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ORIGINAL ARTICLE

Assessment of interstitial lung disease among black rheumatoid arthritis patients

Isabel M. McFarlane[1,2] · Su Yien Zhaz[1,3] · Manjeet S. Bhamra[1,2] · Aaliya Burza[1,4] · Srinivas Kolla[1,5] · Milena Rodriguez Alvarez[1,2] · Kristaq Koci[1,2] · Nicholas Taklalsingh[1,2] · Joshy Pathiparampil[1,2] · Latoya Freeman[1,2] · Ian Kaplan[1,2] · Naureen Kabani[1,2] · David J. Ozeri[1,6] · Elsie Watler[1,2] · Mosab Frefer[1,2] · Vytas Vaitkus[1,2] · Keron Matthew[1,2] · Fray Arroyo-Mercado[1,2] · Helen Lyo[1,2] · Tomasz Zrodlowski[1,2] · Aleksander Feoktistov[1,2] · Randolph Sanchez[1,7] · Cristina Sorrento[1,2] · Faisal Soliman[1,8] · Felix Reyes Valdez[1,9] · Veena Dronamraju[1,2] · Michael Trevisonno[1,2] · Christon Grant[1,2] · Guerrier Clerger[1,2] · Khabbab Amin[1,2] · Makeda Dawkins[1,2] · Jason Green[1,2] · Jane Moon[1,2] · Samir Fahmy[1,4] · Stephen Anthony Waite[1,5]

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Abstract

Background Conflicting reports exist regarding the racial and the gender distribution of rheumatoid arthritis–related interstitial lung disease (RA-ILD). In a major population study of predominately Whites, RA-ILD was reported mainly among smoker middle-aged men. However, recent data suggest that the disease is that of elderly women. Our study aimed to assess the prevalence and identify the gender differences and clinical characteristics of RA-ILD in a predominantly Black population.

Methods Cross-sectional analysis of data obtained from the records of 1142 patients with RA diagnosis by ICD codes of which 503 cases met the inclusion criteria for the study. Eighty-six patients had chronic respiratory symptoms of cough and dyspnea and were further assessed by our multidisciplinary group of investigators. Thirty-two subjects with an established diagnosis of rheumatoid arthritis met the diagnostic criteria for interstitial lung disease.

Results Of the 32 patients with RA-ILD, mean age was 62.6 ± 2.2 (± SEM), 93.7% were females, and 89% Blacks with a BMI = 29.2 (Kg/m^2). Usual interstitial pneumonia (UIP) was found in 24/32 (75%) of the cases. Seventy-two percent of the RA-ILD patient had seropositive RA. Smoking history was reported in 31.3% of the cohort, gastroesophageal reflux disease (GERD) in 32.3%, and cardiovascular disease (CVD) risk factors in 65.6%.

Conclusion Our study indicates RA-ILD among Blacks is predominantly a disease of elderly females with higher rates of GERD and CVD risk factors. Further studies are needed to identify the pathogenetic differences accounting for the gender distribution of RA-ILD among Black and White populations.

Key Points
- *First study to assess ILD among predominantly Black RA patients.*
- *The prevalence of RA-associated ILD was 6.36%, affecting mostly women in their sixth decade with seropositive disease.*
- *COPD was the most common airway disease among non-RA-ILD Black population.*
- *GERD was found in approximately one-third of patients with RA-associated ILD versus one-fifth of those RA patients without any lung disease.*

✉ Isabel M. McFarlane
Isabel.McFarlane@downstate.edu

Su Yien Zhaz
szhaz@shsny.com

Aaliya Burza
Aaliya.Burza@downstate.edu

Srinivas Kolla
Stephen.Waite@downstate.edu

David J. Ozeri
david.ozeri@sheba.health.gov.il

Randolph Sanchez
Randysanchez2011@gmail.com

Faisal Soliman
fas9051@nyp.org

Felix Reyes Valdez
freyesv@montefiore.org

Extended author information available on the last page of the article

Keywords Associated autoimmune disease · Asthma · Chronic obstructive pulmonary disease · Erosive disease · Extra-articular manifestations · Multidisciplinary meetings · Non-specific interstitial pneumonia · Pulmonary function test · Rheumatoid arthritis · Rheumatoid arthritis–related interstitial lung disease · Seropositive rheumatoid arthritis · Therapeutic patterns · Usual interstitial pneumonia

Introduction

RA is a chronic systemic autoimmune disease, with a prevalence of 1% in the Black adult population [1]. It is characterized primarily by proliferating synovitis with systemic inflammation and increasing morbidity and mortality.

Among the extra-articular manifestations of rheumatoid arthritis (RA), interstitial lung disease (ILD) warrants special attention, given the fact that up to 10% of RA patients will eventually develop clinically significant ILD [2–5]. ILD was first described in 1948 when findings ranging from fine to widespread heavy reticulation were noted in chest radiographs (CXR) of patients of RA [6]. Recent studies have found that the prevalence of RA-ILD is increasing, while the incidence is stable over time, perhaps reflecting the prolonged survival among this population [7].

RA-ILD is associated with a higher mortality rate in comparison with RA without ILD likely due to the higher frequency of comorbid conditions including ischemic heart disease, congestive heart failure, and diabetes. Lack of definitive prognostic indicators or gold standard treatment therapies for RA-ILD is a likely explanation for the higher mortality rates observed among these patients [8, 9].

A large population study from Mayo Clinic published in 2010 assessed the incidence, prevalence, and mortality of ILD in RA. This study indicated that the disease typically affects middle-aged men with seropositive RA of about 9 years duration with long-term smoking history [10–12]. The population included in this study was largely Whites [13]. In contrast, a recently published report from December 2018 indicated the RA-ILD occurs mainly among female patients with common co-morbid conditions. Information on the racial classification of the study cohort was not reported since that study was based on claims data [7]. These two conflicting reports suggest racial and gender differences in the prevalence and associations of RA-ILD among different populations. Our study aimed at assessing the prevalence and clinical characteristics as well as comorbidities associated with RA-ILD in a predominantly Black population with RA from two large urban academic medical centers.

Methods

This is a cross-sectional analysis of data obtained from records of RA patients utilizing the International Classification of Diseases Ninth Revision, Clinical Modification and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-9 CM 714.0 and ICD-10 M06.00 thru M06.09). We identified RA as principal or secondary diagnosis including all inpatient discharges between January 1, 2010, to May 30, 2017, that took place at State University of New York (SUNY) Downstate Medical Center and New York City (NYC) Health + Hospitals/Kings County which serve the population of Central Brooklyn, NY.

Prior to the initiation of the study, the protocol was reviewed and approved by the SUNY Downstate Institutional Review Board Study [1080808] and the Office of Research Administration for implementation at NYC Health + Hospitals/Kings County [001252].

We identified the hospital discharges with RA and proceeded to select patients 18 years or older by Jan 1, 2010, to be included in the study. Data abstraction was performed for the selected cases, utilizing a uniform study data collection sheet. We collected demographics and clinical data including smoking history, year of diagnosis, comorbidities, laboratory values, hand imaging, and treatment regimens. Patients who received care at both hospitals were counted once, and data for the individual patient were merged for the purpose of this analysis.

Two investigators (IMM, SYZ) independently reviewed the cases identified by ICD codes to confirm RA diagnosis by the 2010 American College of Rheumatology criteria [14]. We used physician entries (inpatient/outpatient notes and consultations) and presence of disease-modifying anti-rheumatic drugs (DMARDs) in the medication reconciliation or DMARDs prescriptions.

