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Key terms: asbestos-exposed worker; asbestosis; diffusing capacity; emphysema; high-resolution computed tomography; HRCT; lung function

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Impairment of lung function in asbestos-exposed workers in relation to high-resolution computed tomography

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Objectives The aim of the study was to determine the causes of impairment of ventilatory function and diffusing capacity in smoking asbestos-exposed workers (N=590) showing radiological pleural thickenings or pulmonary fibrosis.

Methods High-resolution computed tomography (HRCT) and spirometry were performed, and diffusing capacity was measured. The workers were divided into five groups based on the HRCT scoring: pleural disease (N=190), pulmonary fibrosis (N=68), emphysema (N=148), combined fibrosis and emphysema (N=74), and marked adhesions (N=110). The graded lung function impairment was compared between the groups.

Results Moderate impairment of forced expiratory volume in 1 second [odds ratio (OR) 2.72, 95% confidence interval (95% CI) 1.31–5.57] and forced vital capacity (OR 2.81, 95% CI 1.05–6.89) was associated with the persons with combined fibrosis and emphysema. Marked impairment of diffusing capacity was associated with the combined fibrosis and emphysema (OR 4.94, 95% CI 2.48–9.77) but not with pleural disease (OR 0.21, 95% CI 0.09–0.45) or pulmonary fibrosis (OR 0.36, 95% CI 0.08–1.05). For the persons with combined fibrosis and emphysema, the mean fibrosis score did not differ between normal, slightly reduced, or markedly reduced diffusing capacity, but the emphysema score was significantly higher for the patients with marked impairment than for those with normal diffusing capacity ($P<0.01$).

Conclusions Different profiles of asbestos- and smoking-induced pulmonary or pleural disease were found. The results indicate that the most important factor determining the degree of functional impairment in smoking asbestos-exposed workers is the presence of pulmonary emphysema.

Key terms asbestosis; diffusing capacity; emphysema; lung function.

High-resolution computed tomography (HRCT) is currently the most sensitive imaging method available for detecting structural pulmonary changes caused by emphysema (1, 2), and it has become the method of choice for studying asbestos-induced pulmonary and pleural diseases (3). HRCT is also the most effective method for diagnosing asbestosis and emphysema, and it is superior to pulmonary function tests and chest X-rays for that purpose (4, 5).

Pulmonary fibrosis caused by asbestos exposure (ie, asbestosis) is a diffuse interstitial fibrosis of the lung parenchyma caused by the deposition of asbestos fibers in the lung (6). Emphysema, usually caused by smoking, is defined as a condition of the lung characterized by abnormal permanent enlargement of the air spaces distal to the terminal bronchioles, accompanied by destruction of their walls without significant associated fibrosis (7). It is generally known that asbestosis is associated with restrictive lung function impairment (8) and emphysema with increased air volumes; however, both are associated with decreased diffusing capacity (DL_{CO}). DL_{CO} measurement is commonly used in the follow-up of asbestos-exposed persons (6, 9), and the reduction in DL_{CO} was suggested as preceding changes in chest radiography (10).

Our clinical impression has been that emphysema could play an important role in respiratory disability

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among asbestos-exposed persons, as suggested also in previous studies (11–13). In assessments of the severity of asbestos-induced lung disorders in smokers, the presence of emphysema must be diagnosed for medicolegal and compensational reasons. Although HRCT is widely used, results on the use of HRCT in assessments of lung function impairment in asbestos-induced lung diseases are sparse (13, 14).

Our aim was to assess the causes of eventual respiratory disability in a population of 590 asbestos-exposed workers who were current or previous smokers and showed pleural thickenings or pulmonary fibrosis radiologically. Lung function (spirometric and diffusing capacity variables) was related to findings in HRCT scans, smoking, and asbestos exposure.

