Diagnostic value of Lung Function Test, Chest x-ray, and Pulmonary HR-CT in Detecting Interstitial Lung Disease at the Onset of Inflammatory Rheumatic Diseases

Tobias Jens Hoffmann (✉ tobias.hoffmann@med.uni-jena.de)
Universitatsklinikum Jena https://orcid.org/0000-0003-2959-1126

Peter Oelzner
Jena University Hospital Department of Internal Medicine III

Marcus Franz
Jena University Hospital Department of Internal Medicine I

Ulf Teichgräber
Jena University HospitalDepartment of Diagnostic and Interventional Radiology: Universitatsklinikum Jena Institut fur Diagnostische und Interventionelle Radiologie

Martin Förster
Jena University Hospital: Universitatsklinikum Jena Department of Internal Medicine I

Joachim Böttcher
Jena University Hospital: Universitatsklinikum Jena Department of Internal Medicine III

Claus Kroegel
Jena University Hospital: Universitatsklinikum Jena Department of Internal Medicine I

Christian P. Schulze
Jena University Hospital: Universitatsklinikum Jena

Gunter Wolf
Jena University Hospital: Universitatsklinikum Jena Department of Internal Medicine III

Alexander Pfeil
Jena University Hospital: Universitatsklinikum Jena Department of Internal Medicine III

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Abstract

Objectives: Interstitial lung disease (ILD) is a severe pulmonary complication in inflammatory rheumatic diseases (IRD) and associated with a significantly increased morbidity and mortality. Therefore, ILD screening in patients with IRD is essential. The objective of the present study was to determine the diagnostic value of pulmonary function tests (PFT), chest x-ray (CXR), and high-resolution computed tomography (HRCT) chest imaging in detecting ILD at the onset of IRD.

Methods: The case-control study included 126 patients with new onset of IRD (patients with ILD: *N* = 63; control group: *N* = 63). If pathological findings were observed in the screening tests (CXR or reduced carbon monoxide diffusion [DLCO] < 80 %), patients underwent a pulmonary HRCT. In addition, an immunological bronchioalveolar lavage (BAL) was performed in the ILD group as reference for the detection of ILD.

Results: A reduced DLCO (< 80 %) showed a sensitivity of 83.6 % and specificity of 45.8 % compared to chest x-ray with 64.2 % and 73.6%, respectively, in detecting ILD. The combination of reduced DLCO and CXR revealed a sensitivity of 95.2 % and specificity of 38.7 %. The highest sensitivity (95.2 %) and specificity (77.4 %) was observed for the combination of reduced DLCO, chest x-ray, and pulmonary HRCT.

Conclusion: At the beginning of the disease**,** IRD-patients with ILD show a reduced DLCO which could be a sensitive tool for ILD-screening in IRD at the onset of the disease. Only patients with pathological findings in PFT and chest x-ray should undergo pulmonary HRCT. With this stepwise IRD-associated ILD screening approach, nearly 25 % of HRCT and therefore unnecessary radiation exposure can be avoided.

Introduction

Based on growing insights into immunopathological pathways, rheumatology has changed over the years from a discipline that focused mainly on joint diseases to a wide spectrum of inflammatory rheumatic diseases (IRD), encompassing inflammatory joint diseases, connective tissue diseases (CTD), myositis as well as vasculitis [1–6].

Many IRD present with complex clinical pictures, involving other tissues, of which the lungs are a frequent target of autoimmune-mediated injury (10% – 65% depending on the disease) [7–12]. In addition, lung involvement in IRD is associated with a significant morbidity and one of the leading cause of mortality in patients with systemic sclerosis (SSc) (10-year mortality rate of 31–71%) [13–15]. Among many diverse forms of IRD-associated lung involvements, most common is interstitial lung disease (ILD) which clinical manifestations and severity can vary from subclinical abnormality to dyspnoea, respiratory failure, and death [15–17].

