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Survival analysis of patients with pneumoconiosis followed in occupational medicine clinics: 10 years experience

Melike Yüksel Yavuz[1†], Ayşe Coşkun Beyan[2*†], Merve Ayik Türk[3], Türkan Dizdar Canbaz[4], Ö.Melis Korkmaz Özgüngör[3] and Nur Şafak Alici[5]

Abstract

Background Pneumoconiosis is still the most common occupational disease worldwide. The aim of the study was to evaluate the risk factors affecting survival in patients with pneumoconiosis who were followed up in occupational medicine clinics.

Methods This retrospective descriptive study included all pneumoconiosis patients followed up in occupational medicine clinics between 2013 and 2023. The patients' death records were accessed through the national death notification system.

Results A total of 539 patients were included in the study. During the clinical follow-up, 14 (2.56%) patients had died. The mean overall survival time was 224 ± 13 months. In multiple analyses, silica exposure ($p = 0.029$) and lung cancer development ($p = 0.002$) were associated with survival. There was no difference between stages 0 and 1, stage 2 and stage 3 in terms of age at diagnosis, type of disease and duration of dust exposure (respectively $p = 0.109$, $p = 0.852$).

Conclusions This study showed that exposure to silica as a dust type and the development of lung cancer increased mortality in patients with pneumoconiosis. Determining the factors that may be associated with mortality in patients with pneumoconiosis is important in patient follow-up and in developing preventive measures and policies. It is crucial that the establishment of lung cancer screening programs contribute to life expectancy.

Keywords Pneumoconiosis, Survival analysis, Mortality

†Melike Yüksel Yavuz, Ayşe Coşkun Beyan the authors contribution to work is equal. The authors were identified as the first authors.

*Correspondence:
Ayşe Coşkun Beyan
ayse.coskun@deu.edu.tr
[1]Faculty of Medicine, Pulmonology Department, İzmir Katip Çelebi University, İzmir, Turkey
[2]Present address: Faculty of Medicine, Occupational Medicine Department, Dokuz Eylül University, İzmir, Turkey
[3]Pulmonology Department, HSU, Bozyaka Training and Research Hospital, İzmir, Turkey
[4]Faculty of Medicine, Allergy and Immunology Department, Ege University, İzmir, Turkey
[5]İzmir Suat Seren Chest Diseases and Chest Surgery Training and Research Hospital, Occupational Medicine Clinic, İzmir, Turkey

Introduction

Pneumoconiosis is the most common occupational disease in the world, particularly in developing countries and represents a serious threat to global public health [1]. Pneumoconiosis develops as a result of exposure to dust, smoke, and fibers. The type of pneumoconiosis depends on the inhaled substance [2]. Besides classical pneumoconiosis, new cases from new sectors, such as indium, nylon flock, and nanoparticles-induced interstitial lung diseases, are increasingly recognized. Masanori A [3]. However, silicosis, coal workers' pneumoconiosis and asbestos still represent the current socioeconomical burden. In 2019, the incidence of pneumoconiosis was 2.39/100,000. The number of cases increased by about 61.5% in 2019 compared with 1990. The countries with the highest number of cases are China, India and the United States of America [4]. A 40-year retrospective study in Brazil found that the overall mortality rate in 97 municipalities with active mining was increased in all regions. Deaths are mostly related to men aged over 50 years. It is reported that silica-associated pneumoconiosis is still at the top of the list [5]. Su et al. evaluated 335,424 cases from 19 studies, and the incidence of pneumoconiosis was found to be 0.093 (95% CI 0.085 to 0.135). The risk factors for developing pneumoconiosis were male gender, smoking history, tunnelling work, total dust concentration and being over 50 years of age [6].

According to the CDC, MMWR, Trends in Pneumoconiosis Deaths - United States, 1999–2018 report, between these years, a total of 43,366 people aged 15 years and older had a diagnosis of pneumoconiosis on their death certificates and the overall annual number of pneumoconiosis deaths decreased 40.4%. Asbestosis remains the most frequently reported cause of pneumoconiosis-related mortality, accounting for 60.1% of all pneumoconiosis deaths between 1999 and 2018 [7]. It is observed that there are differences in the frequency of pneumoconiosis according to the mining activities of the countries. 204 countries and regions in a forecast analysis according to disease burden scenarios, global cause-specific disability-adjusted life years (DALYs) and age-standardized and age-standardized DALY rates for pneumoconiosis in 2022 and 2050 are presented as 441.8 and 443.4 [8]. The Global Burden of Disease study found 0.20 million new cases and 0.92 million DALYs for pneumoconiosis in 2019 [9].

Thus, it is very important to determine the factors affecting the progression of the disease after diagnosis, use them for early intervention and use them in surveillance models. This study evaluated risk factors affecting survival in patients diagnosed with pneumoconiosis.

Methods and materials

Study design, setting and selection of participants

This retrospective descriptive study was conducted in İzmir. In Turkey, only authorized health institutions can diagnose occupational diseases. This study included all occupational pneumoconiosis patients diagnosed at two authorized health service provider clinics in the Aegean region. The diagnosis of pneumoconiosis was established based on a thorough work and exposure history, compatible radiological findings and the exclusion of other potential diagnoses [10]. Chest radiography according to ILO standards and spirometry tests were obtained at the time of diagnosis. Occupational history, sociodemographic data, information on dust exposure and diagnosis obtained by occupational medicine specialists. Age at diagnosis was included in the analysis. International Labour Office (ILO) readings of chest radiographs were obtained by at least two different ILO readers. Pneumoconiosis staging is based on ILO categories. Category and stage are grouped with the same number. Simple pneumoconiosis is characterised by opacities of less than 1 cm. Complicated pneumoconiosis occurs with opacities of more than 1 cm (also named large opacities A, B or C) [11]. Simple spirometry tests were evaluated according to the acceptability and repeatability criteria in the American Thoracic Society 2019 guidelines [12].