Study population and methods

Previously 2857 persons with asbestos-related occupational nonmalignant pulmonary or pleural diseases among 18 900 asbestos-exposed persons were diagnosed (15, 16) according to international guidelines (6, 17). Of these, ethnically Finnish smoking men from the Helsinki area and willing to participate in additional studies and, in addition, nonsmokers with asbestosis were included (N=602) (18, 19); however, women (N=10) and two persons with insufficient data were excluded. A total of 590 persons were examined at the Finnish Institute of Occupational Health. Their mean age was 63 (range 38.4–80.8) years, and they had a mean height of 173.9 (range 153–196) cm and a mean weight of 83.6 (range 45–167) kg. They were employed in various construction occupations and had been exposed to asbestos for a mean of 25.9 (range 2–48) years. Most were smokers with a mean of 23.9 (range 0–87.5) pack-years, 3% had never smoked, 70% were ex-smokers (stopped smoking more than 6 months previously), and 27% were current smokers. Lung function test results (spirometry and DL_{CO}) were compared with HRCT findings, intensity of asbestos exposure, and smoking habits. The Ethics Committee of the Finnish Institute of Occupational Health approved the study, and informed consent was obtained from all the participants.

Radiological methods

All the workers underwent chest computed tomography (CT) (Picker pQ 2000; Picker, Chicago, IL, USA) (125 mA, 140 kV, 10 mm collimation) from the costophrenic angle to the apical lungs, as reported in detail earlier (20, 21). In addition the following 1.5-mm slices (HRCT slices; 200 mA, 130 V) were taken from the chest and were used in our analyses: (i) at the level of the carina, (ii) at the level of the dome of the higher diaphragm, (iii) halfway between slices 1 and 2, and (iv) halfway between slice 2 and the lower costophrenic angle. The window level and width were set at 700 and 1000, respectively, for lung and at 40 and 400, respectively, for soft tissue. A classification of the radiological findings for pulmonary tissue and the pleura was developed by radiologists on the basis of classifications recommended previously (20–22). Semiquantitative scoring of the HRCT findings indicating interstitial lung fibrosis in both lungs was made according to an arbitrary scale from 0 to 5 with class 0 as a normal finding (normal finding by all criteria), class 1 as a subnormal finding (1–2 criteria sporadically for the lung periphery; no honeycombing), class 2 as mild fibrosis (at least 2 criteria on both sides and in several slices from the lung periphery; no honeycombing), class 3 as moderate fibrosis (several criteria, which extend deeper into the lung than in class 2; honeycombing as a general rule), class 4 as severe fibrosis (several criteria or associated findings extending deep into the lung; honeycombing; lung architectural change), and class 5 as extreme fibrosis (extreme severe and various fibrotic changes; little normally aerated lung left). If the observers or readers could not match the finding exactly with any given fibrosis class, five subcategories (0/1, 1/2, 2/3, 3/4 and 4/5) were used (ie, a finding coded as 1/2 indicated fibrosis between classes 1 and 2).

Signs of centrilobular, paraseptal, and panlobular emphysema and bullae were classified in both lungs separately, using a similar scale from 0 to 5 without subcategories: 0 (no changes), 1 (faint and few abnormalities, usually in a single slice), 2 (more distant abnormalities in a single slice or abnormalities in two slices), 3 (clear abnormalities in two to five slices), 4 (score between 3 and 5) to 5 (abnormalities widely distributed in the whole lung, in all or most slices). For our analysis, the emphysema scores from these four emphysema types were added up, and the mean scores of both lungs were used in the analysis; hence, the maximum emphysema score was 20. The marked adherences were graded as 0–3: 0 = no adherences, 1 = adherences of the diaphragm or sinuses, 2 = adherences in locations other than the diaphragm or the costophrenic angles, or 3 = converging adherences (ie, so-called “crows’ feet” adherences]. The three categories of adherences were added up from each lung, and the mean scores of both lungs were used. However, the scores of converging (crows’ feet) adherences and the thickness of their underlying pleura were multiplied by 2. The maximum score could thus have been 21. Rounded atelectases were graded as 0–3. A rough description of the pleural thickenings was made using a single parameter (ie, the greatest thickness of pleural thickenings) classified as

0 = 0 mm, 1 = <5 mm, 2 = 5–10 mm, and 3 = >10 mm. All the workers showed some pleural thickening, and the group with pleural disease was formed by the exclusion of other changes found in the HRCT scanning. For additional analyses, the patients were divided into disease groups, as follows: (i) pulmonary fibrosis: fibrosis score for both lungs ≥1, emphysema score = 0, adherence score <5, and rounded atelectasis count = 0; (ii) emphysema: fibrosis score <1 (possibilities 0 or 0/1), adherences score <5, rounded atelectasis count = 0, and emphysema score >0; (iii) combined fibrosis and emphysema: emphysema score >0, fibrosis score ≥1, adherences <5, and rounded atelectasis count = 0; (iv) pleural disease: emphysema score = 0, fibrosis score <1, adherence score <5, and rounded atelectasis count = 0; (v) marked visceral adhesions: adherences ≥5, as well as cases with a rounded atelectasis count of ≥0.

