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Understanding the determinants of health-related quality of life in rheumatoid arthritis-associated interstitial lung disease

Jake G. Natalini, M.D. [a], Jeff J. Swigris, D.O., M.S. [b], Julie Morisset, M.D. [a], Brett M. Elicker, M.D. [c], Kirk D. Jones, M.D. [d], Aryeh Fischer, M.D. [e], Harold R. Collard, M.D. [a], Joyce S. Lee, M.D. [e, *]

[a] Department of Medicine, University of California, San Francisco, USA
[b] Department of Medicine, National Jewish Health, Denver, CO, USA
[c] Department of Radiology, University of California, San Francisco, USA
[d] Department of Pathology, University of California, San Francisco, USA
[e] Department of Medicine, University of Colorado Denver, USA

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ABSTRACT

Rationale: Health-related quality of life (HRQL) is impaired among patients with interstitial lung disease (ILD). Little is understood about HRQL in specific subtypes of ILD.
Objectives: The aim of this study was to characterize and identify clinical determinants of HRQL among patients with rheumatoid arthritis-associated interstitial lung disease (RA-ILD) and compare them to patients with idiopathic pulmonary fibrosis (IPF).
Methods: We identified patients with a diagnosis of RA-ILD and IPF from an ongoing longitudinal cohort of ILD patients. HRQL was measured at their baseline visit using the Short Form Health Survey (SF-36), versions 1 and 2. Regression models were used to characterize and understand the relationship between selected baseline clinical covariates, the physical component score (PCS) and mental component score (MCS) of the SF-36.
Measurements and main results: RA-ILD patients (n = 50) were more likely to be younger and female compared to IPF patients (n = 50). After controlling for age and pulmonary function, RA-ILD patients had a lower HRQL compared to IPF patients, as measured by the PCS ($P = 0.03$), with significant differences in two of four PCS domains – bodily pain ($P < 0.01$) and general health ($P = 0.01$). Clinical covariates most strongly associated with a lower PCS in RA-ILD patients compared to IPF patients were the presence of joint pain or stiffness and dyspnea severity ($P < 0.01$). Mental and emotional health, as measured by the MCS, was similar between RA-ILD and IPF patients.
Conclusion: The physical components of HRQL appear worse in RA-ILD patients compared to IPF patients as measured by the PCS of the SF-36. Differences in the PCS of the SF-36 can be explained in part by dyspnea severity and joint symptoms among patients with RA-ILD.

1. Introduction

Rheumatoid arthritis (RA) is a systemic inflammatory condition characterized by symmetric arthritis and synovial inflammation that leads to progressive joint erosion and eventual deformity[1]. Extra-articular manifestations of RA are common, affecting up to 40% of patients[2]. Pulmonary involvement in RA can manifest in many ways, including interstitial lung disease (ILD)[3]. Interstitial lung disease occurs in approximately 10% of patients with RA, leading to significant morbidity and mortality[4].

Health-related quality of life (HRQL) is impaired among patients with ILD. In addition to the severity of underlying lung disease, factors such as older age, dyspnea severity, and depression appear to be associated with worse HRQL in ILD[5, 6]. Less is understood about HRQL among specific subtypes of ILD. A recent study demonstrated worse HRQL among patients with chronic

* Corresponding author. 12700 E, 19th Ave., C-272, Aurora, CO 80045, USA.
E-mail address: joyce.lee@ucdenver.edu (J.S. Lee).

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Abbreviation list

DLCO	diffusing capacity for carbon monoxide
FVC	forced vital capacity
HRQL	health-related quality of life
ILD	interstitial lung disease
IPF	idiopathic pulmonary fibrosis
MCS	mental component score
PCS	physical component score
PFT	pulmonary function test
RA	rheumatoid arthritis
RA-ILD	rheumatoid arthritis-associated interstitial lung disease
SF-36	Short Form (36) Health Survey
UCSD SOBQ	University of California, San Diego Shortness of Breath Questionnaire for Lung Health
UCSF	University of California, San Francisco

hypersensitivity pneumonitis compared to patients with idiopathic pulmonary fibrosis (IPF)[7]. The difference in HRQL appeared to be explained, in part, by differences in sex, dyspnea severity, and fatigue.

The focus of this study was to characterize HRQL among patients with RA-ILD compared to patients with IPF and to identify any clinical determinants of HRQL among patients with RA-ILD. We hypothesized that patients with RA-ILD would report worse HRQL compared to patients with IPF, primarily due to the presence of articular manifestations of their disease.

