JMS 2023;Vol 6(3):56-67
UDC: 616.24-073.756.8:004
https://doi.org/10.55302/JMS2363056d

THE ROLE OF HIGH-RESOLUTION CT IN THE DETECTION AND DIFFERENTIATION OF PULMONARY CHANGES BETWEEN UIP AND NSIP PNEUMONIA

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Abstract

Introduction: High-resolution computed tomography (HRCT) has a central role in the diagnosis of interstitial lung diseases, particularly in idiopathic pulmonary fibrosis (IPF) that produces a radiological UIP pattern. It is especially important to distinguish it from secondary fibrosis, that is, non-specific interstitial pneumonia (NSIP), which can be detected in numerous conditions, but predominantly in connective tissue diseases. These conditions have a different mechanism of occurrence, approach and response to therapy.

Aim of the study: To analyze the distribution and characteristic radiological findings of interstitial lung changes with HRCT in UIP and NSIP pattern and to show the efficacy of this method in distinguishing these two entities.

Material and methods: High-resolution computed tomography was performed on a 128-slice PHILIPS INCISIVE CT scanner, using 1 mm slices and a high spatial resolution image reconstruction algorithm. A total of 37 patients at the University Clinic for Pulmonology and Allergology-Skopje were examined, of which 14 have non-specific interstitial pneumonia and 23 have usual interstitial pneumonia. The mentioned pulmonary conditions are graded according to the diagnostic HRCT criteria of the Fleischner society guideline for UIP and NSIP pattern.

Results: The analysis of the distribution of the changes refers to their symmetry, apicobasal localization, predominantly basal or subpleural predilection. The type of changes that have been evaluated are: linear reticulations, traction bronchiectasis, ground-glass opacities, lymphadenopathy, the presence of honeycombing which is mandatory in the UIP pattern. Of the total number of patients, 23 showed a UIP pattern on HRCT, 15 of them were men, and 8 were women with a predominant age over 60 years and most were smokers. Out of 14 patients with NSIP pattern, 11 are women and 3 are men. Half of them are under the age of 60, where the smoking status is significantly lower compared to UIP patients.

Conclusion: This article demonstrates HRCT finding and its distribution in UIP pattern associated with idiopathic pulmonary fibrosis and NSIP pattern commonly present in connective tissue diseases. These two entities clearly differ in their specific radiological signs, which is very significant in the therapy and prognosis of interstitial lung diseases.

Keywords: UIP pattern, NSIP pattern, HRCT, interstitial lung diseases

Introduction

Idiopathic pulmonary fibrosis (IPF) is a specific form of chronic, progressive, fibrosing interstitial pneumonia of unknown cause. It occurs primarily in older adults, is limited to the lungs, and is defined by a histopathologic or radiologic UIP pattern. It should be considered in all adult patients with unexplained chronic fatigue, dyspnea, cough, bibasilar inspiratory murmurs, or other symptoms suggestive of multisystem disease. The incidence of IPF increases with advancing age, typically with a presentation consisting of an insidious onset of dyspnea in the sixth and seventh decades [1,2].

Patients with IPF who are younger than 50 years are rare; such patients may subsequently manifest features of the underlying connective tissue diseases that commonly produce an NSIP pattern [5].

IPF is more common in men than women, and the majority of patients have a current or past history of cigarette smoking. Non-specific interstitial pneumonia (NSIP) usually tends to present in middle-aged adults between 40-50 years of age [1].

The overall prevalence is higher in women due to the high association with collagen vascular disease, but the prevalence of idiopathic NSIP is similar in both sexes. In 2011, the American Thoracic Society (ATS), European Respiratory Society (ERS), Japanese Respiratory Society (JRS), and Latin American Thoracic Society (ALAT) collaborated to develop a guideline for the diagnosis and management of IPF in clinical practice [9]. This guideline is based on the evidence-based diagnostic criteria for IPF based on radiological and histological findings, which were later revised in 2018 [15].

Usual interstitial pneumonia (UIP pattern)

Usual interstitial pneumonia (UIP) is a histopathological and radiological pattern of interstitial lung disease, which is characteristic of idiopathic pulmonary fibrosis (IPF).