Lung function methods

Flow-volume spirometry was performed with a rolling-seal spirometer (Mijnhardt BV, Bunnik, Holland) connected to a microcomputer (Medikro MR-3; Medikro, Kuopio, Finland), using the reference values of Viljanen (23), usually on the same day as the CT scan (for practical reasons sometimes with a maximum interval of 2–3 days), although at different hospitals. The flow-volume curve was formed with the envelope method from curves obtained from at least three successive forced expiratory breathing maneuvers, using the standards of the European Respiratory Society (24). The following parameters were measured: forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), the FEV_1/FVC ratio (FEV%), and forced expiratory flow at the level when 50% of the FVC remains exhaled (MEF_{50}). The single breath diffusing capacity for carbon monoxide (DL_{CO}), specific diffusing capacity (DL_{CO} related to alveolar volume, DL_{CO}/VA), and the total lung capacity (TLC) with the helium single-breath dilution method were measured using a Masterlab transfer or a compact lab transfer device (Erich Jaeger, Würzburg, Germany); the mean values from at least two successive measurements were recorded (25). In our analysis, the Viljanen reference values (23) were used to grade the ventilatory function, based on the distribution of values in the reference population. The FEV_1 and FVC values were graded as follows: normal ≥81%, slight 65–80%, moderate 45–64% and severe ≤44% impairment of the predicted value; MEF_{50} values: normal ≥62, slight 35–61% and severe ≤44% impairment of the predicted value; TLC values: normal ≥80%, slight 70–79% and marked ≤69% impairment of the predicted value; DL_{CO}: normal ≥74%, slight 60–73% and marked ≤59% impairment of the predicted value.

The intensity of exposure to asbestos was analyzed on the basis of occupation, the asbestos exposure diminishing in the following order: insulators, plumbers, carpenters, electricians, builders, and others. Smoking was calculated in pack-years.

Statistical methods

Smoking, asbestos exposure, and the scoring of radiological findings were compared between the different disease groups, using an analysis of variance. The results of the lung function tests were calculated as percentages of the predicted values (23), which varied according to age and height for the spirometric values and, for the DL_{CO}/VA, and TLC values, also according to weight. Odds ratios (OR) and 95% confidence intervals (95% CI) were calculated, using the PROG LOGISTIC procedure (SAS/STAT) (26). The graded lung function of each group was compared with that of persons displaying normal lung function, and graded lung function was dealt with as an independent variable and disease group as a dependent variable.

Results

Scoring of the high-resolution computed tomography

The grouping of workers based on the HRCT scoring is presented in table 1, in addition to the anthropometric and smoking data. The fibrosis score for those with combined fibrosis and emphysema was higher than for those with pulmonary fibrosis or marked visceral adhesions at a significance level of 0.05, but at a level of 0.01 the difference was not significant. The emphysema score did not differ between those with emphysema and those with combined fibrosis and emphysema. For marked visceral adhesions, the emphysema score was significantly lower than for emphysema or those with combined fibrosis and emphysema ($P<0.01$). Rounded atelectases were present only in the patients with marked visceral adhesions, with a mean score of 0.405 (SD 0.60).

Exposure

There were slight differences in the duration of asbestos exposure between the groups, but they were not significant (table 1). There was a nonsignificant excess of insulators with combined fibrosis and emphysema and carpenters with emphysema (table 2). Smoking ≥40 pack-years was associated with combined fibrosis and emphysema (OR 2.230, 95% CI 1.044–4.955) and emphysema (OR 2.521, 95% CI 1.338–4.856), as was smoking 30–39 pack-years with emphysema. The presence of smokers with ≥40 pack-years was negatively

Table 1. Anthropometric characteristics, smoking, and exposure data, as well as high-resolution computed tomography (HRCT) scoring of the 590 participants with asbestos exposure. A fibrosis score of <1 for emphysema (EMP) and pleural disease (PD) and an emphysema score of 0 for fibrosis had to be obtained; thus the statistical differences of these comparisons are not indicated. (SD = standard deviation, PF = pulmonary fibrosis, CFE = combined fibrosis and emphysema, ADH = marked visceral adhesions)

