Pathologically Proved Nonspecific Interstitial Pneumonia: CT Pattern Analysis as Compared with Usual Interstitial Pneumonia CT Pattern[1]

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Purpose: To assess the variability of computed tomography (CT) patterns in patients with pathologic nonspecific interstitial pneumonia (NSIP) and to evaluate correlation of CT patterns with new idiopathic pulmonary fibrosis (IPF) classification guidelines, including pathologic diagnosis and predicted mortality.

Materials and Methods: The ethical review boards of the five institutions that contributed cases waived the need for informed consent for retrospective review of patient records and images. The study included 114 patients with *(a)* a pathologic diagnosis of idiopathic NSIP ($n = 39$) or *(b)* a pathologic diagnosis of usual interstitial pneumonia (UIP) and a clinical diagnosis of IPF ($n = 75$). Two groups of independent observers evaluated the extent and distribution of various CT findings and identified the following five patterns: UIP, possible UIP, indeterminate (either UIP or NSIP), NSIP, and suggestive of an alternative diagnosis. CT findings were compared with pathologic diagnoses and outcome from clinical findings by using the log-rank test and Kaplan-Meier curves.

Results: Radiologists classified 17 cases as UIP, 24 as possible UIP, 13 as indeterminate (either UIP or NSIP), and 56 as NSIP. In 35 of 39 patients with pathologic NSIP, a diagnosis of NSIP was made with CT. On the basis of CT interpretations, the mean overall survival time of patients with UIP, possible UIP, indeterminate findings, or NSIP was 33.5, 73.0, 101.0, and 140.2 months, respectively. Outcome of patients with a CT diagnosis of UIP was significantly worse than that of patients with a pattern of possible UIP, indeterminate findings, or NSIP (log-rank test: $P = .013$, $P = .018$, and $P < .001$, respectively).

Conclusion: CT pattern in patients with pathologic NSIP is more uniform than that in patients with pathologic UIP, and CT NSIP pattern is associated with better patient outcome than is CT UIP pattern.

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Idiopathic nonspecific interstitial pneumonia (NSIP) and radiologic and/or pathologic usual interstitial pneumonia (UIP) cases that were diagnosed as idiopathic pulmonary fibrosis (IPF) (hereafter, IPF/UIP) are idiopathic interstitial pneumonias (1). The American Thoracic Society (ATS) and European Respiratory Society (ERS) 2002 Working Group Consensus Classification of Idiopathic Interstitial Pneumonias states that NSIP is a provisional diagnosis. However, the position of NSIP in relation to idiopathic interstitial pneumonias has changed. In a more recent ATS report, NSIP was determined to be a distinct clinical entity (2). On the other hand, the situation with IPF/UIP has also changed. The new ATS, ERS, Japanese Respiratory Society (or JRS), and Latin American Thoracic Association (or ALAT) IPF/UIP guidelines state that the UIP pattern, possible UIP pattern, and patterns inconsistent with UIP on computed tomographic (CT) images can be identified, and criteria are provided. Identification of these CT patterns influences final diagnoses (3).

Although the classification of NSIP and UIP has progressed, further detailed investigation of CT is required. The NSIP and UIP patterns of CT with the new classification guidelines should be established. For example, the pathologic findings and the prognosis of patients with the possible UIP pattern and the pattern that is inconsistent with UIP on the basis of CT findings are still unclear and must be evaluated further. In addition, some cases of NSIP and UIP remain difficult to differentiate radiologically (4–9). One of the reasons for this is that patients with pathologically proved UIP have various CT findings (10,11). Patients with pathologic UIP sometimes have an NSIP pattern or an undifferentiated pattern on thin-section CT images. On the other hand, it remains unknown if patients with pathologically proved NSIP have various CT findings. Thus, CT patterns of pathologic NSIP should be assessed.

The aim of the present study was to assess the variability of CT patterns in patients with pathologic NSIP and to evaluate the correlation of CT patterns with the new IPF guidelines for classification, including pathologic diagnosis and predicted mortality.