Given the poor prognosis, effective screening to improve early diagnosis of IRD-patients with associated ILD is of paramount importance [15, 16]. Currently, national and international guidelines recommend pulmonary high-resolution computer tomography (HRCT) based on the high sensitivity for detecting and

monitoring lung involvement in patients with IRD [17–21]. In addition, immunological bronchoalveolar lavage (BAL) is a diagnostic cornerstone if ILD is suspected [18–22]. A surgical lung biopsy is not clinically necessary in most patients and only used in special circumstances and questions [18].

At the onset and diagnosis of IRD, an organ screening should be performed to detect lung involvement and other manifestations. However, despite the complex, multisystemic disease and risk of ILD with increased morbidity and mortality, only less than half of SSc-patients underwent a basic organ screening at the time of initial diagnosis, as shown in a survey with members of the Scleroderma Society of Canada [23]. According to various studies, 54 % to 65 % of patients with SSc or dermatomyositis presented with lung involvement at the onset of their disease [8, 24]. Consequently, not every patient needs a pulmonary HRCT at initial diagnosis.

The aim of the study was to determine the diagnostic value of pulmonary function tests (PFT), chest x-ray, and HRCT of the lung for identifying patients with ILD at the onset of IRD.

Methods

The study included 126 patients (*N* = 63 with new lung involvement [ILD group] and *N* = 63 without lung involvement [control group]) with initial diagnosis of IRD.

IRD encompassed CTD (systemic lupus erythematosus [SLE], SSc, Sjögren's syndrome, Sharp syndrome), small vessel vasculitis (granulomatosis with polyangiitis [GPA], microscopic polyangiitis [MPA], eosinophilic granulomatosis with polyangiitis [EGPA]) and myositis (dermatomyositis, polymyositis, necrotizing myositis, Jo1-anti-synthetase syndrome). All patients were examined and treated at the Department of Rheumatology, University Hospital Jena/Germany, between 2005 and 2020.

Nearly all participants underwent PFT including forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), total lung capacity (TLC), transfer factor of the lung for carbon monoxide (TLCO), and diffusing capacity for carbon monoxide (DLCO). DCLO < 80 % was considered as a reduced diffusing capacity.

An additional chest x-ray could be performed. Patients with at least one suspicious finding in PFT or chest x-ray underwent pulmonary HRCT. To exclude other causes of lung involvement, immunological BAL was performed in all patients who showed pathological findings in the HRCT.

ILD group (IRD-patients with newly diagnosed lung involvement) (see Table 1):

Table 1
Baseline characteristics of ILD- and control group.

Variable		ILD group number (%)	Control group number (%)	Difference
Number		63 (50.0%)	63 (50.0%)	
Gender	Men	17 (27.0%)	17 (27.0%)	$\chi^2(1) = 0.000$, P = 1.000
	Women	46 (63.0%)	46 (63.0%)	
Age	Median ± SD	58.6 ± 14.2 years	53.8 ± 14.3 years	$t(124)=-1.907$, P = 0.059
IRD	CTD	35 (55.6%)	55 (87.3%)	$\chi^2(3) = 17.732$, P < 0.001, *Cramer´s-V = 0.375*
	Small vessel vasculitis	16 (25.4%)	3 (4.8%)	
	Myositis	12 (19.0%)	5 (7.9%)	
PFT		61 (96.8%)	61 (96.8%)	$\chi^2(1) = 0.000$, P = 1.000
Median ± SD	DLCO	59.4 ± 19.6%	79.9 ± 18.3%	$t(118) = 5.91$, P < 0.001
	TLC	84.4 ± 19.8%	98.5 ± 12.9%	$t(95) = 4.47$, P < 0.001
	FVC	82.3 ± 21.3%	92.6 ± 17.9%	$t(118) = 2.89$, P = 0.005
	FEV_1	82.0 ± 23.4%	92.2 ± 16.6%	$t(104) = 2.78$, P = 0.007
	TLCO	75.0 ± 19.6%	88.1 ± 17.3%	$t(116) = 3.84$, P < 0.001
Chest X-ray		53 (84.1%)	53 (84.1%)	$\chi^2(1) = 0.000$, P = 1.000
Pulmonary HR-CT	Pathological finding	63 (100.0%)	17 (27.0%)	$\chi^2(1) = 43.955$, P < 0.001
	No pathological findings	0 (0.0%)	21 (33.3%)	

