

Pulmonary involvement in rheumatoid arthritis: A cross-sectional study in Iran

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ABSTRACT

Background: Interstitial lung disease (ILD) is a type of pulmonary manifestation in patients with rheumatoid arthritis (RA). Mostly RA-ILD has no symptoms and is only diagnosed by clinical examination, pulmonary function test (PFT), and high-resolution computed tomography (HRCT); hence it seems that the diagnosis of pulmonary involvement in early stages of RA is of great importance. Therefore, we decided to answer this question whether the evaluation of RA patients without pulmonary symptoms using methods such as PFT and HRCT are justifiable and reasonable or not. **Methods:** We conducted a cross-sectional study in a referral rheumatology clinic in Razi hospital of Rasht, Iran. Forty-four consecutive patients, diagnosed with RA, were enrolled. Physical examination of the joints was performed by a rheumatologist. The activity of RA was evaluated in all patients by Disease Activity Score 28. An expert pulmonologist performed the respiratory examination in all participants. Then, all subjects were referred for chest X-ray, PFT, and HRCT of lungs. **Results:** Patients included in this study, 9 (20.45%) males and 35 (79.55%) females, were 21–73 years old and their mean age was 49 ± 13 years. Significant relation between PFT and respiratory complaints was observed ($P = 0.016$). PFT had significant relation with respiratory examinations ($P = 0.009$). Our results indicated a significant relation between disease activity rate and PFT ($P = 0.038$). While HRCT had any significant relation with above items. **Conclusion:** We concluded, using PFT in the respiratory assessment of RA patients can be limited to persons with high disease activity, respiratory complaints, and positive findings in the clinical respiratory examination.

KEY WORDS: High-resolution computed tomography, pulmonary function test, rheumatoid arthritis

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INTRODUCTION

Rheumatoid arthritis (RA) is an inflammatory systemic disease with unknown etiology that is characterized with peripheral symmetric polyarthritis. The prevalence of this disease is about 1% in general population.^[1-3]

Extra-articular manifestations of RA can emerge during the course of the disease and even before the onset of arthritis.^[1]

One of the most important extra-articular manifestations of RA is pulmonary involvement that usually can be seen in patients with a high titer of rheumatoid factor and in smokers.^[4]

Pulmonary involvement in RA patients can be assessed as interstitial pneumonitis and fibrosis, pleural involvement, pulmonary nodule, bronchiolitis obliterans organizing

Access this article online	
Quick Response Code: 	Website: www.lungindia.com
	DOI: 10.4103/0970-2113.173062

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How to cite this article: Zayeni H, Haji-Abbasi A, Foumani SA, Tohidi M, Masooleh IS, Parsa BG, *et al.* Pulmonary involvement in rheumatoid arthritis: A cross-sectional study in Iran. Lung India 2016;33:49-52.

pneumonia, arthritis associated with pulmonary hypertension, and involvements of small and large airways.^[5,6]

Interstitial lung disease (ILD) is another type of pulmonary manifestation in patients with RA that usually has a poor prognosis. Mostly RA-ILD has no symptoms and is only diagnosed by clinical examination, pulmonary function test (PFT), and high-resolution computed tomography (HRCT); so it seems that diagnosis of pulmonary involvement in early stages of RA is of great importance.^[1,4,7-9]

Therefore, we decided to evaluate RA patients in terms of history, clinical examination, chest X-ray (CXR), PFT, and HRCT to ascertain that the evaluation of RA patients without pulmonary symptoms by using the above-mentioned methods is justifiable, reasonable, and cost-effective.

METHODS

We conducted a cross-sectional study in a referral rheumatology clinic in Razi Hospital of Rasht, Iran, during 2011–2012.

In this study, forty-four consecutive patients, diagnosed with RA according to American College of Rheumatology-European League Against Rheumatism classification criteria for RA 2010,^[10] were enrolled. Patients with a history of smoking, known pulmonary diseases, collagen vascular diseases associated with known pulmonary effects and the use of gold, penicillamine, sulfasalazine, methotrexate (MTX) (more than a year), and cytotoxic drugs were excluded from the study.

Demographic and clinical data such as sex, age, occupation, comorbidities, drug history and history of systemic and respiratory symptoms were collected.

A complete physical examination of the joints was performed by an expert rheumatologist in all subjects. The activity of RA was evaluated in all patients by Disease Activity Score 28 (DAS28).^[11]

An expert pulmonologist performed a complete respiratory examination in all participants. Then all subjects were referred for CXR, PFT, and HRCT of lungs.

The Local Ethical Committee approved this study and informed consent for participation in the study was obtained from all subjects.

