A Comparison of Health-Related Quality of Life in Idiopathic Pulmonary Fibrosis and Chronic Hypersensitivity Pneumonitis

Molly Lubin, MD; Hubert Chen, MD, FCCP; Brett Elicker, MD; Kirk D. Jones, MD; Harold R. Collard, MD, FCCP; and Joyce S. Lee, MD

Background: Patients with interstitial lung disease (ILD) have poor health-related quality of life (HRQL). However, whether HRQL differs among different subtypes of ILD is unclear. The aim of this study was to determine whether HRQL was different among patients with idiopathic pulmonary fibrosis (IPF) and chronic hypersensitivity pneumonitis (CHP).

Methods: We identified patients from an ongoing longitudinal cohort of patients with ILD. HRQL was assessed using the Short Form (SF)-36 medical outcomes form (version 2.0). Regression analysis was used to determine the association between clinical covariates and HRQL, primarily the physical component summary (PCS) and mental component summary (MCS) score. A multivariate regression model was created to identify potential covariates that could help explain the association between the ILD subtype and HRQL.

Results: Patients with IPF ($n = 102$) were older, more likely to be men, and more likely to have smoked. Pulmonary function was similar between the groups. The patients with CHP ($n = 69$) had worse HRQL across all eight domains of the SF-36, as well as the PCS and MCS, compared with patients with IPF ($P < .01$ -.09). This pattern remained after controlling for age and pulmonary function ($P < .01$ -.02). Covariates explaining part of the relationship between disease subtype and PCS score included severity of dyspnea ($P < .01$) and fatigue ($P < .01$). Covariates explaining part of the relationship between disease subtype and MCS score included severity of dyspnea ($P < .01$), female sex ($P = .02$), and fatigue ($P = .02$).

Conclusions: HRQL is worse in CHP compared with IPF. HRQL differences between ILD subtypes are explained in part by differences in sex, dyspnea, and fatigue.

CHEST 2014; 145(6):1333–1338

Abbreviations: CHP = chronic hypersensitivity pneumonitis; DLCO = diffusing capacity of the lung for carbon monoxide; HRQL = health-related quality of life; ILD = interstitial lung disease; IPF = idiopathic pulmonary fibrosis; MCS = mental component summary; PCS = physical component summary; SF = Short Form; UCSD-SOBQ = University of California, San Diego Shortness of Breath Questionnaire

The interstitial lung diseases (ILDs) are a heterogeneous group of conditions characterized by varying degrees of pulmonary fibrosis and inflammation. This pathology leads to impairments in pulmonary physiology that affect day-to-day functioning. We know from prior research that patients with ILD tend to have decreased health-related quality of life (HRQL) as compared with population norms.^{1,2} According to common definitions of HRQL, this suggests that their life is marked by decline in physical, social, emotional, and cognitive functioning as a result of their illness.^{3,4}

Although many of the ILDs, such as sarcoidosis and connective tissue disease ILDs, are associated with

extrapulmonary manifestations that may impact HRQL, idiopathic pulmonary fibrosis (IPF) and chronic hypersensitivity pneumonitis (CHP) predominantly affect only the lung. IPF is a progressive, debilitating condition of the aging population with a median survival of 3 years and for which there exists no approved therapy in the United States.⁵ Hypersensitivity pneumonitis is characterized by exposure to an inhaled antigen that leads to inflammation and, in chronic cases, progresses to fibrosis.^{6,7} Although the conditions differ in their underlying pathophysiology, patient demographics, time course, and prognosis, both diseases lead to pulmonary impairment with debilitating effects on daily functioning and HRQL.

Studies have shown that degree of pulmonary impairment is not the only significant driver of poor HRQL in patients with ILD but that other factors, such as dyspnea, depression, and age, matter.^{8,9} Whether differences in HRQL exist among different subtypes of ILD is not well understood. Given the phenotypic differences between IPF and CHP (including age and presence of comorbidities such as depression¹⁰) as well as the lack of treatment available and overall worse prognosis in IPF compared with CHP, we hypothesized that patients with IPF would report worse HRQL compared with patients with CHP. The aim of this study was to determine whether HRQL was different among patients with IPF and CHP and, if present, to identify potential reasons for this difference.