Variable		ILD group number (%)	Control group number (%)	Difference
Immunological BAL		63 (100.0%)	17 (27.0%)	$\chi^2(1) = 72.800$, $p < 0.001$
Origin of the pathologies in HR-CT	ILD in IRD	63 (100.0%)	0 (0.0%)	$\chi^2(4) = 80.000$, $p < 0.001$
	RB-ILD	0 (0.0%)	7 (11.1%)	
	Post-inflammatory change	0 (0.0%)	6 (9.5%)	
	Sarcoidosis	0 (0.0%)	2 (3.2%)	
	Other lung disease	0 (0.0%)	2 (3.2%)	

63 IRD-patients with ILD as newly diagnosed pulmonary involvement were included in the ILD group who met the following requirements:

a) Immunological BAL performed as general gold standard in pulmonary diagnostic, showing no other causes of lung involvement

b) Final diagnosis of ILD in IRD, confirmed by two rheumatologist

Control group (IRD-patients without lung involvement) (see Table 1):

In order to perform a comparison, 63 patients with newly diagnosed IRD without lung involvement acted as control group. These patients also underwent initial lung diagnostics with PFT, chest x-ray, and optional pulmonary HR-CT and immunological BAL in the Department of Rheumatology, University Hospital Jena/Germany. With this stepwise diagnostic approach and the absence of characteristic morphological changes, ILD-manifestations in these IRD-patients were excluded. Exclusion criteria were defined as already known diagnosed IRD.

Statistical analysis

The data were documented in Microsoft Excel® (Microsoft Windows, Redmond Washington, USA). The statistically analysis was performed by IBM SPSS Statistics 25 (IBM SPSS Statistics, Chicago, Illinois, USA, for Windows). At the beginning, a case control matching was performed with the support of IBM SPSS Statistics 25. It was matched by gender, age, PFT, and chest x-ray. The tolerance/fuzz factor for age was 40.

In the following, a descriptive statistic was used to evaluate the data. The sensitivity and specificity were verified by crosstabs and receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC) was used to summarize the diagnostic accuracy of the evaluated diagnostic test. According to Hosmer, a value of 0.5 suggest no discrimination by the test, 0.7 to 0.8 is acceptable, 0.8 to 0.9 is excellent and > 0,9 is considered outstanding [25]. Moreover, the following statistical tests were used to verify differences and to objectify correlations: t-test *(t)* and Pearson´s chi-squared test (χ^2) for independent samples. As correlations coefficients: Cramer´s-V (*Cramer´s-V)* as a measure of the strength of the relationship between more than two dichotomous characteristics. According to Cohen, for the correlation coefficient (Cramer´s-V): Small effect size 0.1 to < 0.3, medium effect size 0.3 to < 0.5, large effect size ≥ 0.5 [26]. A $P < 0.05$ was considered as statistical significant.

Results

Baseline characteristics (see Table 1):

Each group (ILD and control group) encompassed 63 patients (46 female and 17 men). Due to case control matching, there was no significant difference in age, gender or the performance of PFT or chest x-ray. However, in the ILD group were significant more participants with small vessel vasculitis (ILD group: *N* = 16 [25.4%]; control group: *N* = 3 [4.8%]) and myositis (ILD group: n = 12 [19.0%]; control group: n = 5 [7.9%]). Cramer´s-V shows a medium effect size. Table 2 depicts the distribution of all included IRD diseases.

Table 2
Distribution of IRD in the ILD- and control group.

