High-Resolution CT of Benign Asbestos-Related Diseases:
Clinical and Radiographic Correlation

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We prospectively analyzed benign asbestos-related pleural and parenchymal abnormalities on high-resolution CT scans and correlated them with clinical diagnoses in 100 asbestos-exposed workers. All subjects had high-resolution CT scans in conjunction with conventional CT at the time of clinical evaluation. To evaluate for asbestosis, we ranked high-resolution CT scans as high, intermediate, or low probability of asbestosis on the basis of the multiplicity and extent of observed parenchymal changes. By linear regression analysis, the most distinctive high-resolution CT features of asbestosis included thickened nondependent interstitial short lines and parenchymal bands. In 45 subjects satisfying clinical criteria of asbestosis, high-resolution CT probability of asbestosis was high in 38 (84%), intermediate in five (11%), and low in two (4%). In 20 (36%) of 55 subjects without clinical asbestosis, parenchymal abnormalities indicative of a high probability of asbestosis were observed on high-resolution CT. High-resolution CT probability scores had a strong positive correlation with chest radiographic profusion scores ($p < .0001$) and asbestos-related pleural thickening ($p < .0001$). Significant inverse correlations were seen with forced vital capacity ($p < .006$) and single-breath diffusing capacity ($p < .03$), both functional measures of restrictive interstitial lung disease. Neither clubbing nor rales were sufficiently prevalent to have statistical correlation with high-resolution CT scores.

High-resolution CT is sensitive in detecting both pleural and parenchymal abnormalities in the asbestos-exposed subject. Asbestos-related pleural changes are observed more frequently on high-resolution CT than on conventional CT or chest radiography. The probability of asbestosis based on high-resolution CT parenchymal features has a significant correlation with existing clinical determinants of disease, and high-resolution CT can detect abnormality when other methods are not diagnostic.

Fibrosis of the lungs and pleura as a response to the inhalation of asbestos fibers has been recognized for over 80 years. It is estimated that in the United States since 1940 at least 25 million individuals have been exposed to asbestos in their work environments [1].

Histopathologically, asbestosis is initially a multifocal insult with lower-lobe peribronchiolar and subpleural interstitial fibrosis in association with asbestos bodies [2]. In the clinical setting, histologic confirmation is not the standard of practice, and the diagnosis is inferred from symptoms, physical findings, chest radiographic abnormalities, and evidence of lung restriction on pulmonary function testing. Symptoms and physical findings are present only in a small minority of individuals with asbestosis unless advanced disease is present [3]. Similarly, the reductions in lung volumes and diffusing capacity that are the hallmarks of restrictive lung disease are insensitive for the detection of early or mild disease [4, 5]. The chest radiograph is thus relied on frequently for diagnosis, and a clinical diagnosis without radiographic abnormality is often suspect.

High-resolution CT (HRCT) has a greatly increased sensitivity over chest radiography for the detection of diffuse lung abnormalities, although the precise increase in sensitivity has been difficult to document. We recently described the HRCT

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features that are encountered in subjects with clinical asbestosis [6].

Our current study was undertaken to compare HRCT with existing imaging methods for the detection of both pleural and parenchymal disease in asbestos-exposed individuals. We determined which parenchymal abnormalities on HRCT were useful for the diagnosis of asbestosis. In addition, the characterization of pleural disease on HRCT scans was compared with the characterization of pleural disease on chest radiographs and conventional CT scans. Finally, we correlated the results of the HRCT studies with existing clinical determinants of asbestosis.

Subjects and Methods

Subjects

The study group consisted of 100 individuals being evaluated for the potential effects of asbestos exposure. In each case, two International Labour Office (ILO) B-readers (who were not involved in this study) had disagreed about plain film findings regarding the presence of asbestos-related pleural abnormalities or the presence or severity of asbestos-related parenchymal abnormalities. Criteria for inclusion in the study were (1) documented occupational exposure to asbestos; (2) a latency (time from initial exposure) of at least 10 years; and (3) complete clinical evaluation, including chest radiographs, physical examination, and resting pulmonary function tests. Excluded from the study were individuals with other known causes of interstitial lung disease, previous thoracotomy or lung resection, or known malignancy. Twenty-nine of the 100 subjects were included from a prior communication [6].

Clinical Evaluation

Standard high-kilovoltage plain radiographs in the posteroanterior, lateral, and, in most instances, oblique projections were interpreted by consensus between two experienced thoracic radiologists, one of whom was a certified B-reader. The same two radiologists interpreted all images (chest radiographic and CT) in this study. Radiographs were scored according to the ILO 1980 long form [7], and the interpretations included determination of the category and profusion of parenchymal opacities as well as the category (focal or diffuse), site, width, and extent of pleural changes. The readers were aware that all subjects were being evaluated for asbestos exposure but had no knowledge of patient identity or the results of other clinical evaluations, including the previous interpretations of the chest radiographs.