MATERIALS AND METHODS

Study Design and Patient Population

Patients with IPF and CHP were identified from an ongoing longitudinal cohort of patients with ILD seen at the University of California, San Francisco from January 2010 to August 2012. During this time period, only 2% of patients who were eligible for inclusion into the ILD cohort chose to decline. Informed consent was obtained on all patients. The University of California San Francisco Committee on Human Research approved the protocol (10-01592).

Patients with IPF or CHP who had completed an HRQL self-assessment were eligible for our study; no patients were excluded based on this criterion. Patients were excluded if they did not have pulmonary function test data from within 6 months of completing the self-assessment; three patients were excluded based on this criterion. All patients with IPF were diagnosed according to consensus criteria.¹¹ CHP cases were diagnosed by multidisciplinary conference. All hypersensitivity pneumonitis cases were chronic as defined by persistent interstitial changes (reticulation and traction bronchiectasis) on imaging and persistent symptoms (dyspnea or cough). In CHP cases that did not have a surgical lung biopsy, a characteristic high-resolution CT scan¹² and an exposure were required.

Demographic information, pulmonary function test results, and prednisone use at the time of HRQL self-assessment were obtained from the medical record. All other information was obtained from written, patient-administered questionnaires that were completed at the time of the self-assessment. Cough, fatigue, daytime sleepiness, weight loss, and pain were reported by patients

as present or absent. Patients also reported whether they experienced pain at four specific sites (hand/wrist, shoulder, knee, foot/ankle). Patients self-classified as never or ever smokers.

Degree of dyspnea was measured with the University of California San Diego Shortness of Breath Questionnaire (UCSD-SOBQ), which provides a numerical dyspnea score. A higher score indicates greater dyspnea.¹³

HRQL Measurements

HRQL information was obtained from the Short Form (SF)-36 medical outcomes short form (version 2.0), which is a generic instrument for assessing HRQL that has been applied to multiple chronic medical conditions. This instrument has been shown to be a sensitive tool for assessing quality of life and has demonstrated ability to capture changes in clinical status.^{14,15} The SF-36 is made up of questions pertaining to eight domains of quality of life: Physical Functioning, Role-Physical, Bodily Pain, General Health, Emotional Functioning, Role-Emotional, Vitality, and Mental Health. Completion of the form generates scores for the eight individual domains as well as a physical component summary (PCS) score (composed of the domains of Physical Functioning, Role-Physical, General Health, and Bodily Pain) and a mental component summary (MCS) score (composed of the domains of Mental Health, Role-Emotional, Social Functioning, and Vitality). The score for each domain is generated from a set of questions that are weighted equally to provide a total numerical score that can range from zero to 100. The weighted average of the domain scores provides the summary scores, which are transformed to fit a norm-based scale on which the general US population has a mean score of 50 with an SD of 10. Higher scores indicate better quality of life.

Statistical Analyses

Summary data are reported as mean (SD), median (interquartile range), or percentage, unless otherwise stated. Between-group comparisons were performed using an unpaired *t* test or χ^2 test, as appropriate. Univariate and multivariate linear regression models were used to examine the relationship between selected covariates and the PCS (primary outcome variable) and the MCS (secondary outcome variable). All multivariate models were adjusted for age to account for potential confounding and FVC % predicted to account for pulmonary disease severity. Clinical covariates were identified as potential variables that might explain some or all of the association between ILD subtype and HRQL (eg, presence of pain, dyspnea severity) (Fig 1). We tested a series of models to examine the individual effects of potential covariates on the relationship between ILD subtype and HRQL (ie, PCS and MCS). Covariates tested in the multivariate model were selected based on their *P* value on univariate analysis (*P* value cutoff $\leq .01$). Model performance was compared using the model *R*², the coefficient of determination. The model *R*² describes how well the observed data are described by the model (eg, a perfect model would have an *R*² of 1.0). Different models were compared to understand the effect of different covariates, with the goal of achieving the most parsimonious model that best describes the observed data. As a sensitivity analysis, a backward selection model was also used. All statistical analyses were performed using STATA version 11 (StataCorp LP). Significance was defined as a *P* value of $< .05$.