IRD	ILD group	Control group
CTD	**35 (55.6%)**	**55 (87.3%)**
SLE	4	15
SSc	16	19
Sjögren´s syndrome	9	17
Sharp syndrome	6	4
Small vessel vasculitis	**16 (25.4%)**	**3 (4.8%)**
GPA	7	1
MPA	3	1
EGPA	6	1
Myositis	**12 (19.0%)**	**5 (7.9%)**
Myositis/polymyositis	0	1
Dermatomyositis	4	2
Jo1-anti-synthetase syndrome	8	1
Necrotizing myositis	0	1
Total	**63 (100.0%)**	**63 (100.0%)**

Lung function test (see Table 3 and Fig. 1):

Table 3
Area under the curves (AUC), sensitivity and specificity for different cut-offs in the detection of lung involvement in inflammatory rheumatic diseases by different examinations in the ILD group.

Diagnostic procedure	Parameter	AUC (95% CI; P)	Cut-off	Sensitivity	Specificity
PFT	DLCO	0.772 (0.690–0.855; P < 0.001)	< 80%	83.6%	45.8%
			< 70%	67.2%	76.3%
	TLC	0.707 (0.610–0.803; P < 0.001)	< 80%	32.1%	94.6%
			< 70%	23.2%	100.0%
	TLCO	0.686 (0.591–0.781; P = 0.001)	< 80%	57.6%	67.8%
			< 70%	32.2%	84.7%
	FVC	0.648 (0.548–0.747; P = 0.005)	< 80%	47.5%	78.7%
			< 70%	32.2%	91.8%
	FEV_1	0.629 (0.526–0.732; P = 0.015)	< 80%	49.2%	82.0%
			< 70%	33.9%	91.1%
Chest X-ray				64.2%	73.6%
HR-CT				100.0%	55.3%
Immunological BAL				reference	

For DLCO < 80 %, the sensitivity and specificity for the detection of ILD in patients with IRD was 83.6 % and 45.8 %, respectively. DLCO < 70% revealed a sensitivity and specificity of 67.2 % and 67.3 %. Regarding FVC < 80 %, FEV_1 < 80 %, TLC < 80 %, and TLCO < 80 %, a lower sensitivity with a higher specificity was observed.

The highest area under the curve (AUC) was achieved by DLCO (0.772) with an acceptable discrimination according to Hosmer et al. (details see Table 3).

Regarding the differentiation of IRD subgroups, the highest sensitivity with 91.7 % and specificity of 45.8 % was evaluated for DLCO < 80% in patients with myositis. The lowest sensitivity (66.7 %) and specificity (45.8 %) was demonstrated in participants with small vessel vasculitis. For all investigated PFT parameters, we examined whether the respective AUC was significantly different from the reference line (= random). However, the AUC is not significant to the reference line in all vasculitis patients (details see Fig. 1).

Chest x-ray (see Table 3 and Fig. 1):

Chest x-ray revealed a sensitivity of 64.2 % specificity of 73.6 % in detecting ILD in IRD-patients. For IRD-subgroups, the sensitivity was 63.3 % for CTD-patients, 61.5 % for small vessel vasculitis, and 70.0 % for myositis with a specificity of 73.6 % for all three aetiologies.

Pulmonary HRCT and immunological BAL (see Tables 1 and 3):

All ILD group-patients and 60.3 % in the control group underwent a HRCT of the lung. 17 patients (27.0 %) of the control group showed pathological findings, resulting in a sensitivity and specificity of 100.0 % and 55.3 %.

If pathological findings were observed on HRCT, patients were required to undergo an immunological BAL. In consideration of the immunological BAL, morphological changes in the control group in the pulmonary HRCT were mainly interpreted as post-inflammatory (scars) (*N* = 6; 9.5 %) or associated to smoking in the context of respiratory bronchiolitis interstitial lung disease (RB-ILD) (*N* = 7; 11.1 %).