The remaining clinical evaluation included a detailed history of occupational exposure and smoking habits, relevant symptoms of shortness of breath, and the physical findings of auscultatory rales and digital clubbing. Pulmonary function tests included spirometry, lung volumes, and measurements of diffusing capacity for carbon monoxide.

Imaging

Conventional CT scans were obtained on a Picker International 1200SX Scanner (Picker International, Cleveland, OH) by using 10-mm collimation, 140 kVp, 140 mA, and a 2-sec acquisition time. Subjects were imaged supine at full inspiration from above the lung apices to below the posterior costophrenic angles at contiguous 1-cm intervals. IV contrast material was administered when there was a suspicion of hilar or mediastinal disease. Images were reconstructed by using a standard reconstruction algorithm and were photographed at two window settings suitable for viewing the lung parenchyma and the pleura and mediastinum.

HRCT was performed in all subjects immediately after conventional CT and was directed toward the usual pulmonary sites of asbestosis. Scans were obtained at five levels through the lower thorax in both supine and prone positions for a total of 10 images [6]. All images were acquired at full inspiration by using 1-mm collimation, 140 kVp, 110 mA, and a 3-sec acquisition time. Images were reconstructed with a high-spatial-frequency algorithm (designated on the Picker 1200SX software as no. 12). The HRCT images were photographed at three window settings suitable for imaging (1) the lung parenchyma, (2) the pleura and mediastinum, and (3) (a wide window) both the parenchyma and pleura.

Clinical Determination of Asbestosis

The diagnosis of clinical asbestosis was based on our modification of the criteria of the Canadian Task Force on Occupational Respiratory Disease [8] and the American Thoracic Society statement of March 1986 [1]. These use a combination of clinical, functional, and radiographic features in the setting of a documented history of asbestos exposure. We included radiographic pleural disease as a clinical criterion. The diagnostic criteria used for the diagnosis of clinical asbestosis were (1) the radiographic criterion: abnormal chest radiograph of ILO profusion 1/0 or greater; and (2) confirmatory criteria, including auscultatory rales, digital clubbing, forced vital capacity less than 80% predicted, single-breath diffusing capacity less than 80% predicted, and asbestos-related pleural changes (detected on conventional CT). The diagnosis of clinical asbestosis required a documented occupational exposure with (1) an abnormal plain radiograph plus one or more confirmatory criteria or (2) three or more confirmatory criteria.

Scoring of CT Scans

HRCT scans were coded for both asbestos-related pleural and parenchymal disease. Pleural disease was classified according to type (focal plaques or diffuse), location (absent, right, left, or bilateral), calcification (absent or present), and severity (absent, minimal, moderate, or severe) (Fig. 1). Focal plaques were defined as minimal in severity if the plaques were no more than 1 mm thick, 1–3 mm long, and few in number (Fig. 1A); moderately severe plaques were 1–3 mm thick, usually 2–5 cm long, and multiple (Fig. 1B); severe plaques were at least 3 mm thick and extensive and clearly indented the adjacent lung. Diffuse pleural thickening was defined as a thickened sheet of pleura with transverse extent of at least 5 cm, cephalocaudal extent of at least 8 cm, and thickness greater than 3 mm. Conventional CT scans were coded for pleural disease by using the same definitions as for HRCT. Interpretation was separated by at least 6 weeks from the interpretations of the HRCT scans and the chest radiographs.

Parenchymal abnormalities on HRCT were coded:

1. Curvilinear subpleural lines (coded as absent, length <2 cm, length 2–5 cm, length >5 cm) were defined as a linear density within 1 cm of the pleura and parallel to it, as described by Yoshimura et al. [9].

2. Parenchymal bands (coded as absent or present) were defined as linear densities 2–5 cm in length. These bands usually contacted the pleural surface and were distinguishable from pulmonary blood vessels in that they were thicker, did not taper peripherally, and often were oriented in a direction incompatible with normal vessels (Fig. 2).

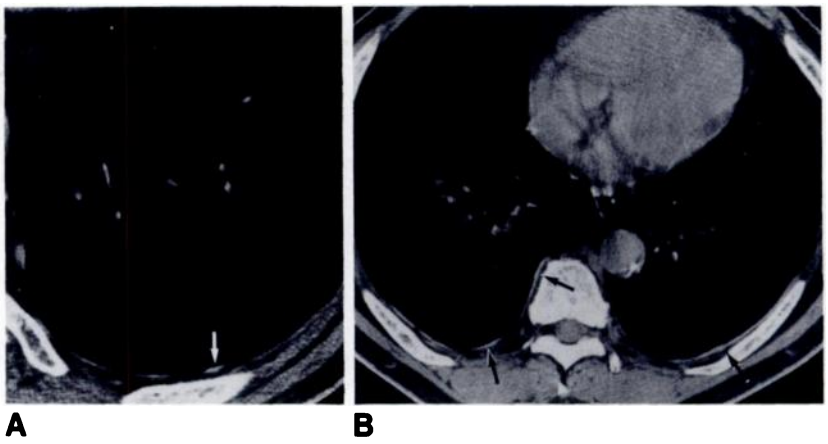


Fig. 1.—High-resolution CT scans of asbestos-related pleural disease.