RESULTS

Patient Characteristics and Clinical Symptoms

We analyzed a total of 171 patients with ILD. Of these, 102 had IPF, and 69 had CHP. Patients with

Manuscript received August 22, 2013; revision accepted December 19, 2013; originally published Online First January 23, 2014.

Affiliations: From the Department of Medicine (Drs Lubin, Collard, and Lee), the Department of Radiology (Dr Elicker), and the Department of Pathology (Dr Jones), University of California, San Francisco, San Francisco, CA; and Genentech (Dr Chen), South San Francisco, CA.

Funding/Support: This publication was supported by the National Center for Advancing Translational Science, National Institutes of Health [UCSF-CTI KL2TR000143].

Correspondence to: Joyce S. Lee, MD, 505 Parnassus Ave M1093, Box 0111, San Francisco, CA 94143; e-mail: joyce.lee@ucsf.edu

© 2014 American College of Chest Physicians. Reproduction of this article is prohibited without written permission from the American College of Chest Physicians. See online for more details. DOI: 10.1378/chest.13-1984

FIGURE 1. This figure demonstrates the suspected relationship between ILD subtype and HRQL. Some of this relationship may be explained by the potential covariates identified in the figure. ILD = interstitial lung disease; HRQL = health-related quality of life.

IPF were older, more likely to be men, and more likely to be ever smokers (Table 1). Patients with CHP were more likely to be taking prednisone at the time of HRQL assessment. Lung function, as measured by FVC % predicted and diffusing capacity of the lung for carbon monoxide (DLCO) % predicted, was similar between both groups.

Patients with CHP more commonly reported pain than patients with IPF (58% vs 42%, $P = .05$). The proportion of patients with CHP reporting fatigue was also greater than that for IPF (87% vs 60%, $P < .01$). Patients with CHP reported a higher severity of dyspnea compared with patients with IPF on the UCSD-SOBQ.

Table 1—Baseline Demographic and Clinical Characteristics of Patients With IPF and CHP

Variable	IPF (n = 102)	CHP (n = 69)	P Value
Age, y	70 ± 8	64 ± 12	< .01
Female sex	26 (25)	51 (74)	< .01
Ever smoker	71 (70)	30 (43)	< .01
FVC % predicted	70 ± 18	65 ± 16	.08
DLCO % predicted	50 ± 17	48 ± 15	.34
Prednisone use at baseline	19 (19)	26 (38)	< .01
Cough	85 (83)	64 (93)	.07
Any pain	43 (42)	40 (58)	.05
Hand/wrist pain	15 (15)	21 (30)	.01
Shoulder pain	12 (12)	19 (28)	< .01
Knee pain	19 (19)	28 (41)	< .01
Foot/ankle pain	19 (19)	23 (33)	.03
Fatigue	61 (60)	60 (87)	< .01
Weight loss	34 (33)	28 (41)	.33
Daytime sleepiness	51 (50)	39 (57)	.4
UCSD-SOBQ score ^a	40.8 ± 26.6	55.8 ± 26.6	< .01

Data are expressed as No. (%) for categorical variables and mean ± SD for continuous variables. CHP = chronic hypersensitivity pneumonitis; DLCO = diffusing capacity of the lung for carbon monoxide; IPF = idiopathic pulmonary fibrosis; UCSD-SOBQ = University of California San Diego Shortness of Breath Questionnaire.¹³

^aHigher score indicates worse dyspnea.

Health-Related Quality of Life

Patients with CHP had lower scores (ie, worse HRQL measurements) across all eight domains of the SF-36 as well as on the PCS (mean, 32.6 ± 10.2 vs 39.2 ± 10.6 ; $P < .01$) and MCS (mean, 43.8 ± 14.2 vs 49.1 ± 11.6 ; $P < .01$) (Fig 2). These differences were statistically significant on all measures except for the Role-Emotional domain, which assesses the inability to carry out necessary activities because of emotional problems ($P = .09$).