The 2018 American Thoracic Society IPF Guideline provides four levels of confidence for a diagnosis of UIP. These include: UIP, probable UIP, indeterminate for UIP, and a pattern suggesting an alternative diagnosis. UIP is defined by subpleural basilar-dominant fibrosis, a honeycombed lung, and the absence of features that would suggest another diagnosis. If there is no honeycombing, the pattern is a "probable UIP" pattern previously called "possible UIP" [4,15].

The histological diagnosis of UIP is based on temporal and spatial heterogeneity, which is the identification of fibrotic lesions in different stages (fibroblastic infiltrates, mature fibrosis and honeycomb) in the same biopsy specimen and architectural parenchymal distortion. Honeycomb, especially if it involves more than 5% of the lung volume, is an almost 100% specific finding. On a typical biopsy, there are areas of normal lung alternating with interstitial fibrosis and honeycombing. The distribution of UIP is characterized by an apicobasal gradient with basal and peripheral subpleural predominance [11].

The inflammation is absent or moderate and is mainly limited to the honeycombing zones. The UIP pattern on HRCT (High-resolution computed tomography) is often associated with the clinical diagnosis of idiopathic pulmonary fibrosis (IPF) which has a life expectancy of 3 to 4 years without treatment.

Patients with a UIP pattern are more likely to be older, male, and smokers. This pattern carries a worse prognosis and an increased risk of death regardless of the underlying cause. More frequent acute exacerbations are also seen with the UIP pattern. It is important to mention that the UIP pattern does not automatically equate to a diagnosis of IPF because other interstitial lung diseases can have this HRCT pattern [2].

Drug toxicity, collagen vascular disease, rheumatoid arthritis, chronic hypersensitivity pneumonitis as well as familial pulmonary fibrosis can also present with this type of pattern [4]. Non-IPF interstitial lung diseases (ILD), which usually have a better survival than IPF, carry similar mortality to IPF if radiological honeycombing is present.

Aim of the study

To analyze the distribution and characteristic radiological findings of interstitial lung changes with HRCT in UIP and NSIP pattern and to show the effect of this method in distinguishing these two entities.

Material and methods

High-resolution computed tomography was performed on a 128-slice PHILIPS INCISIVE CT scanner, using 1 mm slices and a high spatial resolution image reconstruction algorithm. A total of 37 patients were examined at the University Clinic for Pulmonology and Allergology-Skopje, of which 14 patients with non-specific interstitial pneumonia, 23 patients with usual interstitial pneumonia. The mentioned pulmonary conditions are graded according to the diagnostic HRCT criteria of the Fleischner society guideline for UIP and NSIP pattern.

Statistical analysis

The statistical analysis of the data obtained from the research was done in the statistical program SPSS 23.0. Shapiro Wilk's test was used to test the normality of the data distribution. The obtained data are presented tabularly and graphically.

Categorical (attributive) variables are shown with absolute and relative numbers. Numerical (quantitative) variables are shown with mean, standard deviation, minimum and maximum values.

Fisher exact test was used to compare the two groups in terms of qualitative variables, Student t-test was used to compare in terms of quantitative variables.

Statistical significance was defined at the $p<0.05$ level.

Results

A total of 37 subjects participated in the research, of which 14 patients with non-specific interstitial pneumonia, 23 patients with usual interstitial pneumonia.

The gender structure of patients from both groups was statistically significantly different (p=0.0097). Female patients dominated in the NSIP group (78.57% vs. 34.78%), while male patients were the majority in the UIP group (65.22% vs. 21.43%), (table 1).

(p=0.13). The mean age of patients with NSIP and UIP was 60.8 ± 14.2 and 66.3 ± 7.8 years, respectively (table 1).

Table 1. Socio-demographic characteristics of the groups

sex	**groups**			
	n	**NSIP**	**UIP**	**p-level**
Sex n (%)				
female	19	11 (78.57)	8 (34.78)	X^2=6.7
male	18	3 (21.43)	15 (65.22)	*p=0.0097
Age				
n	14		23	t=1.54
mean ± SD	60.8 ± 14.2		66.3 ± 7.8	p=0.13
min- max	30 – 84		53 – 79	

NSIP (non-specific interstitial pneumonia)
UIP (Usual Interstitial Pneumonia)
X2(Chi-square test); t(Student t-test)
*sig p<0.05

Patients with non-specific and common interstitial pneumonia did not differ significantly in terms of HRCT findings for the frequency of reticular opacities, high and low attenuation and mosaic attenuation in the upper and middle lung zones (p>0.05) (table 2).

