Brief Report

Not peer-reviewed version

Comparison of Chest Ct Findings and Pulmonary Function Tests in Non-symptomatic Children with Rheumatic Diseases

Spyridon Prountzos , Kyveli Chiotopoulou , Katerina Kourtesi , Evdoxia Sapountzi , Dafni Moriki , Elpiniki Kartsiouni , Efthymia Alexopoulou , Konstantinos Douros , Lampros Fotis *

Posted Date: 21 August 2024

doi: 10.20944/preprints202408.1591.v1

Keywords: Lung; Pediatrics; Rheumatic Diseases; Spirometry; Tomography, X-ray Computed

Article

Comparison of chest CT Findings and Pulmonary Function Tests in Non-Symptomatic Children with Rheumatic Diseases

Spyridon Prountzos [1], Kyveli Chiotopoulou [2], Evdoxia Sapountzi [3], Katerina Kourtesi [2], Dafni Moriki [4], Elpiniki Kartsiouni [4], Euthymia Alexopoulou [1], Konstantinos Douros [4] and Lampros Fotis [2,*]

[1] 2nd Department of Radiology, ATTIKON General Hospital, National and Kapodistrian University of Athens, Greece; spyttt@gmail.com (S.P.); elpikartiouni@gmail.com (E.A.);
[2] Division of Pediatric Rheumatology, 3rd Department of Pediatrics, ATTIKON General Hospital, National and Kapodistrian University of Athens, Greece; kyvelich@yahoo.gr (K.C.); kourtesikaterina@yahoo.com (K.K.);
[3] 2nd Department of Pediatrics, AHEPA General Hospital, Aristotle University of Thessaloniki, Greece; esapountzi@gmail.com (E.S.);
[4] Division of Pediatric Pulmonology and Allergology, 3rd Department of Pediatrics, ATTIKON General Hospital, National and Kapodistrian University of Athens, Greece; dafnimoriki@yahoo.gr (D.M.); costasdouros@gmail.com (K.D.)
* Correspondence: lafotis@med.uoa.gr; Tel.: +30 210 5832228

Abstract: Lung involvement in rheumatic diseases is a major determinant of patient morbidity and mortality; however, its diagnosis depends on the detection methods used. We compared the incidence of pulmonary involvement in newly diagnosed treatment-naive patients with rheumatic diseases, as assessed by pulmonary function tests (PFTs) and chest high-resolution computed tomography (HRCT). This retrospective study reviewed the symptoms, spirometry results, and HRCT scans of 22 newly diagnosed, treatment-naïve patients and age-matched controls from the University General Hospital "Attikon", Athens, Greece, between January 2021 and December 2023. Correlations between clinical findings and spirometry parameters were tested. HRCT scans revealed lung abnormalities in all patients, including peribronchial wall thickening (61.5%), ground glass opacities (59.1%), parenchymal bands (54.5%), air-trapping (50%), reticular patterns (45.5%), bronchiectatic changes (40.9%), and parenchymal opacities (31.8%). PFTs, performed in 17/22 (77.3%) patients, revealed definite pathology in 5 patients (restrictive: N=4; obstructive: N=1). No association was found between spirometric indices and clinical parameters. The results indicate a higher prevalence of abnormal chest CT than of PFT abnormalities, suggesting that HRCT is more sensitive in detecting early lung involvement in pediatric patients with rheumatic disease and should be considered in the routine evaluation of these patients.

Keywords: Lung; Pediatrics; Rheumatic Diseases; Spirometry; Tomography, X-ray Computed;

1. Introduction

Rheumatic diseases are a group of autoimmune mediated diseases that affect multiple organs, with the lung being a frequently affected target organ. Individual or several components of the respiratory system, including the airways, vessels, parenchyma, pleura, and respiratory muscles, may be related to the illness itself or to the medications used. Lung involvement in rheumatic diseases is a major determinant of patient morbidity and mortality, while the pattern of lung disease is considerably heterogeneous in incidence, prevalence, and severity depending on the underlying rheumatic disease [1,2].

