CHEST

Interstitial Lung Disease in the Elderly

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BACKGROUND: Despite the relationship between idiopathic pulmonary fibrosis (IPF) and advancing age, little is known about the epidemiology of interstitial lung disease (ILD) in the elderly. We describe the diagnoses, clinical characteristics, and outcomes of patients who were elderly at the time of ILD diagnosis.

METHODS: Among subjects from a prospective cohort study of ILD, elderly was defined as age ≥ 70 years. Diagnoses were derived from a multidisciplinary review. Differences between elderly and nonelderly groups were determined using the χ^2 test and analysis of variance.

RESULTS: Of the 327 subjects enrolled, 80 (24%) were elderly. The majority of elderly subjects were white men. The most common diagnoses were unclassifiable ILD (45%), IPF (34%), connective tissue disease (CTD)-ILD (11%), and hypersensitivity pneumonitis (8%). Most elderly subjects (74%) with unclassifiable ILD had an imaging pattern inconsistent with usual interstitial pneumonia (UIP). There were no significant differences in pulmonary function or 3-year mortality between nonelderly and elderly subjects combined or in a subgroup analysis of those with IPF.

CONCLUSIONS: Although IPF was the single most common diagnosis, the majority of elderly subjects had non-IPF ILD. Our findings highlight the need for every patient with new-onset ILD, regardless of age, to be surveyed for exposures and findings of CTD. Unclassifiable ILD was common among the elderly, but for most, the radiographic pattern was inconsistent with UIP. Although the effect of ILD may be more pronounced in the elderly due to reduced global functionality, ILD was not more severe or aggressive in this group.

CHEST 2017; 151(4):838-844

KEY WORDS: aging; elderly; idiopathic pulmonary fibrosis; interstitial lung disease

ABBREVIATIONS: CTD = connective tissue disease; CTD-ILD = connective tissue disease interstitial lung disease; ILD = interstitial lung disease; IPF = idiopathic pulmonary fibrosis; PFT = pulmonary function testing; UIP = usual interstitial pneumonia

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FUNDING/SUPPORT: The authors have reported to *CHEST* that no funding was received for this study.

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DOI: http://dx.doi.org/10.1016/j.chest.2016.11.003

Interstitial lung disease (ILD) encompasses a spectrum of diffuse fibrotic and inflammatory parenchymal injuries. Idiopathic pulmonary fibrosis (IPF) is the ILD most closely related to aging: onset before age 50 years is rare, and the incidence of IPF increases with age.[1] Further, IPF is associated with telomerase mutations, indicating that it may be related to premature aging.[2,3] However, beyond the association of IPF and aging, the epidemiology of other forms of ILD in the elderly is not known.

Currently in the United States, 14% of the population is 65 years or older, and at age 65 years the average life expectancy is 19.3 years.[4] With the population aging, ILD in the elderly is increasingly encountered in clinical practice. In addition, age-related considerations have implications for ILD care. Compared with younger patients, the risks of surgical lung biopsy and immunosuppression are higher for elderly patients.[5-7] Age may also have an impact on survival in ILD. In a large IPF cohort, older age at disease presentation was associated with decreased survival.[8] However, it is not known if ILD is more aggressive at the extremes of age or if age-related comorbidities contribute to poor outcomes. In this prospective study of ILD, we sought to define the diagnoses, clinical characteristics, and outcomes of patients who were elderly at the time of ILD presentation.

Methods

This study was approved by the Institutional Review Board of the University of Pennsylvania (protocol No. 817689) and is compliant with the Health Insurance Portability and Accountability Act. Between 2012 and 2016, patients seen at a tertiary ILD clinic associated with a university-based hospital in the mid-Atlantic United States were serially recruited for study participation and enrolled by informed consent. This is a referral center for a second opinion or consideration of lung transplantation, and many patients had had their disease for years before the first clinic visit. Age of ILD onset was therefore defined as the age at which chest imaging first demonstrated ILD, even if onset was before the first visit to our clinic. Although a universally accepted definition for elderly is lacking, age $\geq$ 65 years is generally considered elderly.[9,10] We used a more conservative age cutoff of 70 years to define elderly for our study. Subjects between 18 and 69 years comprised our nonelderly cohort.

Testing

Chest CT imaging obtained near the time of the first clinic visit was reviewed by a thoracic radiology expert in ILD who was blinded to clinical details. Surgical lung biopsy specimens, explanted lungs, and autopsy samples were reviewed by a pulmonary pathologist with expertise in ILD. Pulmonary function testing (PFT) and a 6-min walk test performed near the time of CT imaging were interpreted according to established criteria.[11] When available, results from yearly follow-up PFT and walking tests were also recorded. A decline in lung function was defined as a 10% or greater decrease in the FVC or a 15% or greater decrease in the diffusing capacity of lung for carbon monoxide (DLCO) in 1 year. Hypoxemia was defined by the need for supplemental oxygen or a saturation $<$ 90% on room air, or both. Study termination outcomes included death or lung transplantation.

Clinical Review

All subjects underwent a detailed history taking and physical examination, with an emphasis on features discriminating between causes of ILD. Diagnoses of ILD were established by a multidisciplinary consensus review including at least two pulmonologists who were expert in ILD, a thoracic radiologist, and a pulmonary pathologist.[12] IPF was diagnosed according to American Thoracic Society/European Respiratory Society/Japanese Respiratory Society/Latin American Thoracic Association criteria.[13] Hypersensitivity pneumonitis was most often established by supportive histopathologic findings in the setting of consistent clinical features. For subjects unable to undergo lung biopsy, a suggestive clinical presentation with an exposure history and imaging features typical for hypersensitivity pneumonitis established the diagnosis. Sarcoidosis was diagnosed according to American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and Other Granulomatous Disorders criteria, and only subjects with interstitial disease were included in our ILD cohort.[14] A clinical diagnosis of connective tissue disease (CTD), with consistent imaging or histopathologic findings of CTD-ILD estabished this diagnosis. In accordance with society statements on the diagnosis of idiopathic interstitial pneumonias and IPF, unclassifiable ILD was subtyped into categories of (1) inadequate data, (2) discordant data, and (3) possible usual interstitial pneumonia (UIP), with radiographic features suggestive of UIP but lacking honeycombing and without a biopsy procedure for further assessment.[13,15] ILD due to chronic aspiration was diagnosed by imaging findings of lower lobe bronchiolitis, with documented tracheal aspiration on a barium swallow study and without an alternative diagnosis to better account for ILD.

Statistical Analysis

Study data were collected and managed using Research Electronic Data Capture electronic data capture tools hosted at the University of Pennsylvania.[16] Comparisons between groups were made using a χ^2 test for categorical data and a one-way analysis of variance for continuous data. For all tests, $P < .05$ determined significance. Data analysis was performed using Stata software, version 13.1 (StataCorp LP).

Results

Demographics

Of the 327 subjects enrolled, 80 (24%) were elderly. Nearly all elderly subjects were white (94%), and most were men (68%) (Table 1). The nonelderly group was significantly more diverse. Surgical lung biopsy procedures were uncommon (9%) among the elderly.