ORIGINAL ARTICLE

Associations between radiographic findings and spirometry in a community exposed to Libby amphibole

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ABSTRACT

Background Among asbestos-exposed individuals, abnormal spirometry is usually associated with parenchymal abnormalities or diffuse pleural thickening. Localised pleural thickening (LPT), the most common abnormality associated with asbestos exposure, is typically thought to be a marker of exposure with little clinical consequence. Our objective was to determine if abnormal spirometry is associated with LPT independent of other abnormalities, using data from community-based screening conducted in Libby, Montana.

Methods Subjects were a subset of screening participants comprising persons with interpretable spirometry and chest radiograph results (n=6475). Chest radiographs were independently evaluated by two or three B readers, and participants were classified by mutually exclusive categories of spirometry outcome: normal, restriction, obstruction or mixed defect.

Results Restrictive spirometry was strongly associated with parenchymal abnormalities (OR 2.9; 95% CI 1.4 to 6.0) and diffuse pleural thickening (OR 4.1; 95% CI 2.1 to 7.8). Controlling for the presence of these abnormalities as well as age, smoking status and other covariates, restrictive spirometry was also associated with LPT (OR 1.4; 95% CI 1.1 to 1.8). The risk of restrictive spirometric findings correlated with the severity of LPT.

Conclusions In this large community-based screening cohort, restrictive spirometry is significantly associated with LPT, indicating that this abnormality may result in lung function impairment. Physicians treating patients exposed to Libby amphibole should be aware that LPT may have functional consequences.

What this paper adds

- In this study of a large community-based cohort with widespread amphibole exposure, we found a statistically significant association between radiographic LPT and restrictive spirometry.
- Among subjects with restrictive spirometry, the odds of functional impairment increased with extent of LPT.
- Physicians treating patients exposed to Libby amphibole should be aware that LPT may have functional consequences.

INTRODUCTION

Pleural fibrosis is the most common outcome associated with inhalation of asbestos.[1] Nevertheless, greater attention is typically devoted to other asbestos-related diseases associated with respiratory impairment and disability: lung cancer, mesothelioma and asbestosis. While asbestosis can cause severe respiratory impairment, pleural fibrosis has traditionally been viewed only as a marker of asbestos exposure with little effect on lung function. This is less true when one considers the type of pleural fibrosis; localised pleural thickening (LPT) is generally regarded as an innocuous lesion, while diffuse pleural thickening (DPT) has been associated with pulmonary function deficits.[2–4]

Libby, Montana, was the site of a vermiculite mining and processing operation 1925–1990. Libby vermiculite contains amphibole fibres that have been characterised as, in decreasing order of abundance, winchite, richterite, tremolite and actinolite,[5–7] Reports of respiratory disease prompted the Agency for Toxic Substances and Disease Registry to initiate a community screening programme there in 2000. Consisting of a health survey, spirometry testing and chest radiograph, the screening programme's purpose was to identify asbestos-related abnormalities among Libby residents. The results from screening showed a high prevalence (18%) of pleural abnormalities detected independently by two or three B readers.[8] There was evidence of pervasive non-occupational amphibole exposure in Libby; self-reports of environmental risk factors were predictive of asbestos-related radiographic abnormalities.[8]

In this study, we examined screening data collected by the Agency for Toxic Substances and Disease Registry to see if radiographic abnormalities are predictive of pulmonary abnormalities and impairment as indicated by spirometry. Our primary goal was to see if LPT is associated with functional impairment independent of parenchymal abnormalities and DPT. Given this association, a secondary goal was to see if the risk of abnormal spirometry is correlated with LPT extent.

METHODS

Informed consent was obtained from all participants (n=7307) under a protocol approved by the Institutional Review Board of the Centers for

Disease Control and Prevention. Eligibility criteria and a description of the questionnaire used are described elsewhere.[8]

Posterior–anterior chest radiographs were offered to adult participants who were not pregnant and were collected following National Institute for Occupational Safety and Health guidelines.[9] Two B readers independently evaluated each radiograph using the 1980 International Labour Office (ILO) Classification.[10] When they disagreed about the presence of pneumoconiosis, a third reader was used. The Agency for Toxic Substances and Disease Registry used the same three readers throughout the screening programme. We defined the following radiographic abnormalities dichotomously:

- Parenchymal abnormalities, detected by at least two readers with profusion ≥1/0
- Pleural calcification, detected in the same hemithorax by ≥2 readers
- DPT, DPT and costophrenic angle obliteration detected in the same hemithorax by ≥2 readers
- LPT, circumscribed pleural plaque on chest wall and/or diaphragmatic pleural thickening detected in the same hemithorax by ≥2 readers, with DPT not detected.

