The Effects of Pleural Plaques on Longitudinal Lung Function in Vermiculite Miners of Libby, Montana

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ABSTRACT

Background: This study was conducted to assess associations of pleural plaques (PP) and longitudinal lung function in vermiculite miners of Libby, Montana who are occupationally exposed to asbestos. High-resolution computed tomography (HRCT) was used to identify asbestos-related findings in former Libby vermiculite miners. We investigated annual lung function decline in miners with PP only and compared them to miners with normal HRCT findings.

Materials and Methods: HRCTs from 128 miners were categorized into the following 4 diagnostic groups: (1) normal computed tomography scan ($n = 9$); (2) PP only ($n = 72$); (3) PP and interstitial fibrosis ($n = 26$) and (4) additional HRCT abnormalities ($n = 21$) such as rounded atelectasis, diffuse pleural thickening, pleural effusions or pulmonary nodules or tumor >1 cm in diameter. Random intercept and slope linear mixed-effect regression models identified differences in lung function decline between miners with asbestos-associated outcomes and those with normal HRCT. Models were adjusted for follow-up time, body mass index, smoking status, latent exposure period and employment years. Interactions for smoking status with age and smoking status with pleural plaque severity were examined.

Results: Miners with PP only did not have an accelerated decline in lung function between 40 and 80 years. Miners with PP and additional HRCT abnormalities displayed significantly accelerated declines in forced expiratory volume in 1 second and diffusing capacity of the lungs for carbon monoxide ($P = 0.05$ and $P < 0.01$, respectively). Plaque severity did not affect lung function decline. However, smokers with extensive plaques displayed accelerated loss in diffusing capacity of the lungs for carbon monoxide and forced expiratory volume in 1 second when compared to nonsmoking miners with mild plaque formation.

Conclusions: PP alone did not significantly affect lung function decline in vermiculite miners of Libby, Montana.

Key Indexing Terms: Pleural plaques; Asbestos; Libby miners; Longitudinal lung function; High-resolution computed tomography and pleural plaques. **[Am J Med Sci 2017;353(6):533–542.]**

INTRODUCTION

Pleural plaques (PP) are the most common noncancerous finding in workers exposed to asbestos.[1] PP are sharply circumscribed, rounded, smooth white nodules composed of bands of interwoven collagen. They normally occur along the posterior parietal pleura but can also be distributed along the surfaces of the diaphragm and pericardium.[2] Single plaques may be present, but bilateral plaques are more common.[1,3,4] PP may enlarge and become calcified over time. A 20-year latent period usually exists between the time of first asbestos exposure and PP development.[1] However, a recent retrospective review observed that vermiculite miners from Libby, Montana displayed subtle pleural abnormalities within a shorter latency period (mean = 8.6 years; range: 1.4-14.7 years).[5]

PP are usually detected incidentally through chest radiography, conventional computed tomography (CT) or high-resolution computed tomography (HRCT).[3] Chest radiographies may display high diagnostic sensitivity for the detection of PP (~96%), but positive predictive value is low (56-79%), as subpleural fat deposits are commonly misinterpreted as PP.[6] HRCT provides both high sensitivity and positive predictive value (96% and 100%, respectively).[6] Therefore, HRCT is most useful for eliminating false-positive diagnoses of PP, such as those caused by subpleural fat deposits.[6]

In 2004, an American Thoracic Society (ATS) document recognized PP as definitive markers of asbestos exposure, but concluded that they were not associated with significant loss in lung function.[1] The document noted that some studies reported an approximately 5% reduction in forced vital capacity (FVC) or mildly diminished diffusion capacity among individuals with PP, but that most individuals maintained well preserved lung function. Furthermore, the document stated that recent longitudinal studies did not observe accelerated decline in those with PP only.[1] Nevertheless, the effects of PP on lung function remain controversial. Two recently published systematic reviews arrived at opposite conclusions regarding the effects of PP on lung function.[7,8] Both agreed that well-designed studies using longitudinal data were superior to cross-sectional studies. However, only 3 HRCT-based longitudinal studies were included in the systematic reviews.[9-11]

