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CASE REPORT

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Lung function not affected by asbestos exposure in workers with normal Computed Tomography scan

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Background: It has been suggested that asbestos exposure affects lung function, even in the absence of asbestos-related pulmonary interstitial or pleural changes or emphysema. Methods: We analyzed associations between well-known asbestos-related risk factors, such as individual cumulative asbestos exposure, and key lung function parameters in formerly asbestos-exposed power industry workers (N = 207) with normal CT scans. For this, we excluded participants with emphysema, fibrosis, pleural changes, or any combination of these. Results: The lung function parameters of FVC, FEV1, DLCO/VA, and airway resistance were significantly associated with the burden of smoking, BMI and years since end of exposure (only DLCO/VA). However, they were not affected by factors directly related to amount (eg, cumulative exposure) or duration of asbestos exposure. Conclusions: Our results confirm the well-known correlation between lung function, smoking habits, and BMI. However, we found no significant association between lung function and asbestos exposure.

KEYWORDS
asbestos dust, asbestos exposure, CT, MDCT, lung function

1 | INTRODUCTION

In the 20th century, due to its excellent physical properties, asbestos was frequently used in workplaces where high temperatures or the need for heat protection demanded the use of insulation materials. Therefore, despite the lack of documented exposure data, an increased risk of asbestos exposure can be assumed for such workplaces, which were frequently found in the power generating industry.[1–4] The development of the use of asbestos in Germany is comparable to other industrialized countries.[5–7] After a series of restrictions, the importation and processing of asbestos and asbestos-containing materials was totally banned in 1993.

As early as the 1950s, asbestos dust was known to be a powerful carcinogen with a long-term effect on the lungs and pleura, causing lung cancer and malignant pleural mesothelioma. Other known effects include nonmalignant changes in lung tissue (asbestosis) and pleura (pleural thickening, eg, plaques), in some cases leading to restrictive lung disease.[5–8]

There is general agreement in the literature that the risk of nonmalignant changes is related to age,[9] cumulative asbestos exposure,[9–13] time since first exposure (latency)[10,11,13,14] and exposure duration.[9,12–14] High levels of cumulative exposure in combination with a history of smoking are usually associated with parenchymal changes.[15] The first cases of asbestos-related diseases may appear a few years after the beginning of exposure, although very long latency periods of several decades are common.[16] Decreased lung function parameters are often associated with these effects, which are frequently combined with the influencing factor of a high BMI, and possibly with a genetically determined predisposition for a specific pathophysiological reaction.[17–24] The relationship between decreased lung function parameters and asbestos-related pulmonary interstitial or pleural changes or emphysema, and the risk factors of asbestos dust and cigarette smoke, have been analyzed in various studies.[25–33]

It is still unclear whether the exposure to asbestos dust affects lung function in the absence of asbestos-related pulmonary interstitial or pleural changes or emphysema visible on multidetector-row CT (MDCT), or whether lung function impairment is always a secondary effect of structural changes in the lung tissue or pleura.[33,34] Therefore, the aim of our study was to examine the association between several known risk factors and various lung function parameters in a group of

asbestos-exposed individuals without any signs of asbestos-related disease on MDCT.

2 | MATERIALS AND METHODS

2.1 | Study design

In the late 1990s enrolment in the survey was started as an internal health program of a major provider of electrical power in Germany. The main purpose of the survey was the early detection of cases with asbestos-related diseases in all active and former employees, who had been exposed to asbestos. All of the 8565 individuals who responded by submitting a signed statement that they had been exposed to asbestos fibers were entered into the study group. The individual cumulative exposure to asbestos was estimated on the basis of job titles, main occupational tasks and self-reported periods of exposure. A computer program based on ambient monitoring data of airborne asbestos fiber concentrations at specific, carefully defined workplaces and periods of exposure was used for these calculations.