Advance in Knowledge

- Radiologic diagnoses of usual interstitial pneumonia (UIP), possible UIP, and idiopathic nonspecific interstitial pneumonia (NSIP) (mean survival period, 33.5, 73.0, and 140.2 months, respectively) were correlated with mortality.

Implication for Patient Care

- Because radiologic NSIP pattern is related to a good prognosis, familiarity with CT NSIP pattern is important when an NSIP diagnosis is made and in the prediction of prognosis in patients with idiopathic interstitial pneumonia.

Materials and Methods

Patients and Diagnoses

The ethical review boards of the five institutions that contributed cases to the present study waived the need for informed consent for retrospective review of patient records and images.

A total of 183 patients who underwent surgical biopsy at one of the four institutions between December 1989 and November 2006 and in whom NSIP or IPF/UIP was diagnosed were included in this study. Surgical biopsy sites were selected by following ATS and ERS guidelines at each institution (1). All biopsy specimens were also reviewed by two lung pathologists (T.V.C., J.F.; 34 and 20 years of experience, respectively), and a diagnosis of NSIP, UIP, or other was made. The two pathologists reviewed the specimens independently with the histologic criteria for diagnosis recommended by the ATS and ERS International Multidisciplinary Consensus Classification and the new ATS report on NSIP (1,2). Disagreements concerning the pathologic diagnosis were resolved by consensus. Other diagnoses were made in 40 patients; these included organizing pneumonia in 13, nonclassifiable fibrosis in seven, airway disease in seven, chronic hypersensitivity pneumonitis in four, acute lung injury in four, desquamative interstitial pneumonia in three, pneumoconiosis in one, and eosinophilic pneumonia in one. These cases were excluded from the study. A total of 143 cases in which the pathologists made a diagnosis of UIP or NSIP were included in the study. Of these, 29 cases subsequently were excluded because CT images were unavailable; the remaining 114 cases were included for analysis. Of the 114 cases, 26 were included in the previous study (10). The study sample consisted of 114 patients with a mean age of 61 years (age range, 25–86 years). A total of 79 men (mean age, 61.3 years; age range, 35–76 years) and 35 women (mean age, 60.5 years; age range, 25–86 years) were included (Tousei General Hospital, n = 48; Kanagawa Cardiovascular and Respiratory Center, n = 48; Kurume University School of Medicine, n = 11; Saiseikai Kumamoto Hospital, n = 7). The 114 patients included 40 current smokers, 28 ex-smokers, and 46 patients who were never smokers. Survival analysis, survival status, and follow-up periods were assessed by review of medical records. Mean and median

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Abbreviations:
ATS = American Thoracic Society
ERS = European Respiratory Society
IPF = idiopathic pulmonary fibrosis
NSIP = nonspecific interstitial pneumonia
UIP = usual interstitial pneumonia

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Conflicts of interest are listed at the end of this article.

follow-up periods for all patients were 56 and 54 months, respectively, during which 49 patients died and 14 were lost to follow-up.

CT Images and Review

CT images were obtained at end inspiration in the supine position for all patients by using a variety of CT units. The mean period from CT scanning to surgical biopsy was 35 days (range, 1–411 days). Protocols consisted of 0.5–2.0-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 range, −700 to −600 HU; window width range, 1200–1500 HU). Images were reviewed in random order by two groups of two radiologists without pathologic or clinical information working independently. All four observers were chest radiologists (K.F., T.J., H.A. and H.S.; 22, 20, 17, and 9 years of experience, respectively). The findings were decided by consensus between the two radiologists in each group. All radiologists were blinded to the pathologic and clinical information. Radiologists evaluated the CT findings, which included the extent of spared areas, ground-glass attenuation with and without traction bronchiectasis, air-space consolidation, honeycombing, intralobular reticular opacities, emphysema, traction bronchiectasis, and presence of subpleural sparing and upper lobe subpleural irregular lines. Definitions of these CT findings were based on the literature (10,12–14). Ground-glass attenuation was defined as hazy increased attenuation that did not obscure the underlying vessels, and it divided into attenuation without and attenuation with traction bronchiectasis. Air-space consolidation was defined as a homogeneous increase in pulmonary parenchymal attenuation. Honeycombing was defined as clustered cystic air spaces that ranged in size from several millimeters to 1 cm, with well-defined thick walls in the subpleural region. Intrareticular opacity was defined as irregular and randomized linear shadows separated by a few millimeters. Traction bronchiectasis was defined as irregular bronchial dilatation within or around areas with parenchymal abnormality. Subpleural sparing was defined as a relative sparing area adjacent to the pleura in the presence of a fibrotic change in the lung field. Upper lobe subpleural irregular line was defined as irregular lines adjacent to the pleura in the upper lobes.