Systemic inflammatory diseases with the highest likelihood of pulmonary involvement are juvenile systemic lupus erythematosus (SLE), scleroderma (systemic sclerosis [SSc]), juvenile dermatomyositis (JDM), mixed connective tissue disease (MCTD), granulomatosis with polyangiitis and juvenile idiopathic arthritis (JIA) [3]. Interstitial lung disease (ILD) is usually the primary and

 doi:10.20944/preprints202408.1591.v1

most frequent presentation of lung involvement in adult patients, while pulmonary artery hypertension and obstructive lung disease may also occur. The incidence of pulmonary complications is lower in childhood, and some forms of diffuse lung disease are unique to infants and children [4]. Nevertheless, clinically significant pulmonary complications are rare in childhood, and, if present, may require changes in disease management [5].

Recognition of pulmonary involvement depends on the methods used to detect the disease. Although various tests are available for assessing lung function, their sensitivity and specificity in detecting lung involvement in newly diagnosed patients are not always consistent with their efficacy in monitoring lung function throughout the course of inflammatory rheumatic disease. [6]. Pulmonary function tests (PFTs), including diffusing capacity of the lungs for carbon monoxide (DLCO) and forced vital capacity (FVC), as well as high-resolution computed tomography (HRCT) are commonly used tools for screening and monitoring ILD in patients with inflammatory rheumatic diseases. HRCT is considered highly sensitive in detecting morphological abnormalities, although its specificity remains unclear, especially in case of unclassifiable changes. Among PFTs, DLCO is considered to have the best predictive value for ILD development, FVC is good for monitoring known lung involvement, whereas total lung capacity assessed by another PFT, body plethysmography, seems to be suitable neither for diagnosis nor monitoring of lung disease in rheumatology [6]. The above highlight the necessity of using reliable diagnostic means, especially when patients are asymptomatic, to enable early intervention.

The present study aimed to compare the incidence of pulmonary involvement in newly diagnosed treatment-naive patients with rheumatic diseases, as assessed by PFTs and chest HRCT. HRCT findings were more prevalent than PFT findings in this study population, denoting the capability of HRCT in detecting subtle structural changes.

2. Materials and Methods

This retrospective study was conducted at the Unit of Pediatric Rheumatology and of Pediatric Pulmonology and Allergology, 3rd Department of Pediatrics, and the Pediatric Radiology Unit, 2nd Department of Radiology of University General Hospital “Attikon”, Athens, Greece, between January 2021 and December 2023.

Chest HRCT scans of children and adolescents under the age of 18 with rheumatic diseases with high risk of ILD performed in our tertiary center between 01/01/2021 and 31/12/2023 were reviewed retrospectively. All patients underwent chest CT examination using paired end-inspiratory and forced-expiratory scan protocol using 1-mm collimation and slice thickness reconstruction algorithm. Only patients with radiological findings were included in the analysis. Parenchymal opacities, ground-glass opacities (GGOs), reticular pattern, honeycombing, parenchymal bands, bronchiectasis, and peribronchial wall thickening were examined. Air trapping was assessed during expiratory scans. The patients were treatment-naïve and had been diagnosed with rheumatic disease for the first time. Exclusion criteria were history of chronic lung or cardiac disease or lower respiratory tract infection history or findings.

Symptoms and spirometry results were also reviewed. Correlations between clinical findings and spirometry parameters (forced expiratory volume in one second [FEV1]% and FVC%) were evaluated by the Spearman’s test.

2. Results

Twenty-two pediatric patients with rheumatic disease (18 females and 4 males), with a mean age of 13 years (age range 3-16 years) underwent chest HRCT and PFTs to assess possible lung involvement.

3.1. Clinical Characteristics

Four children were diagnosed with SLE, four with SSc, three with JDM, three with systemic JIA, three with MCTD, one with microscopic polyangiitis, one with granulomatosis with polyangiitis, one

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 21 August 2024 doi:10.20944/preprints202408.1591.v1

with non-specific vasculitis, one with Behçet's disease, and one with idiopathic pulmonary hemosiderosis (Table 1).