Patient group	Number (N=590)	Age (years)		Weight (kg)		Height (cm)		Pack-years [a]		Exposure (years)		HRCT							
												Fibrosis [b]		Emphysema [c]		Pleural thickening [d] (cm)		Marked visceral adhesions [e]	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Pleural disease	190	60.7	7.9	85.3	12.1	173.8	6.1	19.7	11.4	25.1	9.6	0.72	0.52	0	·	1.63	0.47	0.97	0.87
Emphysema	148	62.4	6.6	79.5	12.2	174.7	6.5	28.2	16.2	27.2	10.0	0.86	0.52	1.70	2.41	1.57	0.51	1.07	0.76
Pulmonary fibrosis	68	64.1	7.0	87.5	14.7	175	6.0	17.3	13.2	27.9	8.8	2.77	0.73	0	·	1.90	0.56	1.24	0.87
Combined fibrosis and emphysema	74	64.7	7.1	82.2	15.9	173.3	5.7	28.5	16.1	25.4	10.5	3.21	1.22	2.15	2.80	1.84	0.64	1.85	1.26
Marked visceral adhesions	110	63.1	7.3	80.7	13.3	174.1	7.3	25.8	16.3	25.3	9.5	2.2	1.4	0.94	1.85	2.30	0.55	5.9	3.6

[a] P<0.05: PF/PD; P<0.01: CFE/PD, CFE/PF, EMP/PD, EMP/PF, ADH/PD, ADH/PF.
[b] P<0.05: CFE/PF, CFE/ADH.
[c] P<0.01: ADH/EMP, ADH/CFE.
[d] Greatest thickness; P<0.01: CFE/EMP, CFE/PD, EMP/PF, PF/ADH, PF/PD, PD/ADH, CFE/ADH.
[e] P<0.01: ADH/PF, ADH/EMP, ADH/PD, ADH/CFE, CFE/PD.

Table 2. Percentage of different occupations in the patient groups.

Patient group	Occupations													
	Builders		Electricians		Carpenters		Plumbers		Insulators		Others		Total number	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Pleural disease	9	4.8	24	12.9	39	21.0	30	16.1	9	4.8	75	40.3	186	100
Emphysema	9	6.1	8	5.4	41	27.7	23	15.5	3	2.0	64	43.2	148	100
Pulmonary fibrosis	8	11.8	8	11.8	13	19.1	6	8.8	3	4.4	30	44.1	68	100
Combined fibrosis and emphysema	3	4.1	3	4.1	13	17.6	6	8.1	13	17.6	36	48.7	74	100
Marked visceral adhesions	12	11.0	9	8.3	21	19.3	11	10.1	7	6.4	49	45.0	109	100

Table 3. Lung function results of the patients in the different patient groups. (pred = predicted value, FVC = forced vital capacity, FEV_1 = forced expiratory volume in 1 second, FEV% = FEV_1/FVC ratio, MEF_{50} = forced expiratory flow at the level when 50% of the FVC remains exhaled, DL_{co} = single breath diffusing capacity for carbon monoxide, VA = alveolar volume, TLC = total lung capacity)

Patient groups	Spirometric variable																			
	FVC (l)		FVC (% of pred)		FEV_1 (l)		FEV_1 (% of pred)		FEV% (%)		FEV% (% of pred)		MEF_{50} (l/s)		MEF_{50} (% of pred)		DL_{CO} (% of pred)		DL_{CO}/VA (% of pred)		TLC (% of pred)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Pleural disease (N=190)	4.2	0.8	91.4	15.0	3.2	0.7	87.5	17.0	76.9	6.6	95.2	8.6	3.4	1.4	70.6	27.9	98.2	14.3	104.8	14.6	90. 2	10.9
Emphysema (N=148)	4.2	0.9	93.8	16.8	3.0	0.8	82.7	20.9	70.6	12.0	87.8	15.2	2.8	1.4	57.5	29.2	57.5	29.2	91.6	18.2	94. 6	13.6
Fibrosis (N=68)	4.0	0.8	88.4	13.9	3.1	0.7	85.4	14.9	78.7	7.5	96.8	9.6	3.5	1.2	73.2	24.3	93.0	15.3	103.6	13.7	86.4	10.9
Combined fibrosis and emphysema (N=74)	3.6	0.8	83.8	16.7	2.5	0.7	72.4	18.6	70.7	14.4	87.3	18.5	2.4	1.4	50.9	29.0	72.4	21.2	84.2	21.8	83.2	14.4
Marked visceral adhesions (N=109)	3.8	0.9	84.1	16	2.7	0.8	73.7	18.7	70.0	11.5	88.213.14		2.5	1.4	50.6	26.8	81.2	17.3	94.1	17.9	83	13.4