The extent of CT findings was evaluated separately in six lung zones (upper, middle, and lower lobes of both lungs). The upper, middle and lower lung zones were divided by the level of the tracheal and inferior pulmonary veins. Readers scored the percentage of lung fields that showed abnormalities in each of the six zones in regard to spared areas, ground-glass attenuation with and without traction bronchiectasis, air-space consolidation, honeycombing, intralobular reticular opacities, and emphysema. The percentage of whole lung was calculated by obtaining an average for the six lung zones.

Traction bronchiectasis was evaluated by summing the number of pulmonary segments with traction bronchiectasis. Subpleural sparing and upper lobe subpleural irregular lines were evaluated as absent or present. Observers also evaluated predominant distribution and asymmetry of CT findings. The distribution was classified as being predominantly lower, peripheral, or peribronchovascular. Asymmetric distribution was assessed as asymmetric extent or progression.

After review of CT findings, observers selected the mostly appropriate diagnosis in the following new UIP classification (3): UIP pattern, possible UIP pattern, or inconsistent with UIP pattern. In addition, cases that were inconsistent with UIP pattern were classified as indeterminate (either UIP or NSIP) pattern, NSIP pattern, or suggestive of alternative diagnosis. CT findings were classified as indeterminate pattern when a heterogeneous abnormality was seen in the lung. For example, areas of reticulation and ground-glass attenuation could be seen in a lung (except for a basal lung), or a cyst and reticulation with broad ground-glass attenuation could be seen. CT images were classified as having the NSIP pattern when they showed broad ground-glass attenuation more than reticulation without or with minimal honeycombing in diffuse or peribronchovascular distribution of predominant lower lobe. CT images were classified as suggestive of an alternative diagnosis when a diagnosis of UIP or NSIP was more appropriate.

The overall extent of various abnormal findings was obtained by averaging the evaluations of the two independent observers. Disagreements with respect to distribution and diagnosis were resolved by consensus. The relationship between CT findings and pathologic diagnosis was evaluated. Moreover, correlation of CT findings and CT diagnosis to survival duration was assessed.

Statistical Analysis

All statistical analyses were performed by using statistical software (SPSS, version 18.0; SPSS, Chicago, Ill). Interobserver variation with regard to the extent of various abnormalities was evaluated by using the Spearman rank correlation coefficient. Interobserver variation of the existence of predominant distribution was analyzed by using the κ statistic (15). Interobserver agreement was classified as poor (κ = 0–0.20), fair (κ = 0.21–0.40), moderate (κ = 0.41–0.60), good (κ = 0.61–0.80), or excellent (κ = 0.81–1.00).

The extent of the individual CT patterns, traction bronchiectasis score, and fibrosis score was assessed by using the Mann-Whitney *U* test. The presence of predominant distribution and the overall impression were analyzed with the Fisher exact test. These statistical analyses of multiple comparisons between CT patterns were applied with Bonferroni correction (.05/4 = .0125). Multivariate logistic regression analysis was used to assess the predictive value of the various CT findings between pathologic UIP and NSIP. Variables in the logistic regression model were selected with the stepwise procedure. Variables were retained in the logistic regression model if they contributed to the explanatory power of the regression equation ($P < .10$).