Table 2. HRCTfindings-upper and middle lung zones

Variable					**p-level**
			NSIP **n (%)**	**UIP** **n (%)**	
Reticular opacities	Peripheral and subpleural	**yes**	11 (78.57)	22 (95.65)	p=0.14
		no	3 (21.43)	1 (4.35)	
	Peribronchovascular	**yes**	2 (14.29)	2 (8.7)	p=0.6
		no	12 (85.71)	21 (91.3)	
High attenuation	Peripheral and subpleural	**yes**	1 (7.14)	1 (4.35)	p=1.0
		no	13 (92.86)	22 (95.65)	
	Peribronchovascular	**yes**	5 (35.71)	4 (17.39)	p=0.25
		no	9 (64.29)	19 (82.61)	
Low attenuation	Peripheral and subpleural	**yes**	5 (35.71)	13 (56.52)	p=0.31
		no	9 (64.29)	10 (43.48)	
	Peribronchovascular	**yes**	2 (14.29)	6 (26.09)	p=0.68
		no	12 (85.71)	17 (73.91)	
Mosaic attenuation (ground glass opacities)	Peripheral and subpleural	**yes**	3 (21.43)	2 (8.7)	p=0.35
		no	11 (78.57)	21 (91.3)	
	Peribronchovascular	**yes**	2 (14.29)	1 (4.35)	p=0.54
		no	12 (85.71)	22 (95.65)	

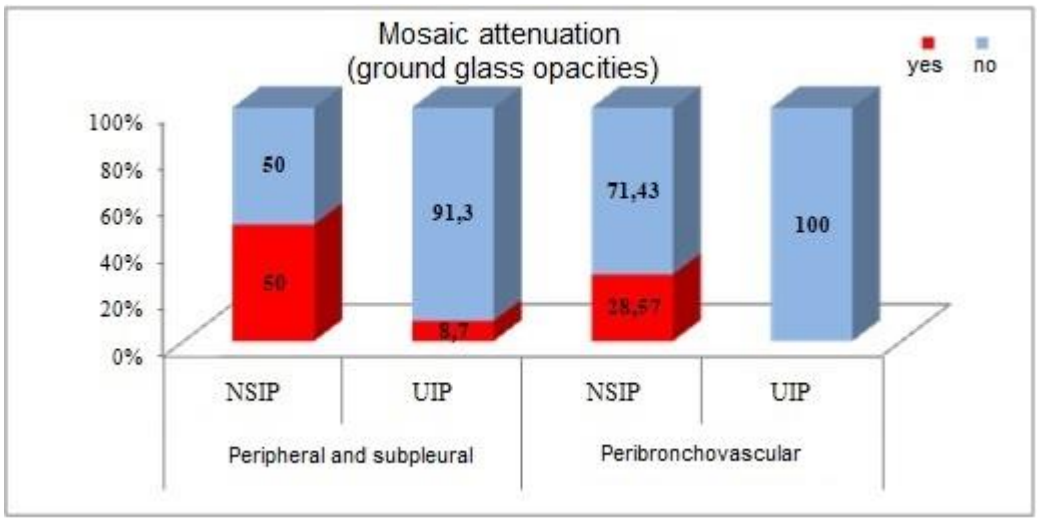
NSIP (non-specific interstitial pneumonia)
UIP (Usual Interstitial Pneumonia)
p(Fisher's exact test)

In the lower lung zones, the HRCT finding regarding the frequency of reticular opacities and attenuation did not differ significantly between the NSIP and UIP groups ($p>0.05$), while the finding regarding the frequency of mosaic attenuation in terms of ground glass opacities was significantly different. depending on the type of interstitial pneumonia ($p<0.05$). Patients with non-specific interstitial pneumonia had a significantly more frequent finding of mosaic attenuation in terms of ground glass opacities peripherally subpleural (50% vs. 8.7%) and peribronchovascular (28.57% vs. UIP pattern 0%).(table 3, figure 1, figure 1a)