RA patients with chronic respiratory symptoms of dyspnea and cough who had been evaluated for RA-related interstitial lung disease with pulmonary function tests (PFTs) by spirometry and/or plethysmography and chest computed tomography were further screened to exclude those who had the diagnosis of ILD prior to the establishment of RA diagnosis.

We also excluded those with drug-induced ILD, sarcoidosis, vasculitis, and pneumoconiosis.

A chest radiologist (SAW), a pulmonary specialist (AB), and a rheumatologist (IMM) reviewed the clinical course, management, pulmonary function tests, and chest computed tomography (CT) images for each patient during the multidisciplinary reviews. When UIP was suspected, it was categorized using the Fleischner Society idiopathic pulmonary fibrosis diagnostic criteria [15]. The CT features considered for a diagnosis of usual interstitial pneumonia (UIP) are honeycombing, reticular pattern, traction bronchiectasis, and

the pattern of distribution (heterogenous and predominantly basal or sub-pleural).

Three diagnostic categories of UIP recognized by the Fleischner Society Criteria are:

- The typical UIP CT pattern features honeycombing, reticular pattern with peripheral traction bronchiectasis or bronchiolectasis in a predominantly basal (occasionally diffuse) and sub-pleural distribution that is often heterogeneous.
- Probable UIP CT pattern consists of a reticular pattern with peripheral traction bronchiectasis or bronchiolectasis in a predominantly basal and sub-pleural distribution that is often heterogeneous. Honeycombing is absent.
- Indeterminate UIP CT pattern demonstrates evidence of fibrosis with some inconspicuous features suggestive of non-UIP pattern in variable or diffuse distribution [15].

Chest CT images demonstrating a homogenous and bilateral pattern of ground-glass opacities associated with fine reticulations, pulmonary volume loss, traction bronchiectasis, and sparing of the sub-pleural space were classified as non-specific interstitial pneumonia (NSIP) [16].

All available PFTs were reviewed during the multidisciplinary meetings. Forced vital capacity (FVC), forced expiratory volume in first second (FEV1), FEV1/FVC ratio, total lung capacity (TLC), and diffusing lung capacity for carbon monoxide (DLCO) values in the most recent PFTs were recorded. A reduction in TLC, FVC, and FEV1 along with a reduction in DLCO was used as supporting evidence suggestive of ILD [17].

Cases deemed during the multidisciplinary reviews to be non-interstitial lung disease were further categorized into airway disease, pleural disease, vascular, and miscellaneous [18].

A musculoskeletal radiologist (SK), who was blinded to the serology results for the cases, reviewed the most recent hand radiographs. Periarticular osteopenia, number of erosions, and joint space narrowing were evaluated utilizing the Simple Erosion Narrowing Score (SENS) [19].

Descriptive statistics using SPSS® version 23 was applied. We used measures of central tendencies and dispersion for continuous variables and frequency distribution for categorical variables. Data is presented as the mean ± standard error of the mean (± SEM). We used *t* test to compare between two groups for continuous variables and ANOVA for multiple comparisons. Chi-square analysis was used for categorical variables.

Results

RA diagnosis was ascertained in 503 subjects from a total number of 1142 records identified by ICD-9 and ICD-10 codes. Figure 1 illustrates the process of selection of the RA patients, with 529 (281 + 241) cases being excluded due to either insufficient data to confirm RA or alternative diagnosis found upon review. Women represented 88% of the study cohort with Blacks accounting for 88.5%, and Hispanics 9.2%. Body mass index (BMI) was mean age was 65 ± 0.67 for women vs. 61 ± 2.19 for men ($p < 0.04$ (Table 1)) 28.9 ± 0.36 (± SEM).

In our cohort, we found a high prevalence of traditional cardiovascular risk factors including hypertension (66.6%), dyslipidemia (41.3%), diabetes (28.5%), and smoking (29.4%) (Table 1) as we previously reported [20]. In addition, among the cardiovascular outcomes examined, myocardial infarction (MI) or known coronary artery disease (CAD) was reported in 19.8%, congestive heart failure in 14.8%. Stroke or transient ischemic attack was reported in 10.1%. Gastroesophageal reflux disease (GERD) was encountered in 20.7%, asthma in 16.5%, chronic obstructive pulmonary disease in 12%, and venous thromboembolic disease in 12.9% of the entire cohort (Table 1).

Of the 503 RA patients, eighty-six had chronic respiratory symptoms of cough and dyspnea that developed after the RA diagnosis and had clinical note entries of suspected RA-related lung disease; pulmonary referral or work up ordered for evaluation of the chronic respiratory symptoms. The multidisciplinary team of this study reviewed the clinical history including date of RA diagnosis, disease course, comorbidities, serologies, therapeutic interventions, chest CT, and serial PFTs (Fig. 1).

Thirty-two cases had PFTs and CT features compatible with ILD [2, 13, 21–23]. The categories of ILD were as follows: typical usual interstitial pneumonia (UIP), 16 cases; probable UIP, 6 cases; and non-specific interstitial pneumonia (NSIP), 8 cases; five cases had lung biopsies confirming ILD diagnosis (one case was respiratory bronchiolitis-ILD). None of the cases was an indeterminate pattern of UIP.

Therefore, the prevalence of ILD in our RA population was (32/503) 6.36% (Table 2).

During the multidisciplinary meetings, the investigators confirmed that the patients under review did not have exposure to asbestos, previous administration of bleomycin, amiodarone, history of hypersensitivity pneumonitis, sarcoidosis, or vasculitis. The CT features more frequently found among the RA-ILD cases were architectural distortion, traction bronchiectasis, low lung volume, peripheral and lower lobe predilection, reticular pattern honeycombing, and ground-glass opacities (Table 3). GERD was more frequent among UIP cases, compared with NSIP population (39% vs. 12.5%) (Figs. 2, 3, and 4).

Two of the eight RA-NSIP cases presented within the first year of RA diagnosis; five of the 32 RA-ILD patients had RA for 7–11 years, and nine patients for more than 20 years.

