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Diagnostic certainty of idiopathic pulmonary fibrosis/usual interstitial pneumonia: The effect of the integrated clinico-radiological assessment

Junya Tominaga[a,b,*], Fumikazu Sakai[b], Takeshi Johkoh[c], Satoshi Noma[d], Masanori Akira[e], Kiminori Fujimoto[f], Thomas V. Colby[g], Takashi Ogura[h], Yoshikazu Inoue[i], Hiroyuki Taniguchi[j], Sakae Homma[k], Yoshio Taguchi[l], Yukihiko Sugiyama[m]

[a] Department of Diagnostic Radiology, Tohoku University School of Medicine, Sendai 9808574, Japan
[b] Department of Diagnostic Radiology, Saitama International Medical Center, Saitama Medical University, Hidaka 3501298, Japan
[c] Department of Radiology, Kinki Central Hospital of Mutual Aid Association of Public School Teachers, Itami 6648533, Japan
[d] Department of Radiology, Tenri Hospital, Tenri 6328552, Japan
[e] Department of Radiology, National Hospital Organization Kinki-Chuo Chest Medical Center, Sakai 5918555, Japan
[f] Department of Radiology and Center for Diagnostic Imaging, Kurume University School of Medicine, Kurume 8300011, Japan
[g] Department of Laboratory Medicine and Pathology, Mayo Clinic, Scottsdale, AZ 85054, USA
[h] Department of Respiratory Medicine, Kanagawa Cardiovascular and Respiratory Center, Yokohama 2360051, Japan
[i] Clinical Research Center, National Hospital Organization Kinki Chuo-Chest Medical Center, Sakai 5918555, Japan
[j] Department of Respiratory Medicine and Allergy, Tosei General Hospital, Seto 4898642, Japan
[k] Department of Respiratory Medicine, Toho University Omori Medical Center, Tokyo 1438541, Japan
[l] Department of Respiratory Medicine, Tenri Hospital, Tenri 6328552, Japan
[m] Department of Medicine, Division of Pulmonary Medicine, Jichi Medical University, Simotsuke 3290498, Japan

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ABSTRACT

Objective: To reevaluate idiopathic pulmonary fibrosis (IPF) cases which had surgical lung biopsy (SLB) for diagnosis of usual interstitial pneumonia (UIP), and examine the influence of computed tomography (CT) findings and clinical information based on diagnostic certainty.
Methods: Ninety-five cases with multidisciplinary diagnoses of IPF were identified from eight institutions. All cases had SLB. Two expert chest radiologists and five expert pulmonologists used a 5-point scale to grade their level of certainty in the diagnosis of a radiological pattern of UIP or a clinical diagnosis of IPF (level 1 "definitely no" to level 5 "definitely yes"). Radiologists independently evaluated thin-section CT images and pulmonologists independently assessed clinical information. The two groups then discussed their diagnosis to obtain a final consensus, and listed alternative diagnoses. Changes in the level of certainty during the diagnostic process were investigated.
Results: The level of certainty for IPF was judged as low (level 1 or 2) in 32 cases (34%) by radiologists and in three cases (3%) by pulmonologists; in the final consensus 39 cases (41%) were judged as low. Chronic hypersensitivity pneumonitis (CHP), interstitial pneumonia associated with collagen tissue diseases (CTD-IP), and idiopathic nonspecific interstitial pneumonia (idiopathic NSIP) were listed as alternative diagnoses.
Conclusions: In this retrospective series, some cases that had UIP confirmed on SLB for IPF diagnosis were classified into a low-level certainty group by expert chest radiologists and pulmonologists. When a diagnosis of IPF is made, the possibility of CHP, CTD-IP, and idiopathic NSIP must be also considered.

1. Introduction

Idiopathic pulmonary fibrosis (IPF) is defined as a specific form of chronic, progressive, fibrosing interstitial pneumonia of unknown cause. IPF shows usual interstitial pneumonia (UIP) pattern pathologically and/or radiologically. By definition, a diagnosis

* Correspondence to: Department of Diagnostic Radiology, Tohoku University School of Medicine, 1-1, Seiryomachi, Aobaku, Sendai, Miyagi 9808574, Japan. Fax: +81 22 717 7316.
E-mail address: jrtomi@jf6.so-net.ne.jp (J. Tominaga).

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of IPF requires the exclusion of other forms of interstitial lung diseases [1].

A joint American Thoracic Society (ATS)/European Respiratory Society (ERS) committee recommended a dynamic diagnostic integration process in which clinicians, radiologists, and pathologists exchange information to reach a multidisciplinary diagnosis of IPF. This recommendation emphasized the need for surgical lung biopsy (SLB) in order to achieve a confident multidisciplinary diagnosis (integration of clinical, radiological, and pathologic diagnosis) in cases that do not show typical clinical and/or radiological findings of IPF [2,3]. Recently, an official ATS, ERS, Japanese Respiratory Society, and Latin American Thoracic Association consensus statement (the current IPF guideline) advocated the updated thin-section computed tomography (CT) criteria: the presence of characteristic UIP findings ("UIP pattern") on thin-section CT images is sufficient for diagnosing IPF/UIP without pathologic evaluation by surgical lung biopsy in appropriate clinical settings [1].