Table 1

Clinical and Pulmonary Function Data

Characteristic	Pathologic UIP Pattern	Pathologic NSIP Pattern	Total
Sex			
Male	55	24	79
Female	20	15	35
Age (y)*	62.9 ± 8.2	57.7 ± 10.7	61.1 ± 9.4
Smoking history			
Never a smoker	29	17	46
Current smoker	29	11	40
Ex-smoker	17	11	28
VC*†	81.7 ± 7.4 (71)	81.4 ± 8.3 (38)	81.6 ± 7.7 (109)
FEV_1/FVC*†	77.0 ± 19.8 (70)	76.2 ± 17.5 (38)	76.7 ± 18.9 (108)

Note.—Unless otherwise indicated, data are numbers of patients. FEV_1 = forced expiratory volume in 1 second, FVC = forced vital capacity, VC = vital capacity.

* Data are mean ± standard deviation.

† Data are percentage predicted values; data in parentheses are the number of patients.

Uni- and multivariate Cox proportional hazards regression models were used to identify independent CT predictors of outcome. For multivariate analysis, variables were selected by using a stepwise procedure. Findings were retained if they contributed to the power of the regression equation ($P < .10$).

Differences in patient survival between the CT categories and pathologic diagnoses were determined by using the log-rank test and displayed by using Kaplan-Meier curves. A P value of less than .05 was considered to indicate a significant difference.

Results

Clinical and Pulmonary Function Test

Clinical data and pulmonary function test results are shown in Table 1. In some cases, pulmonary function data are unavailable.

Interobserver Agreement and Diagnoses

Interobserver agreement of two pathologists was good ($\kappa = 0.73$). Interobserver variability of radiologists is shown in Table 2.

Thin-Section Findings

Thin-section CT findings of all cases are shown in Table 2. At multivariate analysis, CT features that enabled distinction of pathologic UIP and NSIP were extent of intralobular reticular opacity (odds ratio, 1.09) and subpleural spared area (odds ratio, 0.16). The relationships between CT findings and outcome with Cox regression analysis are shown in Tables 2 and 3. At univariate analysis, air-space consolidation, honeycombing, intralobular reticular opacity, and subpleural spared area were significant predictors (hazard ratios: 1.21, 1.35, 1.23, and 0.02, respectively). At multivariate analysis, air-space consolidation, honeycombing, intralobular reticular opacity, and subpleural spared area were significant predictors (hazard ratios: 1.10, 1.24, 1.08, and 0.25, respectively).

CT Patterns

Observers classified 17 patients (15%) as having the UIP pattern (Fig 1), 24 (21%) as having the possible UIP pattern (Fig 2), 13 (11%) as having the indeterminate (either UIP or NSIP) pattern (Fig 3), 56 (49%) as having the NSIP pattern (Fig 4), and four (4%) as having a pattern suggestive of an alternative diagnosis. CT findings of each CT pattern are shown in Table E1 (online). As compared with patients with CT findings classified with a UIP pattern, patients with a possible UIP pattern were less likely to have honeycombing ($P < .001$). Patients with the indeterminate (either UIP or NSIP) pattern were more likely to have ground-glass attenuation with bronchiectasis ($P = .032$), less likely to have peripheral distribution ($P = .011$), and similarly likely to have intralobular reticular opacity ($P = .63$).

A comparison of CT pattern and pathologic diagnosis is shown in Table 4. Patients with the UIP pattern, possible UIP pattern, or indeterminate (either UIP or NSIP) pattern were all deemed to have pathologic UIP, with the exception of one patient. The patients with NSIP pattern at CT were classified as having pathologic UIP ($n = 21$ [38%]) or pathologic NSIP ($n = 35$ [63%]).

CT findings of pathologic UIP and pathologic NSIP in patients with CT NSIP pattern are compared in Table E2 (online). Patients with pathologic UIP pattern were more likely to have honeycombing, reticular opacity, and an upper subpleural irregular line and less likely to have a subpleural spared area.