As the safety precautions after the banning of asbestos in 1993 were rigorous, periods of exposure after this time were not included. Even if short periods of unprotected exposures after 1993 cannot be completely ruled out, fiber concentrations would not have been comparable to those measured prior to the banning of asbestos.[35] Cumulative asbestos exposure was expressed as a product of the total exposure duration and the 8-h time weighted average fiber concentration (in fibers/cubic centimeter × years or "fibre years"). One standard fiber year was defined as an exposure of 1920 work hours accumulated through daily 8-h shifts over 240 workdays spread over 48 weeks with a standard airborne concentration of one fiber per cubic centimeter or 1×10^6 fibers per cubic meter. In order to obtain the information required to calculate the cumulative exposure, a specially designed self-administered questionnaire was sent to each participant prior to examination.

A standard medical examination, including lung function testing (PFT) and an X-ray of the thorax (CXR or MDCT), was started in March 2002.[36] By the end of 2013, a total of 7703 participants had been examined at least once. A routine annual examination including MDCT was restricted to a high-risk group of 338 participants, of whom 273 (3.54%) have been examined at least once. For these participants a higher risk of developing an asbestos-related disease was assumed, due to their cumulative asbestos exposure, smoking habits and age. For participants with a lower cumulative exposure and burden of smoking, who were usually younger, we assumed a lower risk of developing asbestos-related diseases. Those not in the high risk group were routinely examined annually (medium risk) or every 3 years (low risk) using CXR. In the case of equivocal findings on CXR, they received a secondary MDCT ($N = 926$).[37] Thus, a total of 1199 (15.6%) participants was examined with MDCT at least once. Changes in lung tissue and pleura on MDCTs were recorded using the International Classification of Occupational and Environmental Respiratory Diseases (ICOERD).[38–43] MDCTs were evaluated independently by two experienced readers. In cases of disagreement, a consensus reading was used for final assessment. All readers, who were either specialists in thoracic imaging, radiologists or occupational physicians, scored the MDCTs for signs of asbestosis, asbestos-associated pleural disease and any type of emphysema. MDCTs classified as "abnormal" showed at least one of the following: irregular/linear opacity of at least grade 1 in both lower fields, any pleural findings of parietal or visceral pleura or any sign of emphysema. Although not directly related to asbestos exposure, we considered emphysema as an exclusion criterion because it affects lung function and would mask dust related effects not indicated by radiological signs.

The main objective of our analysis was to investigate the influence of various risk factors such as asbestos exposure and smoking habits on lung function in absence of asbestos-related pulmonary interstitial or pleural changes or emphysema. To avoid the effects of possible systematic inter-center bias when comparing results from different examination centers, we used only lung function results carried out at the Institute of Occupational and Social Medicine at RWTH Aachen University (IOSM), which was the biggest and most experienced examination center. As the MDCTs of 652 participants showed signs of emphysema ($n = 79$), asbestos-related changes ($n = 296$), or both ($n = 277$), 207 participants qualified for analysis. A more detailed description of the study population can be found in Felten et al[35] and Eisenhawer et al.[36]

2.2 | Examination with MDCT

Examinations of the whole lung with MDCT were done without administering contrast material and performed during a one breath-hold with the participant in a supine position (SOMATOM Sensation 16, Siemens Medical Solutions, Forchheim, Germany). A standard low-dose MDCT protocol was used: 120 kV, individuals weighing less than 80 kg with $10mAs_{eff}$/individuals weighing 80 kg and more with $20mAs_{eff}$, 16 × 0.75 mm collimation, a rotation time of 0.5 s, and a table feed/rotation of 18 mm. For analysis of soft tissue changes, mediastinal changes, pleural changes, additional asbestos-related changes, and detection of pulmonary nodules, MDCTs were reconstructed using three different methods described in Das et al[44] and Eisenhawer et al.[36]

2.3 | Lung function testing

All PFTs used in this evaluation were done at the outpatient department of the IOSM and usually carried out on the same day as the MDCT. Technical equipment, calibration routine, and standard procedures were consistent for all testing cycles. We used a whole-body plethysmograph, from MasterScreen body CareFusion, Germany, to measure all parameters, including the spirometric values of forced expiratory volume in one second (FEV1,l) and forced vital capacity (FVC,l), air way resistance (R'tot,kPa*s/l), and single-breath carbon monoxide diffusing capacity adjusted for alveolar volume (DLCO/VA,mmol*l/min*kPa) acquired with additional gas transfer equipment by the same manufacturer. The airway resistance was

considered, since the measurement of this value is less affected by the co-operation of the participant. Further, this is an essential lung function parameter for the assessment of obstruction.[45]