***A*, Minimal focal pleural plaques overlie left posterior ribs (*arrow*).**

***B*, With subject supine. Moderate pleural plaques in posterior and paraspinous locations (*arrows*).**

3. Thickened interstitial short lines (coded as absent or present and by location) were seen in the subpleural parenchyma and represented thickened septal and intralobular lines (Figs. 2 and 3). Septal lines corresponded to branches of the pulmonary venules and lymphatics within a connective tissue envelope. When thickened, septal lines appeared as short, discrete lines that contacted the pleural surface peripherally. Occasionally they could be seen to arborize from the distal branching points of pulmonary veins 1–2 cm from the pleural surface [10]. Intralobular lines represented the intralobular arterioles and bronchioles with their surrounding interstitium that arborized within the secondary pulmonary lobule. They appeared as dotlike, linear, or Y-shaped branching structures 5–10 mm from the pleura. When abnormal, they appeared thickened, were more numerous, and often contacted the pleura peripherally. Separation of subpleural septal lines from intralobular lines was not always possible on HRCT, although septal lines usually were nonbranching and their proximal origin was 1–2 cm from the pleural surface, whereas subpleural intralobular lines frequently branched and generally were closer to the pleura (5–10 mm) [10].

4. Subpleural dependent density (coded as absent or present and by thickness) was defined as a band 2–30 mm thick of poorly marginated, increased lung density paralleling the dependent pleura and obscuring the underlying lung morphology (Fig. 4).

5. Honeycombing (coded as absent or present) was defined as areas of lung containing small, cystlike spaces less than 1 cm in diameter with thickened walls. Most commonly, honeycombing was subpleural in location and predominated in the posterior lower lobes (Fig. 5). The adjacent pleura frequently was thickened.

Prone and supine images were obtained with HRCT. The differences in appearance of the lung between the two positions were coded systematically. Specifically, we evaluated changes in parenchymal bands (absent or present), interstitial short lines (resolved or

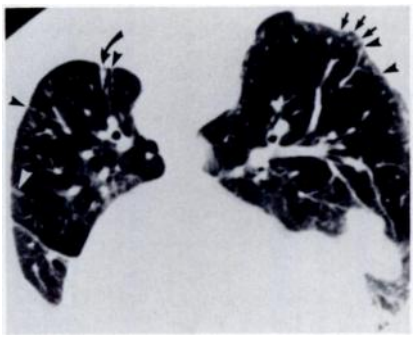


Fig. 2.—High-resolution CT scan with subject prone shows discrete parenchymal band in left base that contacts pleural surface (*curved arrow*). Thickened interstitial structures are evident in subpleural parenchyma bilaterally, including dotlike structures (*straight arrows*) and thickened short lines (*arrowheads*).

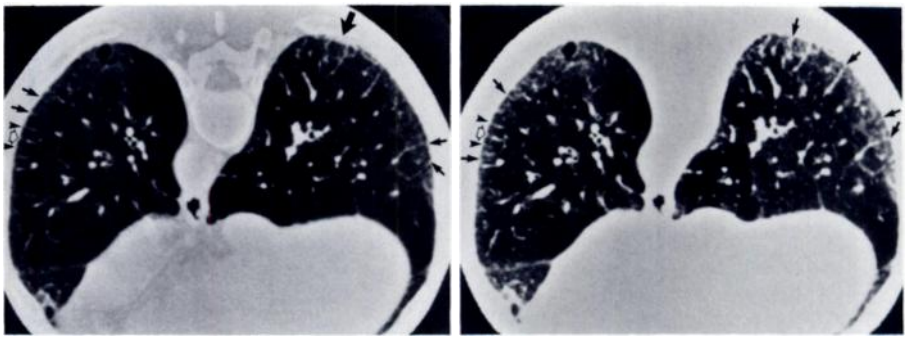
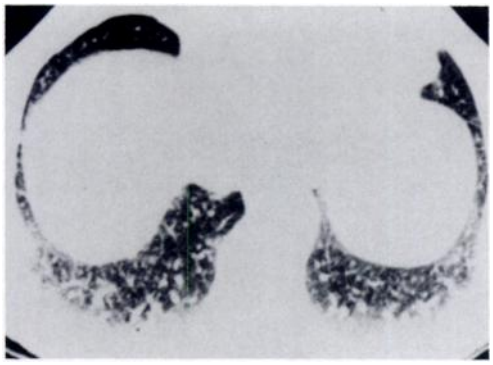


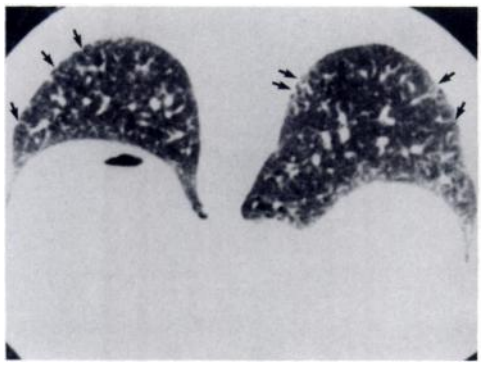
Fig. 3.—High-resolution CT scans with subject prone, displayed at two CT window parameters used for interpretation of lung parenchyma.