Table 3. HRCT findings – lower zones

Lower zones					
Variable					**p-level**
			NSIP **n (%)**	**UIP** **n (%)**	
Reticular opacities	Peripheral and subpleural	**yes**	12 (85.71)	22 (95.65)	p=0.54
		no	2 (14.29)	1 (4.35)	
	Peribronchovascular	**yes**	2 (14.29)	0	p=0.14
		no	12 (85.71)	23 (100)	
High attenuation	Peripheral and subpleural	**yes**	4 (28.57)	2 (8.7)	p=0.17
		no	10 (71.43)	21 (91.3)	
	Peribronchovascular	**yes**	7 (50)	6 (26.09)	p=0.17
		no	7 (50)	17 (73.91)	
Low attenuation	Peripheral and subpleural	**yes**	5 (35.71)	16 (69.57)	p=0.09
		no	9 (64.29)	7 (30.43)	
	Peribronchovascular	**yes**	2 (14.29)	6 (26.09)	p=0.68
		no	12 (85.71)	17 (73.91)	
Mosaic attenuation (ground glass opacities)	Peripheral and subpleural	**yes**	7 (50)	2 (8.7)	*p=0.014
		no	7 (50)	21 (91.3)	
	Peribronchovascular	**yes**	4 (28.57)	0	*p=0.015
		no	10 (71.43)	23 (100)	

NSIP (non-specific interstitial pneumonia)
UIP (Usual Interstitial Pneumonia)
p(Fisher's exact test)
*sig p<0.05



Patients with non-specific and usual interstitial pneumonia did not differ significantly in terms of frequency of findings of predominantly basal subpleural and subpleural distribution (p>0.05), while they differed significantly in terms of frequency of findings of symmetrical distribution (p=0.0013), asymmetric distribution (p=0.015), homogeneous distribution (p=0.0013), heterogeneous distribution (p=0.0003), apicobasal distribution (p=0.0003) and the finding of subpleural sparing (p=0.047).

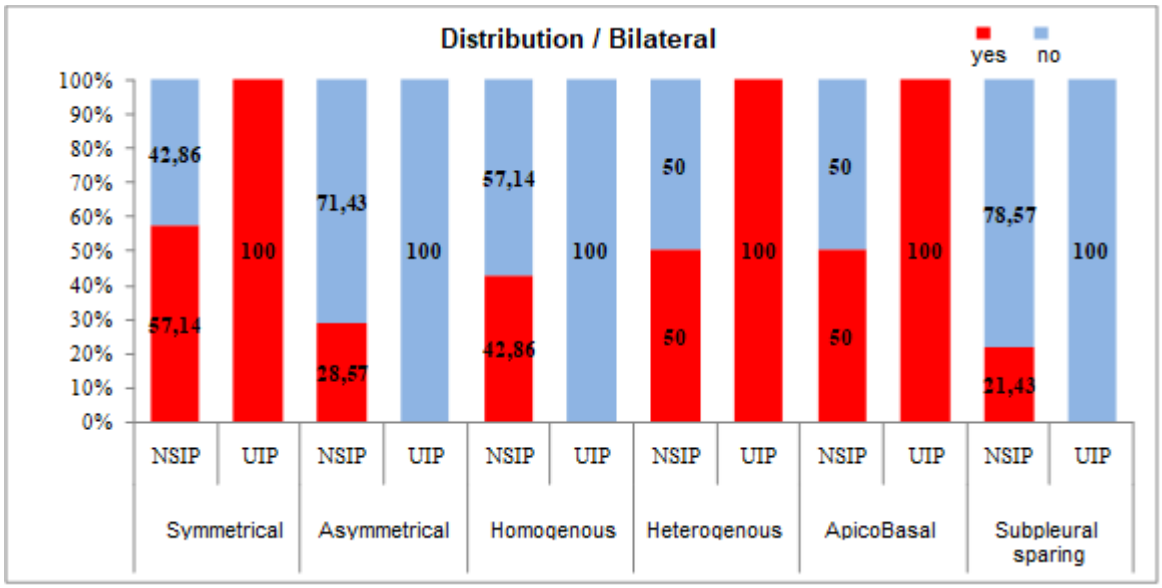
Symmetric distribution was significantly more often detected in patients from the UIP group (100% vs. 57.14%), asymmetric distribution significantly more often in patients from the NSIP group (28.57% 0%), homogeneous distribution significantly more often in patients from the NSIP group (42.86% vs. 0%), heterogeneous distribution significantly more often in patients from the UIP group (100% vs. 50%), apicobasal distribution also significantly more often in patients from the UIP group (100% vs. 50%), subpleural sparing significantly more often in patients from the NSIP group (21.43% versus 0%).