associated with pleural disease (OR 0.265, 95% CI 0.121–0.545) or pulmonary fibrosis (OR 0.212, 95% CI 0.068–0.545), as was smoking, 10–19 pack-years (OR 0.351, 95% CI 0.140–0.804) or 20–29 pack-years (OR 0.349, 95% CI 0.155–0.743).

Spirometry results

The lung function results of the groups are presented in table 3, and the occurrence of different gradings of the spirometric values is shown in table 4. Severe, moderate,

Table 4. Comparison of values of forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) between the patient groups. The measured FEV_1 values were related to reference values of Viljanen (23) and graded as follows: 0 = severe, ≤44% of predicted value; 1 = moderate, 45–64% of predicted value; 2 = slight, 65-80% of predicted value; 3 = normal, ≥81% of predicted value. The statistically significant values are shown in boldface. (OR = odds ratio, 95% CI = 95% confidence interval, grading = grading of the spirometric variables)

Patient group	FEV_1				FVC			
	Crude value		Adjusted value [a]		Crude value		Adjusted value [a]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Severe versus normal grading								
Pleural disease (N=190)	**0.34**	**0.14–0.71**	**0.32**	**0.12–0.75**	0.86	0.32–2.09	0.55	0.17–1.58
Emphysema (N=148)	1.42	0.70–2.77	1.27	0.59–2.66	1.26	0.50–3.06	1.75	0.57–5.13
Fibrosis (N=68)	0.52	0.12–1.53	0.67	0.15–2.19	1.27	0.29–3.91	1.65	0.32–6.33
Combined fibrosis and emphysema (N=73)	**3.41**	**1.40–7.76**	2.48	0.91–6.24	1.30	0.30–4.01	0.89	0.15–3.80
Marked visceral adhesions (N=107)	1.57	0.67–3.37	1.97	0.81–4.47	0.53	0.08–1.89	0.9	0.13–3.55
Moderate versus normal grading								
Pleural disease (N=190)	**0.35**	**0.19–0.63**	**0.45**	**0.23–0.83**	0.56	0.22–1.27	0.59	0.22–1.41
Emphysema (N=148)	0.76	0.40–1.36	0.63	0.32–1.16	0.67	0.24–1.59	0.65	0.23–1.58
Fibrosis (N=68)	**0.28**	**0.07–0.80**	**0.32**	**0.07–0.94**	0.57	0.09–2.00	0.58	0.09–2.11
Combined fibrosis and emphysema (N=73)	**3.59**	**1.79–7.09**	**2.72**	**1.31–5.57**	**2.99**	**1.19–6.89**	**2.81**	**1.05–6.89**
Marked visceral adhesions (N=107)	**3.14**	**1.78–5.5**	**2.98**	**1.65–5.34**	1.63	0.62–3.77	1.56	0.59- 3.66
Slight versus normal grading								
Pleural disease (N=190)	**0.48**	**0.30–0.75**	0.66	0.40–1.09	**0.57**	**0.35–0.91**	0.66	0.40–1.09
Emphysema (N=148)	1.03	0.64–1.63	0.93	0.56–1.51	0.68	0.40–1.11	**0.57**	**0.33–0.95**
Fibrosis (N=68)	1.04	0.55–1.88	1.19	0.62–2.24	1.12	0.57–2.08	1.28	0.64–2.45
Combined fibrosis and emphysema (N=73)	**2.74**	**1.47–5.11**	**2.21**	**1.15–4.23**	1.34	0.71–2.44	1.11	0.57–2.09
Marked visceral adhesions (N=107)	1.4	0.81–2.38	1.31	0.72–2.26	**2.27**	**1.39–3.66**	**2.23**	**1.35–3.64**