For analysis, results of FVC, FEV1, and DLCO/VA were set in relation to the corresponding reference values. Here, the 2012 published reference value equations of the Global Lungfunction Initiative (GLI)[46] were used for FVC and FEV1. For DLCO/VA we used the equations of the European Coal and Steel Community (ECSC).[47–49] For R'tot the raw measurement was used. FVC and FEV1 results below the lower limit of normal (LLN), DLCO/VA measurements below 80% and R'tot measurements above 0.3kPa*s/l were classified as abnormal.

2.4 | Characteristics of the study population

The general characteristics of the study population are summarized in Table 1.

The 207 male participants showed a mean cumulative asbestos exposure of 49.0 (0.1-844.9) fiber years, accumulated over the mean exposure duration of 21.4 years. Due to the mean cumulative asbestos exposure, the cohort can be regarded as highly exposed to asbestos dust. In comparison, the individuals who were excluded due to asbestos-related diseases had a significantly higher exposure with regard to latency, duration of exposure and time since end of exposure (Table S1). Although our study group was less exposed with regard to cumulative asbestos exposure (49 fiber years vs 63,7 fiber years), this difference was not significant.

The standard deviation of the cumulative asbestos exposure is extremely large, due to the different workplaces of the participants. The cohort includes for example participants working in management (low asbestos exposure) as well as participants who regularly attended in technical turbine revisions (technical inspection, maintenance, and repair of turbines) with extreme levels of asbestos exposure and were therefore highly exposed to asbestos dust. In regards to smoking status, 43 (20,8%) participants reported being active smokers, 111 (53.6%) being ex-smokers, and 53 (25.6%) reported that they had never smoked. The mean tobacco exposure was 34.4 pack years, taking into consideration only active and ex-smokers. With 98.5% and 95.8%, respectively, of the age adjusted reference values the mean values for FVC and FEV1 are very close to the expected results (Table 2).

Likewise, the values for DLCO/VA and R'tot were in the range of the expected results of the general population. The FVC results for 11 participants and the FEV1 results for 22 participants were below the LLN. In two participants the DLCO/VA values were below the 80% limit of the corresponding reference values and in another 67 the results for R'tot were above 0.3 (kPa*s/l) indicating obstructive lung disease. Based on these measurements, the lung function of approximately one third of the participants (n = 74) was classified as abnormal.

TABLE 1 Study population of formerly asbestos-exposed power industry workers with no radiological changes on MDCT (n = 207)

	N (%)	Mean (SD)	Range
Age at examination (years)	207 (100)	61.2 (9.5)	36.4-79.9
BMI[a] (kg/m^2)	207 (100)	30.3 (4.1)	22.7-45.2
Pack years, smokers[b]	154 (100)	34.4 (23.7)	1-120
Asbestos exposure (years)	207 (100)	21.4 (9.3)	1-42
Cumulative exposure[c] (fiber/cc × years)	207 (100)	49.0 (114.2)	0.1-844.9
Latency[d] (years)	207 (100)	36.2 (9.8)	13-60
Time since end of exposure (years)	207 (100)	14.8 (4.6)	9-37

[a]Body mass index.
[b]Including active smokers at time of examination and ex-smokers (n = 154).
[c]In fibers/cubic centimeter—years, based on a standard fiber year with a standard airborne fiber concentration of one fiber per cubic centimeter.
[d]Time since beginning of exposure.

2.5 | Ethics review and approval

This study was approved by the local ethics committee of the Medical Faculty of the RWTH Aachen University (EK 043/09). Each participant has given written consent to participate.