Table 4. HRCT distribution

Distribution/Bilateral				
variable				**p-level**
		NSIP **n (%)**	**UIP** **n (%)**	
Predominantly basal subpleural	**yes**	11 (78.57)	20 (86.96)	p=0.65
	no	3 (21.43)	3 (13.04)	
Subpleural	**yes**	10 (71.43)	20 (86.96)	p=0.39
	no	4 (28.57)	3 (13.04)	
Symmetrical	**yes**	8 (57.14)	23 (100)	**p=0.0013
	no	6 (42.86)	0	
Asymmetrical	**yes**	4 (28.57)	0	*p=0.015
	no	10 (71.43)	23 (100)	
Homogenous	**yes**	6 (42.86)	0	**p=0.0013
	no	8 (57.14)	23 (100)	
Heterogenous	**yes**	7 (50)	23 (100)	***p=0.0003
	no	7 (50)	0	
Apicobasal	**yes**	7 (50)	23 (100)	***p=0.0003
	no	7 (50)	0	

Subpleural sparing	**yes**	3 (21.43)	0	*p=0.047
	no	11 (78.57)	23 (100)	

NSIP (non-specific interstitial pneumonia)
UIP (Usual Interstitial Pneumonia)
p(Fisher's exact test)
*sig p<0.05; **sig p<0.01; ***sig p<0.0001



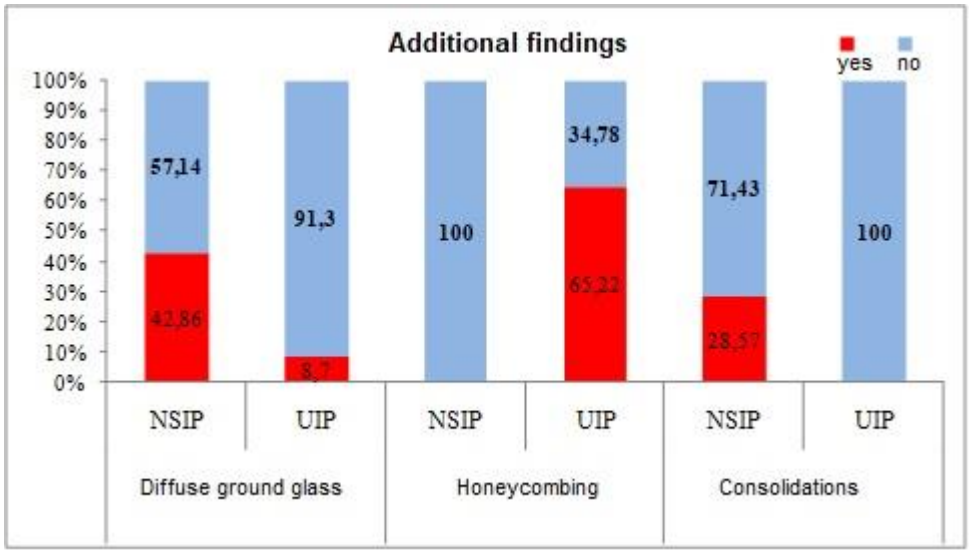
The results shown in Table 5 for the additional finding present a significantly more frequent finding of diffuse ground glass in the NSIP group (42.86% vs. 8.7%, p=0.034), honeycombing in the UIP group (65.22% vs. 0%, p=0.00007), and consolidations in the NSIP group (28.57% vs. 0%, p=0.015).