During initial diagnosis, the patients reported no or mild respiratory symptoms. Nine (40.9%) patients reported early fatigue during exercise, and six (27.3%) reported dry cough. Three patients reported dyspnea (13.6%) (Table 1).

Table 1. Demographics and clinical symptoms of enrolled patients.

Variable	Categories	N (%)
Sex	Female	18 (81.8%)
	Male	4 (18.2%)
Age (in years)		mean 13.05 (±3.169, min 3, max 16)
Cough	Yes	6 (27.3%)
	No	16 (72.7%)
Dyspnea	Yes	3 (13.6%)
	No	19 (87.4%)
Fatigue	Yes	9 (40.9%)
	No	13 (59.1%)
Disease	Systemic lupus erythematosus	4 (18.2%)
	Systemic sclerosis	4 (18.2%)
	Juvenile dermatomyositis	3 (13.6%)
	Systemic Juvenile Idiopathic Arthritis	3 (13.6%)
	Mixed connective tissue disease	3(13.6%)
	Microscopic polyangiitis	1(4.5%)
	Granulomatosis with polyangiitis	1(4.5%)
	Non-specific vasculitis	1(4.5%)
	Behçet's disease	1(4.5%)
	Idiopathic Pulmonary Hemosiderosis	1(4.5%)

3.2. HRCT findings

Chest CT findings revealed parenchymal opacities in 7 patients (31.8%), GGOs in 13 (59.1%), reticular pattern in 10 (45.5%), honeycombing in 1 (4.5%), parenchymal bands in 12 (54.5%), bronchiectatic changes in 9 (40.9%), peribronchial wall thickening in 19 (61.5%), and air-trapping in the form of mosaic attenuation during expiratory scans in 11 patients (50%) (Table 2).

3.3. Pulmonary Function Test Results

PFTs were available in 17 patients (77.3%), which revealed a restrictive pattern in 4 patients (18.2%), while only 1 patient (4.5%) had an obstructive pattern (Table 3).

Non-parametric testing using Spearman's tests revealed no association between the spirometric indices and the presence of cough, dyspnea, or fatigue.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 21 August 2024 doi:10.20944/preprints202408.1591.v1

Table 2. HRCT scan findings.

Variable	Categories	N (%)
HRCT scan	Yes	22 (100%)
	No	0 (0%)
Parenchymal opacities	Yes	7 (31.8%)
	No	15 (68.2%)
Ground-glass opacities	Yes	13 (59.1%)
	No	9 (40.9%)
Reticular pattern	Yes	10 (45.5%)
	No	12 (54.5%)
Honeycombing	Yes	1 (4.5%)
	No	21 (95.5%)
Parenchymal bands	Yes	12 (54.5%)
	No	10 (45.5%)
Bronchiectatic changes	Yes	9 (40.9%)
	No	13 (59.1%)
Peribronchial wall thickening	Yes	19 (61.4%)
	No	3 (13.6%)
Mosaic attenuation	Yes	11 (50.0%)
	No	11 (50.0%)

Table 3. Pulmonary function test findings.

Variable	Categories	N (%)
PFTs	Yes	17 (77.3%)
	No	5 (22.7%)
FVC (%)		Mean (±SD) 90.71 (±13.331)
FEV_1 (%)		Mean (±SD) 95.06 (±17.541)
FEV_1 / FVC		Mean (±SD) 91.488 (±8.632)
FEF_{25-75}		Mean (±SD) 105.35 (±51.741)
Restrictive pattern	Yes	4 (18.2%)
	No	18 (81.8%)
Obstructive pattern	Yes	1 (4.5%)
	No	21 (95.5%)

FEF25-75, forced expiratory flow over the middle one-half of the FVC; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; PFT, pulmonary function test.

4. Discussion

This study assessed pulmonary involvement in 22 children with newly diagnosed rheumatic diseases who underwent chest HRCT and PFTs. The study aimed to compare the incidence of pulmonary involvement as detected by these methods in treatment-naïve patients with mild or absent respiratory tract symptoms. Lung involvement was quite prevalent in this patient cohort. All children had abnormal chest CT findings and 5 of them had definite pathology on PFTs in the form of restrictive or obstructive pattern.