The Relationship Between ILD Subtype and PCS

ILD subtype was associated with the PCS in unadjusted analysis (standardized coefficient, 0.30; $P < .01$). In addition to ILD subtype, several covariates were associated with the PCS in unadjusted analyses (Table 2). Younger age, female sex, worse pulmonary function, the severity of dyspnea, and the presence of pain, fatigue, cough, or daytime sleepiness were significantly associated with worse PCS scores. Prednisone use was not associated with PCS ($P = .36$). After adjustment for age and pulmonary function, the ILD subtype remained independently associated with the PCS ($P < .01$) (Table 3).

The covariates most strongly associated with PCS included presence of pain (standardized coefficient = -0.43 , $P < .01$), severity of dyspnea (standardized coefficient = -0.67 , $P < .01$), presence of fatigue (standardized coefficient = -0.44 , $P < .01$), and presence of daytime sleepiness (standardized coefficient = -0.25 , $P < .01$). A prediction model including the covariates of severity of dyspnea and fatigue, in addition to ILD subtype, age, and FVC % predicted, explained 50% of the observed variance in physical health status, as indicated by the model R^2 (model 5, Table 3). Pain was not included in the final model given the incorporation of the Bodily Pain domain in the computation of the PCS, and daytime sleepiness was not included in the final model given its collinearity with fatigue ($P < .01$). Last, the addition of sex to this model provided no additional explanatory power, and, thus, it was not included in the model. ILD subtype was not a significant predictor in the final model, and when ILD subtype was removed from model 5, the model R^2 remained unchanged (model 6, Table 3). Backward selection modeling yielded similar results (data not shown).

The Relationship Between ILD Subtype and MCS

ILD subtype was associated with the MCS in unadjusted analysis (standardized coefficient = 0.10, $P = .01$). In addition to ILD subtype, several covariates were associated with the MCS in unadjusted analyses (e-Table 1). Female sex, severity of dyspnea, and the

FIGURE 2. Bar graph compares Short Form-36 HRQL scores in idiopathic pulmonary fibrosis (dark gray) and chronic hypersensitivity pneumonitis (light gray). Higher scores indicate better quality of life. * $P = .02$, ** $P < .01$. See Figure 1 legend for expansion of abbreviation.

presence of fatigue or daytime sleepiness were significantly associated with worse MCS scores. Prednisone use was not associated with MCS ($P = .76$). After adjustment for age and pulmonary function, ILD subtype remained independently associated with the MCS ($P = .02$) (e-Table 2).

The covariates most strongly associated with MCS included female sex (standardized coefficient = -0.34 , $P < .01$), severity of dyspnea (standardized coefficient = -0.43 , $P < .01$), presence of fatigue (standardized coefficient = -0.11 , $P < .01$), and presence of daytime sleepiness (standardized coefficient = -0.29 , $P < .01$). A prediction model including the covariates of presence of fatigue and severity of dyspnea, in addition to

ILD subtype, age, lung function, and female sex, explained 33% of the observed variance in MCS, as indicated by the model R^2 (model 6, e-Table 2). The addition of daytime sleepiness to this model provided no additional explanatory power, and, thus, it was not included in the final model. ILD subtype was not a significant predictor in the final model, and when ILD subtype was removed from the final model, the model R^2 was unchanged (model 7, e-Table 2). Backward selection modeling yielded similar results with the exception of including presence of pain ($P = .02$) as a covariate (data not shown).

DISCUSSION

This study demonstrates that level of HRQL impairment, as assessed by PCS and MCS scores, is different between two subtypes of ILD, IPF and CHP, and is independent of age and pulmonary disease severity. Key covariates partly explaining the association between ILD subtype and PCS are dyspnea and fatigue; key covariates between ILD subtype and MCS are dyspnea, female sex, and fatigue.

