IPF patients; 28 (8.7%) had a family history of interstitial pneumonia. Regarding complications among the IPF patients, diabetes was observed in 10%, COPD in 4.0%, and lung cancer in 3.1%. Disease severity

Abbreviations: ALAT, Latin American Thoracic Association; ATS, American Thoracic Society; COPD, Chronic Obstructive Pulmonary Disease; ERS, European Respiratory Society; FVC, Forced Vital Capacity; IIPs, Idiopathic Interstitial Pneumonias; IPF, Idiopathic Pulmonary Fibrosis; JRS, Japanese Respiratory Society; KL-6, Krebs von den Lungen-6; NAC, N-acetylcysteine; NSIP, Non-specific Interstitial Pneumonia; PaO_2, Partial Pressure of Arterial Oxygen; SP-A, Surfactant Protein-A; SP-D, Surfactant Protein-D; SpO_2, Oxygen Saturation by pulse oximetry; VC, Vital Capacity; %DLco, % predicted diffusing capacity for carbon monoxide; %VC, % predicted vital capacity

☆The Diffuse Lung Diseases Research Group by a Ministry of Health, Labour and Welfare Grant-in-Aid for Scientific Research.

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