Table 4. HRCT Additional findings

Additional findings				
variable				**p-level**
		NSIP **n (%)**	**UIP** **n (%)**	
Diffuse ground glass	**yes**	6 (42.86)	2 (8.7)	*p=0.034
	no	8 (57.14)	21 (91.3)	
Residual ground glass findings	**yes**	9 (64.29)	11 (47.83)	p=0.5

	no	5 (35.71)	12 (52.17)	
Traction bronchiectasis	**yes**	13 (92.86)	22 (95.65)	p=1.0
	no	1 (7.14)	1 (4.35)	
Honeycombing	**yes**	0	15 (65.22)	***p=0.00007
	no	14 (100)	8 (34.78)	
Bronchiolectasis / bronchioceles	**yes**	11 (78.57)	15 (65.22)	p=0.48
	no	3 (21.43)	8 (34.78)	
Irregular septal thickening	**yes**	5 (35.71)	4 (17.39)	p=0.25
	no	9 (64.29)	19 (82.61)	
Consolidations	**yes**	4 (28.57)	0	*p=0.015
	no	10 (71.43)	23 (100)	
Nodular changes	**yes**	3 (21.43)	1 (4.35)	p=0.14
	no	11 (78.57)	22 (95.65)	
Emphysema	**yes**	2 (14.29)	2 (8.7)	p=0.62
	no	12 (85.71)	21 (91.3)	
Lymphadenopathy	**yes**	12 (85.71)	18 (78.26)	p=0.68
	no	2 (14.29)	5 (21.74)	

NSIP (non-specific interstitial pneumonia)
UIP (Usual Interstitial Pneumonia)
p(Fisher's exact test)
*sig p<0.05; ***sig p<0.0001



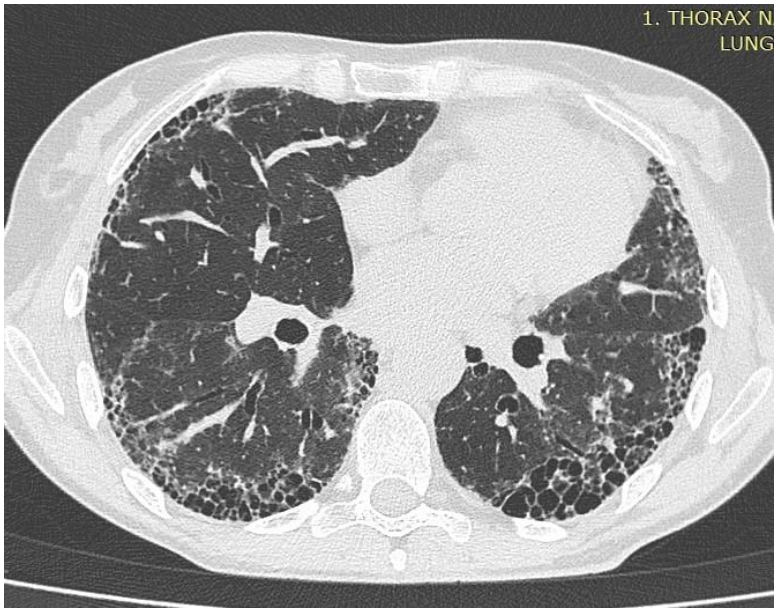


Figure 1. UIP pattern in IPF Peripheral distribution of disease, the coarse reticular pattern with honeycombing and the absence of much ground-glass change.

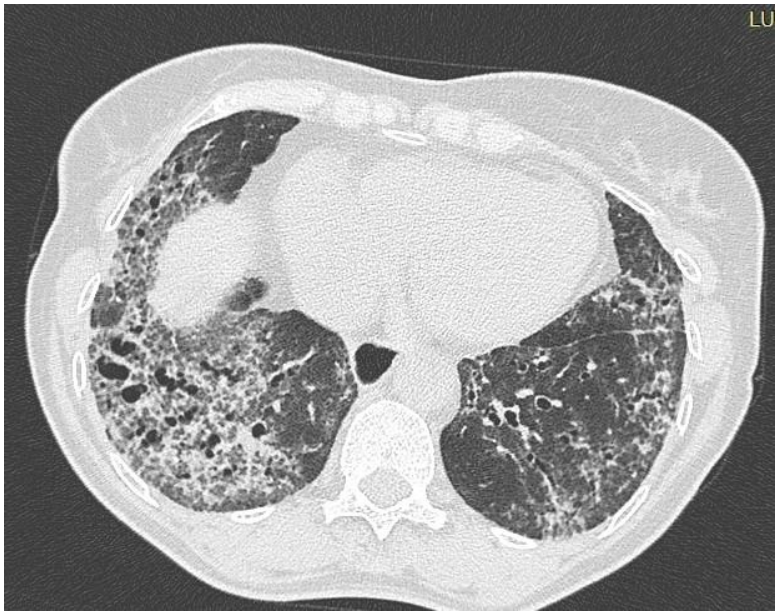


Figure 2. NSIP pattern in SLE Less peripheral distribution of disease than in idiopathic pulmonary fibrosis and the widespread ground-glass change, no honeycombing

Discussion

The differentiation between UIP and NSIP is very important because the treatment and prognosis are different between these two entities. Key features favoring the diagnosis of NSIP over UIP are symmetrical bilateral ground-glass-type opacities with fine reticulations and sparing of the immediate subpleural space. The presence of a macrocystic honeycomb lung is virtually diagnostic of UIP.