We hypothesize that the worse quality of life seen in CHP is largely due to these key covariates and not underlying pulmonary disease subtype or severity. In support of this hypothesis, removal of pulmonary disease subtype in the multivariate models for PCS and MCS did not alter the model performance (as

Table 2—Unadjusted Associations Between Clinical Covariates and the Physical Component Score

Variable	Standardized Coefficient (SE)	P Value
Age	0.20 (0.08)	.01
Female sex	−0.19 (1.70)	.01
FVC % predicted	0.38 (0.05)	<.01
DLCO % predicted	0.25 (0.05)	<.01
UCSD-SOBQ score ^a	−0.67 (0.02)	<.01
Any pain	−0.43 (1.37)	<.01
Fatigue	−0.44 (1.70)	<.01
Cough	−0.19 (2.57)	.02
Daytime sleepiness	−0.25 (1.67)	<.01
Weight loss	−0.15 (1.78)	.06
Prednisone use	0.07 (0.10)	.36

See Table 1 legend for expansion of abbreviations.

^aHigher score indicates worse dyspnea.

Table 3—Relationship Between ILD Subtype and the Physical Component Score: Multivariate Analysis

Model	Diagnosis of IPF vs CHP	Age	FVC, % Predicted	Female Sex	UCSD-SOBQ	Fatigue
Model 1 $R^2 = 0.21$	0.22 (<.01)	0.08 (.28)	0.34 (<.01)	...	...	...
Model 2 $R^2 = 0.22$	0.15 (.07)	0.09 (.24)	0.35 (<.01)	−0.13 (.12)	...	...
Model 3 $R^2 = 0.47$	0.13 (.05)	0.01 (.84)	0.14 (.04)	...	−0.57 (<.01)	...
Model 4 $R^2 = 0.32$	0.13 (.08)	0.05 (.50)	0.31 (<.01)	...	...	−0.34 (<.01)
Model 5 $R^2 = 0.50$	0.10 (.15)	0.00 (.96)	0.14 (.03)	...	−0.50 (<.01)	−0.18 (.01)
Model 6 $R^2 = 0.49$	...	0.02 (.72)	0.15 (.02)	...	−0.51 (<.01)	−0.20 (.01)

Data are presented as standardized β coefficients (P value). ILD = interstitial lung disease. See Table 1 legend for expansion of other abbreviations.

measured by the model R^2), indicating that the observed variance is accounted for by the other covariates. Notably, however, only 50% of the observed variance in physical health status was explained by our models. This further suggests that the determinants of HRQL in ILD are complex and that other, unmeasured factors influence HRQL in ILD.

Our findings build on previous work in ILD by demonstrating that increased dyspnea correlates strongly with increased impairment in HRQL. In this study, dyspnea was one of the strongest determinants of HRQL (both PCS and MCS), as reflected by its standardized coefficient on univariate analysis. Notably, the severity of dyspnea has a stronger association with poor HRQL than does the severity of pulmonary impairment.^{8,9} Some studies have shown that degree of dyspnea in ILD increases with decreasing pulmonary function,^{2,14} but it is unclear what additional factors make dyspnea more severe in some patients than in others. Dyspnea has been strongly associated with depression score and functional status and moderately associated with pulmonary function.¹⁰ In this study, dyspnea was found to be more severe in CHP than in IPF. This difference was not explained by available measures of pulmonary disease severity (FVC and DLCO). There are likely additional physiologic, psychologic, both factors that contribute to a greater sensation of dyspnea and worse HRQL in patients with CHP, and understanding these more clearly could improve quality of life for this patient population.

This study also demonstrated the impact of pain on HRQL in ILD. We found that 58% of patients with CHP and 42% of patients with IPF reported pain in their joints and extremities and that this was a major determinant of the PCS score. The cause of the pain experienced in our ILD cohort is unclear; we did not have detailed data on pain. Bajwah et al¹⁶ reported that among 45 patients with ILD in their last year of life, 29% experienced chest pain and an additional 9% experienced generalized pain. Ryerson et al¹⁰ also found that pain was strongly correlated with depression in an ILD cohort of 52 patients.