CT Patterns of Abnormality and Mortality

Kaplan-Meier survival curves and their relation to the pattern of abnormalities on CT images are shown in Figure 5. Mean survival of patients with CT findings interpreted as having a UIP pattern, possible UIP pattern, indeterminate pattern, or NSIP pattern were 33.5, 73.0, 101.0, and 140.2 months, respectively, Outcome of patients with a UIP pattern was significantly worse than that of patients with a possible UIP pattern, indeterminate findings, or an NSIP pattern (log-rank test: $P = .013$, $P = .018$, $P < .001$, respectively), and the

Table 2

Extent of CT Findings and Predictors of Outcome on Univariate Analysis with Cox Proportional Hazards Regression Models

					Interobserver Variability		Predictor of Outcome	
CT Finding	Pathologic UIP Pattern	Pathologic NSIP Pattern	*P* Value	All	*r* Value	*P* Value	Hazard Ratio	95% Confidence Interval
Spared area	61.0 ± 16.0*	64.1 ± 13.4*	.52	62.0 ± 15.1*	0.53	<.001	0.99	0.97, 1.01
Ground-glass attenuation without traction bronchiectasis	4.9 ± 6.2*	7.2 ± 6.2*	.003†	5.7 ± 6.3*	0.57	<.001	0.97	0.93, 1.02
Ground-glass attenuation with traction bronchiectasis	13.5 ± 8.8*	12.6 ± 8.1*	.69	13.2 ± 8.5*	0.67	<.001	1.01	0.98, 1.04
Air-space consolidation	4.4 ± 5.6*	5.7 ± 5.4*	.14	4.9 ± 5.6*	0.83	<.001	1.03	0.98, 1.08
Honeycombing	1.5 ± 3.3*	0.2 ± 1.2*	<.001†	1.0 ± 2.8*	0.44	<.001	1.19	1.11, 1.27
Intralobular reticular opacity	9.9 ± 5.5*	5.2 ± 4.3*	<.001†	8.3 ± 5.6*	0.56	<.001	1.07	1.03, 1.12
Emphysema	1.7 ± 4.4*	1.8 ± 4.0*	.51	1.8 ± 4.3*	0.82	<.001	0.94	0.86, 1.02
Segments of traction bronchiectasis	13.8 ± 4.0‡	11.9 ± 4.0‡	.01	13.1 ± 4.1‡	0.68	<.001	1.19	1.08, 1.31
Subpleural spared area	7§	12§	.007†	19§	0.21	.19	0.09	0.01, 0.67
Upper subpleural linear shadow	63§	12§	<.001†	75§	0.43	.005	2.99	1.44, 6.19
Lower predominance	57§	33§	.34	90§	0.40	.002	0.60	0.32, 1.12
Peripheral predominance	59§	17§	<.001†	76§	0.57	<.001	1.90	0.97, 3.73
Peribronchovascular predominance	11§	16§	.003†	27§	0.81	<.001	0.49	0.21, 1.16
Asymmetry	10§	2§	.22	12§	0.19	.019	2.25	1.01, 5.05

* Data are mean percentage of lung parenchyma ± standard deviation.

† Difference was significant ($P < .05$).

‡ Data are mean ± standard deviation. Scores are defined in Materials and Methods.

§ Data are number of cases with a feature.

UIP group at CT (UIP pattern and possible UIP) and the inconsistent with UIP group (indeterminate and NSIP pattern) were compared. The UIP group as defined by CT (mean survival, 57 months) had a significantly worse outcome than did the inconsistent with UIP group (mean survival, 130.2 months) ($P < .001$). In patients with an NSIP pattern at CT, those with pathologic UIP (mean survival, 105.0 months) had a worse outcome than did those with pathologic NSIP (mean survival, 169.5 months); however, the difference was not significant ($P = .12$) (Fig 6).

Table 3

Predictors of Outcome in Multivariate Analysis with Cox Proportional Hazards Regression Models

CT Finding	Hazard Ratio	95% Confidence Interval
Air-space consolidation	1.10	1.04, 1.17
Honeycombing	1.24	1.14, 1.34
Intralobular reticular opacity	1.08	1.03, 1.14
Subpleural spared area	0.25	0.06, 1.06