***A*, Extended window (width = 2000, level = −750) shows numerous bilateral interstitial short lines in subpleural lung that contact pleura peripherally (*small solid arrows*). Subpleural dependent density was present on supine images and persists in right base (*large arrow*). Thickened septa marginate subpleural pulmonary lobule (*arrowheads*). Intralobular structure is seen centrally in lobule (*open arrow*). Focal bulla is in left base.**

***B*, With narrower window (width = 1000, level = −750), thickened subpleural interstitial lines (*solid arrows*) are better contrasted with more normal central interstitium. Lobular architecture is seen, including septal (*arrowheads*) and intralobular (*open arrow*) lines. Subpleural distribution of abnormality was typical in asbestos-exposed subjects.**



A



B

Fig. 4.—High-resolution CT of dependent density and septal thickening.
***A*, Scan with subject supine shows dependent density posteriorly, obscuring underlying lung morphology.**
***B*, Scan with subject prone shows clearing of dependent density. Numerous thickened interstitial short lines (*arrows*) are visible. Vascular distension would resolve in prone position.**

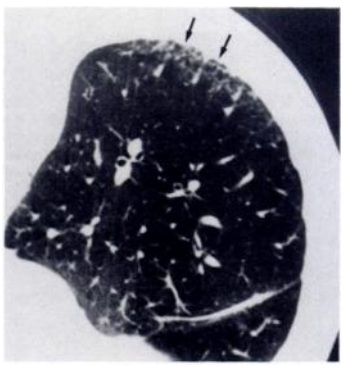


Fig. 5.—High-resolution CT scan with subject prone shows focal subpleural honeycombing and interlobular septal thickening at right base (*arrows*).

persistent), curvilinear subpleural lines (resolved or persistent), dependent density (complete clearing, incomplete clearing, or persistent), and subpleural abnormalities revealed by resolution of dependent density (absent or present) (Fig. 3).

Probability Scores for HRCT Scans

Both the lung window and extended window settings were used to observe the lung parenchyma. On the basis of the presence, extent, and distribution of parenchymal abnormalities, HRCT scans were scored independently on a five-point scale for asbestosis by each of the two radiologists: 1 = normal; 2 = abnormal but of low probability for asbestosis; 3 = abnormal, intermediate probability for asbestosis; 4 = abnormal and of moderately high probability for asbestosis; and 5 = abnormal and of high probability for asbestosis. For each scan, the separate scores were averaged to derive a consensus score. From this, scans were assigned high (score ≥ 4), intermediate (score 3–3.5), or low (score < 3) probability.

Results

The study group was relatively homogeneous (average age, 62 ± 10 years; range, 34–85). The subjects all had occupational exposure to asbestos, 85 in shipyards and 15 in construction. The mean duration of exposure to asbestos was 21 ± 11 years (range, 2–45). The mean latency, meaning interval from first exposure to evaluation, was 37 ± 10 years (range, 12–59), so that all subjects were at least 10 years from initial exposure to asbestos. Twenty-seven subjects had never smoked. The remaining 73 subjects had a current or temporally remote smoking history. Of these, 27 subjects had a cumulative history of less than 20 pack-years and half had stopped smoking for over 1 year.

Clinical asbestosis was established in 45 subjects (Table 1). Of these, 35 had a chest radiograph of ILO profusion score of 1/0 or greater plus one or more confirmatory criteria. Ten of the 45 had a chest radiograph of ILO profusion less than 1/0, and diagnosis was by three or more confirmatory criteria. Of the 35 subjects with abnormal chest radiographs, HRCT probability scores for asbestosis were high in 30 (86%), intermediate in four (11%), and low in one (3%). Of the 10 subjects who did not have chest radiographic profusion abnormalities but did have multiple confirmatory criteria, the HRCT probability of asbestosis was high in eight, intermediate in one, and low in one. The difference in probability scores between these two subgroups was not significant ($p = .64$, Wilcoxon rank sum test).

TABLE 1: Relationship of HRCT Probability Scores to Clinical Diagnosis of Asbestosis

Clinical Diagnosis	No. of Subjects	HRCT Probability of Asbestosis		
		Low	Intermediate	High
Asbestosis:				
Abnormal chest radiograph	35	1	4	30
Normal chest radiograph	10	1	1	8
Subtotal	45	2	5	38
No asbestosis	55	25	10	20
Total	100	27	15	58

Note.—HRCT = high-resolution CT.

Fifty-five subjects did not satisfy criteria for clinical asbestosis. None had an abnormal chest radiograph by ILO standards. The HRCT probability score for asbestosis in these 55 was high in 20 (36%), intermediate in 10 (18%), and low in 25 (45%). The probability scores in this group were significantly different from the 45 subjects with the clinical diagnosis of asbestosis ($p < .001$, Wilcoxon rank sum test).