2.6 | Statistical analysis

The aim of the analysis was to investigate the effect of exposure to asbestos dust on key lung function parameters in individuals with no radiological signs of emphysema or asbestos-related pulmonary interstitial or pleural changes. Therefore, univariate and multivariate regression analyses were conducted with $FVC_{\%}$, $FEV_{\%}$, $DLCO/VA_{\%}$, and R'tot as dependent variables. The risk factors of age (at time of examination), body mass index (BMI), smoking status (never-, ex-, and active smoker) and smoking history (pack years) were used as independent variables not related to asbestos. Furthermore, we used key factors related to occupational history and dust exposure, which are known to be associated with typical radiological changes, namely duration of asbestos exposure, latency, time since end of exposure and fiber years as a measure of cumulative exposure. In multivariate analysis, the models were fitted by using a stepwise selection algorithm, combining aspects of forward and backward selection.

First, we summarized the main characteristics of the study population using descriptive statistics. Measures of central tendency, of variability and contingency tables for categorical data were reported.

TABLE 2 Study population of formerly asbestos-exposed power industry workers with no radiological changes on MDCT (n = 207)

	N (%)	Mean (SD)	Range
FVC (%)[a]	207 (100)	98.5 (14.4)	59.4-137.5
FEV1 (%)[a]	207 (100)	95.8 (17.9)	43.4-136.6
DLCO/VA (%)[a]	191 (92.3)	111.4 (16.6)	67.6-159.8
R'tot	206 (99.5)	0.28 (0.14)	0.10-1.15

[a]% of reference value.

Second, we investigated the association between the study variables and the spirometric results, starting with scatterplots which did not contradict the assumption of a linear relationship. For this reason, univariate and multivariate linear regression was applied to assess the effect of the study variables.

Third, we used analysis of variance (ANOVA) to investigate differences in lung function between never-smokers, ex-smokers, and smokers. Further, the effect of the asbestos-related risk factors was individually examined by multivariate linear regression for never-smokers, ex-smokers, and smokers. All statistical analyses were performed using SPSS software Version 20 (IBM).

3 | RESULTS

3.1 | Lung function and risk factors

Descriptive statistics pointed to a linear relationship between the risk factors of age, BMI, burden of smoking, cumulative asbestos exposure, latency, duration of exposure, time since end of exposure and the lung function parameters $FVC_{\%}$, $FEV1_{\%}$, $DLCO/VA_{\%}$, and R'tot. Therefore, we based our analysis on univariate and multivariate linear regression models. For all considered lung function parameters, number of pack years and BMI were found to have a significant effect in the univariate analyses (Table 3).

In addition, a significant effect of the time since end of exposure on DLCO/VA became obvious. None of the risk factors related to duration and amount of asbestos exposure showed a significant association with the considered lung function parameters in univariate analysis.

Furthermore, in multivariate analysis for every considered lung function parameter, pack-years, and BMI showed a significant effect and were therefore included in the regression model (Table 4).

While these were the only variables included for FVC, FEV1, and R'tot, the age at time of examination showed some effect on $DLCO/VA_{\%}$. None of the risk factors related to duration and amount of asbestos exposure showed a significant effect on any of the considered lung function parameters either in univariate or in multivariate analysis. Furthermore, investigations using regression models adjusted for the previously determined risk factors (Table S2), did not show a significant association for any of the asbestos-related risk factors.

However, ANOVA showed statistically significant differences between the smoking subgroups with regard to FVC, FEV1, DLCO/VA, R'tot, and age (Table 5). In contrast, the three groups did not vary significantly with regard to the asbestos-related risk factors.

In comparison to the group of never-smokers, the ex-smokers showed a slight reduction in FEV1, whereas the other lung function parameters showed no significant differences. In contrast, the mean FVC, FEV1 and DLCO/VA values of the smokers were significantly lower compared to the results of the never-smokers and ex-smokers. Furthermore, the mean R'tot value of the smokers was significantly higher than that of the never-smokers.