2. Materials and methods

2.1. Study design and patient population

Patients with RA-ILD and an equal number of patients with IPF were identified from an ongoing longitudinal cohort of patients with ILD seen at the University of California, San Francisco (UCSF) from March 2010 to September 2015. The diagnosis of RA-ILD was made prospectively by multidisciplinary discussion. The diagnosis of IPF was made using consensus criteria[8, 9]. Patients with IPF were matched to the RA-ILD patients by date of their initial ILD clinic visit due to a change in administration of the Short Form Healthy Survey (SF-36), from version 2 to version 1 in 2013. The parent study protocol was reviewed and approved by the UCSF Institutional Human Subject Review Committee (10−01592).

Patients were included in this study if they completed the SF-36 HRQL questionnaire at the time of enrollment. Patients were excluded from this study if they did not have pulmonary function tests (PFTs) within six months of completion of the HRQL self-assessment.

A standardized questionnaire was used to collect baseline patient demographic information, patient reported co-morbidities (e.g., sleep apnea, diabetes mellitus), and symptoms (e.g., fatigue, cough, weight loss, heartburn, joint pain or stiffness). Presence or absence (yes/no) of symptoms was determined based on survey responses to questions such as “Do you cough?” and “Do you experience joint pain or stiffness?”. The degree of dyspnea was measured using the University of California, San Diego Shortness of Breath Questionnaire (UCSD SOBQ), a validated numerical dyspnea-scoring tool in which a higher score corresponds to worse dyspnea [10].

2.2. Health-related quality of life measurements

HRQL was measured using the SF-36, versions 1 and 2. The SF-36 is a validated instrument for assessing HRQL and has been applied to a variety of chronic medical conditions, including IPF [7, 11, 12]. The SF-36 is comprised of questions pertinent to eight domains of HRQL: physical functioning, role − physical, bodily pain, general health, vitality, social functioning, role − emotional, and mental health. The weighted averages of the domain scores are used to generate two summary scores: a physical component score (PCS) and a mental component score (MCS). The individual domain scores and summary scores are transformed to fit a norm-based scale on which the 1998 general U.S. population has a mean score of 50 with a standard deviation of 10. Higher scores indicate a better HRQL. Previous studies have confirmed that norm-based scores generated from version 1 are directly comparable to norm-based scores generated from version 2[13].

2.3. Statistical analyses

Comparisons between RA-ILD and IPF patients were performed using an unpaired *t*-test or Chi-squared test. Univariate and multivariate linear regression models were applied to characterize the relationship between select covariates and the PCS and MCS scores. Standardized coefficients were generated to allow comparison between estimates. All multivariate models included age to adjust for potential confounding and percent predicted forced vital capacity (FVC%) to adjust for disease severity. A series of multivariate models were developed to examine the effects of potential covariates on HRQL in RAILD (with the goal of achieving the most parsimonious model that best described the observed data) and to identify potential variables that might explain some or all of the differences in HRQL between ILD subtypes (i.e., RA-ILD and IPF). Covariates were selected based on their performance in the univariate analyses ($P \leq 0.10$). The coefficient of determination (R^2) was used to characterize model performance. All statistical analyses were performed using STATA version 11 (College Station, TX). Statistical significance was defined as a P value of <0.05.

3. Results

3.1. Patient characteristics and clinical symptoms

This study included 50 RA-ILD patients and 50 IPF patients. Compared to IPF patients, RA-ILD patients were more likely to be younger and female (Table 1). Lung function, based on FVC% and percent predicted diffusing capacity for carbon monoxide (DLCO%), and smoking were similar between groups.

RA-ILD patients were more likely than IPF patients to be taking prednisone at the time of HRQL assessment (90% vs. 38%, $P < 0.01$). The presence of joint pain or stiffness was more common in RA-ILD patients (92% vs. 44%, $P < 0.01$). Dyspnea severity, as measured by the USCD SOBQ, and presence of fatigue, cough, and weight loss were similar between patients with RA-ILD and IPF.

3.2. Health-related quality of life

Patients with RA-ILD had more impaired HRQL than IPF patients as measured by the PCS of the SF-36 (31.5 ± 8.7 vs. 36.0 ± 11.4, $P = 0.03$) (Fig. 1). Two out of four domains that contribute to the PCS, bodily pain and general health, were significantly lower in RA-ILD compared to IPF. The overall MCS, including its four contributing domain scores, was similar between RA-ILD and IPF patients (46.7 ± 12.7 vs. 47.6 ± 12.0, $P = 0.72$).