Interobserver variability between the two radiologists in assigning HRCT probability scores was evaluated. In 65 subjects, the scores (five-point scale) were identical; in 32 subjects, scores differed by one point; and in three subjects, scores differed by two points.

Relationship of HRCT Scores to Radiographic ILO Profusion Scores

The relationship of the HRCT probability scores of asbestosis to the chest radiographic ILO profusion scores is shown in Table 2. Sixty-five subjects had ILO profusion scores lower than 1/0. Of these, HRCT probability scores of asbestosis were low in 26 (40%), intermediate in 11 (17%), and high in 28 (43%). Thirty-three subjects had ILO profusion scores of category 1 (score of 1/0, 1/1, or 1/2). Of these, HRCT scores were of low probability in one (3%), intermediate probability in four (12%), and high probability in 28 (85%). Of two subjects with ILO profusion scores of 2/1 or higher, both had an HRCT score of high probability of asbestosis.

Correlation of HRCT Features to Probability Scores of Asbestosis

The HRCT probability scores for asbestosis were derived subjectively on the basis of the presence and extent of specific parenchymal features. Persistence of these features after the subject was moved from the supine to prone position was important. Pleural abnormalities were not used to establish an HRCT probability score of asbestosis. Regression analysis of the observed parenchymal features relative to the HRCT probability score of asbestosis was performed in order to (1) provide an objective measure of the frequency and importance of each feature and (2) rank the HRCT features according to their contribution in determining the probability score of asbestosis.

Correlations between the multiple HRCT features and probability scores are shown in Table 3. Of individual features, nondependent interstitial short lines were most highly correlated ($r = .74$, $p < .0001$). Specifically, these were interstitial lines apparent *only* in the prone position because of obscuration by dependent density when the subject was supine. Interstitial thickening, visible in the supine position, also had a strong correlation ($r = .59$, $p < .0001$). Parenchymal bands in both prone ($r = 0.55$, $p < .0001$) and supine ($r = .52$, $p < .0001$) positions were likewise strongly correlated. Dependent density and curvilinear subpleural lines had no significant correlation with HRCT probability scores. By using analysis of variance, the rank and additive effect of the individual HRCT features were determined. Nondependent interstitial short lines alone had the highest correlation ($r^2 = .55$, $p < .0001$). The addition of dependent interstitial short lines increased the r^2 to .58 ($p < .0001$). Parenchymal bands in the prone position increased the r^2 to .76 ($p < .0001$). Addition of the remaining HRCT features did not improve the correlation further. Honeycombing was seen on CT in only seven subjects; because of this low occurrence rate, honeycombing did not contribute to the diagnostic correlations. However, when honeycombing was present, it always was associated with a high probability score of asbestosis.

TABLE 2: Relationship of HRCT Probability Scores of Asbestosis to Chest Radiographic ILO Profusion Scores

ILO Profusion Score	No. of Patients with HRCT Probability Score		
	Low	Intermediate	High
<1/0	26	11	28
1/0	0	2	10
1/1	1	2	12
1/2	0	0	6
2/2	0	0	1
3/3	0	0	1

Note.—HRCT = high-resolution CT; ILO = International Labour Office.

TABLE 3: Correlation of High-Resolution CT Parenchymal Features to Probability Score of Asbestosis

Feature	Correlation Coefficient (r)	Level of Significance (p)
Thickened interstitial lines (prone)	.74	<.0001
Thickened interstitial lines (supine)	.59	<.0001
Parenchymal bands (prone)	.55	<.0001
Parenchymal bands (supine)	.52	<.0001
Subpleural density (prone)	.24	<.06
Dependent subpleural density	.15	NS
Curvilinear subpleural lines	.10	NS

Note.—Correlations are Pearson product-moment correlations. NS = not significant.

Pleural Disease

Pleural disease was common in this group. Pleural plaques were evident on chest radiographs in 49 individuals (bilateral in 38 and unilateral in 11). With conventional CT, unequivocal plaques were shown in 56 subjects (53 moderate and three severe), and an additional 25 subjects had minimal plaques. With HRCT, 64 subjects had unequivocal plaques (58 moderate and six severe), and minimal plaques were evident in another 29. Thus, on HRCT, only seven subjects were considered to be completely free of pleural abnormality.

Diffuse pleural thickening was evident in seven subjects. In two subjects, it was discovered by all three techniques; in the other five, it was seen with only one or two techniques (chest radiography, two; conventional CT, four; HRCT, one). In all seven subjects with diffuse pleural thickening, the HRCT probability score for asbestosis was high (score = 5).

Pleural calcification was seen in 13 subjects on chest radiography, in 16 on conventional CT, and in 20 on HRCT. Chest radiographic interpretations of pleural calcification were not corroborated in three of 13 on conventional CT and in four of 13 on HRCT. In 15 of the 16 instances in which pleural calcification was seen on conventional CT, it was also seen on HRCT; in only one case was pleural calcification seen on conventional CT not imaged also on HRCT.