Combination of chest x-ray and DLCO (see Table 4 and Fig. 1):

Table 4
Sensitivity and specificity for different combinations and cut-offs of diagnostic procedures in the detection of lung involvement in patients with IRD in the ILD group.

Diagnostic procedure	Parameter	Cut-off	Sensitivity	Specificity
Combination of **PFT** and **chest X-ray**	DLCO and/or chest X-ray	< 80%	95.2%	38.7%
		< 70%	88.7%	64.5%
	TLC and/or chest X-ray	< 80%	69.4%	73.8%
		< 70%	64.5%	77.0%
	TLCO and/or chest X-ray	< 80%	78.7%	58.1%
		< 70%	68.9%	69.4%
	FVC and/or chest X-ray	< 80%	80.6%	66.1%
		< 70%	71.0%	74.2%
	FEV_1 and/or chest X-ray	< 80%	80.6%	66.1%
		< 70%	71.0%	74.2%
Combination of **PFT** and **HRCT**	DLCO and HRCT	< 80%	83.6%	83.1%
		< 70%	67.2%	88.1%
	TLC and HRCT	< 80%	32.1%	98.2%
		< 70%	23.2%	100.0%
	TLCO and HRCT	< 80%	57.6%	81.4%
		< 70%	32.2%	91.5%
	FVC and HRCT	< 80%	47.5%	93.4%
		< 70%	32.2%	95.1%
	FEV_1 and HRCT	< 80%	50.8%	93.4%
		< 70%	33.9%	95.1%
Combination of **1. PFT** and **chest X-ray** and **2. HRCT**	1. DLCO and/or chest X-ray and 2. HRCT	< 80%	95.2%	77.4%

The combination of chest x-ray and DLCO < 80 % resulted in a sensitivity and specificity of 95.2 % and 38.7 %, respectively. In patients with CTD, small vessel vasculitis, and myositis, chest x-ray combined with

DLCO was associated with an increase of sensitivity (CTD: 94.1 %, small vessel vasculitis: 93.8 %, myositis: 100.0 %) with a specificity of 38.7 %.

Combination of chest x-ray, DLCO, and pulmonary HRCT (see Table 4):

If the first chest x-ray and DLCO (< 80 %) were combined and in the following pulmonary HR-CT was added (if ≥ 1 pathologic finding present), a sensitivity and specificity of 95.2 % and 77.4 % was achieved. In total, with this stepwise approach 24.7 % of HRCT could be avoided, with a false negative rate of only 4.8 %.

Discussion

The aim of the present study was to determine the diagnostic value of PFT, chest x-ray, and pulmonary HRCT in detecting ILD in newly diagnosed patients with IRD.

Based on new therapeutic options (e. g. Nintedanib) for IRD-associated lung involvement in form of ILD as well as the increased mortality in patients with chronic systemic autoimmune diseases and pulmonary manifestations, evaluation of the lungs at the time of IRD-diagnosis is essential [27, 28]. On the other hand, not all IRD patients show a lung involvement [7, 29, 30].

Chest x-ray

In our study, the sole use of chest x-ray yielded a low sensitivity (64.2 %) and a moderate specificity (73.6 %) in detecting ILD. Similar results were reported by Hax et al. and a simple clinical decision rule developed by Steele et al. showed a sensitivity and specificity of 58.6 % to 88.7 % and 60.0 %, respectively, in identifying ILD using physical examination or/and chest x-ray [29, 30].