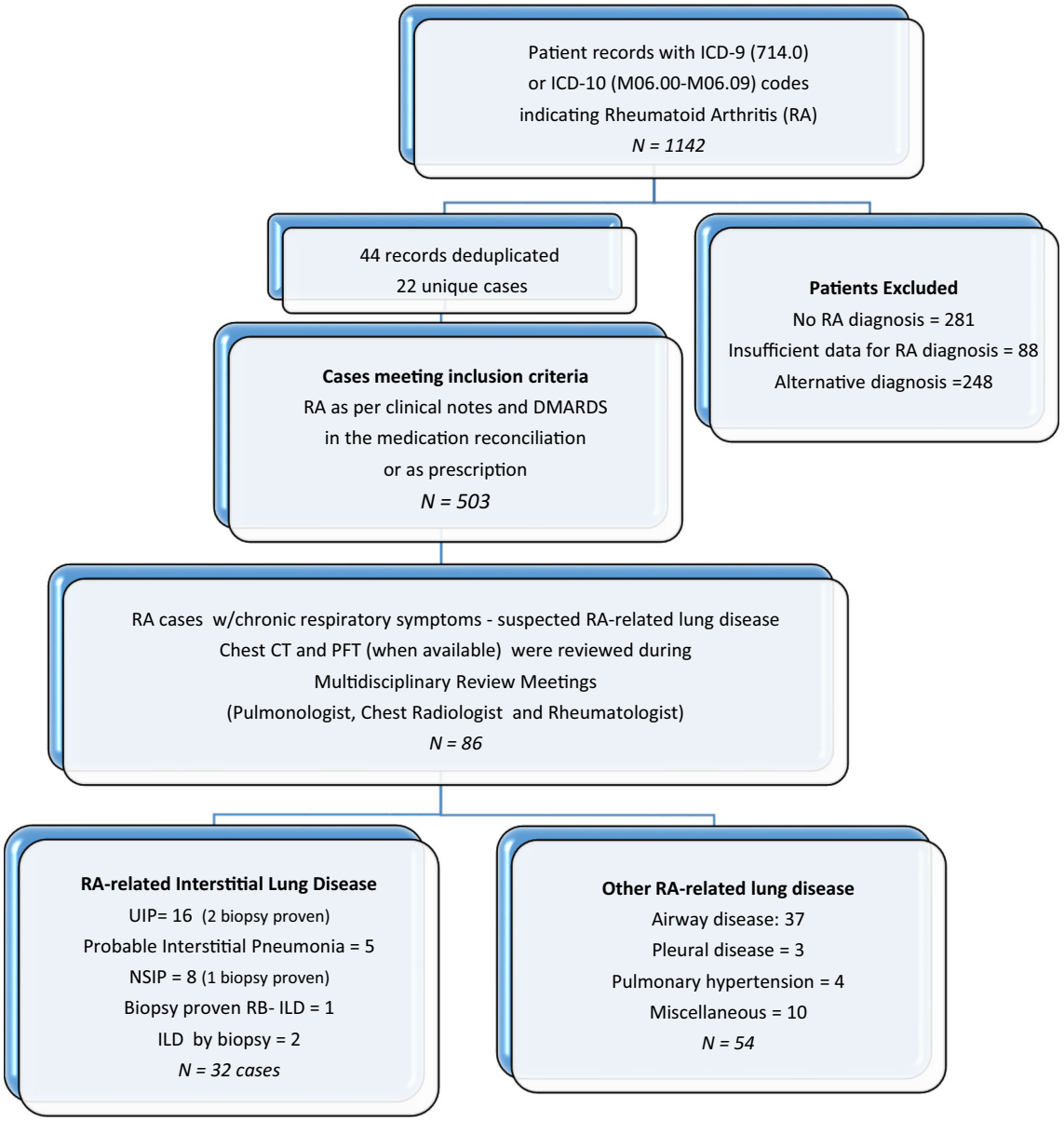

Fig. 1 Selection process for RA cases. ACOS asthma COPD Overlap Syndrome, COPD chronic obstructive pulmonary disease, DMARDs disease-modifying anti-rheumatic drugs, PFTs pulmonary function tests RB-ILD respiratory bronchiolitis interstitial lung disease, NSIP non-specific interstitial pneumonia, UIP usual interstitial pneumonia

Nine of the 32 (37.5%) UIP patients were seropositive for either rheumatoid factor (RF) or anti-citrullinated peptide antibodies (ACPA) and 33.3% had positive anti-nuclear antibodies. A second autoimmune disease was found in 31.2% (10/32) of the RA-ILD cases and in 50% of the NSIP patients (Table 4).

PFTs had been obtained in 46.5% (40/86) of the patients who were reviewed by the multidisciplinary investigators with 40.62% (13/32) of the patients in the RA-ILD group had PFTs recorded. The values for FVC, TLC, and DLCO were lower in RA-ILD vs. RA with other lung disease groups; however, only the FEV1/FVC ratio between the groups reached statistical significance (Table 5).

Cases not meeting RA-ILD inclusion criteria by CT features were classified as follows: airway disease which included chronic obstructive pulmonary disease (COPD), 19 cases; restrictive lung disease, 6 cases; asthma, 3 cases; chronic atelectasis with scarring, 3 cases, with 2 cases reported for each of the following categories: asthma-COPD overlap syndrome, obliterative bronchiolitis, and bronchiectasis. Pleural disease group includes two cases of pleural plaques and one case of pleural effusion; vascular pathology, 4 cases of pulmonary hypertension (PAH); and mixed pathologies, ten other cases including pneumonia (2 cases), COPD-adenocarcinoma, infection-metastasis, PAH-bronchiectasis, PAH-chronic venous thromboembolism,

Table 1 Total study population characteristics

Total number of patients: 503	
Percentage of women	87.9%
Percentage of men	12.1%
Women's mean age (± SEM) years	65 ± 0.68
All patients' age in years (± SEM) years	64 ± 0.6
BMI (mean ± SEM)	28.9 ± 0.36
BMI ≥ 30 Kg/m^2	37.2%
Race/ethnicity	
White	7.2%
Black	88.5%
Hispanics	9.2%
Asian Pacific Islander	0.6%
Native American	0.2%
Smoking	
Non-smoker	70.6%
Ever smoker	29.4%
Comorbidities	
Hypertension	66.6%
Hyperlipidemia	41.3%
Diabetes mellitus	28.5%
CAD or AMI	19.8%
Congestive heart failure	14.8%
Prior cerebrovascular accident	10.1%
Atrial fibrillation	8.4%
GERD	20.7%
Asthma	16.5%
COPD	12.0%
VTE	12.9%
Cancer	11.9%
Prior sepsis	11.6%
Hepatitis C	2.6%
HIV	2.2%
Hepatitis B	1.1%
Other autoimmune disease	
Systemic lupus erythematosus	11.4%
Sjögren's syndrome	2.4%
Mixed connective tissue disease	1.1%
Undifferentiated connective tissue disease	0.9%
Systemic sclerosis	0.9%
Polymyositis	0.7%
Idiopathic inflammatory myopathy	0.6%

Percentages were calculated based on the number of patients with data available on the measure. *CAD*, coronary artery disease; *MI*, myocardial infarction; *BMI*, body mass index; *SEM*, standard error of the mean

Table 2 RA cases assessed by the multidisciplinary investigators*

	n = 86
RA-related ILD	32
Typical usual interstitial pneumonia	16 (50%)
Probable usual interstitial pneumonia	5 (15.6%)
Non-specific interstitial pneumonia Cellular appearance NSIP (2 cases) Organizing pneumonia NSPI (1 case)	8 (25%)
Biopsy-proven RB-ILD	1 (3.3%)
Biopsy proven RA-ILD	2 (6.25%)
Non-ILD lung disease	54
Airway disease	
Chronic obstructive pulmonary disease	19 (35.2%)
Restrictive lung disease	6 (11.1%)
Asthma	3 (5.5%)
Chronic atelectasis/scarring	3 (5.5%)
Asthma-COPD overlap syndrome	2 (3.7%)
Obliterative bronchiolitis	2 (3.7%)
Bronchiectasis	2 (3.7%)
Pleural disease	
Pleural plaque	2 (3.7%)
Pleural effusion	1 (1.8%)
Vascular	
Pulmonary hypertension	4 (7.4%)
Miscellaneous lung disease	10 (18.5%)

COPD, chronic obstructive pulmonary disease; *RB-ILD*, respiratory bronchiolitis-interstitial lung disease; *NSIP*, non-specific interstitial pneumonia

*Multidisciplinary investigators (chest radiologist, pulmonary, and rheumatology specialists)

scarring-bronchiectasis, fibrosis/cystic air disease, undetermined pathology, and a normal chest.

