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Added value of prone CT in the assessment of honeycombing and classification of usual interstitial pneumonia pattern☆

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ABSTRACT

Objective: To retrospectively investigate whether prone CT improves identification of honeycombing and classification of UIP patterns in terms of interobserver agreement and accuracy using pathological results as a reference standard.

Materials and methods: Institutional review board approval with waiver of patients' informed consent requirement was obtained. HRCTs of 86 patients with pathologically proven UIP, NSIP and chronic HP between January 2011 and April 2015 were evaluated by 8 observers. Observers were asked to review supine only set and supine and prone combined set and determine the presence of honeycombing and UIP classification (UIP, possible UIP, inconsistent with UIP). The diagnosis was regarded as correct when UIP pattern on CT corresponded to pathological UIP.

Results: Interobserver agreement of honeycombing identification among radiologists was only fair on the supine and combined set (weighted κ = 0.31 and 0.34). Additional review of prone images demonstrated a significant improvement in interobserver agreement (weighted κ) of UIP classification from 0.25 to 0.33. Prone CT conferred a significant improvement in interobserver agreement of UIP classification for trainee radiologists (from 0.10 to 0.34) while no improvement was found for board-certified radiologists (from 0.35 to 0.31). There were no significant differences in the accuracy of UIP pattern with reference to pathological results between the supine and combined set (78.8% (145/184) and 81.3% (179/220), P = 0.612).

Conclusion: Additional review of prone CT can improve overall interobserver agreement of UIP classification among radiologists with variable experiences, particularly for less experienced radiologists, while no improvement was found in honeycombing identification.

1. Introduction

Idiopathic pulmonary fibrosis (IPF) is the most common type of idiopathic interstitial pneumonia (IIP) with the characteristic of chronic and progressive fibrosis [1]. In addition to the grave prognosis of IPF, it is important to differentiate IPF from other IIPs as two new drugs for the treatment of IPF have recently been introduced [2,3] and patients with IPF may benefit from drug therapy. Therefore, early detection and accurate diagnosis of IPF has become increasingly important.

The most recent consensus guidelines by American Thoracic Society (ATS)/European Respiratory Society (ERS)/Japanese Respiratory Society (JRS)/LatinAmerican Thoracic Association (ALAT) state that the diagnosis of IPF can be made based on the CT appearance ofusual interstitial pneumonia (UIP) pattern alone obviating the need for a surgical biopsy in the appropriate clinical setting [4]. This change removes a rare but substantial risk of morbidities and potentially fatal

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complications accompanied by surgical biopsy [5]. Therefore, CT plays a critical role in diagnosis of IPF as well as in evaluation of disease status in IPF patients.

Among typical CT features of UIP pattern, which include basal- and subpleural-predominant reticular opacities and honeycombing in the absence of atypical findings, honeycombing is the mainstay of the criteria defining UIP, possible UIP, and inconsistent with UIP patterns. However, at best moderate interobserver agreement in honeycombing identification even among expert radiologists was noted, which was due to the mimickers of honeycombing such as traction bronchiectasis, large cysts and emphysema [6]. Moreover, interobserver agreement of UIP classification based on the ATS/ERS/JRS/ALAT criteria was also only moderate among thoracic radiologists, irrespective of their levels of experience [7]. Therefore, it is imperative to improve observer agreement on the updated CT criteria for IPF for it to be widely applied in routine practice.

Obtaining CT in the prone position in patients with IIP or suspicious of IIP has long been proposed [8]. The value of prone CT in IIP is mainly in differentiating true lung pathology from dependent opacities. Due to the predominant involvement of basal and subpleural areas in IPF, this is particularly important in enabling detection of early fibrosis and characterization of basal lung pathology [9]. However, to our knowledge, there have been no studies evaluating the added value of prone CT in honeycombing identification and UIP classification.

The purpose of our study was to retrospectively investigate whether prone CT improves identification of honeycombing and classification of UIP patterns in terms of interobserver agreement and accuracy using pathological results as a reference standard.

2. Materials and methods

Our institutional review board of Asan Medical Center approved this retrospective study and the requirement for informed consent was waived.