PFT

Caron et al. and Nihtyanova et al. reported that a reduced DLCO (< 80 %) is associated with lung complications in patients with IRD [31, 32]. In our present study, DLCO < 80 % revealed a sensitivity of 83.6 % and specificity of 45.8 %. This was in accordance with data reported by Bernstein et al. showing a sensitivity of 80.0 % and specificity of 51.0 % in detecting ILD in early SSc [24]. Showalter and co-workers demonstrated a sensitivity and specificity of 92.0 % and 32.0 % for DLCO < 80 % in SSc-patients [33]. In addition, different studies showed similar sensitivities and specificities for other PFT-parameters: Suliman et al. and Showalter et al. demonstrated a sensitivity and specificity of 37.5 % to 69.0 % and 73.0 % to 92.0 %, respectively, for FVC < 80 % [33, 34]. In our study, in patients with myositis a reduced DLCO < 80 % was mostly associated with ILD (sensitivity: 91.7 %). This was also shown in different studies, yielding a sensitivity of 88.0 % to 100.0 % for DLCO < 80 % and 44.4 % to 92.9 % for restrictive PFT patterns in patients with myositis, polymyositis or dermatomyositis [8, 35–38]. However, in our study DLCO < 80 % in

patients with small vessel vasculitis showed a sensitivity and specificity of 66.7 % and 45.8 % for detecting ILD, without significant deviation of the AUC from the reference line in the ROC analysis for all parameters. According to Newall et al., there were no significant differences for FVC, TLCO or FEV_1 between patients with or without ILD [39]. Rosenberg et al. showed sensitivities of 36 % (DLCO), 55 % (FEV_1), and 41 % (FVC) [40]. This can be explained to a large extent by the different manifestations of these diseases [41].

HRCT and immunological BAL

In our study, HRCT showed the highest sensitivity (100.0 %) with a specificity of 55.3 %. Thus, our results are consistent with the majority of studies, regarding HRCT generally as the gold standard for the diagnosis of ILD [8, 29, 30, 33, 34, 36, 38]. In addition, the evidence-based European consensus statements for identification and management of ILD in SSc recommend that SSc-patients should be screened for ILD using HRCT, particularly if they are showing one or more risk factors [19]. However, it should be emphasized that HR-CT is highly sensitive in detecting pulmonary morphologic changes, but IRD-patients do not necessarily have ILD despite the presence of these changes. That is the reason why patients were partially excluded in some studies [33, 34].

Only a few publications additionally focus on biopsy or immunological BAL to confirm the diagnosis of ILD [35, 37, 40]. Our present study demonstrated the utility of the immunological BAL. The HRCT shows a lack of specificity with 55.3 %, 17 patients showed morphological abnormalities in the pulmonary HRCT, but they were due to post-inflammatory changes (scars), smoker associated or other lung diseases. A immunological BAL could compensate this lack of specificity. Until now, comparable studies do not exist in the present literature for the assessment of the importance of the immunological BAL.

Combined examinations

As described in the literature before, also our study showed that a combination of several parameters of PFT did not increase specificity without a significant loss of sensitivity in detecting ILD [33, 34].

We revealed a sensitivity and specificity to 93.7 % and 39.7 % if using a combination of PFT (DLCO < 80 %) and chest x-ray. Bernstein et al. and Steele et al. used similar algorithms, but FVC and FEV_1 instead of DLCO [24, 30]. They could achieve a sensitivity and specificity of 54.5 % to 74.1 % and 45.7 % to 83.3 %, respectively. Suliman et al. showed a sensitivity and specificity of 59.0 % and 65.8 % by using FVC < 80% or DLCO < 70 % [34]. With these algorithms, 40 % to 45 % of patients with ILD would be scored as false negatives. However, a screening algorithm in patients with newly diagnosed IRD should be highly sensitive (even accepting a poorer specificity), because it is already a pre-selected population with high risk of pulmonary involvement and high mortality over time.

A potential limitation of our study is the fact that we performed HRCT in IRD-patients with a DCLO < 80 %. Regarding the rules for the application of ionizing radiation, patients with a DLCO > 80 % underwent no pulmonary HRCT or only in justified individual cases. Consequently, the diagnostic value of the presented algorithm could be potentially overestimated, because an HCRT was not performed on every study participant.

Conclusion

ILD in patients with inflammatory rheumatic diseases are associated with increased morbidity and mortality, whereas new effective treatment options are now available. Consequently, screening methods are crucial for early diagnosis of lung involvement.