In addition to pathologic considerations, NSIP also differs from UIP based on the following clinical features: younger age, predominantly in women, amenability to steroid therapy, longer overall survival, and relatively preserved pulmonary function. NSIP is associated with connective tissue disease more often than UIP, while UIP is the predominant pattern in IPF [10].

Our study is focused on the comparison and evaluation of the distribution of the UIP pattern versus the NSIP pattern in high-resolution computed tomography. The gender structure of patients from both groups was statistically significantly different. Female patients predominated in the NSIP versus UIP group (78.57% vs. 34.78%), while male patients were the majority in the UIP group (65.22 vs. 21.43%). When distributing the findings of reticular opacities, high and low attenuation and mosaic attenuation in the upper and middle lung zones, no significant difference was observed in patients with UIP and NSIP ($p>0.05$) which correlates with the available world literature.

In the lower lung zones, there was a significant difference in the findings regarding the frequency of mosaic attenuation (ground glass opacities) depending on the type of interstitial pneumonia ($p<0.05$). Patients with NSIP have a significantly more frequent finding of mosaic attenuation peripherally subpleural (50% vs. 8.7%) and peribronchovascular (28.57% vs. UIP pattern 0%). In patients with NSIP and UIP, the radiological findings were significantly different in terms of symmetrical distribution ($p=0.0013$), asymmetrical distribution ($p=0.015$), homogeneous distribution ($p=0.0013$), heterogeneous distribution ($p=0.0003$).), apicobasal distribution ($p=0.003$) and finding of subpleural sparing ($p=0.047$).

Symmetric distribution was significantly more often detected in patients from the UIP group (100% vs. 57.14%), asymmetric distribution significantly more often in patients from the NSIP group (28.57% 0%), homogeneous distribution significantly more often in patients from the NSIP group (42.86% vs. 0%), heterogeneous distribution significantly more often in patients from the UIP group (100% vs. 50%), apicobasal distribution also significantly more often in patients from the UIP group (100% vs. 50%), subpleural sparing significantly more often in patients from the NSIP group (21.43% versus 0%).

The results shown in table 5 for the additional finding present a significantly more frequent finding of diffuse ground glass in the NSIP group (42.86% vs. 8.7%), honeycomb lung in the UIP group (65.22% vs. 0%), and consolidations in the NSIP group (28.57% vs. 0 %).

Out of a total of 37 patients, 20 are active or former cigarette smokers, predominantly male, where the UIP pattern prevails. While in the remaining 17 patients who are non-smokers, the NSIP pattern dominates, predominantly in women. In 7 male patients with UIP pattern, industrial and construction workers prevail (workers in glassworks, ironworks, oil industry, paints and varnishes), and the rest are non-specific, while in women there is no particular professional predilection. Primary connective tissue diseases such as systemic lupus erythematosus, systemic sclerosis, dermatopoliomyositis, rheumatoid arthritis, antisynthetase syndrome, overlapping syndromes were diagnosed in 8 out of 14 patients with NSIP pattern, and in the remaining 6 patients NSIP pattern was detected on HRCT with unknown etiology. In a recent study, most patients diagnosed with idiopathic NSIP met the criteria for the definition of undifferentiated connective tissue disease, a newly described distinct entity [11].

Conclusion

Although there are limitations in the differentiation between UIP and NSIP patterns, HRCT plays a key role in their diagnosis. A relative peribronchovascular distribution, diffuse bilateral ground-glass opacities, and subpleural sparing are more common in NSIP, whereas honeycombing and subpleural distribution are more characteristic of UIP.[8] HRCT as the method of choice together with the radiologist plays a significant role especially in patients who refuse open lung biopsy, which is particularly important in their further treatment and appropriate therapy [13,14].

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