[a] Adjusted for age, asbestos exposure duration, and smoking.

or slight FEV_1 impairment was positively associated with combined fibrosis and emphysema, but negatively with pleural disease. Moderate FEV_1 impairment was associated negatively with pulmonary fibrosis. Moderate FEV_1 impaiment was also associated with marked visceral adhesions. Moderate FVC impairment was positively associated with combined fibrosis and emphysema, as was slight impairment positively associated with marked visceral adhesions (table 4). Severe MEF_{50} impairment was positively associated with combined fibrosis and emphysema (OR 1.96, 95% CI 1.01–3.77) and marked visceral adhesions (OR 3.37, 95% CI 1.92–5.94) and negatively with pleural disease (OR 0.38. 95% CI 0.22–0.66) and pulmonary fibrosis (OR 0.18, 95% CI 0.05–0.47). Slight MEF_{50} impairment was associated positively with marked visceral adhesions (OR 2.01, 95% CI 1.19–3.42).

Total diffusing capacity

Marked DL_{CO} impairment was significantly associated with combined fibrosis and emphysema (about fivefold risk), as was slight DL_{CO} impairment (twofold risk) (table 5). Marked or slight impairment was negatively associated with pleural disease, as was marked impairment with pulmonary fibrosis. A slight reduction in DL_{CO} was associated with marked visceral adhesions (table 5).

Totals of 53%, 12%, and 6% of the DL_{CO} values were lower than the reference limit for combined fibrosis and emphysema, pulmonary fibrosis, and pleural disease, respectively. The DL_{CO} values were significantly lower for the insulators than for the electricians or the group of "other" professions ($P<0.05$).

The grading of DL_{CO} was significantly associated with the mean fibrosis and emphysema scores of the patients with combined fibrosis and emphysema (table 6). The mean fibrosis score did not significantly differ among those with normal, slight, or marked DL_{CO} impairment. However, the total emphysema score was significantly higher for the patients with slight impairment ($P<0.05$) and for those with marked impairment, compared with those showing normal DL_{CO} values ($P<0.01$). When the DL_{CO} impairment was analyzed according to the emphysema type, the presence of centrilobular, paraceptal, or panlobular emphysema did not significantly differ between emphysema and combined fibrosis and emphysema.

Specific diffusing capacity

Impairment in DL_{CO}/VA occurred mainly in those with combined fibrosis and emphysema, for whom about a threefold occurrence in marked and slight impairment was found. Slight DL_{CO}/VA impairment was associated with marked visceral adhesions. Marked or slight DL_{CO}/VA impairment was negatively associated with pleural disease and pulmonary fibrosis (table 5).

Total lung capacity

A twofold occurrence of marked TLC impairment was apparent for patients with combined fibrosis and

Table 5. Comparison of single breath diffusing capacity for carbon monoxide (DL_{CO}) in relation to alveolar volume (VA) and total lung capacity (TLC) between the groups. The statistically significant values are shown in boldface. (normal = DL_{CO} ≥74 when compared with the predicted value of Viljanen (23), slight = DL_{CO} 60–73% of the predicted value, marked = ≤59% of the predicted value, grading = grading of DL_{CO}, DL_{CO}/VA, and TLC)