The HRCT probability score for asbestosis had a strong correlation with severity of pleural plaques, whether detected by conventional CT ($r = .46$) or HRCT ($r = .39$); both correlations were significant at the $p < .0001$ level. Latency from

initial exposure also had a positive correlation with severity of pleural plaques detected by conventional CT ($r = .30$) or HRCT ($r = .22$); these correlations were significant at the $p < .002$ and the $p < .02$ levels, respectively.

Correlation of HRCT Probability Scores with Clinical Criteria

These data were analyzed by linear regression analysis for correlation between the results of HRCT probability score for asbestosis and the individual clinical criteria (Table 4). The highest positive correlation was seen between HRCT probability score and the ILO profusion score ($r = .49$, $p < .0001$). The next highest correlation with HRCT was that of asbestos-related pleural disease as seen on conventional CT ($r = .47$, $p < .0001$). Of the two confirmatory pulmonary function studies, inverse correlations were found with respect to both forced vital capacity (percentage predicted) and single-breath diffusing capacity (percentage predicted); these correlations were significant at the $p < .006$ and $p < .03$ levels, respectively. Neither rales nor clubbing had a significant correlation with the HRCT probability scores. Both of these clinical findings were relatively uncommon, with rales being present in 14 subjects and clubbing in six.

Other parameters, including both latency and duration of occupational exposure, smoking history, and pulmonary function tests of obstruction (forced expiratory volume, 1 sec/forced vital capacity), were studied by correlation analysis to determine correlation with the HRCT score. Latency and duration of exposure are covariables in that they are related. In this study, latency had a small but significant correlation with HRCT score ($r = .32$, $p < .002$), but duration of exposure did not ($p > .5$). Similarly, neither smoking history nor tests of airflow obstruction were correlated with HRCT probability scores of asbestosis.

Discussion

With the commercial exploitation of asbestos over the last century, asbestos-related interstitial lung fibrosis has become a major public health concern. Asbestosis has been reported in a variety of occupational settings as well as in family contacts of asbestos-exposed workers [11, 12]. In clinical practice, the diagnosis of asbestosis is established from a combination of physical, physiologic, and radiographic abnormalities in the context of a documented history of fiber exposure. Although none of the clinical criteria are specific, multiple abnormalities in the exposed individual are strong presumptive evidence for asbestosis. The diagnosis is problematic when only few physical or functional findings are present, or when exposure history is combined with smoking, which may result in abnormalities that can confuse the interpretation of pulmonary function tests or chest radiographs.

Conventional CT has been suggested for evaluating both pleural and parenchymal changes of asbestos exposure [13–16]. Early trials in subjects with asbestos exposure found that conventional CT sections of 13 mm thickness were significantly more sensitive than chest radiographs in detecting pleural thickening. The greater sensitivity of CT was attributed to the fact that pleural thickening was most common in paravertebral and posterolateral locations, which are difficult to visualize on chest radiographs [14]. In addition, CT identified parenchymal fibrosis in 33% of the subjects, whereas radiographs were interpreted as abnormal in only 17%. In these CT studies, interstitial fibrosis appeared as areas of coarse honeycombing. Loss of normal gravity-dependent perfusion was also described in areas of fibrosis [14, 15]. More recently, Begin et al. [16] analyzed the usefulness of conventional CT scans relative to posteroanterior and four-view radiographs of the chest for detecting asbestos-related pleuroparenchymal fibrosis in 127 workers. When analyzing total (summed) pleuroparenchymal scores, they found that the three methods yielded comparable results. However, CT scans did not recognize asbestosis in 19% of 53 subjects in whom chest radiographs were abnormal (ILO profusion $\geq 1/0$). CT did identify significantly more pleural calcifications than the other methods did.

The disparities in the early studies with conventional CT and the limitations of clinical criteria in diagnosing asbestosis stimulated our study with HRCT. Our patient group was generated from prior interobserver disagreement on ILO interpretation of chest radiographs regarding minimal asbestos-related parenchymal or pleural disease. Use of the HRCT technique of thin collimation with high-spatial-frequency reconstruction algorithms provides spatial resolution at the submillimeter level and reduces volume-averaging effects (which may be confusing on conventional CT) [17]. HRCT can detect pathologic changes not evident on chest radiographs in several conditions, including lymphohematogenous metastatic disease [18], interstitial pneumonias, and other idiopathic or acquired fibroses of lung [19].

TABLE 4: Correlation of High-Resolution CT Probability Scores and Clinical-Functional Criteria of Asbestosis

Clinical-Functional Criterion	Correlation Coefficient (r)	Level of Significance (p)
Chest radiographic profusion score	.49	<.0001
Pleural thickening (conventional CT)	.47	<.0001
Forced vital capacity (% predicted)	−.28	<.006
Single-breath diffusing capacity (% predicted)	−.22	<.03
Rales	NS	NS
Digital clubbing	NS	NS

Note.—Correlations are Pearson product-moment correlations. NS = not significant.