Spirometry was offered to all participants. Testing followed American Thoracic Society guidelines[11] and was performed by a qualified technician using a Jaeger Masterscope spirometer (CareFusion, San Diego, California, USA). Patient effort categories were based on institutional guidelines, and test result quality was evaluated using American Thoracic Society guidelines.[11] Results with patient effort rated 'acceptable' or 'suboptimal' were retained, while those rated as 'questionable' or 'uninterpretable' were excluded. Patients with acceptable effort had three acceptable manoeuvres, of which two were reproducible, while patients with suboptimal effort had one or two acceptable manoeuvres and did not always meet reproducibility criteria. Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1) and FEV_1/FVC ratio were recorded. Predicted values based on the lower limit of normal (LLN) were calculated using published reference equations.[12] Participants' pulmonary function was classified into mutually exclusive categories: normal (FEV_1/FVC ≥ LLN and FVC ≥ LLN), obstructive (FEV_1/FVC < LLN and FVC ≥ LLN), restrictive (FEV_1/FVC > LLN and FVC < LLN) and mixed (FEV_1/FVC < LLN and FVC < LLN).[13]

SAS V.9[14] was used for all statistical analysis. To examine reader agreement, we calculated unweighted and weighted κ statistics[15] using SAS PROC FREQ. We used logistic regression to investigate the association between abnormal spirometry and radiographic abnormalities. A model was fitted for each spirometric outcome, with the outcome (ie, normal, obstructive, restrictive or mixed spirometry) serving as the dependent variable. The odds of having each type of abnormal spirometry was estimated using subjects with normal spirometry as the reference, factoring the categorical covariates shown in table 1: sex, age, smoking history, body mass index (BMI), exposure group

Table 1 Distribution (n (row %)) of selected characteristics of participants by spirometry outcome

	Total	Normal	Restrictive	Obstructive	Mixed
All	6476	5004 (77)	693 (11)	564 (9)	215 (3)
Male	3187	2373 (75)	381 (12)	319 (10)	114 (4)
Female	3289	2631 (80)	312 (9)	245 (7)	101 (3)
Age (years)					
18–39	1679	1462 (87)	65 (4)	143 (9)	9 (1)
40–59	3124	2441 (78)	352 (11)	251 (8)	80 (3)
60+	1673	1101 (66)	276 (17)	170 (10)	126 (8)
Cigarette smoking					
Never	3001	2602 (87)	235 (8)	152 (5)	12 (<1)
Ever	3474	2401 (69)	458 (13)	412 (12)	203 (6)
BMI (kg/m^2)					
Under weight (<18.5)	60	33 (55)	7 (12)	9 (15)	11 (18)
Healthy (18.5 to <25)	1824	1436 (79)	106 (6)	215 (12)	67 (4)
Over weight (25 to <30)	2400	1914 (80)	197 (8)	212 (9)	77 (3)
Obese (30 to <40)	1922	1443 (75)	308 (16)	120 (6)	51 (3)
Morbidly obese (≥40)	270	178 (66)	75 (28)	8 (3)	9 (3)
Exposure group*					
Occupational	2536	1864 (74)	316 (12)	263 (10)	93 (4)
Household contact	832	639 (77)	96 (12)	76 (9)	21 (3)
Resident	3023	2437 (81)	272 (9)	218 (7)	96 (3)
Length of residence in Libby (years)					
0–13	1465	1139 (78)	157 (11)	112 (8)	57 (4)
14–21	1606	1326 (83)	120 (7)	126 (8)	34 (2)
22–33	1703	1328 (78)	170 (10)	156 (9)	50 (3)
≥34	1660	1180 (71)	241 (15)	166 (10)	73 (4)
Number of pathways†					
None apparent	139	109 (78)	15 (11)	12 (9)	3 (2)
1–3	1799	1433 (80)	164 (9)	134 (7)	68 (4)
4–5	1701	1329 (78)	181 (11)	145 (9)	46 (3)
≥6	2837	2133 (75)	333 (12)	273 (10)	98 (3)
SOB‡	2423	1564 (65)	422 (17)	254 (10)	183 (8)

*Occupational: occupational exposure to vermiculite or asbestos; household contact: household contact of a Libby vermiculite worker; resident: Libby residents with neither occupational exposure to vermiculite/asbestos nor household contact exposure to a Libby vermiculite worker.
†Number of community exposure pathways for vermiculite.
‡Self-reported shortness of breath.