Patient group	DL_{CO}				DL_{CO}/VA				TLC			
	Crude value		Adjusted value [a]		Crude value		Adjusted value [a]		Crude value		Adjusted value [a]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Marked versus normal grading												
Pleural disease (N=190)	**0.24**	**0.11–0.46**	**0.21**	**0.09–0.45**	**0.34**	**0.15–0.70**	**0.32**	**0.12–0.72**	**0.47**	**0.26–0.83**	**0.43**	**0.22–0.78**
Emphysema (N=148)	1.36	0.77–2.35	1.15	0.62–2.06	**2.07**	**1.09–3.69**	1.89	0.97–3.64	0.72	0.39–1.25	0.66	0.35–1.19
Fibrosis (N=68)	**0.30**	**0.07–0.85**	0.36	0.08–1.05	0.43	0.10–1.22	0.54	0.12–1.64	1.08	0.48–2.21	1.23	0.53–2.61
Combined fibrosis and emphysema (N=73)	**5.51**	**2.93–10.22**	**4.94**	**2.48–9.77**	**3.53**	**1.74–6.88**	**2.81**	**1.27–5.99**	**2.13**	**1.12–3.92**	**2.05**	**1.02–3.96**
Marked visceral adhesions (N=107)	1.44	0.74–2.68	1.78	0.88–3.43	0.62	0.23–1.39	0.72	0.26–1.69	**1.92**	**1.07–3.36**	**2.19**	**1.2–3.9**
Slight versus normal grading												
Pleural disease (N=190)	**0.43**	**0.22–0.78**	**0.32**	**0.12–0.72**	**0.05**	**0.00–0.24**	**0.06**	**0.00–0.29**	0.59	0.30–1.07	0.56	0.28 -1.06
Emphysema (N=148)	0.91	0.48–1.65	0.70	0.36–1.31	1.65	0.78–3.35	1.25	0.57–2.59	**0.19**	**0.06–0.48**	**0.18**	**0.05–0.47**
Fibrosis (N=68)	0.55	0.19–1.29	0.68	0.22–1.68	**<0.001**	**·· –0.38**	**<0.001**	**·· –0.52**	1.72	0.78–3.51	1.85	0.81–3.89
Combined fibrosis and emphysema (N=73)	**2.05**	**1.02–3.96**	**2.81**	**1.27–5.99**	**3.49**	**1.53–7.47**	**3.21**	**1.34–7.26**	1.52	0.66–3.15	1.51	0.64–3.28
Marked visceral adhesions (N=107)	**3.26**	**1.84–5.7**	**3.25**	**1.78–5.84**	**2.57**	**1.22–5.19**	**2.48**	**1.15–5.15**	**3.17**	**1.73–5.7**	**3.06**	**1.65–5.58**

[a] Adjusted for age, asbestos exposure duration, and smoking.

emphysema (table 5). Pleural disease was negatively associated with marked impairment, as was emphysema with slight impairment in the TLC values. Marked visceral adhesions displayed a twofold increased occurrence in marked and threefold increased occurrence in slight TLC impairment. When TLC was analyzed according to occupation, the insulators showed significantly lower TLC values (P=0.02) than the group of "other" occupations.

Discussion

In our study of smoking asbestos-exposed workers, emphysema scoring assessed with HRCT appeared to be a strong determinant of lung function impairment in patients with combined pulmonary emphysema and fibrosis, who displayed the most severely reduced FEV_1, DL_{CO}, and TLC values. Persons with "pure" lung fibrosis showed, at most, slight ventilatory impairment and a slight reduction in DL_{CO}, although their fibrosis score approached that of persons with combined disease.

Several authors have investigated the simultaneous effect of asbestos exposure and smoking on the lungs; in some studies an additive effect of asbestos exposure and cigarette smoking on lung function was suggested (27–29). It was also suggested that smoking could augment the inflammatory process in pulmonary fibrosis, causing its progression to interstitial fibrosis (30). These earlier studies were performed without the use of CT scanning, and it may be that, using ordinary roentgenograms, it has not been possible to differentiate early asbestosis from small emphysema blebs. When the relationship between HRCT findings and smoking was analyzed (22), smoking appeared to increase all emphysema signs but to diminish the signs of fibrosis, as also shown in our study. Persons with combined disease had smoked additional numbers of pack-years when compared with those with pulmonary fibrosis only. Their fibrosis score was only slightly increased in comparison with that of patients with pulmonary fibrosis; however, they had developed severe signs of emphysema.

In our study, lung fibrosis was usually slight or moderate. This finding was not likely to have been dependent on the radiological scoring system, which had been carefully validated earlier (19, 20, 22) Workers with heavy asbestos exposure (eg, asbestos miners) were not included in the study, in which an excess of the most

Table 6. Grading of total diffusing capacity for those with combined fibrosis and emphysema in relation to the mean fibrosis and emphysema scores in the variance analysis. One patient lacked information on diffusing capacity (N=73).