In Table 6, we present a comparison of the cohorts of RA-related ILD, other RA lung disease, and the RA only population. GERD was encountered at a rate of 32.3% and 34% among the patients with ILD and other lung diseases respectively versus 18% for RA only patients. Sepsis occurred at a higher rate among patients with other lung diseases. Cancer rate was 11.9% for the entire cohort of RA patients with 12.5% being breast cancer among RA-ILD population. Among those with other RA lung disease, the cancer rate was 9.25%. There were no statistically significant differences among the groups in regard to other clinical parameters, inflammatory markers, presence of RF or ACPA positivity, or SENS scores.

We recorded glucocorticoid use in 68% of the RA patients with other lung diseases versus 50% among patients with RA-related ILD. Methotrexate, biologics, and the combination of steroids, disease-modifying anti-rheumatic drugs (DMARDs), and biologics use were the lowest among RA-ILD (16%, 12%, and 21.9% respectively). Only one patient in the RA-ILD category had received rituximab. DMARDS and biologics were used with low frequency among RA patients with other lung diseases (see Table 7).

Table 3 Chest Computed Tomography Findings

Chest CT features	RA-ILD ($N = 32$)	RA + other lung disease ($N = 54$)	p value
Architectural distortion	86.2%	7.4%	< 0.001
Traction bronchiectasis	75.9%	1.9%	< 0.001
Low lung volume	72.4%	1.9%	< 0.001
Peripheral and lower lobe predilection	69.0%	1.9%	< 0.001
CT reticular pattern	65.5%	3.7%	< 0.001
Honeycombing	55.2%	1.9%	< 0.001
Ground-glass opacities	51.7%	14.8%	= 0.001
Patchy consolidations	17.2%	1.9%	< 0.001

Seventeen of the 32 patients with RA-ILD continued to receive care at our institutions by the time this cross-sectional analysis was completed. Four patients expired, three belonging to the UIP category with death occurring at 5 years and 19 years after ILD diagnosis. The NSIP patient expired within the first year of RA-ILD diagnosis. The other 13 patients were alive as per clinic/progress notes.

Given the current interest in COPD, asthma, and RA, we examined further our RA patients with a clinical diagnosis of COPD. Smoking rates were as follows: 55.5% were former smokers while only 22.2% were current smokers among our COPD patients. Seropositivity (either RF or ACPA) was present in 38.6% of the COPD patients with 28% of them being double seropositive.

For asthma, 12% of the patients were reported as former smokers and 25% as current smokers. Seropositive RA (either RF or ACPA) was recorded in 89.7% and double seropositivity in 47.2%. The SENS for the hand radiographs (maximum = 62), which adds the total number erosions (up to 32) and total number of joint space narrowing (up to 30), for the COPD group had a mean score of 32.71 ± 6.5 (± SEM), and for asthma, the SENS was 25.42 ± 7.4 (± SEM).

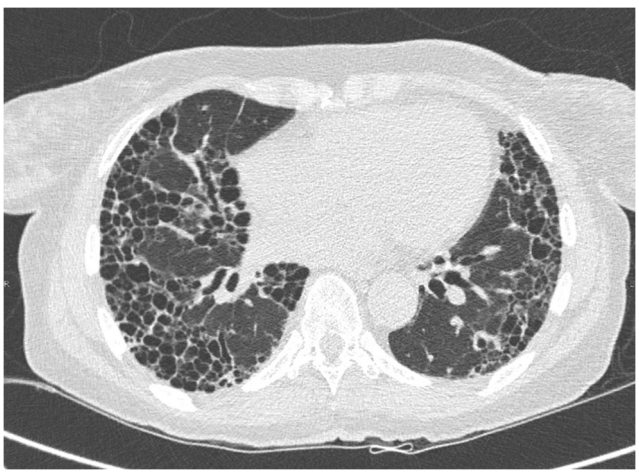

Fig. 2 Typical usual interstitial pneumonia. CT image demonstrating peripheral and basilar severe honeycombing, with architectural distortion and traction bronchiectasis

Discussion

In our predominantly Black RA population, ILD was found with a prevalence of 6.36%, which is consistent with previously published reports; given that the patterns of ILD in connective tissue disease resemble those seen in idiopathic pulmonary fibrosis, we were able to apply the Fleischner Society Criteria for UIP [7, 13, 15]. Consistent with the current literature, the UIP was the most CT pattern encountered. Our RA-ILD population consisted mainly of females (93.75%) with a mean age of 62.65 years. This is contrary to previous reports indicating middle-aged men as the predominant population affected by ILD [13]. Smoking history reported among our population was 31%, less than half of that reported in the Mayo Clinic study (64%) [13].

The difference in the rate of smoking in addition to the fact that males are heavier smokers (higher serum cotinine levels among male smokers) compared with female smokers could explain the gender discrepancy encountered between our RA-ILD population predominantly composed of women compared with the RA-ILD population from Mayo Clinic [24].

Half of our RA-ILD patients had double seropositivity [7, 22]. The length of RA disease was more than 10 years in about 59% of the RA-ILD cases, finding consistent with the current knowledge that the risk of RA-ILD increases over time [13].

The fact that only 35% (6/17) of the RA-ILD cases had RA for more than 20 years of disease could be explained by the high mortality rate, in which only a smaller number of ILD cases live past 20 years of disease. NSIP developing within the first year of RA diagnosis was found in a quarter of the patients; it has been described that cases with NSIP pattern on chest CT will be read as UIP pattern on lung biopsy which is known to be linked to increased mortality [25].

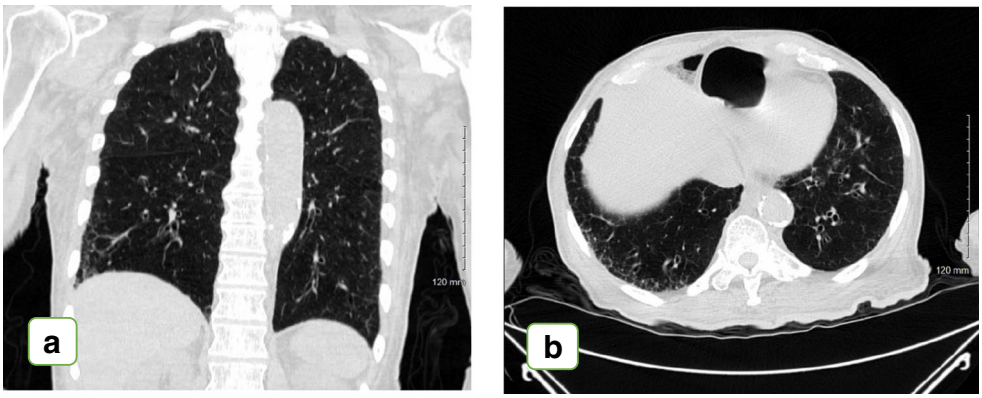

Fig. 3 Probable usual interstitial pneumonia (**a**, **b**). CT demonstrates basal, sub-pleural, and peripheral distribution of reticulation, with peripheral traction bronchiectasis, distorted airways, and relatively minimal honeycombing

Our RA-ILD population had a higher prevalence of a second auto-immune disease (31.25%), in contrast with recent reports on the co-existence of RA and other autoimmune diseases in 23.4% of the patients which appears to be an important characteristic among our patients [26, 27].