(occupational, household contact or residential), length of residence in Libby, number of non-occupational exposure pathways and self-reported shortness of breath. All models controlled for the presence of parenchymal abnormalities. Regression models were evaluated using likelihood ratio tests and fit statistics such as the Hosmer–Lemshow goodness-of-fit test.

Again using logistic regression, we then modelled the odds of restriction and obstruction by the degree of extent and width of radiographic pleural thickening. Using ILO classification results, a separate index for degree of LPT and DPT for each participant was calculated using a method described by Bourbeau *et al*[2] (with a possible range of 0–24). The average index score from two or three readers was then categorised as 'none' (index=0), 'modest' (index <median score, 2.5, for all participants with LPT or 3.0 for those with DPT) or 'high' (index ≥2.5 for LPT or ≥3.0 for DPT).

We also fit a generalised logit model estimating the risk of severity of functional impairment predicted among participants with restrictive spirometry and a high degree of LPT. Severity of functional impairment was defined as: mild, per cent predicted (PP) FEV_1 >70%; moderate, PP FEV_1 50%–69%; and severe, PP FEV_1 <50%.[13]

Finally, to see if excess abnormal spirometry occurred among participants, we compared their results to national data from the Third National Health and Nutrition Examination Survey (NHANES III) using indirect standardisation for age, race, BMI and smoking status. We used NHANES III sampling weights to derive the expected prevalence of abnormal spirometry and calculated 95% CIs assuming that observed data had a Poisson distribution.[16]

RESULTS

A subset of all participants (n=6476) had both interpretable spirometry and chest radiographs. Of 831 persons excluded from this analysis, 599 had no radiograph due to being a minor with the remaining adults excluded for various reasons: 64 had missing interpretability of spirometry, 145 had uninterpretable spirometry and 23 had no radiograph. Table 1 shows the distribution of subject characteristics by spirometry outcome. The majority had normal spirometry (n=5003, 77%); 693 (11%) were categorised with restrictive abnormality, 564 (9%) with obstructive and 215 (3%) with mixed. The prevalence of restrictive and mixed spirometry increased with age, while that of obstruction ranged 8%–10% for all age categories. Excluding underweight participants, the prevalence of restriction increased while that of obstruction decreased with increasing BMI. Current or former smokers had a higher prevalence of abnormal spirometry compared with non-smokers (87% vs 69%). There were no strong trends between prevalence of abnormal spirometry with surrogates of amphibole exposure (ie, exposure category, residence duration in Libby and number of exposure pathways).[8] Radiographs of 5355 participants were reviewed by two and 1118 by three B readers. Expressed as proportions of the total number of readings (n=14 064), in 9345 (66%) readings, radiograph quality was rated good, 4509 (32%) acceptable without technical defect, 81 (<1%) acceptable with technical defect and image quality was missing for 129 (1%). When two readers (readers 'A' and 'B') were used, agreement beyond chance was good for both the presence of parenchymal and any pleural abnormalities (κ=0.70 and 0.71, respectively). Agreement was fair when the initial readers' results were compared with the third reader (reader 'C') for parenchymal (A vs C κ=0.40; B vs C κ=0.31) and pleural abnormalities (A vs C κ=0.38; B vs C κ=0.30).