The first descriptive report of HRCT findings in asbestosis [9] was in a group of subjects judged to have disease by virtue of ILO profusion abnormalities. Nineteen patients were imaged only in the supine position by using slice thicknesses of 1.5 or 10 mm. In addition to areas of discrete honeycombing, a curvilinear subpleural line occurred in 79% of subjects that was thought to be the consequence of the initial stage of fibrosing bronchioloalveolitis. HRCT findings were not correlated with physiology or other determinants of clinical asbestosis.

Recently, we characterized abnormalities on HRCT scans in subjects satisfying physical, plain radiographic, and pulmonary function criteria of asbestosis that are demonstrated consistently and are not observed in similar-age control patients without history of asbestos exposure or diffuse lung process [6]. In our present study, probability scores of asbestosis were subjectively derived by the two readers on the basis of the presence of multiple HRCT features. Statistical evaluation provided an objective measure of those HRCT features that were most significant in determining these scores. Those features included (1) thickened interstitial short lines and (2) parenchymal bands. Frequently, thickened short lines were visible on both prone and supine images; however, in many cases, discrete lines were obscured by dependent density in the supine position and were definable only when nondependent in the prone images. Honeycombing was not seen often, but when present, was always associated with a high probability of asbestosis. Curvilinear subpleural lines and dependent subpleural density occurred in many subjects and did not help to diagnose asbestosis. In our subjects, curvilinear subpleural lines commonly resolved when the involved lung was nondependent, indicating that they are affected by gravity and are not always sites of fibrosis. If these lines persisted when nondependent, they were invariably associated with other parenchymal abnormalities suggestive of asbestosis.

In our subjects, lung abnormalities on HRCT were typically multifocal. This scattered distribution is compatible with histopathologic descriptions of asbestosis until late in the disease. Affected areas frequently are subtle and continuous with uninvolved lung, such that sampling of multiple sites is required to confirm disease [2]. In addition, HRCT abnormalities predominated in the posterior regions of the lower lobes, in keeping with pathophysiologic observations that fibers tend to accumulate in the peripheral regions of the lung bases, presumably because of the effects of posture and gravity [11]. For evaluation of fixed structural changes, the prone position renders the posterior subpleural lungs nondependent and free of gravitational effects on perfusion (specifically, vascular distension) and ventilation.

The spatial resolution of conventional CT permits visualization of some of the HRCT features of asbestosis, in particular, parenchymal bands. However, discrete interstitial lines in the lung periphery that are visible with HRCT are below the limits of conventional CT resolution. Instead, reticular patterns or peripherally branching arcades (representing summation of branching intrapulmonary vessels and their thickened interstitial investiture) may be seen in the dependent parenchyma of asbestos-exposed individuals. Unfortunately, both gravity and variations in inspiratory volume may cause striking differences in the appearance of the dependent lung. For these reasons, our technique with prone HRCT provides a greater degree of confidence in evaluating fine interstitial detail and eliminates the effect of gravity on the lung.

HRCT correlates significantly with existing clinical criteria of asbestosis. The strongest correlation of HRCT probability scores is with chest radiographic profusion scores because both techniques show morphologic derangement. Currently, an abnormal chest radiograph generally is considered to be the most confirmatory of existing criteria for the diagnosis of clinical asbestosis [1]. Plain radiographic interpretation by the ILO classification is now standard in the clinical assessment of subjects with asbestos exposure; in some diagnostic schemes, parenchymal profusion abnormalities are an essential criterion for the diagnosis of asbestosis [8]. Irregular parenchymal opacities coupled with characteristic pleural changes in a person with known exposure usually present little diagnostic difficulty. However, substantial interstitial fibrosis must be present to be evident on plain radiographs [20]. Lesions that are too small to be individually resolved must be present in sufficient concentration before their summation exceeds the threshold of visibility. The relationship between chest radiographic profusion scores and pathologically confirmed asbestosis corroborates the insensitivity of chest radiographs. In a recent study [21], autopsy specimens from 138 asbestos workers who had died of lung cancer were examined. The authors found a limited correlation between radiographic and pathologic asbestosis; 18% of those with parenchymal fibrosis had normal chest radiographs. Similarly, Gaensler et al. [22] reported normal radiographs in 26% of subjects in whom asbestosis was determined by open-lung biopsy or necropsy. Studies assessing observer variation in interpretation of profusion scores in the ILO classification system indicate that the lowest (most nearly normal) profusion categories have the highest observer error [20]. Therefore, subtle or early asbestosis is not only poorly registered on radiographs but also is least consistently characterized.