DLCO combined with chest x-ray proved to be a potential screening tool for detecting lung manifestations in IRD-patients. Based on the high sensitivity of DLCO in combination with chest x-ray, all patients with a reduced DLCO (< 80 %) or/and a suspicious chest x-ray findings should undergo pulmonary HRCT. To detect inflammatory activity in the lungs and to exclude other diseases for differential diagnosis, a immunological BAL should also be performed. With our stepwise approach algorithm, nearly 25 % of HRCT can be avoided. In addition, given the often impairing ILD-therapy with side effects, the diagnosis should not be made on the basis of HRCT alone.

Abbreviations

BAL Bronchoalveolar lavage

CTD Connective tissue disease

CXR Chest x-ray

DLCO Diffusing capacity for carbon monoxide

EGPA Eosinophilic granulomatosis with polyangiitis

FEV_1 Forced expiratory volume in 1 second

FVC Forced vital capacity

GPA Granulomatosis with polyangiitis

HRCT High-resolution computer tomography

ILD Interstitial lung disease

IPF Idiopathic pulmonary fibrosis

IRD Inflammatory rheumatic diseases

MPA Microscopic polyangiitis

PFT Pulmonary function tests

RB-ILD Respiratory bronchiolitis interstitial lung disease

ROC Receiver operating characteristic

SLE Systemic lupus erythematosus

TLC Total lung capacity

TLCO Transfer factor of the lung for carbon monoxide

Key Messages

- Inflammatory rheumatic diseases were associated with interstitial lung disease, whereas the screening procedure at the onset of inflammatory rheumatic diseases is unclear
- Diffusing capacity for carbon monoxide (DLCO < 80 %) should be used to identify IRD-patients who require further lung imaging
- The combination of reduced DLCO (< 80 %), chest x-ray and pulmonary high-resolution computer tomography yielded the highest sensitivity and specificity in detecting of interstitial lung disease manifestation in the onset of inflammatory rheumatic diseases
- DLCO is a screening marker in inflammatory rheumatic diseases-associated interstitial lung disease

Declarations

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Authors´ contributions

AP and TH designed the study, analysed the data, performed the statistical analysis, wrote the manuscript and revised the manuscript. TH, MF and MF performed the data collection and participated on the statistical analysis. GW, PCS, UT, PO and JB edited and drafted the manuscript. CK was involved in the development of the study design and collected the BAL-data. AP and TH revised the manuscript. All authors read and approved the final manuscript.

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Data availability statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

All examinations were performed in accordance with the rules and regulations of the local Human Research and Ethics Committee of the Friedrich-Schiller-University Jena (Germany). The study is registered under the following number: “2020-1845-Daten”. All chest x-rays and HRCT were obtained for clinical routine and not for study purposes.

Consent for publication

Not applicable.

Competing Interests

All author declared no conflicts of interest.