2.1. Study population

We (M.K. and J.B.S.) performed a search of our hospital's electronic medical records and radiology information systems for patient selection. From January 2011 to April 2015, patients who underwent surgical biopsy for the diagnosis of UIP, nonspecific interstitial pneumonia (NSIP) and chronic hypersensitivity pneumonitis (CHP) were included. The diagnosis of IIP and CHP was achieved based on the updated diagnostic criteria through multidisciplinary involvement of experienced clinical experts, radiologists, and pathologists [1,4,10,11]. Among initial 96 patients, patients without HRCT prior to surgical biopsy ($n = 4$) and patients with HRCT longer than three months prior to surgical biopsy ($n = 2$) were excluded. Patients with underlying connective tissue disease ($n = 3$) and lung cancer ($n = 1$) were also excluded. Finally, 86 patients (mean age, 62.1 years ± 9.5; range, 38–78) were included in our study. There were 53 patients with pathologically proven UIP (mean age, 64.6 years ± 8.1; range, 49–78), 29 patients with pathologically proven NSIP (mean age, 56.9 years ± 9.6; range, 38–75), and 4 patients with pathologically proven CHP (mean age, 67.5 years ± 9.6; range, 51–75) (Table 1).

All patients underwent wedge resection for pathological diagnosis. The median time interval between HRCT and surgical biopsy was 3.5 days (range, 0–88 days). The latest CT prior to the surgical resection was used for the analysis.

2.2. CT acquisition

HRCT images were obtained for all patients using Siemens CT scanners (Somatom Sensation 16 and Somatom Definition; Siemens Medical Systems, Forchheim, Germany). CT scans were performed for all patients in the supine and prone position at full inspiration and without contrast enhancement. CT scans were obtained with 120–140 kVp; 100–200 mAs; 1-mm slice thickness; collimation of 0.75 mm; and reconstruction with enhancing kernels of B60f. The slice intervals were 5 mm in the supine CT and 10 mm in the prone CT. Regarding the radiation dose, dose-length product was obtained from dose report and effective dose was calculated from product of DLP and conversion factors ($0.017\ mSv \times mGy^{-1} \times cm^{-1}$) [12]. Total radiation dosage including prone CT was 7.7 mSv ± 1.8 and prone CT accounted for 1.2 mSv ± 0.5.

2.3. Image analysis

Eight observers (S.J.W., D.K.H., L.H.J., L.S.M., L.S.Y., P.H.J., C.J.A., P.K.J.) with varying levels of experience in interpretation of chest CT imaging were included; five observers (S.J.W., D.K.H., L.H.J., L.S.M., L.S.Y.) were board-certified radiologists with varying levels of experience in IIP imaging (mean = 11 years, range = 1–26) and three observers (P.H.J., C.J.A., P.K.J.) were trainee radiologists. Two review sets, one consisting of supine images only (supine set) and another consisting of supine and prone images (combined set) of the 86 patients arranged in a different order, were distributed to the eight observers. All observers were blind to the clinical and pathological results and performed evaluations of the two sets at a 1-month interval. The observers were asked to determine the presence or absence of honeycombing and to evaluate whether the images were compatible with UIP, possible UIP or inconsistent with UIP patterns as defined by the ATS/ERS/JRS/ALAT criteria [4]. When UIP pattern on CT determined by observers corresponded to pathological UIP, we regarded the diagnosis as correct.

2.4. Statistical analysis

Multirater Fleiss κ statistics were used to measure interobserver agreement for honeycombing identification and interobserver agreement of UIP pattern classification [13]. Cohen κ statistics were applied to determine intraobserver agreement for honeycombing identification. κ values for intraoberver agreement were averaged for both board-certified radiologists and trainee radiologists, which resulted in a mean with 95% confidence interval.

The strength of the intra- and interobserver agreement indicated by

Table 1
Demographic data of patients with IPF, NSIP and chronic HP.

Characteristic	IPF	NSIP	Chronic HP	*P* value*
Sex				< 0.001
Male	41 (77)	12 (41)	2 (50)	
Female	12 (23)	17 (59)	2 (50)	
Age (y)				< 0.001
Mean ± standard deviation	64.6 ± 8.1	56.9 ± 9.6	67.5 ± 9.6	
Range	49–78	38–75	51–75	

Note. Numbers in parentheses are percentages. *$P < 0.05$ indicates significant difference between IPF and NSIP.