In addition, we carried out an analysis of the association of the asbestos-related risk factors and lung function using regression

TABLE 3 Predictors of change of lung function in asbestos-exposed subjects according to univariate linear regression of various risk factors ($n = 207$)

	FVC (%)[a]			FEV1 (%)[a]			DLCO/VA (%)[a]			R'tot (kPa*s/l)		
	B	95%CI	*P*-value	B	95%CI	*P*-value	B	95%CI	*P*-value	B	95%CI	*P*-value
Cumulative exposure[b]	0.009	0.008, 0.03	0.29	0.01	−0.01, 0.03	0.27	−0.02	−0.04, 0.005	0.13	0.000	−0.001, 0.000	0.09
Exposure duration[c]	0.06	0.15, 0.28	0.57	0.04	−0.23, 0.31	0.78	0.01	−0.27, 0.27	0.93	−0.004	−0.01, 0.002	0.19
Latency[c]	0.01	−0.19, 0.21	0.91	−0.04	−0.29, 0.21	0.75	−0.13	−0.38, 0.12	0.31	−0.002	−0.008, 0.004	0.53
Time since end of exposure[c]	−0.19	−0.62, 0.23	0.37	−0.34	−0.87, 0.20	0.22	−0.59	−1.09, −0.08	0.02	0.008	−0.004, 0.02	0.19
Smoking[d]	−0.14	−0.22, −0.07	0.000	−0.29	−0.32, −0.14	0.000	−0.13	−0.22, −0.04	0.005	0.005	0.002, 0.007	0.000
Body mass index[e]	−1.07	−1.53, −0.60	0.000	−0.92	−1.51, −0.32	0.003	1.04	0.48, 1.60	0.000	0.04	0.03, 0.05	0.000
Age at examination[c]	0.07	−0.14, 0.28	0.49	0.08	−0.19, 0.34	0.57	0.11	−0.15, 0.38	0.40	−0.001	−0.007, 0.005	0.72

[a]% of reference value.
[b]In fibers per cubic centimeter and years, based on one standard fiber year with an airborne fiber concentration of one fiber per cubic centimeter.
[c]In years.
[d]In pack years, based on 20 cigarettes per day for 1 year.
[e]In kg/m^2.

TABLE 4 Formerly asbestos-exposed power industry workers with no changes on MDCT: multivariate regression models for the effect of non-asbestos risk factors on the main the lung function parameters ($n = 207$)

	FVC (%)[a]			FEV1 (%)[a]			DLCO/VA (%)[a]			R'tot (kPa*s/l)		
	B	95%CI	*P*-value	B	95%CI	*P*-value	B	95%CI	*P*- value	B	95%CI	*P*- value
Body mass index[b]	−0.97	−1.43, −0.51	0.000	−0.75	−1.32, −0.18	0.01	1.28	0.72, 1.84	0.000	0.04	0.02, 0.05	0.000
Smoking[c]	−0.12	−0.20, −0.05	0.001	−0.21	−0.30, −0.12	0.000	−0.16	−0.25, −0.07	0.000	0.004	0.002, 0.006	0.000
Age at examination[d]	–	–	–	–	–	–	0.26	0.002, 0.51	0.048	–	–	–

[a]% of reference value.
[b]In kg/m^2.
[c]In pack years, based on 20 cigarettes per day for 1 year.
[d]In years.

analysis stratified by smoking status. The analysis within the group of never-smokers enables us to analyze the associations in the absence of the burden of smoking. However, it should be taken into account that the stratified analysis leads to a loss of power. For the never-smokers we adjusted for BMI and for the ex-smokers and smokers for BMI and pack years (Table 6).

A significant association between the risk factors related to duration and amount of asbestos exposure and the considered lung function parameters was not observed in any of the three subgroups of never-smokers, ex-smokers, or smokers.

4 | DISCUSSION

Inhalation of dust particles, including tobacco smoke and asbestos dust, causes impairment of lung function. The overlying effects of ageing and a possible genetically determined predisposition for a specific pathophysiological reaction resulting in decreased lung function parameters are frequently combined with the influencing factor of a high BMI. The relationship between the risk factors of asbestos dust and cigarette smoke as well as the asbestos-related pulmonary interstitial or pleural changes or emphysema and decreased lung function parameters have been analyzed in various studies.[25–33] The impact of these asbestos-related changes on lung function parameters and clinical status, especially those which are limited or not clearly visible on conventional CXR, is still controversial. However, there is agreement that isolated pleural plaques and pleural thickening, especially with an increase in the involvement of the pleura and signs of visceral pleural involvement are associated with increased impairment of lung function.[28,29,31,43,48,50–57]