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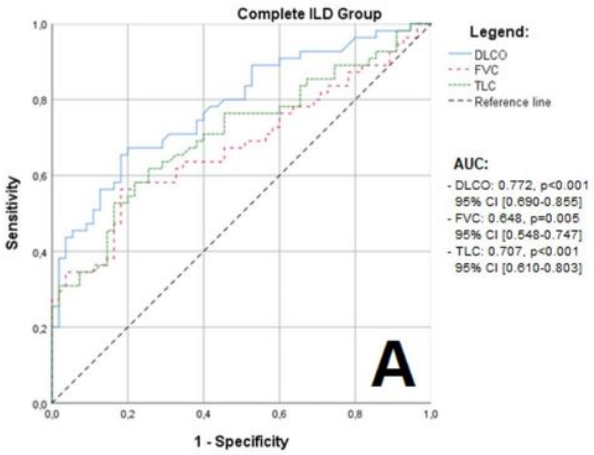
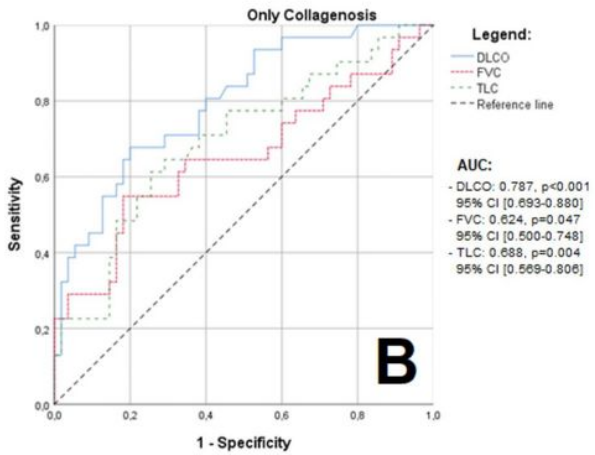
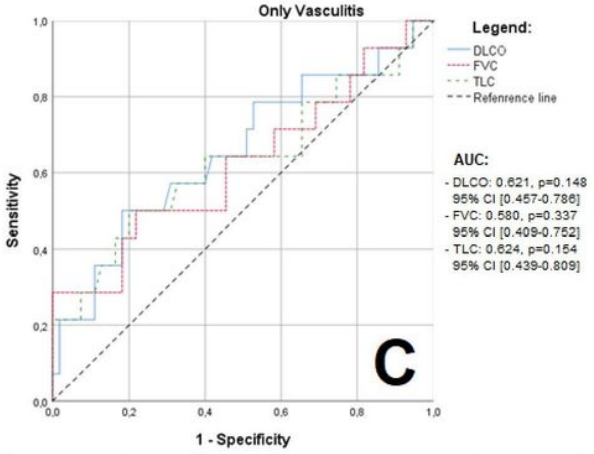
Figures



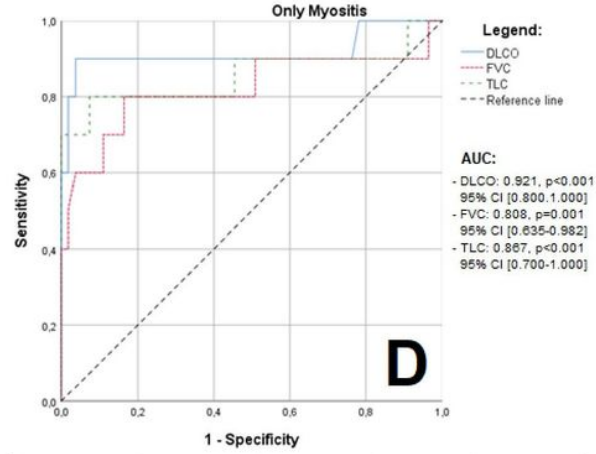
Complete	DLCO < 80 %	DLCO < 70 %	Chest X-ray	Combination
Sensitivity	83.6 %	67.2 %	64.2 %	95.2 %
Specificity	45.8 %	76.3 %	73.6 %	38.7 %



Collagenosis	DLCO < 80 %	DLCO < 70 %	Chest X-ray	Combination
Sensitivity	88.2 %	67.6 %	63.3 %	94.1 %
Specificity	45.8 %	76.3 %	73.6 %	38.7 %



Vasculitis	DLCO < 80 %	DLCO < 70 %	Chest X-ray	Combination
Sensitivity	66.7 %	46.7 %	61.5 %	93.8 %
Specificity	45.8 %	76.3 %	73.6 %	38.7 %



Myositis	DLCO < 80 %	DLCO < 70 %	Chest X-ray	Combination
Sensitivity	91.7 %	91.7 %	70.0 %	100.0 %
Specificity	45.8 %	76.3 %	73.6 %	38.7 %

Figure 1

ROC curve analysis as well as sensitivity and specificity of different cut-off´s in DLCO, chest X-ray, and a combination (DLCO < 80 % or/and pathological findings in chest X-ray) in relation to subpopulations of the ILD group A: complete ILD group; B: CTD group; C: vasculitis group; D: myositis group