Discussion

In the group of patients studied, it was especially difficult to differentiate idiopathic NSIP from IPF/UIP on the basis of CT images (8); radiologic diagnoses that were discordant with pathologic diagnoses were encountered. Many studies have reported predictive CT findings in the diagnosis of interstitial pneumonia (7,8,12,13). For example, ground-glass attenuation, honeycombing, upper lobe subpleural linear shadows, subpleural sparing, and peribronchovascular distribution all have been reported to be predictive of outcome, and all of these findings were predictive features in the present study at univariate analysis. However, subpleural sparing and peribronchovascular distribution were not often seen (31% and 44%, respectively, in patients with pathologic NSIP). Twelve of 39 patients with pathologic NSIP had an upper lobe subpleural linear shadow in this study. In addition, ground-glass attenuation, intralobular reticular opacity, and honeycombing were selected with multivariate analysis in the present study. Thus, it was thought that important CT findings for distinguishing pathologic UIP and NSIP were presence of honeycombing, reticular opacity, and areas with ground-glass attenuation. However, ground-glass attenuation and reticular opacity often coexist, and the complexity of these findings causes confusion in diagnosis.

Figure 1

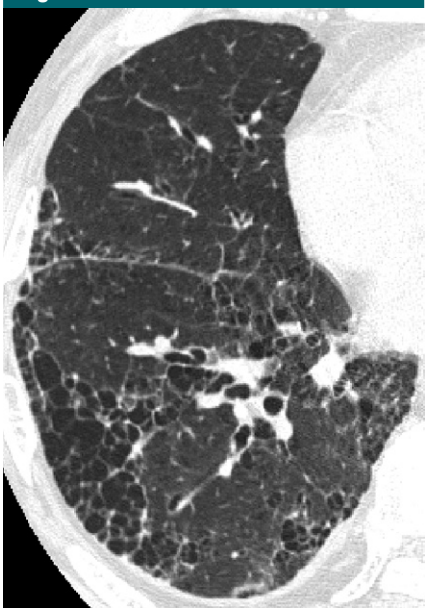

Figure 1: UIP pattern in a 69-year-old man. Transverse thin-section (1-mm) CT image through the right lower lobe shows broad honeycombing in a predominantly peripheral distribution. Pathologic diagnosis of UIP was made.

Figure 2

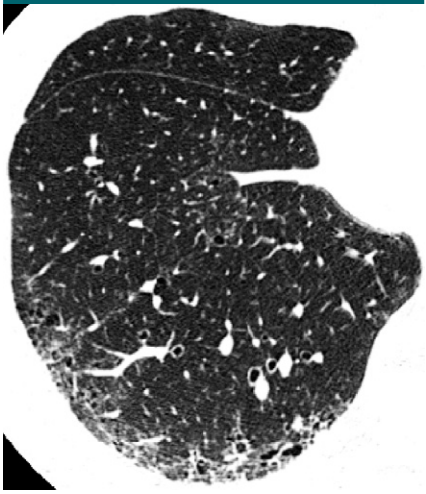

Figure 2: Possible UIP pattern in a 53-year-old man. Transverse thin-section (0.5-mm) CT image through the right lower lobe shows intralobular reticular opacity, ground-glass opacity with traction bronchiectasis, and microcysts in a predominantly peripheral distribution. Pathologic diagnosis of UIP was made.

Figure 3

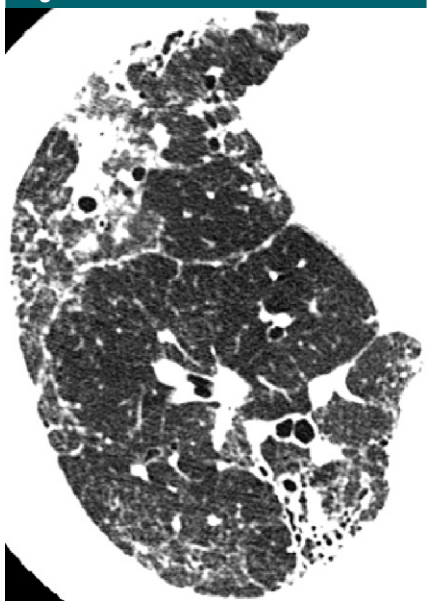

Figure 3: UIP or NSIP pattern in a 73-year-old man. Transverse thin-section (0.5-mm) CT image through the right lower lobe shows ground-glass opacity, intralobular reticular opacity, and traction bronchiectasis. Impression of CT findings was heterogeneous, and the findings were not in a predominantly peripheral distribution. Pathologic diagnosis of UIP was made.

