[Original Research]

CHEST

Air Pollution Exposure Is Associated With Lower Lung Function, but Not Changes in Lung Function, in Patients With Idiopathic Pulmonary Fibrosis

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BACKGROUND: Air pollution exposure is associated with acute exacerbation, disease progression, and mortality in patients with idiopathic pulmonary fibrosis (IPF). The objective of this study was to describe the impact of air pollution exposures on disease severity, as well as changes in lung function, in patients with IPF.

METHODS: Using home spirometers and symptom diaries, 25 patients with IPF prospectively recorded FVC weekly for up to 40 weeks. Residential addresses were geocoded to estimate weekly mean air pollution exposures for ground-level ozone (O_3), nitrogen dioxide (NO_2), and particulate matter < 2.5 or 10 μm in aerodynamic diameter ($PM_{2.5}$ and PM_{10}, respectively). The dependence of weekly clinical measurements on preceding levels of each pollutant was assessed with the use of linear mixed models, yielding beta-coefficients with 95% CIs, using varying lag times.

RESULTS: Lower mean FVC % predicted was consistently associated with increased mean exposures to PM_{10} in the 2 to 5 weeks preceding clinical measurements (range, –0.46 to –0.39 [95% CI, –0.73 to –0.13]; $P < .005$). Lower mean FVC % predicted over the study period was inversely related to mean levels of NO_2 (–0.45 [95% CI, –0.85 to –0.05]; $P = .03$), $PM_{2.5}$ (–0.45 [95% CI, –0.84 to –0.07]; $P = .02$), and PM_{10} (–0.57 [95% CI, –0.92 to –0.21]; $P = .003$), averaged over the study. Weekly changes in FVC and changes over 40 weeks were independent of pollution exposures.

CONCLUSIONS: Higher air pollution exposures were associated with lower lung function, but not changes in lung function, in patients with IPF. Further studies are needed to characterize the mechanisms underlying this relationship. CHEST 2018; ■(■):■-■

KEY WORDS: epidemiology (pulmonary); interstitial lung disease; mobile health

ABBREVIATIONS: IPF = idiopathic pulmonary fibrosis; NO_2 = nitrogen dioxide; O_3 = ozone; $PM_{2.5}$ = particulate matter < 2.5 μm in aerodynamic diameter; PM_{10} = particulate matter < 10 μm in aerodynamic diameter; UCSD-SOBQ = University of California San Diego Shortness of Breath Questionnaire; VAS = visual analog scale

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Idiopathic pulmonary fibrosis (IPF) is a progressive parenchymal lung disease of complex etiology.[1] FVC and subjective symptom assessments such as dyspnea scores are commonly used to characterize disease severity or progression in patients with IPF. Although these outcomes are typically measured intermittently at intervals of 3 to 6 months, recent data suggest that more frequent longitudinal assessments may improve the precision of change estimates over time.[2] Repeated monitoring is feasible and informative in patients with IPF, using hand-held spirometers to measure FVC and self-administered questionnaires to measure dyspnea.[2,3] Short-term changes in symptoms do not seem to be associated with short-term changes in lung function, and it is unknown what factors affect the short-term variability of FVC in these patients.

Air pollution is a ubiquitous exposure and a well-established risk factor for adverse health outcomes, including all-cause and respiratory mortality.[4-8] Short-term increases in air pollution exposures are associated with subsequent increases in exacerbations and hospitalizations in patients with asthma or COPD,[9-12] as well as an increased risk of bronchiolitis obliterans in patients following a lung transplant.[13] Air pollution exposure has been proposed as a risk factor for the development of interstitial lung disease, with plausible biologic mechanisms.[14] Ozone (O_3) and nitrogen dioxide (NO_2) are associated with an increased risk of acute exacerbation of IPF, whereas mortality risk increases with greater exposures to particulate matter < 2.5 or 10 μm in aerodynamic diameter ($PM_{2.5}$ and PM_{10}, respectively).[15,16] Recent data further suggest that higher exposures to PM_{10} are associated with more rapid decline in lung function in patients with IPF.[17] The effect of air pollution exposures on disease severity and on short-term changes in lung function and dyspnea in patients with IPF is unknown.

The objective of the present study was to define the relationship between air pollution exposure, lung function, and dyspnea in patients with IPF by using weekly home spirometry and self-administered questionnaires. We further examined the relationship between air pollution exposure and changes in lung function and dyspnea over time. Some of these results have previously been presented in abstract form.[18]

Patients and Methods

Study Population

Patients were prospectively recruited from the longitudinal interstitial lung disease program at the University of California San Francisco between January and September 2014. Eligibility criteria included a diagnosis of IPF (according to current consensus guidelines),[1] residence in the state of California, and no concomitant participation in a blinded drug treatment trial of IPF therapy. Each patient's most recent high-resolution CT scan of the chest was reviewed by an investigator (K. A. J.) to ensure that the extent of emphysema was $< 10\%$, although the scans were not formally scored by a chest radiologist. The local institutional review board approved this study, and all patients provided written informed consent (University of California San Francisco Human Research Protection Program Committee on Human Research; institutional review board no. 13-11433).

Measurements

Patients were enrolled in a longitudinal prospective cohort for up to 40 weeks. At the baseline visit, each patient's age, sex, smoking history, and complete residential address were recorded. An office-based spirometry meeting American Thoracic Society/European Respiratory Society standards[19] was performed at baseline, measuring absolute values and the percent predicted of FVC.

Home Monitoring

Each patient was provided a personalized hand-held spirometer that met American Thoracic Society/European Respiratory Society performance standards (Spiro PD version 1.0; PMD Healthcare) and received one-on-one instruction in its use. Hand-held spirometry was performed weekly for up to 40 weeks. The spirometer provided real-time feedback to the patient to support proper spirometric technique and to optimize compliance. Three maneuvers were performed at each weekly assessment, with the highest values recorded for FEV_1 and FVC. The device was not blinded, and patients were able to see their recorded values.

Prior to spirometry, patients also completed two weekly questionnaires to measure dyspnea severity, for up to 40 weeks: the University of California San Diego Shortness of Breath Questionnaire (UCSD-SOBQ)[20] and a 10-point visual analog scale (VAS) (e-Fig 1). Permission was obtained for use of the UCSD-SOBQ in this study. Patients recorded a weekly diary documenting the estimated duration of time spent away from home over the previous week. Weekly measurements were omitted if the patient indicated that he or she was away from home for > 72 h that week. Upon study completion, patients returned their diaries and symptom scores and had their home spirometry data uploaded from the device.

Air Pollution Exposures

Air quality data were obtained from the California Air Resources Board for individual patients based on their geocoded residential address. The Air Resources Board is a branch of the California Environmental Protection Agency, providing quality-controlled air quality data from across the state. Data were collected for O_3, NO_2, $PM_{2.5}$, and PM_{10}. Pollutant concentrations were calculated at the following levels, in order of decreasing preference: A = from nearest air monitoring site; B = from the county average; C = from the air basin average; or D = no near site, county, or air basin average, depending on data availability. Mean levels of each pollutant were determined for the week prior to any recorded lung function or dyspnea measure. All exposure levels were adjusted for temperature and humidity. Weekly levels for each pollutant were compared vs the US Environmental Protection Agency's national ambient air quality standards.[21]