It is known that disease-modifying antirheumatic drugs are associated with pulmonary toxicity [7]. Patients included in this study were treatment-naive and newly diagnosed and had no history of previous medical treatments, thus rendering any potential side-effects of drug treatment unfeasible.

HRCT scans revealed various lung abnormalities in all study patients and included abnormalities in the lung parenchyma such as GGOs (59.1%), parenchymal bands (54.5%), reticular patterns (45.5%), and parenchymal opacities (31.8%), as well as abnormal airway findings such as peribronchial wall thickening (61.5%), air-trapping in the form of mosaic attenuation during expiratory scans (50%), and bronchiectatic changes (40.9%). In contrast, PFTs, performed in 77.3% of the patients, only identified abnormal lung function in 5 of 22 patients (22.7%). These results indicate a higher prevalence of abnormal chest CT findings than of PFT abnormalities, suggesting that HRCT is more sensitive in detecting early lung involvement in pediatric patients with rheumatic disease. However, previous studies in pediatric cohorts have shown variable results in this regard. In the studies by Huang et al. [8] and Lilleby V et al. [9], significantly more patients showed PFT than chest CT abnormalities. Specifically, in the study by Huang et al, 56.3% of children with newly diagnosed rheumatic disease had abnormal PFT and 16.7% had abnormal HRCT findings. Importantly, half of the patients with abnormal HRCT findings did not have concurrent PFT abnormalities [8]. Similarly, Lilleby et al. found that PFTs were abnormal in 37% of their patients with childhood-onset SLE, while only 8% showed abnormal CT findings [9]. Consistently with our results, Veiga et al. showed that, in their cohort of patients with childhood-onset SLE, 70% had abnormal CT findings, which were minimal in 43% [10]. This study, along with our data, is aligned with studies in adult patients that have reported a high prevalence of chest CT abnormalities suggestive of lung involvement and ILD mostly in asymptomatic patients with rheumatic diseases who have normal PFTs [11]. In an older study by Panigada et al, 10/17 patients (58.8%) with juvenile SSc had pulmonary involvement, 9 by both PFTs and HRCT and 1 by PTFs only, while for the remaining 7 patients who had no respiratory symptoms, no chest radiographic changes, and presented normal PFTs values, no HRCT was performed [12].

A previous study evaluated the effectiveness of a stepwise diagnostic screening approach, incorporating PFTs, chest radiography, and pulmonary HRCT, for detecting ILD in adult patients with newly diagnosed immune-related diseases [13]. The study found that, among PFTs, a DLCO <80% had a high sensitivity (83.6%) but lower specificity (45.8%), whereas FVC, total lung capacity, and FEV1 were not reliable for diagnosing ILD. Chest X-ray had a low sensitivity (64.2%) and moderate specificity (73.6%), and HRCT had the highest sensitivity (100.0%) but lower specificity (55.3%) in detecting ILD. Similar to our study in pediatric patients, the most common HRCT findings in these adult patients were GGOs. The combination of PFTs (DLCO <80%) and chest X-ray increased sensitivity and specificity, suggesting that patients with reduced DLCO or suspicious chest X-ray findings should undergo HRCT to confirm ILD and exclude other pulmonary conditions. [13].

Because of radiation exposure in HRCT and the fact that many asymptomatic patients show no disease progression, HRCT is not used as a mandatory initial work-up and/or for disease monitoring despite yielding more accurate results regarding ILD than PFTs [6]. Nevertheless, chest CT scan is considered the gold standard method for defining structural abnormalities [14]. Modern CT scanners have enabled for fast scan times, that produce super low-dose examinations, with achieved doses measured in dose-length products (DLPs) of as low as 7.66 mGy*cm per examination [15]. Our study's revelation of prevalent lung involvement in asymptomatic pediatric rheumatic patients, as evidenced by HRCT, not only underscores the subclinical nature of pulmonary manifestations in these diseases but also verifies the efficiency of HRCT in identifying early structural changes before functional impairment becomes apparent, highlighting its potential role in early diagnosis and intervention. Further, our study's results support the use of HRCT in the routine evaluation of pediatric rheumatic patients. The ability of HRCT to detect subtle lung changes could be crucial in guiding clinicians toward more aggressive or protective treatment regimens, especially in diseases known for their pulmonary toxicity, such as SSc and JDM. Our findings align with previous research indicating that lung involvement in rheumatic diseases can be heterogeneous and may not always correlate with clinical symptoms or PFT results [6]. This reinforces the need for a comprehensive diagnostic approach, including sensitive imaging techniques like HRCT, to capture the full spectrum of pulmonary involvement.