Of 50 participants with parenchymal abnormalities, the majority had abnormal spirometry with restriction being most common (n=16, 32%), followed by mixed (n=8, 16%) and obstruction (n=5, 10%). Of 771 participants with pleural calcification, DPT or LPT detected by two or more readers, 483 (63%) had normal spirometry. With reader agreement on the involved hemithorax, among all subjects, 254 (4%) had pleural calcification, 58 (1%) had DPT and 708 (11%) had LPT. Among participants with pleural calcification, restriction was the most common abnormality (n=62; 24%), followed by obstruction (n=23; 9%) and mixed (n=22; 9%). Among participants with DPT, restriction was also most common (n=26; 45%), followed by mixed (n=8; 14%) and obstruction (n=5; 9%). Forty-nine had unilateral DPT; among those with bilateral DPT, six had a mixed and four had a restrictive defect. The majority (n=463; 65%) of participants with LPT had normal spirometry; restriction was the most common abnormality (n=146; 21%), followed by obstruction (n=57; 8%) and mixed (n=42; 6%).

Table 2 shows the influence of radiographic abnormalities on spirometry, controlling for covariates. Despite being rare, parenchymal abnormalities were significantly predictive of restrictive and mixed spirometry. When models were fitted for individual categories of pleural abnormalities, DPT had the strongest association with restrictive spirometry despite DPT being nearly as rare as parenchymal abnormalities. Pleural calcification was also significantly associated with restrictive impairment. LPT had the weakest association with restriction but was statistically significant.

Table 3 shows the association between restriction/obstruction and the degree of DPT and LPT. The odds of restriction increased monotonically with the degree of both DPT and LPT width and extent. This increase was marked for restriction when the severity of DPT was greater than the median severity (OR 5.6;

Table 2 Odds of abnormal spirometry by radiographic abnormality and covariates* (ORs (95% CI), row %)

Model	Restriction	Obstruction	Mixed
Parenchymal abnormalities (profusion ≥1/0; n=50)†	**2.9 (1.4 to 6.0), 32**	1.1 (0.4 to 2.9), 10	**2.7 (1.1 to 7.4), 4**
Pleural calcification in the same hemithorax (n=254)†	**1.7 (1.2 to 2.4), 24**	0.8 (0.5 to 1.3), 9	1.4 (0.8 to 2.5), 9
Diffuse pleural thickening (n=58)†	**4.1 (2.1 to 7.8), 45**	1.1 (0.4 to 3.2), 9	2.3 (0.9 to 5.9), 14
Localised pleural thickening (n=708)‡	**1.4 (1.1 to 1.8), 21**	0.8 (0.5 to 1.0), 8	1.1 (0.7 to 1.7), 6

Statistically significant associations are in bold.
*All models control for parenchymal abnormality, age, sex, smoking history, body mass index, exposure group, number of exposure pathways, duration of residence in Libby and shortness of breath. The mixed defect logistic models use collapsed age group definitions to avoid zero cells. Models include interaction terms when appropriate.
†As seen by at least two B readers.
‡As seen by at least two B readers. Defined as circumscribed plaque on the chest wall and/or diaphragm in the same hemithorax with diffuse pleural thickening not detected.

Table 3 Odds of restrictive and obstructive spirometry by degree of radiographic pleural abnormality and covariates* (ORs (95% CI))

	Row n	Restriction	Obstruction
DPT†			
Index=0	6341	1	1
0<index ≤ median (3.0)	78	**2.1 (1.1 to 3.8)**	1.9 (0.9 to 3.8)
Index > median	57	**5.6 (2.7 to 11.6)**	1.7 (0.6 to 4.9)
LPT‡			
Index=0	5416	1	1
0<index ≤ median (2.5)	561	1.3 (1.0 to 1.7)	1.0 (0.7 to 1.4)
Index > median	499	**1.9 (1.5 to 2.5)**	0.9 (0.6 to 1.3)

Statistically significant associations are in bold.
*All models control for parenchymal abnormality, age, sex, smoking history, body mass index, exposure group, number of exposure pathways, duration of residence in Libby and shortness of breath.
†Pleural abnormality index calculated by converting in-profile diffuse thickening widths from 'a', 'b' and 'c' to 1, 2 and 3, then multiplying in-profile widths by in-profile extents and adding face-on extents, and summing the result for each hemithorax. Average severity from two or three B readers used. Possible range of severity index: 0–24. The sum of participants with a DPT abnormality index score >0, n=135, is greater than number of participants with DPT presented in table 2 due to counting participants with DPT detected by only one reader.
‡Pleural abnormality index calculated by converting in-profile localised thickening widths from 'a', 'b' and 'c' to 1, 2 and 3, then multiplying in-profile widths by in-profile extents and adding face-on extents, and summing the result for each hemithorax. Average severity from two or three B readers used. Possible range of severity index: 0–24. The sum of participants with an LPT abnormality index score >0, n=1060, is greater than number of participants with LPT presented in table 2 due to counting participants with LPT detected by only one reader.
DPT, diffuse pleural thickening; LPT, localised pleural thickening.