Four cases of breast cancer were encountered (12.5%) among the UIP RA-ILD patients with no lung cancer being detected in this group.

PFTs were available in about 40.6% (13/32) of the RA-ILD cases, revealing parameters consistent with loss of pulmonary elasticity with restrictive lung deficit and low diffusion capacity.

These PFT results reflect the common pattern of physiological abnormalities seen in interstitial lung diseases characterized by a restrictive ventilatory defect and reduced diffusing capacity (DLCO). The statistically significant FEV1/FVC ratio, found when comparing RA-ILD vs. RA with other lung diseases, also underlines that the ILD process favors more FVC reduction than reduction in FEV1. Additionally in ILD, DLCO is typically reduced to a greater extent than can be expected by the reduction in lung volumes only [28].

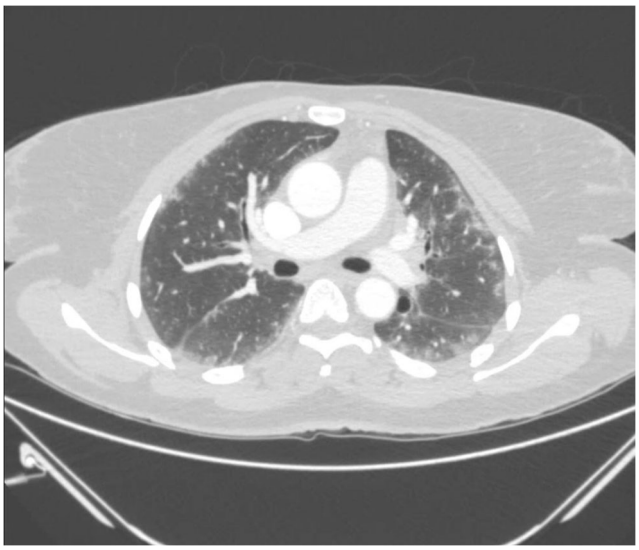

Fig. 4 Non-specific interstitial pneumonia (NSIP). CT images demonstrate predominantly peripheral ground-glass opacities with no evidence of fibrosis. Subpleural sparing in the lingula is appreciated. Findings consistent with cellular NSIP

The most commonly seen chest CT features, in descending order, were architectural distortion, traction bronchiectasis, low lung volume, and the typical predilection for the lung periphery and the lower lobes. Reticular pattern, honeycombing, and ground-glass opacities were also found in two-thirds to about half of the patients. Our RA-ILD patients had a mean SENS slightly higher than the rest of the population, likely representing aggressive disease.

The 54 cases that underwent multidisciplinary review and deemed to be non RA-ILD cases were studied further and classified into categories of RA with other lung diseases [18]. Sixty-eight percent of the patients had airway disease. COPD was the most common, followed by restrictive lung disease. Our data suggests higher airway disease compared with previous reports where airway disease prevalence was between 31 and 60% of the RA populations [18, 29, 30]. Pulmonary hypertension was found in 7.4% of the RA with other lung disease group.

The eleven cases of RA with other lung diseases in the miscellaneous category contain pathology ranging from COPD and lung cancer, infection, pulmonary hypertension with bronchiectasis, fibrosis/cystic changes to undetermined pathology which would explain the chronic respiratory symptoms of the patients in this group.

The reassignment of cases that were once considered "RA-related lung disease," by clinician's notes highlights the importance of pursuing a multidisciplinary approach in the evaluation of suspected cases. A multidisciplinary review is already a proven strategy in the diagnosis of ILD that leads to early diagnosis and thorough discussion of treatment plans and monitoring plans that take into account the patient's other comorbid conditions [31].

When we consider our entire RA population, the clinical diagnosis of COPD was found at a rate higher than previously reported (12% vs. 8.1%) [32]. It has been postulated that RA is associated with an increased risk of COPD with a hazard ratio of 1.52 as per the results of a matched prospective cohort within the Nurses' Health Study. Smoking did not explain

Table 4 Comparison between the two ILD groups

	UIP cases (typical, probable, and biopsy proven) ($N = 24$)	Non-specific interstitial pneumonia ($N = 8$)
Age in years ± SD	63.2 ± 12.1	60.9 ± 14.5
Smoking history	25%	50%
GERD	37.5%%	12.5%
Cancer (number of cases)	4 (breast)	none
At least 1 CV risk factor	62.5%	75%
3 or more CV risk factors	33.3%	37.5%
Years since RA diagnosis		
Within 1 year	0	2
< 5 years	1	–
7–11 years	3	2
> 20 years	4	–
>30 years	3	2
Associated with IIM	1 (ASS)	1 (PM)
Other autoimmune disease	2 (SSc; SjS)	2 (MCT, SSc)
Associated with SLE	3	1
Seropositive (either RF or ACPA)	37.5%	50%
Double seropositive (RF + ACPA+)	6.25%	25%
ANA positive	33.3%	12.5%

ACPA, anti-citrullinated peptide antibody; ANA, anti-nuclear antibodies; *ASS*, anti-synthetase syndrome; *IIM*, idiopathic inflammatory myopathy; *ILD*, interstitial lung disease; *MCTD*, mixed connective tissue disease; *UIP*, usual interstitial pneumonia; *SSc*, systemic sclerosis; *SjS*, Sjögren's syndrome

fully the association between COPD and RA. Other risk factors such as seropositivity were thought to be implicated in the pathogenesis of COPD associated with RA [32].

However, in our RA-COPD population, we found high rates of smoking history (46/60) (77%) with only 38.6% of the patients being seropositive for either RF or ACPA, making smoking an attractive common soil hypothesis for the comorbidity of COPD and RA in our predominately Black female population.

Another important finding in our study is the nearly double rate of asthma among our population compared with previously published reports (12% vs. 6.6%) [33, 34].

A possible explanation to the higher rate of asthma among our patients is the relatively higher smoking rate compared with that of the entire RA population (37.3% vs. 29.54%) for RA-asthma and RA-only group respectively. 89.7% of the RA asthma patients were seropositive with almost half of them being double seropositive highlighting the possible common immunologic mechanisms for these 2 autoimmune disorders [35, 36]. However, the number of erosions and joint space narrowing as calculated by SENS did not point to a more aggressive disease among asthmatics when compared with the entire RA cohort (25.42 ± 7.4 vs. 35.53 ± 2.05).