Both PFTs and HRCT are commonly used in conjunction to provide a comprehensive assessment of lung involvement in rheumatic disease. However, PFTs tend to be used more frequently due to their non-invasive nature and ease of repeated measurements, whereas HRCT is often reserved for cases where PFTs indicate significant abnormalities or where clinical suspicion of ILD is high [1]. HRCT is highly sensitive for detecting ILD, even in early or asymptomatic stages. It can identify structural lung changes that may not yet be evident on pulmonary function tests PFTs. Although

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 21 August 2024 doi:10.20944/preprints202408.1591.v1

more sensitive, its specificity can be lower, especially when it comes to distinguishing between different types of lung abnormalities. While HRCT involves radiation exposure, advances in CT technology have reduced this risk [15]. However, in pediatric populations, the concern about long-term radiation effects remains, especially for repeated scans. Despite these concerns, HRCT is still recommended for screening in high-risk pediatric patients [8]. PFTs, particularly measures like DLCO have moderate sensitivity. They may miss early or mild ILD, especially in cases where structural changes precede functional impairment. PFTs are generally more specific than sensitive. A reduced DLCO may suggest ILD, but normal PFT results do not rule out the presence of early ILD. Due to being non-invasive and easily repeatable, PFTs are often preferred for initial assessments and ongoing monitoring, especially in cases where clinical suspicion of ILD is low [16].

The detection of interstitial lung disease (ILD) in both pediatric and adult patients with rheumatic diseases presents distinct challenges. In adults, HRCT and PFTs are widely recognized as crucial tools for screening and monitoring ILD, with HRCT being highly sensitive in detecting early structural abnormalities, even before functional impairments manifest, as indicated by reduced pulmonary function parameters like FVC and DLCO [17]. A recent guideline published by the American College of Rheumatology and the American College of Chest Physicians for people with systemic autoimmune rheumatic disease at increased risk of developing ILD, conditionally recommended screening with HRCT chest and PFTs over PFTs alone [17]. Similarly, in pediatric populations, as discussed in our study, HRCT has shown a higher prevalence of detecting lung abnormalities compared to PFTs [8]. Our findings revealed that for children with rheumatic diseases that exhibited abnormalities on HRCT, PFTs identified definite pathology in only a minority of patients (22.7%)

For pediatric patients with rheumatic diseases, the choice between HRCT and PFTs should be carefully considered. HRCT, while more sensitive, carries radiation risks, particularly in children. PFTs are safer but may miss early ILD [16]. The decision often hinges on the clinical context, the specific rheumatic disease, and the presence of symptoms or other risk factors for ILD. This evidence highlights the necessity of utilizing HRCT as a complementary tool to PFTs in children with rheumatic diseases. Particularly in pediatric cases, where early detection and intervention are critical for preventing long-term morbidity, the integration of HRCT into routine screening protocols could be invaluable. Future research should continue to refine the balance between the sensitivity of HRCT and the safety of its use, especially in younger populations.

Certain limitations of our study must be considered. First, the sample size was relatively small, since recruitment of newly diagnosed and treatment naïve patients is challenging. Second, our cohort of patients comprised several different entities of rheumatic diseases, each having a different incidence of lung involvement. Third, our hospital is one of many pediatric hospitals in the metropolitan area of Attika; hence, the location and other reasons may have contributed to a selection bias. Therefore, multicenter longitudinal studies are necessary to identify lung involvement in different rheumatic diseases, response to treatment, and prognosis in the future and our results should be verified in follow-up studies. Nonetheless, to the best of our knowledge, this is the largest study on pulmonary involvement in Greek children with treatment-naive, newly diagnosed rheumatic diseases suggesting chest CT scanning as a first-line evaluation tool for structural lung abnormalities.

