Can We Predict the Survival of Idiopathic Pulmonary Fibrosis Patients? Sleep Must Be Re-appreciated

Commentary on Kolilekas et al. Sleep oxygen desaturation predicts survival in idiopathic pulmonary fibrosis. *J Clin Sleep Med* 2013;9:593-601

Paschalis Steiropoulos, M.D., Ph.D.

Sleep Unit, Department of Pneumology, Medical School, Democritus University of Thrace, Greece

Idiopathic pulmonary fibrosis (IPF) is a specific form of chronic, progressive, fibrosing interstitial pneumonia of unknown cause, occurring in adults and confined to the lungs. Clinical trials of potential treatments have failed to affect the progression of disease or the survival of patients with IPF, despite substantial advances in immunomodulatory and antifibrotic therapies.^{1,2}

Interestingly, the clinical course of IPF is variable, with some patients deteriorating rapidly and others remaining in a relatively stable condition. The prognosis of IPF is poor with a median survival of 2 to 3 years from the time of diagnosis¹⁻³ and is equivalent to that of many forms of cancer. This shortened survival has been associated with several factors such as: older age at presentation, extensive cigarette smoking, lower body mass index (BMI), more severe physiologic impairment, greater radiologic extent of disease, and the development of other complications or conditions, e.g., pulmonary hypertension, emphysema, pulmonary embolism, and bronchogenic cancer.^{1,4}

In this issue of *Journal of Clinical Sleep Medicine*, Kolilekas et al.⁵ have prospectively examined the impact of several parameters of sleep disordered breathing on survival of 31 consecutive treatment naive patients with IPF. The authors have highlighted that sleep in IPF is a stressful hypoxemic “practice” even more intense to that of maximal exercise, as assessed by cardiopulmonary exercise test. Sleep oxygen desaturation was linked to the severity of the underlying lung damage and the coexistence of obstructive sleep apnea (OSA).

In agreement with previous reports,⁶⁻⁸ prevalence of OSA is high in IPF patients and has atypical characteristics, such as the lack of association between BMI and AHI and the reported tiredness or fatigue instead of daytime sleepiness. This high prevalence of OSA can be attributed to other factors, such as the reduction of lung volume in IPF patients, which increases pharyngeal collapsibility and airway resistance. Indeed, lung volume dependence seems to be more pronounced in OSA patients.⁹

What is more important about this study is that it proposes novel markers for predicting survival in IPF patients, which are easily obtained with a polysomnographic study. Repeated desaturations and extended periods of low saturation during sleep may contribute to the pathological and pathophysiological changes in the pulmonary tissue, negatively affecting patients’ prognosis through aggravation of pulmonary arterial hypertension. Awareness of these parameters in patients with IPF can

potentially help in discriminating those with a lower life expectancy. Accurate risk prediction is essential both for the patient and the attending physician. The patient needs to know the disease prognosis in order to plan his/her remaining time, while the physician has to estimate the right time to propose the appropriate therapeutic intervention. Finally, risk stratification in IPF might be helpful for the design of clinical trials, where the outcome of therapeutic interventions in patients with good or poor prognosis could be compared.

The real value of this study, though, is that it raises an important question: Could the amelioration of oxygen desaturation with CPAP in IPF patients with concomitant OSA have a survival benefit, especially under the spectrum of the absence of an effective treatment for IPF? Indeed, CPAP treatment has been effective in ameliorating systemic inflammatory markers and markers of tissue hypoxia in OSA patients¹⁰ and in improving quality of life in IPF patients with OSA¹¹ despite therapeutic difficulties or poor compliance.¹²

This study, despite its limitations, makes an important contribution to literature by identifying, for the first time, sleep parameters as predictors of survival in IPF. Future studies are necessary in order to confirm and possibly to expand these results by demonstrating which of the sleep parameters can reliably add predictive value to current prediction models for survival. Additional work through randomized controlled trials is also required to shed light to this important question: can CPAP treatment delay lung fibrosis or prolong survival in IPF patients with OSA?

CITATION

Steiropoulos P. Can we predict the survival of idiopathic pulmonary fibrosis patients? Sleep must be re-appreciated. *J Clin Sleep Med* 2013;9(6):603-604.

REFERENCES

1. Raghu G, Collard HR, Egan JJ, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med* 2011;183:788-824.
2. King TE Jr, Pardo A, Selman M. Idiopathic pulmonary fibrosis. *Lancet* 2011;378:1949-61.
3. Hernandez G, Fernandez R, Lopez-Reina P, et al. Incidence, prevalence, and clinical course of idiopathic pulmonary fibrosis: a population-based study. *Chest* 2010;137:129-37.

4. Ley B, Collard HR, King TE Jr. Clinical course and prediction of survival in idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med* 2011;183:431-40.
5. Kolilekas L, Manali E, Vlami K, et al. Sleep oxygen desaturation predicts survival in idiopathic pulmonary fibrosis. *J Clin Sleep Med* 2013;9:593-601.
6. Mermigkis C, Chapman J, Golish J, et al. Sleep-related breathing disorders in patients with idiopathic pulmonary fibrosis. *Lung* 2007;185:173-8.
7. Lancaster LH, Mason WR, Pamell JA, et al. Obstructive sleep apnea is common in idiopathic pulmonary fibrosis. *Chest* 2009;136:772-8.
8. Mermigkis C, Stagaki E, Tryfon S, et al. How common is sleep-disordered breathing in patients with idiopathic pulmonary fibrosis? *Sleep Breath* 2010;14:387-90.
9. Onal E, Leech JA, Lopata M. Relationship between pulmonary function and sleep-induced respiratory abnormalities. *Chest* 1985;87:437-41.
10. Steiropoulos P, Kotsianidis I, Nena E, et al. Long-term effect of continuous positive airway pressure therapy on inflammation markers of patients with obstructive sleep apnea syndrome. *Sleep* 2009;32:537-43.
11. Mermigkis C, Bouloukaki I, Antoniou KM, et al. CPAP therapy in patients with idiopathic pulmonary fibrosis and obstructive sleep apnea: does it offer a better quality of life and sleep? *Sleep Breath* 2013 Feb 6. [Epub ahead of print]
12. Mermigkis C, Mermigkis D, Varouchakis G, Schiza S. CPAP treatment in patients with idiopathic pulmonary fibrosis and obstructive sleep apnea--therapeutic difficulties and dilemmas. *Sleep Breath* 2012;16:1-3.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication March, 2013

Accepted for publication March, 2013

Address correspondence to: Paschalis Steiropoulos, M.D., Ph.D., Sleep Unit, Department of Pneumology, Medical School, Democritus University of Thrace, 68100 Alexandroupolis, Greece; Tel: +302551075333; Fax: +302551076106; E-mail: pstirop@med.duth.gr

DISCLOSURE STATEMENT

The author has indicated no financial conflicts of interest.