Here, we perform a retrospective longitudinal analysis from serial pulmonary function test (PFT) records of miners who were occupationally exposed to Libby amphibole asbestos (LAA). The vermiculite mine was located 6 miles northeast of Libby, Montana. Libby is a town of approximately 2,600 people, located 40 miles south of the Canadian border and 20 miles east of the Idaho panhandle. In 1963, W.R. Grace & Company purchased the mine. The vermiculite was found to be contaminated with LAA, and in 1990 the mine was closed. LAA is composed of winchite (80%), richterite (12%), tremolite (6%) and other asbestiform minerals (2%).[12] In 2014, we published a cross-sectional analysis from this cohort. In it, we found no significant differences in mean lung function for miners with PP only when compared to miners with normal HRCT.[13]

For the current analysis, our primary goal is to investigate longitudinal lung function decline among LAA-exposed miners with PP only, when compared to miners with LAA exposure but normal HRCT scans. We also investigated longitudinal decline based on severity of plaque formation. Preliminary results of this study have been previously reported as a conference abstract.[14]

METHODS

Study Population

All miner medical records were de-identified prior to investigation. The University of South Carolina Institutional Review Board approved the study protocol (ID#:Pro00020158) prior to medical record examination.

Analysis was conducted from a convenience sample of former Libby vermiculite miners who applied or were enrolled in the Libby Medical Program (LMP) between April 2000 and September 2012. This program was established for W.R. Grace & Company employees, their household contacts, and residents of Libby, with identified asbestos-related abnormalities. We examined the medical records from miners who were occupationally exposed to LAA, and thus, had higher exposure than those with household or environmental exposures.[15,16]

Inclusion Criteria

To be included in this analysis, miners underwent 1 HRCT scan that had been peer reviewed by a board-certified university-based thoracic radiologist. At least 2 serial PFTs inclusive of spirometry, lung volumes via plethysmography, and carbon monoxide lung diffusion capacity (DLCO) were also needed. A minimal 3-year follow-up was required between each miners' first and last PFT. Furthermore, at least 1 PFT needed to be performed within 3 years of the HRCT.

HRCT Peer Review

The LMP received 2 independent readings of the HRCTs that were done locally in Libby. When disagreement occurred between the readers, the HRCT scans were sent for independent peer review to resolve the differences.

HRCT Classification

HRCT results were used for miner group assignment. Miners were assigned to 1 of the following 4 groups: normal CT scan (NCTS), pleural plaques only (PPO), pleural plaques and interstitial fibrosis (PPIF) or other CT abnormalities (OCTA). The OCTA group contained miners with rounded atelectasis, diffuse pleural thickening, pleural effusions, or pulmonary nodules or tumors >1 cm in diameter. Diffuse pleural thickening was considered to be distinctly different from PP and defined as homogenous pleural thickening extending along the lateral chest wall over multiple rib interspaces and included "blunting" of the corresponding costophrenic angle.[17]

For PPO miners, the severity of PP was divided into the following 3 categories: (1) mild (single, unilateral or sparsely distributed plaques), (2) moderate (bilateral plaques) and (3) extensive (bilateral, calcified and widely distributed plaques).

Pulmonary Function

PFTs were performed between January 1988 and September 2012, in accordance with the American Thoracic Society (ATS)/European Respiratory Society guidelines.[18-20] Outcome variables examined were as follows: FVC (FVC percent predicted), forced expiratory volume in 1 second (FEV_1 percent predicted), total lung capacity (TLC percent predicted) and DLCO (DLCO percent predicted). Percent predicted values were determined using ATS suggested or validated reference equations.[21-25]

Statistical Analysis

Repeated measures regression analysis was performed to determine intercept and slope differences between HRCT groups using random intercept and slope linear mixed models (LMM).[26,27] PPO, PPIF and OCTA miner groups were compared to NCTS miners. Age was nested within each miner group for slope analyses and centered at 40 years. Inferences were made based on the estimated slope between 40 and 80 years. Fixed effects considered were smoking status at the time of initial follow-up (heavy $\geq$15 pack-years; mild $<$15 pack-years and never smoker), body mass index (BMI), time since first occupational asbestos exposure to HRCT (years) and years of employment. For the PPO group, we also performed a random coefficients analysis to identify plaque severity association with decline in lung function. We considered statistical significance to be at $\alpha \leq 0.05$ for fixed effects and $\alpha \leq 0.10$ for interaction terms. Manuscript statistical procedures and results were also independently, professionally reviewed before submission (Analysis Factor,