Table 5 Comparison of PFTs results among the RA lung disease groups

	RA-ILD (available PFTs = 13/32)	RA + other lung disease (available PFTs = 27/54)	*p* value
FVC (± SEM) liters	1.76 ± 0.17	2.05 ± 0.10	NS
FVC percentage of predicted	66.92 ± 6.78	78.2 ± 4.07	NS
FEV_1 (± SEM) liters	1.43 ± 0.14	1.44 ± 0.09	NS
FEV_1 percentage of predicted	71.17 ± 7.46	68.85 ± 3.9	NS
FEV1/FVC ratio (± SEM)	84.17 ± 3.63	74.3 ± 3.09	0.005
TLC (± SEM) liters	3.53 ± 0.29	3.94 ± 0.16	NS
TLC percentage of predicted	67.94 ± 6.44	79.88 ± 3.8	NS
DLCO (± SEM) ml/mmHg/min	9.67 ± 1.17	11.75 ± 0.94	NS
DLCO percentage of predicted	43.67 ± 3.74	53.85 ± 3.50	NS

DLCO, diffusing capacity for carbon monoxide; *FEV1*, forced expiratory volume in first second; *FVC*, forced vital capacity; *ILD*, interstitial lung disease; *PFTs*, pulmonary function tests; *TLC*, total lung capacity

Table 6 Demographic and clinical characteristics of the study populations*

Clinical features	RA-ILD ($n = 32$)	RA + other lung disease ($n = 54$)	RA only (no lung disease) ($n = 417$)
Female	93.75%	90.74%	86.8%
Age in years (± SEM)	62.65 ± 2.21	66.35 ± 1.74	64.67 ± 0.74
Never smoker	68%	48.9%	73.3%
Current smoker	6.3%	14.9%	11.9%
Former smoker	25%	36.2%	14.8
VTE	3.4%	21.2%	12.5%
GERD	32.3%	34%	18%
Cancer	12.5%	9.25%	11.3%
Prior sepsis	6.7%	19.6%	10.9%
Episode of ARDS w/sepsis	0%	7.1%	3.9%
BMI (Kg/m^2)	29.05 ± 1.85	27.75 ± 1.02	29.06 ± 0.38
White blood cell count (± SEM)	7.93 ± 0.58	7.64 ± 0.5	8.03 ± 0.24
Hematocrit (± SEM)	34.54 ± 0.95	35.46 ± 0.79	35.21 ± 0.33
Hemoglobin (± SEM)	10.84 ± 0.34	11.34 ± 0.26	12.53 ± 0.64
Platelets (± SEM)	314.23 ± 30.57	278.35 ± 17.42	278 ± 5.93
ESR (± SEM)	78.06 ± 9.61	68.54 ± 5.79	60.66 ± 2.38
CRP (± SEM)	52.21 ± 16.23	47.73 ± 11.76	48.56 ± 4.68
RA subcutaneous nodules	0%	2%	5.6%
RA duration of disease >10 years	58.8%	57.1%	53.9%
BMI < 20 Kg/m^2	10.3%	7.8%	7.2%
BMI > 30 Kg/m^2	24.1%	27.5%	39.6%
Abnormal hand radiographs	92.9%	96.4%	94.7%
Periarticular osteopenia	92.9%	92.9%	95.9%
SENS (± SEM)	33.44 ± 8.05	27.57 ± 4.43	30.61 ± 2.05
Presence of joint erosions	57.1%	64.3%	67.8%
Presence of joint space narrowing	57.1%	71.4%	69.9%
Immunological and inflammatory markers of the study populations			
CRP > 10 mg/L **	77.3%	65.7%	61.4%
ESR > 42 mm/h ***	70%	72.5%	61.3%
ANA	50%	47.8%	37.2%
Positive rheumatoid factor (RF)	55.6%	78.6%	76.6%
Positive ACPA	40.6%	76.2%	68.5%
Either RF+ or ACPA+	72.2%	82.1%	86.4%
Double seropositive (RF+/ACPA+)	31.6%	78.3%	50.9%

Percentages were calculated based on the number of patients with data available on the measure

RF, rheumatoid factor; *ACPA*, anti-citrullinated peptide antibody; *ESR*, erythrocyte sedimentation rate; *CRP*, C reactive protein

*Comparison between the 3 groups of the study population revealed no significant differences between the groups on any of the specified parameters (P = NS)

The prevalence rate of cancers encountered in our RA population was 11.9%, which falls at a higher rate than previously reported of 6.3% and most recently 4.16% when non melanoma skin cancer was excluded [37, 38].

Interestingly, the malignancies found among the 4 UIP patients were breast cancer that is the least reported in published series. Another interesting finding is the absence of lung cancer in our populations, which is the most frequently reported cancer among ILD patients. The reasons for this discrepancy are not clear, except that our population is predominately women where the incidence of breast cancer is much higher than that reported in men.

Further studies are needed to understand the higher overall risk of malignancy among our RA population. Possible risk factors include higher rates of obesity, smoking, advanced age, and use of steroids and immunosuppressive drugs, as well as high levels of inflammatory markers among our patients.

Table 7 Therapeutic regimens

Medication pattern	RA-ILD ($n = 32$)	RA + other lung diseases ($n = 54$)	RA only ($n = 417$)	p value
Current steroids	50%	68.1%	54.8%	NS
Methotrexate	16%	37%	42.4%	NS
Other DMARDs	50%	52.4%	41%	NS
Current biologics	12%	15.9%	16.5%	NS
On steroids-DMARDs-biologics	21.9%	50%	34.5%	0.02
DMARDS-biologics	28.1%	14.8%	28.3%	NS

In regard to the therapeutic patterns, the lower use of MTX and biologics found among the RA-ILD cases is expected given their possible association with ILD and shorten survival reported with the use of tumor necrosis factor inhibitors (TNFi), before Rituximab began to be more frequently used.

Finally, our study is limited by the retrospective nature of the analysis, lack of available RA-specific disease activity measurements and survival outcomes for all of the cases. Alive status was only ascertained in 17 cases of the 32 cases with RA-ILD. Inaccuracy in coding explains the number of cases in which RA diagnosis was not found in the clinical documentation. We plan a prospective study to ascertain the survival predictors among our RA population with a special focus on RA-related ILD.

Most of the examinations on our study were routine supine chest CTs limiting our ability to diagnose subtle or early ILD. Dependent densities are common in the posterior subpleural aspects of the lungs on CT scans. This finding is usually attributable to micro-atelectasis; however, it can represent subtle early interstitial lung disease, without examining prone imaging routinely performed on high-resolution computed tomography.

Although our study populations had PFT available for 40.62% of the RA-ILD and 50% for the non RA-ILD group, having PFT's for all cases would have been ideal. PFTs support the diagnosis of ILD although the pattern is non-specific. In addition, in 15% (6/40) of our study cases, baseline PFTs were available. Serial PFTs provide valuable information determining the disease progression and response to therapy or lack of [17]. Having an exercise-induced gas exchange difference would have further enhanced the diagnostic and monitoring value of the PFTs; however, 6-min walk tests were not available in the cases with low DLCO. There is also data missing at random, which we believe is harmless and does not represent a systematic bias.

Conclusion

This is the first study to evaluate lung disease in our predominantly Black RA population assessed by group multidisciplinary experts in rheumatology, pulmonary, and chest radiology. In contrast to previous report from Mayo Clinic indicating that the RA-ILD is typically a disease of White men (58.7%) with high rate of smoking (64%), our study suggests that RA-ILD among Blacks is predominantly a disease of females (93.7%) with high rates of RA seropositivity, GERD, and CVD risk factors. In support of our results, a recent report derived from the US claims data indicates that RA-ILD is predominant among female RA patients (70%).

Smoking history rate among our population was 31%, which is less than half of that reported in the Mayo Clinic study (64%). This together with the fact that men tend to smoke much heavier than women provide at least a partial explanation for the gender differences reported in our study, compared with the Mayo Clinic cohort. Nevertheless, further studies are necessary to identify the pathogenetic mechanisms accounting for the gender differences in the distribution of RA-ILD among Black and White populations.

Finally, among our cohort of RA patients with other lung disease, airway diseases such as COPD, restrictive lung disease, and asthma were the most frequently reported diagnoses. These findings are consistent with the established literature in this area.