95% CI 2.7 to 11.6). The odds of restriction for LPT only became statistically significant when severity was greater than the median severity.

Table 4 shows the risk of mild, moderate and severe functional impairment among participants with restrictive spirometry and high degree of LPT width/extent compared with subjects with LPT index score of 0. The risk of impairment correlated with the degree of LPT extent/width and was statistically significant for the 'mild' and 'moderate' functional impairment categories, but not for severe impairment, likely due to small numbers.

Comparing our results with NHANES revealed a rate ratio of 1.1 for obstruction (observed=576, expected=527.9; 95% CI 1.0 to 1.2) and 1.3 for restriction (observed=776, expected=587.9; 95% CI 1.2 to 1.4). These observed values include all adult participants with spirometry and thus differ slightly from table 1.

DISCUSSION

Using community-based screening data from a population with a high prevalence of pleural abnormalities, we found an association between LPT and restrictive spirometry. The magnitude of this association was less than those of parenchymal abnormalities and DPT with restriction, but even after controlling for these abnormalities the association with LPT remained statistically significant. The risk of restrictive abnormalities relative to the degree of LPT extent/width showed a dose–response relationship, becoming statistically significant among participants with the greatest LPT extent and width. We also found a correlation between risk of functional impairment and LPT among participants with restrictive spirometry and a high degree LPT extent/width. These results indicate that severe LPT may result in respiratory symptoms in addition to serving as a marker of asbestos exposure.

Table 4 Odds of functional impairment* among participants with restrictive spirometry and a high LPT index score† versus those with restrictive spirometry and an index score of 0‡

Severity of functional impairment	n	OR (95% CI)
Normal	292	1
Mild	63	**1.7 (1.3 to 2.5)**
Moderate	50	**2.1 (1.4 to 3.2)**
Severe	6	2.3 (0.8 to 6.7)

Statistically significant associations are in bold.
*American Thoracic Society definitions used for severity of spirometry: mild, forced expiratory volume in one second (FEV_1) per cent predicted >70%; moderate, FEV_1 per cent predicted 50%–69%; and severe, FEV_1 per cent predicted <50%.
†Pleural abnormality index calculated by converting in-profile circumscribed plaque widths from 'a', 'b' and 'c' to 1, 2 and 3, then multiplying in-profile widths by in-profile extents and adding face-on extents, and summing the result for each hemithorax. Average index from two or three B readers used. Possible range of pleural abnormality index: 0–24. High LPT index score defined as >2.5 (the median value for all subjects with LPT).
‡Model controls for parenchymal abnormality, age, sex, smoking history, body mass index, exposure group, number of exposure pathways, duration of residence in Libby and shortness of breath.
LPT, localised pleural thickening.

Our models controlled for exposure group; consequently, the association between LPT and restrictive spirometry holds for persons with non-occupational exposure. Pathways for community exposures in Libby (eg, using amphibole-contaminated vermiculite for gardening or insulation, recreating in contaminated areas) were common.[8] While the prevalence of pleural abnormalities was previously correlated to the number of these exposure pathways,[8] we failed to detect an association between them and abnormal spirometry (table 1). Although studies of cohorts with occupational asbestos exposure have shown that LPT can result in restrictive spirometry,[2] we were unable to identify other studies where this association was found among persons with residential exposure only. However, the Libby cohort has strong associations between restrictive spirometry and parenchymal abnormalities and DPT similar in magnitude to those found in studies of occupational cohorts.[1 2 17–21]