Asbestosis leads primarily to signs of restricted ventilation with a decrease of FVC.[25,28,33,54,58] Smoking-associated opacities in heavy smokers are difficult to distinguish from mild asbestosis, and smoking related emphysema is the primary cause of obstructive lung disease with a decrease of FEV1, FEV1/FVC, and diffusing capacity.[59] Some concern has been raised that "asbestos-exposed workers may present lung function impairments even in the absence of radiological evidence of asbestos-related pleural fibrosis or asbestosis."[33] However, the basic assumption that lung function impairment with clinical significance always has a structural equivalent visible on sensitive radiography has rarely been addressed.[34] In order to test the hypothesis that some effective pathological mechanism or unknown additional confounders may impact lung function without radiological signs, we analyzed occupational asbestos exposure data and lung function results of power industry workers without signs of asbestos-related abnormalities or emphysema on MDCT.

We focused primarily on two aspects, namely the comparison of lung function results with current reference values (GLI for FVC and FEV1; ECSC for DLCO/VA) to detect a possible overall impairment of lung function in our cohort, and secondly the correlation of asbestos-related risk factors (cumulative asbestos dose and exposure duration) with FEV1, FVC, DLCO/VA, and R'tot results. The characteristics of our cohort, as shown in Table 1, were well suited for analysis. Further, the fact that smokers (defined in our study as active smokers at time of

TABLE 5 Analysis of variance for lung function parameters and risk factors for never-smokers, ex-smokers and Smokers

	Mean (SD)			ANOVA	
	Neversmokers (*N* = 53)	Ex-smokers (*N* = 111)	Smokers (*N* = 43)	*F*	*P*-value
FVC (%)[f]	101.7 (15.7)[c]	99.3 (13.6)[c]	92.3 (12.9)[a,b]	5.83	0.003
FEV1 (%)[f]	100.6 (18.1)[c]	96.6 (18.0)[c]	87.7 (14.8)[a,b]	6.79	0.001
DLCO/VA (%)[f]	114.6 (13.3)[c]	114.0 (15.4)[c]	99.4 (19.1)[a,b]	13.06	0.000
R'tot (kPa*s/l)	0.24 (0.14)[c]	0.28 (0.14)	0.32 (0.20)[a]	3.07	0.048
Age at examination (years)	61.0 (9.1)	62.5 (8.8)[c]	57.9 (10.7)[b]	3.89	0.022
Body mass index (kg/m^2)	29.6 (3.7)	30.6 (3.9)	30.4 (4.9)	1.01	0.37
Cumulative exposure (fiber/cc × years[d])	55.1 (122.2)	52.1 (120.8)	33.4 (83.5)	0.51	0.60
Asbestos exposure (years)	21.3 (8.7)	22.3 (9.2)	19.3 (9.9)	1.60	0.20
Latency[e] (years)	35.6 (8.7)	37.4 (9.4)	34.0 (11.8)	2.06	0.13
Time since end of exposure (years)	14.3 (4.0)	15.1 (5.2)	14.6 (3.9)	0.58	0.56

[a]Significantly different from never-smokers ($P < 0.05$).
[b]Significantly different from ex-smokers ($P < 0.05$).
[c]Significantly different from smokers ($P < 0.05$).
[d]In fibers/cubic centimeter—years, based on one standard fiber year with an airborne fiber concentration of one fiber per cubic centimeter.
[e]Time since beginning of exposure.
[f]% of reference value.

examination and ex-smokers) and individuals with a high BMI (mean around 30) were well represented, despite the strict selection process admitting only MDCT-normal participants, allowed for a meaningful analysis of the impact these factors had on lung function.

The slightly reduced mean values for FVC and FEV1 in comparison with the reference values (Table 2) are in line with similar evaluations of asbestos-exposed cohorts. The tendency of rather high values for DLCO/VA with a mean of more than 111% may be seen as an effect of the high BMI values of the cohort. This was mainly due to the fact that an increased BMI was significantly associated with decreased VA (Table S3). An association with DLCO could not be observed. This may indicate an unsuitable age adaptation of the reference values for DLCO/VA. The high proportion of participants (35.7%) with lung function values classified as "abnormal" was mainly caused by individuals with an increased airway resistance, which was consistent with the fact that about three quarters of the cohort were former or active smokers.