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Author contributions I.M.M. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Conceptualization: I.M.M., D.J.O.; Methodology: I.M.M., S.Y.Z.L., D.J.O.; Validation: I.M.M., S.Y.Z., M.S.B., E.W., C.S.S.; Formal analysis: I.M.M., M.S.B., C.S.S., M.R.A.; Investigation: I.M.M., S.Y.Z., M.S.B., M.R.A., K.K., N.T., I.K., S.K., S.A.W., A.B., J.P., N.K., E.W., M.F., V.V., J.G., K.M., F.A.-M., H.L., R.A.S., F.S., F.M.R., V.D., M.T., C.G., C.G., K.A., L.F., M.D. T.Z.; Data curation: I.M.M., S.Y.Z.L., M.S.B. E,W.; Writing—original draft: I.M.M., M.R.A., A.B.; Writing—review and editing: I.M.M., M.S.B., S.Y.Z., M.R.A., S.F., J.M.,A.F., A.B., S.A.W., D.J.O.; Visualization: S.A.W., M.S.B., J.M., M.R.A. I.M.M.; Project administration, S.Y.Z.L., I.M.M., M.S.B.

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Compliance with ethical standards

Prior to the initiation of the study, the protocol was reviewed and approved by the SUNY Downstate Institutional Review Board Study [1080808] and the Office of Research Administration for implementation at NYC Health + Hospitals/Kings County [001252].

Disclosures None.

References

1. Greenberg JD, Spruill TM, Shan Y, Reed G, Kremer JM, Potter J, Yazici Y, Ogedegbe G, Harrold LR (2013) Racial and ethnic disparities in disease activity in patients with rheumatoid arthritis. Am J Med 126(12):1089–1098
2. Olson AL, Swigris JJ, Sprunger DB, Fischer A, Fernandez-Perez ER, Solomon J, Murphy J, Cohen M, Raghu G, Brown KK (2011) Rheumatoid arthritis-interstitial lung disease-associated mortality. Am J Respir Crit Care Med 183(3):372–378
3. Ahmad K, Barba T, Gamondes D, Ginoux M, Khouatra C, Spagnolo P, Strek M, Thivolet-Béjui F, Traclet J, Cottin V (2017) Interstitial pneumonia with autoimmune features: clinical, radiologic, and histological characteristics and outcome in a series of 57 patients. Respir Med 123:56–62
4. Assayag D, Elicker BM, Urbania TH, Colby TV, Kang BH, Ryu JH, King TE, Collard HR, Kim DS, Lee JS (2014) Rheumatoid arthritis-associated interstitial lung disease: radiologic identification of usual interstitial pneumonia pattern. Radiology. 270(2):583–588
5. Chan EC, Kelly, C 2013 Interstitial lung disease in rheumatoid: a review Arthritis Research UK. Reports on the Rheumatic Diseases, Series 7, Topical Reviews No 3
6. Ellman P, Ball RE (1948) Rheumatoid disease with joint and pulmonary manifestations. Br Med J 2(4583):816–820
7. Raimundo K, Solomon JJ, Olson AL, Kong AM, Cole AL, Fischer A, Swigris JJ (2019) Rheumatoid arthritis-interstitial lung disease in the United States: prevalence, incidence, and healthcare costs and mortality. J Rheumatol 46(4):360–369
8. Hyldgaard C, Hilberg O, Pedersen AB, Ulrichsen SP, Lokke A, Bendstrup E et al (2017) A population-based cohort study of rheumatoid arthritis-associated interstitial lung disease: comorbidity and mortality. Ann Rheum Dis 76(10):1700–1706
9. Johnson C (2017) Recent advances in the pathogenesis, prediction, and management of rheumatoid arthritis-associated interstitial lung disease. Curr Opin Rheumatol 29(3):254–259
10. Kelly CA, Saravanan V, Nisar M, Arthanari S, Woodhead FA, Price-Forbes AN, Dawson J, Sathi N, Ahmad Y, Koduri G, Young A, on behalf of the British Rheumatoid Interstitial Lung (BRILL) Network (2014) Rheumatoid arthritis-related interstitial lung disease: associations, prognostic factors and physiological and radiological characteristics–a large multicentre UK study. Rheumatology (Oxford) 53(9):1676–1682
11. Tsuchiya Y, Takayanagi N, Sugiura H, Miyahara Y, Tokunaga D, Kawabata Y, Sugita Y (2011) Lung diseases directly associated with rheumatoid arthritis and their relationship to outcome. Eur Respir J 37(6):1411–1417
12. Zhang Y, Li H, Wu N, Dong X, Zheng Y (2017) Retrospective study of the clinical characteristics and risk factors of rheumatoid arthritis-associated interstitial lung disease. Clin Rheumatol 36(4): 817–823
13. Bongartz T, Nannini C, Medina-Velasquez YF, Achenbach SJ, Crowson CS, Ryu JH, Vassallo R, Gabriel SE, Matteson EL (2010) Incidence and mortality of interstitial lung disease in rheumatoid arthritis: a population-based study. Arthritis Rheum 62(6):1583–1591
14. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO 3rd et al (2010) 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis 69(9):1580–1588
15. Lynch DA, Sverzellati N, Travis WD, Brown KK, Colby TV, Galvin JR, Goldin JG, Hansell DM, Inoue Y, Johkoh T, Nicholson AG, Knight SL, Raoof S, Richeldi L, Ryerson CJ, Ryu JH, Wells AU (2018) Diagnostic criteria for idiopathic pulmonary fibrosis: a Fleischner Society White Paper. Lancet Respir Med 6(2): 138–153
16. Mueller-Mang C GC, Schmid K, Stiebellehner L, Bankier AA (2007) What every radiologist should know about idiopathic interstitial pneumonias. Radiographics. 27:595–615
17. Martinez FJ, Flaherty K (2006) Pulmonary function testing in idiopathic interstitial pneumonias. Proc Am Thorac Soc 3(4):315–321
18. Marcucci E, Bartoloni E, Alunno A, Leone MC, Cafaro G, Luccioli F, Valentini V, Valentini E, la Paglia GMC, Bonifacio AF, Gerli R (2018) Extra-articular rheumatoid arthritis. Reumatismo. 70(4): 212–224
19. Dias EM, Lukas C, Landewe R, Fatenejad S, van der Heijde D (2008) Reliability and sensitivity to change of the Simple Erosion Narrowing Score compared with the Sharp-van der Heijde method for scoring radiographs in rheumatoid arthritis. Ann Rheum Dis 67(3):375–379
20. McFarlane IM, Zhaz Leon SY, Bhamra MS, Burza A, Waite SA, Rodriguez Alvarez M et al (2019) Assessment of cardiovascular disease risk and therapeutic patterns among urban black rheumatoid arthritis patients. Med Sci (Basel) 7(2)
21. Koduri G, Norton S, Young A, Cox N, Davies P, Devlin J, Dixey J, Gough A, Prouse P, Winfield J, Williams P, on behalf of ERAS (Early Rheumatoid Arthritis Study) (2010) Interstitial lung disease has a poor prognosis in rheumatoid arthritis: results from an inception cohort. Rheumatology (Oxford) 49(8):1483–1489
22. Mira-Avendano I, Abril A, Burger CD, Dellaripa PF, Fischer A, Gotway MB, Lee AS, Lee JS, Matteson EL, Yi ES, Ryu JH (2019) Interstitial lung disease and other pulmonary manifestations in connective tissue diseases. Mayo Clin Proc 94(2):309–325
23. Raghu G, Remy-Jardin M, Myers JL, Richeldi L, Ryerson CJ, Lederer DJ, Behr J, Cottin V, Danoff SK, Morell F, Flaherty KR, Wells A, Martinez FJ, Azuma A, Bice TJ, Bouros D, Brown KK, Collard HR, Duggal A, Galvin L, Inoue Y, Jenkins RG, Johkoh T, Kazerooni EA, Kitaichi M, Knight SL, Mansour G, Nicholson AG, Pipavath SNJ, Buendía-Roldán I, Selman M, Travis WD, Walsh S, Wilson KC, American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Latin American Thoracic Society (2018) Diagnosis of idiopathic pulmonary fibrosis. An official ATS/ERS/JRS/ALAT clinical practice guideline. Am J Respir Crit Care Med 198(5):e44–e68
24. McFarlane SI, von Gizycki H, Salifu M, Deshmukh M, Manieram M, Gebreegziabher Y et al (2007) Alcohol consumption and blood pressure in the adult US population: assessment of gender-related effects. J Hypertens 25(5):965–970
25. Flaherty KR, Thwaite EL, Kazerooni EA, Gross BH, Toews GB, Colby TV, Travis WD, Mumford JA, Murray S, Flint A, Lynch JP 3rd, Martinez FJ (2003) Radiological versus histological diagnosis in UIP and NSIP: survival implications. Thorax. 58(2):143–148
26. Simon TA, Kawabata H, Ray N, Baheti A, Suissa S, Esdaile JM (2017) Prevalence of co-existing autoimmune disease in rheumatoid arthritis: a cross-sectional study. Adv Ther 34(11):2481–2490
27. Rodriguez Alvarez M, Bhamra M, Velayudhan V, Cuascut F, Freeman L, Yien Zhaz S et al. 2019 FRI0687 neuromyelitis spectrum disorders associated with autoimmune diseases: differences in clinical characteristics and mri findings