Some studies of asbestos-exposed workers have shown an association between LPT and restriction. Controlling for the presence of DPT and parenchymal abnormalities, Jarvholm and Sanden [22] found reduced FVC and FEV_1 among workers with pleural plaques. Miller *et al*[21] found an association between pleural fibrosis and reduced FVC in a multivariate model that controlled for the presence of parenchymal abnormalities but not DPT. Similarly, Schwartz *et al*[19] found significant decrements in FVC among asbestos-exposed workers with LPT after controlling for the effects of both parenchymal abnormalities and DPT. In that study, the prevalence of parenchymal abnormalities with profusion ≥1/0 was 8.3% (102/1223) compared with <1% (50/6475) among all participants and 1.7% (42/2536) among those with occupational asbestos exposure in our study, suggesting much lower asbestos exposure levels in Libby (on the basis of prevalence of parenchymal abnormalities). Thus, our observed association between LPT and restriction may be generalisable to persons with low-level asbestos exposures. We attempted to improve upon prior studies by using multivariate models that simultaneously controlled for potential confounders of the LPT-restriction association (eg, parenchymal abnormalities and DPT, age, BMI). A recent study of chrysotile miners and millers used this approach and found increased risk of restriction in the presence of pleural abnormalities (OR=3.27; 95% CI 1.63 to 6.56) but did not differentiate between LPT and DPT.[23] This risk estimate for restriction is consistent with those of our study, falling between our estimates for LPT and DPT (table 2). However, the LPT-restriction association has been an inconsistent finding with some studies finding no association with the presence of radiographic LPT[20] or the surface area of LPT on high-resolution CT (HRCT) scans.[24 25] Despite the crudeness of ILO categories for plaque extent and width, our finding of a correlation between severity of restriction and degree of radiographic abnormalities makes

sense; intuitively one would expect decreased lung compliance as LPT covers a larger surface of the pleura. Supporting this finding, increasing LPT extent on HRCT was recently associated with reduced FVC.[26]

A caveat of this study is the body habitus of participants; 4591 (71%) were classified as overweight or obese (table 1). Obesity is associated with reduced FVC and restrictive changes[27] as well as increased perception of circumscribed pleural thickening.[28] Evidence for potential confounding can be seen in the high prevalence of restriction among obese participants (table 1). In addition, some argue that the excess of pleural abnormalities in this cohort may be due in part to obesity with subpleural fat being misclassified as plaque in up to 30% of the cases.[29] To offset the confounding effect of obesity, we controlled for BMI in all models. Among the studies cited above, only one controlled for BMI.[23] Unlike study cohorts comprising workers who were healthy enough for employment, participants in this study represent the spectrum of a community in terms of age, body habitus and health. Notably, comparing screening participants with a national population resulted in a statistically significant excess of restrictive spirometry even while adjusting for confounders, including BMI.

Other limitations include the unavailability of more sophisticated pulmonary function test results, potential reader bias and the low sensitivity of radiographs for pneumoconiosis. A criticism of using spirometry alone in measuring FVC without tidal volumes is that one cannot detect the loss of expiratory reserve volume from obesity.[30] We recognise this as a limitation of using screening data unintended for research and, again, we attempted to control for obesity by including BMI in all statistical models. Regarding reader bias, we acknowledge the readers were aware of the exposures in Libby, and no negative radiographs were deliberately included as controls. Still, the readers were highly experienced, each radiograph was reviewed independently by two or three readers, and reader agreement was good for the majority of the subjects. We did not detect evidence for differential agreement among cases versus controls; thus, poor reader agreement would have likely biased our results towards the null. Finally, compared with radiography, several studies have shown greater sensitivity of HRCT for asbestos-related pleural[31–33] and parenchymal abnormalities.[34 35] Furthermore, the authors of some studies linking radiographic LPT to restrictive spirometry have concluded that it was not LPT itself causing restriction but parenchymal fibrosis undetectable by conventional radiography.[19 36] Thus, although our analysis controlled for the presence of parenchymal abnormalities, our observed association between LPT and restriction may be due to 'subradiographic' fibrosis.[37] We were able to examine HRCT data for a subset (n=353) of Libby screening participants from a separate study,[38] in which 12 (3%) participants without parenchymal abnormalities on radiograph did have them on HRCT, indicating while uncommon subradiographic asbestosis may account for some restrictive spirometry we attributed to LPT. A study of the association between LPT on HRCT and pulmonary function in Libby residents representing the spectrum of pleural abnormalities should be considered.

In conclusion, in this cohort of community screening participants, LPT is statistically associated with restrictive spirometry. This association correlated with the degree of LPT extent. Physicians treating patients exposed to Libby amphibole should be aware that LPT may have functional consequences. Consideration should be given to conducting future studies that explore the clinical significance of asbestos-related LPT in both occupational and community cohorts.

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