5. Conclusions

The present study's investigation into pulmonary involvement in pediatric patients with newly diagnosed rheumatic diseases highlights the critical role of HRCT in detecting lung abnormalities that are not apparent through clinical symptoms alone or through PFTs. This is particularly relevant given the heterogeneous nature of lung disease in rheumatic conditions and the potential for significant morbidity and mortality associated with such complications. The study advocates for the inclusion of HRCT in the initial evaluation of these patients and calls for further research to refine diagnostic and monitoring strategies, ultimately aiming to improve long-term respiratory health in this vulnerable population.

Author Contributions: Conceptualization, SP, EA, KD and LF.; methodology, SP, KD, LF.; formal analysis, KD; writing—original draft preparation, SP, KC, ES, KK, DM, EK ; writing—review and editing, EA, KD, LF; supervision, KC, KK, LF. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of ATTIKON General Hospital, NKUA EBD494, date 02/07/2024.

Informed Consent Statement: Patient consent was not mandated according to current practice for retrospective studies in our institution when only a secondary review of imaging data is undertaken

Data Availability Statement: The clinical data supporting the findings of this study are available from the corresponding author upon reasonable requests via email: lafotis@med.uoa.gr

Conflicts of Interest: The authors declare no conflicts of interest

References

1. Ha, Y.J.; Lee, Y.J.; Kang, E.H. Lung involvements in rheumatic diseases: update on the epidemiology, pathogenesis, clinical features, and treatment. *Biomed Res Int* **2018**, *2018*, 6930297. doi: 10.1155/2018/6930297
2. Richardson, A.E.; Warrier, K.; Vyas, H. Respiratory complications of the rheumatological diseases in childhood. *Arch Dis Child* **2016**, *101*, 752–758. doi: 10.1136/archdischild-2014-306049
3. Dell, S.D.; Schneider, R.; Yeung, R. Pulmonary involvement in the systemic inflammatory diseases of childhood. In *Kendig's Disorders of the Respiratory Tract in Children*, 9th ed.; Wilmott, R.W., Deterding, R., Li, A., Ratjen, F., Sly, P., Zar, H.J., Bush, A., Eds.; Elsevier, Amsterdam, Netherlands, 2019; pp. 850–875.e7.
4. Griese, M. Chronic interstitial lung disease in children. *Eur Respir Rev* **2018**, *27*, 170100. doi: 10.1183/16000617.0100-2017
5. Dell, S.; Cernelc-Kohan, M.; Hagood, J.S. Diffuse and interstitial lung disease and childhood rheumatologic disorders. *Curr Opin Rheumatol* **2012**, *24*, 530–540. doi: 10.1097/BOR.0b013e328356813e
6. Hoffmann, T.; Oelzner, P.; Teichgräber, U.; Franz, M.; Gaßler, N.; Kroegel, C.; Wolf, G.; Pfeil, A. Diagnosing lung involvement in inflammatory rheumatic diseases-Where do we currently stand?. *Front Med (Lausanne)* **2023**, *9*, 1101448. doi: 10.3389/fmed.2022.1101448
7. Hallowell, R.W.; Horton, M.R. Interstitial lung disease in patients with rheumatoid arthritis: Spontaneous and drug induced. *Drugs* **2014**, *74*, 443–450. doi: 10.1007/s40265-014-0190-z