In our present study, of 35 subjects with ILO profusion scores of 1/0 or greater, HRCT was of high probability for asbestosis in 30 (86%) and was abnormal and of intermediate probability in four (11%). Only one subject whose ILO profusion was abnormal had a relatively normal HRCT scan. The chest radiographic opacities in this subject may represent changes other than those of asbestos exposure. Of the remaining 65 subjects in whom radiographs were normal, 10 had combinations of criteria sufficient for the clinical diagnosis of asbestosis; in these 10, HRCT scans were of high probability in eight (80%). In the remaining 55 subjects without clinical asbestosis, one-third had abnormalities on HRCT identical to those seen in subjects with clinical asbestosis. Although we do not have pathologic proof of parenchymal disease in these individuals, these HRCT findings probably define abnormalities that involve geographically too little parenchyma to be evident on either radiographs or resting pulmonary function tests.

Our results indicate a strong relationship between asbes-

tosis and asbestos-related pleural disease. Although pleural and parenchymal abnormalities may occur independently of one another, we found a significant correlation between the severity of pleural disease and the presence and severity of asbestosis. Perhaps the strongest of the pleural manifestations in predicting asbestosis was the presence of diffuse pleural thickening; these subjects all had a high probability of asbestosis. However, diffuse pleural thickening was present in too few patients to have high statistical correlation with HRCT probability scores.

The pathogenesis of asbestos-related parietal pleural plaques is not known. Coated asbestos bodies are conspicuously absent on light microscopy of these lesions; however, with electron microscopy, most plaques clearly contain many small fibers below the limits of resolution of light microscopy [11, 23]. This observation has led to the theory that small fibers, which are present in all inhaled asbestos dust, migrate through the lung parenchyma and visceral pleura to the parietal pleural space, where they become lodged in the lymphatics (which are exclusive to the parietal pleura). Morgan et al. [24] used radioactively labeled asbestos fibers in rats and observed that the fibers were diffusely spread in the lungs at 2 days after inhalation; however, after more than 100 days, the radioactivity was concentrated in subpleural foci. In a study with guinea pigs [25], fibers too small to be resolvable with light microscopy were shown to produce asbestosis. Although these small fibers do not result in the intense inflammatory reaction characteristic of long fibers, they appear to provoke a low-grade inflammatory response that may progress to interstitial fibrosis. The ultimate subpleural distribution of short fibers and their presence in the fibrous parietal pleural plaques of asbestos exposure may explain the high correlation between pleural and parenchymal fibrosis that we observed, as well as the consistent subpleural location of early interstitial changes that we saw on HRCT.

Finally, latency from exposure had a strong correlation with the observation of pleural plaques: the longer the latency, the more severe the pleural disease. The findings from our study and epidemiologic experience seem to indicate that both pleural disease and interstitial pulmonary fibrosis are progressive when HRCT is used for assessment. It is possible but unlikely in this group that subjects exposed at an earlier time had more severe exposure to asbestos and thus had more severe disease.

HRCT scans had a significant inverse correlation with parameters of lung function that measure interstitial lung disease, specifically forced vital capacity (percentage predicted) and single-breath diffusing capacity (percentage predicted). Given the limited distribution of abnormalities on HRCT in many of these subjects, it is not surprising that tests of pulmonary function often were within the limits of normal despite morphologic derangement on HRCT. Disparities between chest radiographic and functional measures of early asbestosis are well known. In a study of 1069 asbestos-exposed workers [4], although vital capacity and diffusing capacity were progressively reduced with increasing radiographic profusion, both values remained above 85% of mean standardized values even in subjects with radiographic profusion scores of 1/2 or greater, suggesting that these functional measures are insensitive to early or mild radiographic disease.

HRCT probability scores for asbestosis had no relationship to smoking history. Cigarette smoking is known to have a synergistic effect with asbestos exposure on the parenchymal opacities seen on chest radiographs [26]. In addition, none of the individual features on HRCT were correlated with smoking history. This suggests that HRCT may distinguish between the effects of asbestos exposure and smoking, which frequently are coincidental in this population.

Our observations suggest that HRCT is sensitive for the morphologic detection of pleural and parenchymal abnormalities in asbestos-exposed subjects. In applying these HRCT criteria to a population of workers with documented asbestos exposure, we ascribe these abnormalities to dust inhalation. Pleural disease, especially when bilateral or multifocal, is relatively specific for asbestos. However, parenchymal abnormalities similar to those we describe may occur in other interstitial diseases such as idiopathic interstitial fibrosis. In the context of a group with documented occupational dust exposure in whom there is no other known cause of interstitial disease, we have applied the same presumptions of causal relationship inherent in other clinical methods used to diagnose asbestosis. HRCT scans have significant correlation with existing radiographic and functional criteria of clinical asbestosis, with the strongest correlations seen with chest radiographic opacities. Although direct examination of lung tissue is considered the most reliable means of diagnosing asbestosis, open-lung biopsy cannot be advocated in the routine evaluation of these individuals. The specificity of HRCT will be defined by longitudinal assessment of exposed individuals and by tissue analysis obtained from subjects in special circumstances or at necropsy. The submillimeter spatial resolution attainable with HRCT offers the potential for disease detection when other clinical methods are nondiagnostic. We conclude that HRCT can complement the evaluation of asbestos-exposed subjects when other criteria are equivocal or absent for parenchymal fibrosis.

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