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Clinical findings and outcomes in patients with possible usual interstitial pneumonia

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KEYWORDS
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Summary
Background: Patients with possible usual interstitial pneumonia (UIP) constitute a substantial group, and their clinical characteristics and outcomes are not well defined. We compared the clinical characteristics and survival between patients with possible UIP and the UIP pattern.
Methods: We evaluated 62 patients with possible UIP and 544 patients with the UIP pattern. Both groups were diagnosed by clinical characteristics and high-resolution computed tomography (HRCT) findings. Two radiologists performed radiological evaluation based on the new idiopathic pulmonary fibrosis (IPF) guidelines. Two risk-stratification methods were used to compare UIP pattern and possible UIP patients.
Results: The groups had similar demographic and clinical characteristics. Pulmonary function tests revealed no significant differences in lung volumes between the 2 groups. However, DLCO was significantly lower with the UIP pattern than with possible UIP ($p = 0.004$). Multivariate analysis showed age, sex, and carbon monoxide diffusing capacity (DLCO) as important independent variables for survival. The UIP HRCT pattern did not affect survival (hazard ratio, 0.83; 95% confidence interval, 0.51–1.24; $p = 0.32$). Possible UIP was not associated with prognosis when independent predictors for survival rate and propensity score were considered. In the case-control study, the 3-year survival rate was 44.6% in the UIP pattern group and 56.8% in the possible UIP group ($p = 0.16$).

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Conclusions: Clinical characteristics and outcomes were similar in possible UIP and UIP patients, except for differences in DLCO. The UIP pattern itself did not affect survival.

Introduction

Idiopathic pulmonary fibrosis (IPF), the most common diffuse fibrosing lung disease, has an unknown etiology and very poor prognosis [1]. This disease is confined to the lungs and is characterized by the histological and radiological patterns of usual interstitial pneumonia (UIP) [1—2]. IPF affects men more than women, and the patients are usually over 50 years of age. The median survival of IPF patients ranges from 2 to 3 years [3—6]. IPF symptoms are nonspecific at onset, with the most prominent being dyspnea on exertion and non-productive cough.

According to a 2011 international statement, an accurate IPF diagnosis is possible with a multidisciplinary discussion among clinicians, radiologists, and pathologists experienced in the diagnosis of IPF [7]. The diagnosis of IPF remains challenging. Many patients meet the clinical criteria, but do not fulfill all of the imaging criteria for the UIP pattern in high-resolution computed tomography (HRCT). These patients are usually classified as 'possible UIP', and the international statement recommends performing a lung biopsy for diagnosis in these cases [7]. In clinical practice, biopsy is often avoided because of its invasive nature and associated morbidity and mortality, and patients often refuse the procedure. Therefore, the ability to identify patients with IPF by using only HRCT and clinical findings would be helpful. Until now, one large cohort study has been reported based on clinical data on the clinical course and survival of patients with possible UIP [8].

The progression of honeycombing in fibrotic idiopathic interstitial pneumonia and extent of idiopathic pulmonary fibrosis has been reported [9—10]. However, it is yet to be ascertained whether possible UIP progresses to a UIP pattern in a clinical setting.

We undertook this study to define the clinical characteristics, progression of CT findings, and outcomes of patients with possible UIP to ascertain if the clinical characteristics of possible UIP are different from the UIP pattern.

Methods

Subjects and study design

We conducted a retrospective cohort study, analysis of patients with possible UIP, and IPF patients with the UIP pattern served as the controls. The patients had been diagnosed over a 126-month period (August 1, 2002—January 31, 2011). The Institutional Review Board (IRB) of Keimyung University, Dongsan Medical Center, approved this study (IRB 12-197). The review board did not require informed consent for retrospective review of the patients' HRCT images and records. The inclusion criteria were patients diagnosed with either the UIP pattern or possible UIP, as defined by the recently published international consensus statement [7] who had undergone at least 1 HCRT during the 126-month period. The exclusion criteria were clinical evidence of connective tissue diseases and lung fibrosis caused by drugs or occupational or environmental exposure (i.e., hypersensitivity pneumonitis). Two experienced chest radiologists performed the radiological assessment (SM Ko and BH Rho) based on the new IPF guidelines [7]. We searched for the term 'interstitial pneumonia' or 'pulmonary fibrosis' in the differential diagnoses of our hospital's chest CT reading records from 2002 to 2011, and found 919 individual patients matching the search criteria. The radiologists selected UIP pattern and possible UIP cases from the 919 cases. They were blinded to the original diagnosis. We included 544 patients with the UIP pattern and 62 patients with possible UIP in our final study population.

Data collection

For every patient, demographic (sex, age, and smoking history), clinical (dyspnea), physiological (resting oxygen saturation and pulmonary function tests), and imaging (HRCT) data were collected electronically from the medical records. Further, we collected follow-up HRCT data in patients initially diagnosed as possible UIP. IPF guidelines recommend that the UIP pattern meets all of the following criteria: the disease is predominantly subpleural and basilar in distribution, reticular in appearance, and is associated with honeycombing in the absence of inconsistent features that suggest another diagnosis [7]. A possible UIP pattern was defined according to the above criteria, but without honeycombing. The key feature for differentiating between possible UIP and UIP pattern is the presence or absence of honeycombing. We defined honeycombing in HRCT according to the Fleischner Society statement [11]: clustered cystic air spaces, typically of comparable diameters of approximately 3—10 mm, but occasionally as large as 2.5 cm, usually with a subpleural location. These spaces are characterized by definable walls, with cysts typically lined up adjacent to each other.

Statistical analysis

The data are presented as mean (SD) for continuous variables and number of subjects (%) for categorical variables. Categorical variables were compared by using the Fisher exact test or Pearson's χ^2 test, as appropriate. Continuous variables were compared by using the Mann—Whitney U test or Student t test, after checking for normality with the Kolmogorov—Smirnov test. A univariate analysis using Cox