We found a significant association between the lung function parameters $FVC_{\%}$, $FEV1_{\%}$, $DLCO/VA_{\%}$, and R'tot, and the risk factors of smoking and BMI, which is in agreement with the literature and well known. Furthermore, DLCO/VA was correlated with the time since end of exposure and the age at time of examination. These results may also point to an inaccurate age-adaptation of the DLCO/VA reference values, which are currently under revision by the DLCO-Task Force of the GLI (www.lungfunction.org).

There is a general agreement in the literature that lung function parameters are strongly affected by smoking habits, as we have also seen in our data. As the strong effect of smoking may obscure the effects of the asbestos-related risk factors on lung function, we further analyzed these associations separately for never-smokers, ex-smokers, and active smokers. The ANOVA test showed significant differences between never-smokers, ex-smokers, and smokers with regard to lung function and age, but not asbestos exposure. Never-smokers showed no impairment of lung function, indicated by the means of FVC, FEV1, DLCO/VA, and R'tot. Ex-smokers had slightly, but not significantly, decreased mean values, with the strongest deviation for FEV1 (96.6%). In contrast, smokers had significantly reduced mean values for all considered lung function parameters.

The findings for the ex-smokers seem to be unusual. However, a possible explanation for this might be the mean time since quitting smoking of 20.12 years. In addition, 75.67% (84 of 111) of the ex-smokers stopped smoking more than 10 years ago. There are indications that smoking cessation prevents accelerated decline in lung function and with longer times of smoking abstinence lung function normalizes.[60,61]

In univariate analysis we found an association between DLCO/VA and the time since end of exposure. We found no correlation between the considered lung function parameters and the variables determining the amount and duration of exposure to asbestos. In particular, no association between these variables and the lung function parameters could be observed in the never-smokers. Therefore, we did not find an effect of asbestos dust exposure on lung function in the absence of asbestos-related pulmonary interstitial or pleural changes or emphysema visible on MDCT.

Our homogenous, heavily exposed group was carefully selected on the basis of sensitive MDCT-scans and the judgment of two experienced readers. This careful selection of the study group might have introduced a selection bias, which could not be avoided since we wanted to consider the effect of asbestos exposure without asbestos-related pulmonary interstitial or pleural changes or emphysema. The use of individual exposure estimates for all participants ensured the best possible data and the use of a single examination center avoided a likely bias caused by inter-center variation due to the use of different equipment or different examination routines. Only for the examinations carried out at the IOSM could it be ensured that the examination routine and equipment remained consistent for the whole time.

TABLE 6 Formerly asbestos-exposed power industry workers with no changes on MDCT: linear regression of the main asbestos- and time-related risk factors of lung function separately for never-smokers, ex-smokers and smokers