28. D OD (1998) Physiology of interstitial lung disease. In: Schwarz M, King T Jr (eds) Interstitial lung disease. Marcel Dekker, Hamilton, pp 51–70
29. Scott DL, Wolfe F, Huizinga TW (2010) Rheumatoid arthritis. Lancet. 376(9746):1094–1108
30. Verstappen SM, Lunt M, Luben RN, Chipping J, Marshall T, Khaw KT et al (2013) Demographic and disease-related predictors of abnormal lung function in patients with established inflammatory polyarthritis and a comparison with the general population. Ann Rheum Dis 72(9):1517–1523
31. De Sadeleer LJ, Meert C, Yserbyt J, Slabbynck H, Verschakelen JA, Verbeken EK et al (2018) Diagnostic ability of a dynamic multidisciplinary discussion in interstitial lung diseases: a retrospective observational study of 938 cases. Chest. 153(6):1416–1423
32. Sparks JA, Lin TC, Camargo CA Jr, Barbhaiya M, Tedeschi SK, Costenbader KH, Raby BA, Choi HK, Karlson EW (2018) Rheumatoid arthritis and risk of chronic obstructive pulmonary disease or asthma among women: a marginal structural model analysis in the Nurses' Health Study. Semin Arthritis Rheum 47(5): 639–648
33. Dougados M, Soubrier M, Antunez A, Balint P, Balsa A, Buch MH, Casado G, Detert J, el-zorkany B, Emery P, Hajjaj-Hassouni N, Harigai M, Luo SF, Kurucz R, Maciel G, Mola EM, Montecucco CM, McInnes I, Radner H, Smolen JS, Song YW, Vonkeman HE, Winthrop K, Kay J (2014) Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). Ann Rheum Dis 73(1): 62–68
34. Lai NS, Tsai TY, Koo M, Lu MC (2015) Association of rheumatoid arthritis with allergic diseases: a nationwide population-based cohort study. Allergy Asthma Proc 36(5):99–103
35. Rolfes MC, Juhn YJ, Wi CI, Sheen YH (2017) Asthma and the risk of rheumatoid arthritis: an insight into the heterogeneity and phenotypes of asthma. Tuberc Respir Dis (Seoul) 80(2):113–135
36. Shaw M, Collins BF, Ho LA, Raghu G (2015) Rheumatoid arthritis-associated lung disease. Eur Respir Rev 24(135):1–16
37. Raheel S, Crowson CS, Wright K, Matteson EL (2016) Risk of malignant neoplasm in patients with incident rheumatoid arthritis 1980-2007 in relation to a comparator cohort: a population-based study. Int J Rheumatol 2016:4609486
38. Wang YH, Zhang GH, Zhang LL, Luo JL, Gao L, Zhao MS (2018) Clinical characteristic of 74 cases of malignant tumor in rheumatoid arthritis. Beijing Da Xue Xue Bao 50(6):986–990

Affiliations

Isabel M. McFarlane[1,2] · Su Yien Zhaz[1,3] · Manjeet S. Bhamra[1,2] · Aaliya Burza[1,4] · Srinivas Kolla[1,5] · Milena Rodriguez Alvarez[1,2] · Kristaq Koci[1,2] · Nicholas Taklalsingh[1,2] · Joshy Pathiparampil[1,2] · Latoya Freeman[1,2] · Ian Kaplan[1,2] · Naureen Kabani[1,2] · David J. Ozeri[1,6] · Elsie Watler[1,2] · Mosab Frefer[1,2] · Vytas Vaitkus[1,2] · Keron Matthew[1,2] · Fray Arroyo-Mercado[1,2] · Helen Lyo[1,2] · Tomasz Zrodlowski[1,2] · Aleksander Feoktistov[1,2] · Randolph Sanchez[1,7] · Cristina Sorrento[1,2] · Faisal Soliman[1,8] · Felix Reyes Valdez[1,9] · Veena Dronamraju[1,2] · Michael Trevisonno[1,2] · Christon Grant[1,2] · Guerrier Clerger[1,2] · Khabbab Amin[1,2] · Makeda Dawkins[1,2] · Jason Green[1,2] · Jane Moon[1,2] · Samir Fahmy[1,4] · Stephen Anthony Waite[1,5]

[1] Department of Internal Medicine, Division of Rheumatology, Division of Pulmonary and Critical Care and Division of Radiology, State University of New York Downstate Medical Center and New York City Health & Hospitals Kings County, Brooklyn, NY 11203, USA

[2] Department of Internal Medicine, Division of Rheumatology, SUNY-Downstate Medical Center, Health & Hospitals Kings County, Brooklyn, NY 11201, USA

[3] Samaritan Medical Center Department of Rheumatology, Watertown, NY 13601, USA

[4] Department of Medicine, Division of Pulmonary and Critical Care State, SUNY Downstate Medical Center, Health & Hospitals Kings County, Brooklyn, NY 11201, USA

[5] Department of Radiology, SUNY Downstate Medical Center, Health & Hospitals Kings County, Brooklyn, NY 11201, USA

[6] Sheba Medical Center, 6100000 Tel Aviv, Israel

[7] Department of Rheumatology, Hahnemann Hospital, Philadelphia, PA 19019, USA

[8] Department of Geriatrics, New York Presbyterian Brooklyn Methodist Hospital, Brooklyn, NY 11201, USA

[9] Department of Family and Social Medicine, Montefiore Medical Center Albert Einstein College of Medicine, Bronx, NY 10468, USA