Statistical analysis

The analysis was performed by *t*-test, Chi-square, and Fisher's exact tests. All statistical analyses were done by SPSS software 17.0 (Kivuto Solutions Inc, Ottawa, ON, CA). A *P* < 0.05 was considered significant.

RESULTS

Patients included in this study, 9 (20.45%) males and 35 (79.55%) females, were 21–73 years old and their mean age was 49 ± 13.

Symptoms and respiratory findings of patients were listed in Table 1.

Of the forty-four RA patients, 41 subjects were in their 1st year of the disease and among them only two individuals (4.5%) had systemic symptoms (including fever and weight loss).

Dyspnea and chest pain were the most common complaints of patients (10 patients [22.7%] and 12 patients [22.3%], respectively), and crackles were the most common finding in the respiratory examination of patients heard in all subjects in the bibasilar areas. Stridor, decreased respiratory sounds, abnormal bronchial sound, and clubbing were not found in these patients.

Table 2 shows HRCT findings and pulmonary function test findings were summarized in Table 3.

Among the 44 participants, nine individuals had no CXR and one person, due to obesity, could not undergo

Table 1: Symptoms and respiratory findings of patients

	n=44 (%)
Symptoms	
Fever	1 (2.3)
Weight loss	2 (4.6)
Dyspnea	10 (22.7)
Dry cough	6 (13.6)
Productive cough	8 (18.2)
Hemoptysis	0
Chest pain	12 (27.3)
Respiratory findings	
Wheezing	2 (4.5)
Crackles	5 (11.4)
Pleural friction rub	1 (2.2)

Table 2: HRCT findings of patients

	n=43 (%)
HRCT findings	
Nodule	7 (16.2)
Fibrosis	19 (44)
Cyst	2 (4.6)
Bronchiectasis	
Localized	6 (13.9)
Generalized	8 (18.6)
Bronchiolectasia	2 (4.6)
Air trapping	12 (28)

HRCT: High-resolution computed tomography

Table 3: Pulmonary function test findings of patients

	n=44 (%)
Pulmonary function test findings	
Normal	21 (47.7)
Air trapping	17 (38.6)
Obstructive	
Mild	1 (2.3)
Moderate	1 (2.3)
Total	2 (4.5)
Restrictive	
Mild	2 (4.5)
Moderate	2 (4.5)
Total	4 (9)

HRCT procedures. Only one of the subjects (2.9%) had abnormal findings in CXR (reticular opacities). The most common findings in patients' HRCTs were fibrosis and bronchiectasis (19 patients [44%] and 14 patients [32.5%], respectively). In addition, air trapping was the most abnormal finding in patients' PFTs.

Of the 23 subjects with respiratory complaints, 15 patients (65.2%) had abnormal HRCTs and 16 patients (69.2%) had abnormal PFTs. On the other, among the participants who did not have respiratory complaints, 15 patients (71.4%) had abnormal HRCTs and 7 patients (33.3%) had abnormal PFTs. These findings showed no significant relation between respiratory complaints and HRCT findings, while the significant relation between PFT and respiratory complaints was observed ($P = 0.659$ and 0.016 , respectively).

All patients with abnormal clinical respiratory examination (seven subjects) had abnormal HRCTs and abnormal PFTs, while among the subjects with normal respiratory examination, 23 patients (62.2%) had abnormal HRCTs and 16 patients (43.2%) had abnormal PFTs. According to these data, there was no significant relation between clinical respiratory examination and HRCT findings, while PFT had significant relation with respiratory examination ($P = 0.578$ and 0.009 , respectively).

We observed that among patients, who had respiratory complaints and abnormal respiratory examination, 19 subjects (70.4%) had abnormal HRCTs and 18 subjects (66.7%) had abnormal PFTs but in subjects who had no respiratory complaints and abnormal respiratory examination, 11 patients (64.7%) had abnormal HRCTs and 5 patients (29.4%) had abnormal PFTs. These findings did not show significant relation between HRCT and total of respiratory complaints and abnormal respiratory examination, while PFT had significant relation with both of these positive findings ($P = 0.694$ and 0.016 , respectively).

The average disease activity of patients, based on DAS28, was 3.84 ± 1.21 . Of the 15 patients with low disease activity (DAS28 < 3.2), 6 patients (40%), among the 23 subjects with moderate disease activity ($3.2 \leq \text{DAS28} \leq 5.1$), and 11 patients (47.8%) and in all patients (6 persons) with high disease activity (DAS28 > 5.1) PFTs were abnormal. These results indicated a significant relation between disease activity rate and PFT ($P = 0.038$).