Figure 4

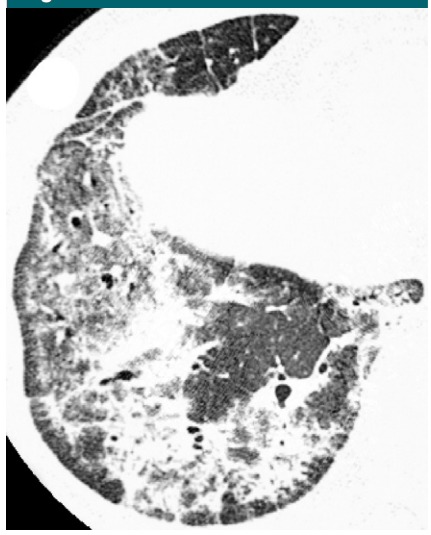

Figure 4: NSIP pattern in a 47-year-old woman. Transverse thin-section (0.5-mm) CT image through right lower lobe shows broad ground-glass opacity and traction bronchiectasis. Subpleural area shows sparing. Pathologic diagnosis of NSIP was made.

In the present study, CT patterns were categorized as UIP pattern, possible UIP pattern, or pattern inconsistent with UIP according to the new IPF/UIP guidelines (3). As a result, most cases with either the UIP pattern or the possible UIP pattern at CT were determined to be pathologic UIP. This CT classification was well correlated with pathologic diagnosis. However, many cases in which the pattern was inconsistent with UIP at CT were deemed to be UIP at pathologic analysis. Thus, cases with a pattern inconsistent with UIP were divided into three patterns: indeterminate pattern, NSIP pattern, and pattern suggestive of an alternative diagnosis. Cases with the indeterminate pattern were categorized as inconsistent with UIP according to the criteria in the new guidelines because of broad ground-glass attenuation, lack of a peripheral distribution, or both. However, findings that include a broad extent of intralobular reticular opacity may lead to diagnosis of indeterminate pattern at CT. As a result, a pathologic diagnosis of UIP was made in most cases with an indeterminate pattern. Nevertheless, patients with the NSIP pattern on CT images included those with pathologic UIP. A previous study reported that patients with pathologically proved UIP had great variability in CT findings, and some patients with pathologic UIP had an NSIP pattern or a pattern suggestive of an alternative diagnosis at CT (8,11). The present study also showed the same results. In contrast, patients with pathologic NSIP almost always have the NSIP pattern on CT images. Namely, CT findings in patients with pathologic NSIP are less variable than those in patients with pathologic UIP.

The present study showed that the outcome of UIP was worse than that of NSIP; this finding was similar to the findings of previous studies (2,16,17). In addition, in the present study, the outcome of patients with the atypical UIP pattern, including those with possible UIP or indeterminate patterns, was

Table 4

Comparison between Each CT Pattern and Pathologic Diagnosis

Finding	UIP Pattern	Possible UIP	UIP or NSIP	NSIP	Suggestive of Alternative Diagnosis
Pathologic UIP	16	23	12	21	3
Pathologic NSIP	1	1	1	35	1

Note.—Data are numbers of patients.

Figure 5

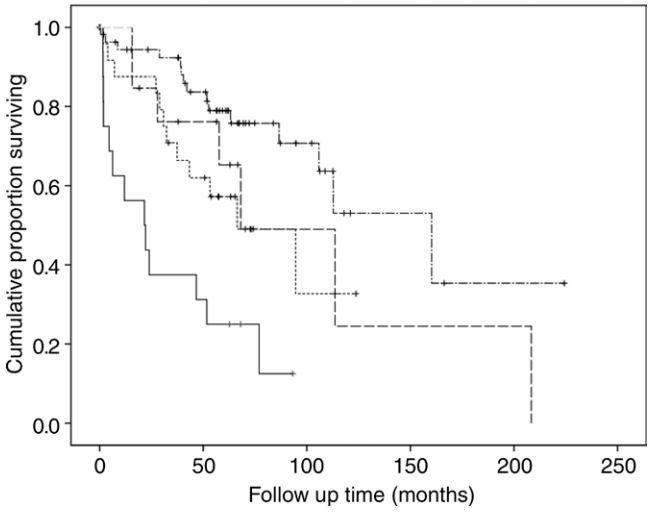

Figure 5: Kaplan-Meier survival curves for patients with UIP pattern ($n = 17$, solid line), possible UIP pattern ($n = 24$, dotted line), UIP or NSIP pattern ($n = 13$, dashed line), and NSIP pattern ($n = 56$, dashed and dotted line).