Worse HRQL in patients with CHP compared with IPF was unexpected and contrary to our initial hypo-

thesis. The existing literature does not provide an explanation for this finding. A potential explanation could be age. Patients with CHP were younger than the patients with IPF, and younger age was found to be associated with worse quality of life. Although age was adjusted for in the multivariate analysis, statistical adjustment may not fully account for the influence of age on HRQL. The COPD literature has demonstrated that depression, anxiety, and HRQL tend to be worse among younger patients.^{17–19} Younger patients with a severe disease may perceive themselves as more sick, symptomatic, or disabled in relation to their same-age peers than do older patients, for whom it is more common to experience functional limitations, shortness of breath, fatigue, and other symptoms. Another potential confounder could be female sex. The CHP cohort had more women than the IPF cohort, and female sex was an independent predictor of low MCS score. This finding is similar to that of several studies showing that depression and anxiety are more common among women with COPD than men with COPD.^{20,21}

Since CHP is linked to environmental exposures, there may be socioeconomic differences between exposed and unexposed populations. Socioeconomic disparity between the two groups could have contributed to differing access to health care as well as differing rates of physical and mental comorbidities. Indeed, studies in patients with asthma have demonstrated that environmental exposures in the home or neighborhood can mediate the relationship between socioeconomic status and HRQL.²² We did not have reliable socioeconomic and comorbidity data and were unable to include this in our analysis. Although prednisone use at baseline was different between patients with IPF and patients with CHP, prednisone use was not associated with HRQL as measured by the PCS and MCS. We did not have information on duration of ILD diagnosis, response to treatment, or use of other immunomodulatory drugs (eg, azathioprine, mycophenolate mofetil) in this cohort, which could all impact HRQL. Last, all patients were drawn from a tertiary referral center, and, thus, these findings may have less generalizability to the general population of patients with ILD.

In summary, HRQL is measurably worse in patients with CHP than in patients with IPF, primarily because of increased symptoms of dyspnea and fatigue in the CHP cohort. Our data suggest that management of patients with IPF and CHP should include not only assessment and treatment of the biologic disease but also aggressive management of dyspnea and fatigue, as targeting these covariates may aid in further ameliorating the impact of ILD on HRQL. Further research is needed to better understand the discrepancy in HRQL between patients with IPF and CHP.

ACKNOWLEDGMENTS

Author contributions: Dr Lee takes responsibility for the content of the manuscript, including the data and analysis.

Dr Lubin: contributed to conception and design; data acquisition, analysis, and interpretation; revision of the manuscript for important intellectual content; and final approval of the version to be published.

Dr Chen: contributed to analysis and interpretation of the data, revision of the manuscript for important intellectual content, and final approval of the version to be published.

Dr Elicker: contributed to the acquisition of the data, revision of the manuscript for important intellectual content, and final approval of the version to be published.

Dr Jones: contributed to the acquisition of the data, revision of the manuscript for important intellectual content, and final approval of the version to be published.

Dr Collard: contributed to conception and design; data acquisition, analysis, and interpretation; revision of the manuscript for important intellectual content; and final approval of the version to be published.

Dr Lee: contributed to conception and design; data acquisition, analysis, and interpretation; revision of the manuscript for important intellectual content; and final approval of the version to be published.

Financial/nonfinancial disclosures: The authors have reported to CHEST the following conflicts of interest: Dr Chen is employed by Genentech. Drs Lubin, Elicker, Jones, Collard, and Lee have reported that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

Role of sponsors: The sponsors had no role in the design of the study, the collection and analysis of the data, or the preparation of the manuscript.

Additional information: The e-Tables can be found in the "Supplemental Materials" area of the online article.