Moreover, 11 patients (73.3%) in low DAS28, 16 patients (69.6%) in moderate DAS28, and 3 patients (50%) in high DAS28 group had abnormal HRCTs; but these results did not show significant relation between disease activity rate and HRCT ($P = 0.527$).

Gender had no significant relation with respiratory complaints, clinical respiratory examination, HRCT, PFT,

and activity of RA disease ($P = 1.0, 0.619, 1.0, 1.0,$ and 0.689 , respectively).

In addition, this study showed that HRCT findings had significant relation with aging, unlike PFT.

DISCUSSION

Rheumatoid arthritis mostly is seen in the 25-55 year age group. Patients usually experience morning stiffness lasting at least 30 min that often improves gradually after physical activity.^[1] Pulmonary involvement is one of the most important extra-articular manifestations of RA. Results of a prospective study about RA showed that RA-ILD is the second cause of mortality in these patients.^[12] ILD characterized with dry cough and increasing dyspnea with restricting pattern in spirometry. The major risk factor of RA-ILD to be prevented is smoking.^[1,7]

Diagnosis of RA-ILD is based on clinical examination, PFT, and HRCT. Bronchoscopy and broncho-alveolar lavage were used in some past studies for the diagnosis of RA-ILD, but these instruments are usually used to rule out other diffuse pulmonary diseases and are not necessary in the diagnosis of RA-ILD.^[8]

A total number of registered patients in our study were 50 individuals, but six of them withdrew from participation because of personal reasons.

In the present study, female participants were approximately four times more than men, while in past similar studies, the ratio of women to men was about 2-3 to 1.^[13] This difference is likely due to considering smoking as an exclusive criterion for participants in the present study; because in our society, due to cultural issues, smoking is more common in men as compared to women.

Previous studies have shown that pulmonary involvement in RA patients is associated with aging, a higher severity of the disease, higher titers of rheumatoid factor, and male gender.^[5,14-16] In our study, PFT and HRCT findings had no significant differences in two gender groups that may be due to small sample size and elimination of smokers from this study; because smoking is a preventable risk factor for ILD.

DAS28 is a system to determine the disease activity in RA patients that is based on the evaluation of 28 joints and also erythrocyte sedimentation rate or C-reactive protein lab results of patients.^[11] In the recent study, abnormal PFT had significant relation with increasing disease activity (based on DAS28), unlike abnormal HRCT. These results are similar to Al-Tayyar *et al.* study.^[17] Hence, we can conclude that DAS28 can be a predictor factor for abnormal PFT and, with increasing disease activity in RA patients, serial PFTs can be helpful in assessment, and prediction of pulmonary involvement.

In our study, with the increasing frequency and severity of clinical examination findings and respiratory complaints, abnormal PFTs also increased significantly, unlike HRCT findings but in Youssef's study, patients' respiratory complaints had significant relation with both PFT and HRCT findings.^[18] The results of our study support this issue that HRCT, regardless of respiratory symptoms or clinical examination as independent parameters, can have positive findings and in the evaluation of asymptomatic patients, using of HRCT is more rational than PFT.

The most common finding in abnormal HRCTs, in the present study, was bronchiectasis (with the prevalence of 38.6%) that was approximately similar to reported the prevalence in Perez and Cortet studies (30% and 30.5%, respectively).^[19,20]

On the other hand, in recent study, the most common PFT finding was air trapping (with the prevalence of 36.8%) that indicates the involvement of small airways; also the prevalence of air trapping in Perez study was 32%.^[20]

Use of MTX (10–20 mg/week) is associated with the progression of RA-ILD regarding MTX pneumonitis was reported between 1% and 11% in RA patients who were treated with MTX.^[21] Hence, in this study, to eliminate the confounding effect of this drug, we excluded the patients, who used this drug for more than 1 year, while in past similar studies use of MTX was not limited in the subjects.

This study indicates using PFT in respiratory assessment of RA patients may be limited to persons with high grades of disease activity (based on DAS28), respiratory complaint and positive findings in clinical respiratory examination, while the assessment of respiratory involvement in these patients, using HRCT, may be planned regardless of disease activity, respiratory complaint, and clinical respiratory examination.

We warranted further studies with a larger sample size and a control group for comparison with the results of healthy subjects.

Acknowledgments

The authors thank all the colleagues' at the Guilan University of Medical Sciences, Rasht, Iran who were coordinate in this research.

Financial support and sponsorship

Funding is Guilan University of Medical Sciences.

Conflicts of interest

There are no conflicts of interest.

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