Figure 6

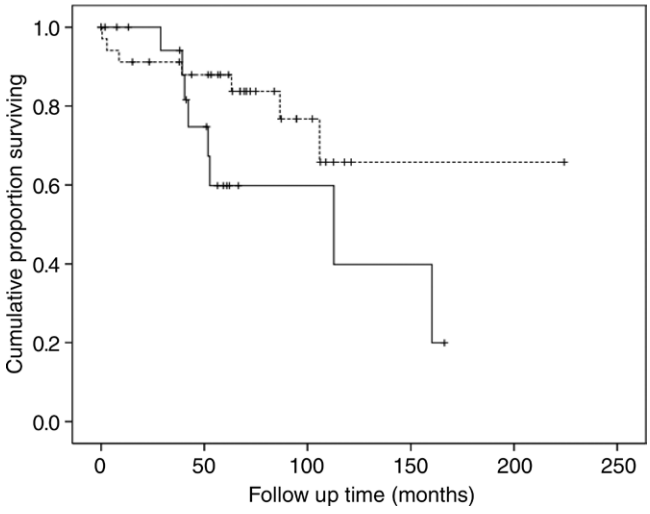

Figure 6: Kaplan-Meier survival curves for patients with pathologic UIP and radiologic NSIP pattern ($n = 21$, solid line) and patients with pathologic NSIP and radiologic NSIP pattern ($n = 35$, dotted line).

significantly better than the outcome of patients with the UIP pattern. This result is the same as that in a previous study (18). However, another study reported that there was no significant difference in outcome between patients with typical CT findings of UIP and those with atypical findings (10). Causes for this discrepancy remain unclear. This discrepancy could be caused by the relatively small number of cases or by the selection bias. Moreover, there was no significant difference in the present study between pathologic UIP with a radiologic NSIP pattern and pathologic NSIP with a radiologic NSIP pattern. However, the survival curves seemed to show a worse outcome for pathologic UIP with a radiologic NSIP pattern. This would explain why some patients with pathologic NSIP and a radiologic NSIP pattern had a poor outcome in the early period. This result calls for further investigation.

The present study had several limitations. First, the study was retrospective. Treatments given to patients were not identical, and this may have influenced the evaluation of outcome. Second, the study included only patients who underwent surgical biopsy; thus, there was a selection bias that resulted in a higher proportion of patients with atypical CT findings of IPF/UIP than what would be seen in daily clinical practice. In the present study, there was a high proportion of cases with the pattern inconsistent with UIP, and this would be influenced by selection bias. Third, the interval between CT and surgical biopsy in some patients was long. However, the longest interval was 1 year 2 months (411 days). We thought this would not significantly influence the result. Fourth, this was a multicenter study. Thus, adaptions of the surgical biopsy, CT protocol, and clinical process, such as treatment, were not standardized. These differences would affect survival. Fifth, CT patterns were compared with only pathologic diagnosis in this study. IPF and NSIP should be diagnosed with a multidisciplinary discussion. Sixth, this study was limited to correlation of initial CT findings with survival data. It did not include

correlations of survival or CT data with functional parameters. Seventh, interobserver agreement on CT pattern was not very good. However, the results of consensus were well correlated with pathologic diagnoses. This could be why the readers did not always use the criteria of CT diagnosis. More experience with the criteria or consensus between multiple readers should lead to correct diagnoses.

In conclusion, ground-glass attenuation, intralobular reticular opacity, and honeycombing were the most important findings used to differentiate NSIP from UIP. Although patients with pathologically proved IPF/UIP showed variable CT patterns, those with pathologically proved NSIP showed less variable CT patterns. CT patterns of UIP and NSIP were significantly correlated with pathologic diagnosis and outcome.

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