REFERENCES

- De Vries J, Drent M. Quality of life and health status in interstitial lung diseases. *Curr Opin Pulm Med*. 2006;12(5):354-358.
- Chang JA, Curtis JR, Patrick DL, Raghu G. Assessment of health-related quality of life in patients with interstitial lung disease. *Chest*. 1999;116(5):1175-1182.
- Ware JE Jr. Conceptualization and measurement of health-related quality of life: comments on an evolving field. *Arch Phys Med Rehabil*. 2003;84(4 suppl 2):S43-S51.
- Edgell ET, Coons SJ, Carter WB, et al. A review of health-related quality-of-life measures used in end-stage renal disease. *Clin Ther*. 1996;18(5):887-938.
- Raghu G, Collard HR, Egan JJ, et al; ATS/ERS/JRS/ALAT Committee on Idiopathic Pulmonary Fibrosis. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med*. 2011;183(6):788-824.
- Ohshimo S, Bonella F, Guzman J, Costabel U. Hypersensitivity pneumonitis. *Immunol Allergy Clin North Am*. 2012;32(4):537-556.
- Costabel U, Bonella F, Guzman J. Chronic hypersensitivity pneumonitis. *Clin Chest Med*. 2012;33(1):151-163.
- Swigris JJ, Kuschner WG, Jacobs SS, Wilson SR, Gould MK. Health-related quality of life in patients with idiopathic pulmonary fibrosis: a systematic review. *Thorax*. 2005;60(7):588-594.
- Coelho AC, Knorst MM, Gazzana MB, Barreto SS. Predictors of physical and mental health-related quality of life in patients with interstitial lung disease: a multifactorial analysis. *J Bras Pneumol*. 2010;36(5):562-570.
- Ryerson CJ, Berkeley J, Carrieri-Kohlman VL, Pantilat SZ, Landefeld CS, Collard HR. Depression and functional status are strongly associated with dyspnea in interstitial lung disease. *Chest*. 2011;139(3):609-616.
- American Thoracic Society. Idiopathic pulmonary fibrosis: diagnosis and treatment. International consensus statement. American Thoracic Society (ATS), and the European Respiratory Society (ERS). *Am J Respir Crit Care Med*. 2000;161(2 pt 1):646-664.
- Lynch DA, Newell JD, Logan PM, King TE Jr, Müller NL, Can CT distinguish hypersensitivity pneumonitis from idiopathic pulmonary fibrosis? *AJR Am J Roentgenol*. 1995;165(4):807-811.
- Eakin EG, Resnikoff PM, Prewitt LM, Ries AL, Kaplan RM. Validation of a new dyspnea measure: the UCSD Shortness of Breath Questionnaire. University of California, San Diego. *Chest*. 1998;113(3):619-624.
- Tzanakis N, Samiou M, Lambiri I, Antoniou K, Siafakas N, Bouros D. Evaluation of health-related quality-of-life and dyspnea scales in patients with idiopathic pulmonary fibrosis. Correlation with pulmonary function tests. *Eur J Intern Med*. 2005;16(2):105-112.
- Swigris JJ, Brown KK, Behr J, et al. The SF-36 and SGRQ: validity and first look at minimum important differences in IPF. *Respir Med*. 2010;104(2):296-304.
- Bajwah S, Higginson IJ, Ross JR, et al. Specialist palliative care is more than drugs: a retrospective study of ILD patients. *Lung*. 2012;190(2):215-220.
- Mangueira NM, Viega IL, Mangueira Mde A, Pinheiro AN, Costa Mdo R. Correlation between clinical parameters and health-related quality of life in women with COPD. *J Bras Pneumol*. 2009;35(3):248-255.
- Lou P, Zhu Y, Chen P, et al. Prevalence and correlations with depression, anxiety, and other features in outpatients with chronic obstructive pulmonary disease in China: a cross-sectional case control study. *BMC Pulm Med*. 2012;12:53.
- Cleland JA, Lee AJ, Hall S. Associations of depression and anxiety with gender, age, health-related quality of life and symptoms in primary care COPD patients. *Fam Pract*. 2007;24(3):217-223.
- Naberman K, Azpeitia A, Cantoni J, Miravittles M. Impairment of quality of life in women with chronic obstructive pulmonary disease. *Respir Med*. 2012;106(3):367-373.
- Di Marco F, Verga M, Reggente M, et al. Anxiety and depression in COPD patients: the roles of gender and disease severity. *Respir Med*. 2006;100(10):1767-1774.
- Trupin L, Katz PP, Balmes JR, et al. Mediators of the socioeconomic gradient in outcomes of adult asthma and rhinitis. *Am J Public Health*. 2013;103(2):e31-e38.