Grading of diffusing capacity	Number		Scores			
			Fibrosis [b]		Emphysema [a]	
	N	%	Mean	SD	Mean	SD
Normal	34	46.6	2.99	1.07	0.81	0.90
Slight impairment	18	24.7	3.25	1.20	2.66	2.41
Marked impairment	21	28.8	3.46	1.45	3.95	3.92

[a] Differed significantly between all gradings at levels of P<0.05 and P<0.01 between normal and severe impairment.
[b] Did not differ between the different gradings of diffusing capacity.

intensively exposed occupation (ie, insulators) occurred in the group with combined fibrosis and emphysema. Of the 35 insulators, 13 (37%) had developed combined disease, whereas, in the remaining professions, the percentage of combined disease varied from 6% to 14%. Although it is difficult to quantify asbestos exposure exactly according to occupation, the insulators were the most heavily asbestos-exposed workers in our study. Our material was collected for a screening study, and more precise information on asbestos exposure was not available. When the insulators were compared with the remaining occupations, reduced DL_{CO} values (<74% of the predicted value) occurred in 45% of the insulators, more than the workers in the remaining occupations (between 11.5% and 27.5%).

Persons with emphysema showed smoking histories similar to those with combined disease. In the emphysema group the number of insulators was low, but the next most intensively exposed occupations, plumbers and carpenters, were well represented. However, neither the intensity of smoking nor the differences in asbestos exposure was sufficient to explain why some workers developed emphysema only and some had combined fibrosis and emphysema. Therefore, individual susceptibility to smoking, asbestos, or both may also have played a role.

In our study, the lung function results were graded according to the reference values (23). A similar grading is used as the basis for economic compensation for impairment resulting from occupational lung diseases in Finland. Several attempts at a correlation analysis, variance analysis or multivariate analysis throughout the entire volume of patient data were attempted. However, we did not find these useful because the lung function impairment overlapped between the diagnoses, necessitating classification according to "pure" disease groups.

Patients with marked adherences were the most diverse patient group; however, adhesions resulted in a mainly restrictive functional impairment, as expected. Pleural thickenings were found among all the workers, and we cannot exclude their effects on lung function. Although our interest was not specifically focused on pleural thickenings, the odds ratios for pleural thickenings were usually very low (<1), indicating normal lung function. Recent evidence has suggested that pleural thickenings are of minor importance in lung function impairment (14). In our study, no nonsmoking control group was available because these analyses were originally performed in a study screening for asbestos-induced cancer (19). Ethically, an HRCT study on nonsmokers unexposed to asbestos could be difficult to undertake.

DL_{CO} is regarded as a sensitive measure of parenchymal disease and was suggested to serve in the separation of persons with well-established asbestosis from those who do not have radiologically detectable alterations (9). Our study, however, indicates that, in the follow-up or early phases of asbestosis in smoking asbestos-exposed persons, a reduction in DL_{CO} is more a reflection of the development of emphysema than of pulmonary fibrosis. This finding does not, however, reduce the value of DL_{CO} measurements for asbestos-exposed workers.

Small-airway disease has been described by several investigators as associated with asbestos exposure (9, 12, 31, 32), caused by the accumulation of asbestos bodies in the walls of respiratory bronchioles (9). We could not distinguish small-airway disease in the HRCT scans; however, the profiles of reduced expiratory flows and volumes in asbestos exposure were also found for those with combined fibrosis and emphysema and also for those with adherences, characterized by lowered values for FEV_1/FVC ratio, FEV_1, and MEF_{50}. The most severely impaired MEF_{50} was found for those with adherences, and this finding may also partially be explained by the airway compression involved in restrictive pulmonary processes.

TLC was measured with the helium single-breath method and thus excluded nonventilated trapped air, which could explain the TLC reduction observed in some cases. This possibility was actually confirmed in clinical examinations because, for those with a reduced TLC value, volume spirometry with the helium steady-state method was also performed. These measurements were, however, not included in our present study, because only a small number of the patients were examined with this alternative method. However, this omission is not likely to have caused bias because the most important findings dealt with the DL_{CO} results.

We found no association between the duration of asbestos exposure and the development of lung diseases in our patients, in contrast to Staples et al (11) and Al Jarad et al (33), possibly due to the rather similar asbestos exposure durations of the patients. On the other hand, variation in the intensity of asbestos exposure in our population may also explain the absence of this association in comparison with the situation in earlier studies (11, 33).

In conclusion, our results indicate that the presence of emphysema in asbestos-exposed workers was the predominant factor in the impairment of pulmonary function in the persons with slight-to-moderate asbestosis. Smoking appears to be the most important cofactor in the development of functional impairment. However, these findings do not fully explain why some of these smoking asbestos-exposed persons developed emphysema only and the others developed both emphysema and fibrosis.

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