8. Huang, H.; Hu, Y.; Wu, Y.; Ding, F.; Xu, X.; Jin, Y.; Jin, Y.; Bao, Y. Lung involvement in children with newly diagnosed rheumatic diseases: characteristics and associations. *Pediatr Rheumatol Online J* **2022**, *20*. doi: 10.1186/s12969-022-00731-5
9. Lilleby, V.; Aaløkken, T.M.; Johansen, B.; Førre, Ø. Pulmonary involvement in patients with childhood-onset systemic lupus erythematosus. *Clin Exp Rheumatol* **2006**, *24*, 203–208. doi: 10.1177/0961203316629554
10. Veiga, C.S.; Coutinho, D.S.; Nakaie, C.M.; Campos, L.M.; Suzuki, L.; Cunha, M.T.; Leone, C.; Silva, C.A.; Rodrigues, J.C. Subclinical pulmonary abnormalities in childhood-onset systemic lupus erythematosus patients. *Lupus* **2016**, *25*, 645–651. doi: 10.1177/0961203316629554
11. Oman Medical Journal-Archive n.d. Available online: https://www.omjournal.org/articleDetails.aspx?coType=1&aId=192 (accessed on 28 April 2024).
12. Panigada, S.; Ravelli, A.; Silvestri, M.; Granata, C.; Magni-Manzoni, S.; Cerveri, I.; Dore, R.; Tomà, P.; Martini, A.; Rossi, G.A.; Sacco, O. HRCT and pulmonary function tests in monitoring of lung involvement in juvenile systemic sclerosis. *Pediatr Pulmonol* **2009**, *44*, 1226–1234. doi: 10.1002/ppul.21141
13. Hoffmann, T.; Oelzner, P.; Franz, M.; Teichgräber, U.; Renz, D.; Förster, M.; Böttcher, J.; Kroegel, C.; Schulze, P.C.; Wolf, G.; Pfeil, A. Assessing the diagnostic value of a potential screening tool for detecting early interstitial lung disease at the onset of inflammatory rheumatic diseases. *Arthritis Res Ther* **2022**, *24*, 107. doi: 10.1186/s13075-022-02786-x
14. Zulian, F.; Balzarin, M.; Birolo C. Recent advances in the management of juvenile systemic sclerosis. *Expert Rev Clin Immunol* **2017**, *13*, 361–369. doi: 10.1080/1744666X.2017.1243467.
15. Alexopoulou, E.; Prountzos, S.; Raissaki, M.; Mazioti, A.; Caro-Dominguez, P.; Hirsch, F.W.; Lovrenski, J.; Ciet, P. Imaging of acute complications of community-acquired pneumonia in the paediatric population-from chest radiography to MRI. *Children (Basel)* **2024**, *11*, 122. doi: 10.3390/children11010122
16. Wells, A., Denton, C. Interstitial lung disease in connective tissue disease—mechanisms and management. *Nat Rev Rheumatol* **2014**, **10**, 728–739. https://doi.org/10.1038/nrrheum.2014.149
17. Johnson SR, Bernstein EJ, Bolster MB, Chung JH, Danoff SK, George MD, Khanna D, Guyatt G, Mirza RD, Aggarwal R, Allen A Jr, Assassi S, Buckley L, Chami HA, Corwin DS, Dellaripa PF, Domsic RT, Doyle TJ, Falardeau CM, Frech TM, Gibbons FK, Hinchcliff M, Johnson C, Kanne JP, Kim JS, Lim SY, Matson S, McMahan ZH, Merck SJ, Nesbitt K, Scholand MB, Shapiro L, Sharkey CD, Summer R, Varga J, Warrier A, Agarwal SK, Antin-Ozerkis D, Bemiss B, Chowdhary V, Dematte D'Amico JE, Hallowell R, Hinze AM, Injean PA, Jiwrajka N, Joerns EK, Lee JS, Makol A, McDermott GC, Natalini JG, Oldham JM, Saygin D,

 doi:10.20944/preprints202408.1591.v1

Lakin KS, Singh N, Solomon JJ, Sparks JA, Turgunbaev M, Vaseer S, Turner A, Uhl S, Ivlev I. 2023 American College of Rheumatology (ACR)/American College of Chest Physicians (CHEST) Guideline for the Screening and Monitoring of Interstitial Lung Disease in People with Systemic Autoimmune Rheumatic Diseases. Arthritis Rheumatol. **2024**;76 :1201-1213. doi: 10.1002/art.42860