In daily clinical practice, for the diagnosis of IPF/UIP, both pulmonologists and radiologists evaluate clinical information and CT images, and exchange their opinions to reach a consensus (clinico-radiological diagnosis). Although the decision whether or not to perform SLB is crucial problem, it is indicated when there are atypical clinical information and/or CT findings. Hence, it is clinically significant to elucidate the features of atypical cases and the diagnostic process in clinico-radiological-practice, especially, how the atypical cases were abstracted. The purpose of the present study was to reevaluate IPF cases which had SLB for diagnosis of UIP and examine the influence of CT findings and clinical information based on the diagnostic certainty.

2. Materials and methods

2.1. Materials

Our institutional review boards approved this multi-institutional retrospective study, and the requirement for patient approval or informed consent was waived (in compliance with the Health Insurance Portability and Accountability Act).

We evaluated hospital records of 95 patients (78 men, 17 women; median age 63 years, range 40–79 years) with an established a multidisciplinary diagnosis of IPF at one of the eight participating institutions (three university hospitals and five tertiary hospitals). The years of diagnosis were from 1992 to 2010. All the patients had undergone thin-section CT, and were subjected to SLB for pathological examination (82 by video-assisted thoracoscopic surgery; 12 by open lung biopsy; and one by lobectomy for concomitant lung cancer). All cases were pathologically diagnosed as UIP by the local pathologist and finally diagnosed as IPF by a multidisciplinary discussion among the pulmonologist, radiologist and the pathologist in each institution.

2.2. Data collection

Chest physicians who contributed cases completed a standard questionnaire that included the patients' symptoms, past history, family history, smoking history, environmental exposure to a potentially offending agent (occupational exposure to dust, contact with birds, or use of humidifiers), serum rheumatologic tests (rheumatoid arthritis test [RA], rheumatoid arthritis particle agglutination [RAPA], and antinuclear antibody [ANA]), serum biomarker tests (Krebs von der Lungen-6 [KL-6], surfactant protein-D [SP-D]), and the results of physical examinations and pulmonary function tests. Table 1 summarizes the clinical information extracted from the standard questionnaires.

Table 1
Clinical characteristics of 95 patients diagnosed with IPF/UIP.

Clinical characteristics	Number of patients
Chief complaint	
Cough	33 (35)
Dyspnea	33 (35)
Abnormal shadow on chest radiograph	27 (28)
Chest pain	1 (1)
General fatigue	1 (1)
Smoking history	
Current smoker	22 (23)
Ex-smoker	51 (54)
Never smoker	22 (23)
History of environmental exposure	
Occupational exposure to dust	28 (29)
Contact with birds	17 (18)
Use of humidifiers	2 (2)
Any of environmental exposure	44 (46)
Auscultatory findings	
Fine crackle positive	70 (90)
Serum rheumatologic test	
RA positive	14 (15)
RAPA positive	12 (13)
ANA positive	28 (29)
Any of serum rheumatologic test positive	39 (41)
Serum biomarker test	
KL-6 (>500 U/mL)	65 (87)
SP-D (>110 ng/mL)	52 (83)
Pulmonary function test	
Restrictive impairment (%VC < 80%)	52 (87)
Diffusion impairment (%DLCO < 80%)	52 (83)

Values indicate the number of cases. The numbers in parenthesis represent the percentage. ANA: antinuclear antigen; RA: rheumatoid arthritis test; RAPA: rheumatoid arthritis particle agglutination; KL-6: Krebs von der Lungen-6; SP-D: Surfactant protein D; VC: volume capacity; DLCO: diffusion capacity of the lung for carbon monoxide. KL-6 and SP-D data in serum biomarker tests were obtained for 75 and 63 patients, respectively. %VC and %DLCO data in pulmonary function tests were obtained for 89 and 84 patients, respectively.

Using a variety of scanners, end-inspiration thin-section CT images were obtained in the supine position within two months of SLB. The protocols consisted of 0.5–2-mm collimation sections reconstructed with a high spatial frequency algorithm at 1- or 2-cm intervals. Images were photographed at window settings appropriate for viewing the lung parenchyma (window level, −600 to −700 hounsfield units; window width, 1200–1500HU). In a few cases, continuous CT images with a 1.0-mm slice thickness were available. All images were anonymized and provided in an electronic format (DICOM or JPEG) at resolutions of 72 or 300 pixels/inch.

2.3. Pathologic re-review

A lung pathologist with 35 years' experience microscopically reexamined all the pathologic specimens blinded to the clinical information and thin-section CT findings, and reconfirmed the histological diagnosis of UIP.

2.4. Study organization scheme

Study observers consisted of two groups: a radiological arm comprising two expert chest radiologists, each with 28 years' experience of chest CT interpretation, and a clinical arm comprising five expert pulmonologists with 26–33 years' experience. All observers knew that IPF/UIP had been previously diagnosed at the participating institutions and that the pathologic diagnosis had been confirmed on re-review. Each arm received the thin-section CT images and clinical information separately and sequentially in alternate order as outlined below and in Table 2 (Step 1R, 2R,