	FVC (%)[a]			FEV1 (%)[a]			DLCO/VA (%)[a]			R'tot (kPa*s/l)		
	B	95%CI	*P*-value	B	95%CI	*P*-value	B	95%CI	*P*-value	B	95%CI	*P*-value
Never-smokers[d] (*n* = 53)												
Cumulative exposure (fiber/cc × years[b])	−0.01	−0.05, 0.02	0.47	−0.009	−0.05, 0.03	0.68	−0.01	−0.04, 0.02	0.43	0.00	−0.001, 0.001	0.80
Asbestos exposure (years)	−0.35	−0.87, 0.16	0.17	−0.46	−1.04, 0.13	0.12	0.17	−0.26, 0.60	0.43	−0.001	−0.02, 0.01	0.87
Latency[c] (years)	−0.39	−0.90, 0.12	0.13	−0.41	−1.001, 0.18	0.17	0.08	−0.35, 0.52	0.70	0.003	−0.01, 0.02	0.68
Time since end of exposure (years)	−0.17	−1.29, 0.96	0.77	0.21	−1.09, 1.51	0.75	−0.42	−1.35, 0.52	0.37	0.02	−0.01, 0.05	0.23
Ex-smokers[e] (*n* = 111)												
Cumulative exposure[a] (fiber/cc × years)	0.01	−0.01, 0.03	0.18	0.02	−0.009, 0.05	0.18	−0.01	−0.04, 0.01	0.24	0.00	−0.001, 0.00	0.29
Asbestos exposure (years)	0.02	−0.24, 0.29	0.86	0.10	−0.25, 0.45	0.58	0.10	−0.22, 0.41	0.54	−0.004	−0.01, 0.004	0.32
Latency[b] (years)	−0.05	−0.32, 0.22	0.71	−0.04	−0.39, 0.32	0.84	−0.03	−0.36, 0.29	0.84	−0.004	−0.01, 0.004	0.35
Time since end of exposure (years)	−0.24	−0.71, 0.24	0.33	−0.44	−1.06, 0.19	0.17	−0.39	−0.94, 0.16	0.16	0.001	−0.01, 0.02	0.98
Smokers[e] (*n* = 43)												
Cumulative exposure[a] (fiber/cc × years)	0.003	−0.04, 0.05	0.90	0.003	−0.05, 0.06	0.90	−0.03	−0.11, 0.05	0.43	−0.001	−0.002, 0.00	0.14
Asbestos exposure (years)	0.20	−0.18, 0.58	0.29	0.16	−0.31, 0.63	0.49	−.029	−0.99, 0.42	0.41	0.001	−0.01, 0.01	0.90
Latency[b] (years)	0.17	−0.15, 0.50	0.29	0.14	−0.25, 0.54	0.47	−0.37	−0.98, 0.24	0.22	0.002	−0.008, 0.01	0.66
Time since end of exposure (years)	0.22	−0.72, 1.15	0.65	0.24	−0.91, 1.39	0.68	−1.41	−3.22, 0.41	0.12	0.02	−0.02, 0.05	0.34

[a]% of reference value.
[b]In fibers/cubic centimeter—years, based on a standard fiber year with a standard airborne fiber concentration of one fiber per cubic centimeter.
[c]Time since beginning of exposure.
[d]Results adjusted for BMI.
[e]Results adjusted for BMI and pack years.

Further, the DLCO/VA and R'tot results of the pulmonary function tests were available only for the examinations carried out at the IOSM. Full information on all participants regarding the two most important non-occupational potential influencing factor of lung function, namely smoking history and BMI, was particularly important for obtaining meaningful results. The exposure estimates for asbestos could not be based on objective fiber measurements at the actual workplaces of the participants. Nevertheless, compared to other studies, which also investigated the adverse health effects of asbestos, they are likely to be the best approximation for asbestos exposure.

5 | CONCLUSIONS

Our study group of asbestos-exposed power industry workers, without any radiographic changes on MDCT, showed no significant lung function impairment. The slightly reduced mean values of FVC and FEV1 were fully explained by the effects of smoking. The tendency to high DLCO/VA values was due to the association of increased BMI and decreased VA. Furthermore, this might indicate an unsuitable age adaptation of the reference values of DLCO/VA. Consequently, we found no evidence that asbestos exposure without concordant MDCT-abnormalities had any effect on FVC, FEV1, DLCO/VA, or R'tot. In cases of clinically relevant lung function impairment without characteristic abnormalities on MDCT, exposure to asbestos dust seems to be an unlikely cause.

AUTHORS' CONTRIBUTIONS

CS extracted and analyzed the relevant data, interpreted the results and drafted the manuscript, MKF organized the cohort, managed the survey data and examined participants, CE coordinated the examination of participants and examined participants, MD evaluated the radiological method and data and revised them critically for important radiological content, TK conceived the study, designed the building of the cohort and the framework of the survey. All authors read and approved the final manuscript.

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ETHICS APPROVAL AND INFORMED CONSENT

The study was performed at the Institute for Occupational Medicine at the RWTH Aachen University. It was approved by the local ethics committee of the Medical Faculty of the RWTH Aachen University (EK 043/09). Each participant has given written consent to participate.

DISCLOSURE (AUTHORS)

The authors report no conflicts of interest.

DISCLOSURE BY AJIM EDITOR OF RECORD

Rodney Ehrlich declares that he has no conflict of interest in the review and publication decision regarding this article.

DISCLAIMER

None

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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