Smoking status was based on the CDC definitions of smoking status [13]. Current smoker: A person who has smoked 100 cigarettes in his or her lifetime and who currently smokes cigarettes. Former smoker: A person who had smoked at least 100 cigarettes in their lifetime but had quit smoking at the time of the interview. Never smoker: A person who has never smoked or has smoked less than 100 cigarettes in their lifetime.

Information on the history of lung cancer and tuberculosis was obtained from patients' current and past medical records. A lifetime history of tuberculosis was recorded. Use of personal protective equipment was based on workers' self-report. Work history and exposure information were classified based on occupational medicine specialists' opinions using qualitative risk assessment. According to the regulations of Turkey, the size of the workplace is defined as micro-enterprise with less than 10 employees, small enterprise with less than 50 employees, medium enterprise with less than 250 employees and large enterprise with more than 250 employees [14].

Premature death compares life expectancy with the actual age at death and is expressed in 'years of life lost. Years of potential life lost (YPLL) and years of life lost (YLL) were used as an indicator of premature mortality [15, 16, 17]. Life expectancy of patients by year of death was obtained from the Turkey Statistical Institute [18].

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Statistical methods

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 23.0 (IBM Corp., Armonk, NY). Continuous variables were presented as mean ± SD if the data was normally distributed and median [min-max] if not normally distributed. Categorical variables were presented as numbers and percentages; n (%). The normal distribution of continuous variables was investigated by normality tests. The 10-year overall survival (OS) analysis was performed with the Kaplan-Meier test. At first, variables affecting OS were analysed by univariate analysis; the Pearson's chi-square test to investigate the impact of categorical variables and the independent samples t-test for continuous variables. After that, multivariate analysis was performed with the Cox regression model to identify independent risk factors. Hazard ratios (HRs) with a 95% confidence interval (CI) were calculated. The follow-up periods of patients were considered as the period from the diagnosis until the last follow-up. Correlation between quantitative variables was performed using the Pearson correlation coefficient. The level of statistical significance was considered as $p < 0.05$.

Results

The study analysed data from 539 patients. 99.6% (537) of the patients were male and the median age was 42 [min:23-max:79] years. At the time of diagnosis, 29.1% of patients had comorbidities. The most common comorbidities were hypertension and diabetes mellitus. Asthma was present in 12 (2%) patients and COPD in 19 (3.5%) patients before the diagnosis of pneumoconiosis. Among the attributed sectors, the most common are ceramics production 24.5%, dental technicians 22.4%, coal mining 16.9% and quartz mining 15.2%. The median dust exposure time was 16 years [min:2- max:40] years. 51.9% of patients had been employees of a large enterprise. The type of dust exposed was dust silica 89.6%, metal dust 21.7%, coal dust 17.4%, asbestos 2% and other 7.4%, respectively. Among the pneumoconiosis, silicosis accounted for 67.3%, mixed dust pneumoconiosis for 26.2%, coal workers' pneumoconiosis for 3.9%, asbestosis for 0.2% and other for 2.4%. The other group included welder's lung, hard metal lung, siderosilicosis and metal worker's lung. 50.8% of patients had stage 1 disease. 75.9% of patients had simple pneumoconiosis. Information was obtained that 3 patients were registered with a cancer diagnosis at the National Cancer Registry Centre. 27.1% of the patients were complicated by tuberculosis. While being evaluated for pneumoconiosis in the occupational disease department, 27.1% of patients were diagnosed with an additional occupational disease. Of the surviving patients, 27.6% were never smokers, and 72.4% were former and current smokers. Among the deceased patients, 21.4% were never smokers and 78.6% were former and current smokers. Univariate analyses showed no significant association between smoking status and survival ($p = 0.067$). Demographic data and clinical characteristics of surviving and deceased patients are presented in Table 1. Age, silica exposure, simple/complicated pneumoconiosis, development of lung cancer, history of tuberculosis and additional occupational disease diagnoses were found to be associated with survival time (Table 2).

There was no statistically significant difference in age at diagnosis, type of disease and duration of dust exposure between stages 0 and 1, stage 2 and stage 3 (Table 3).

During the clinical follow-up, 14 (2.56%) of the total 539 enrolled workers had died. Survival functions of all patients and overall survival status according to stages are presented in Figs. 1 and 2. The mean overall survival time was 224 ± 13 months. In total, YPLL for the 14 patients who died was 31.8 years. The average YLL was 27.2 years.

Simple spirometry parameters FEV1, FVC and FEV1/FVC were associated with survival time. The median values of FEV1, FVC, FEV1/FVC and DLCO were 86 [20], 90 [19], 79 [10] and 80% [34], respectively. DLCO was not included in the analysis because of the small number of cases. The relationship between the values of pulmonary function parameters of surviving patients and deceased patients is presented in Table 4. Age was positively correlated with exposure time, while FEV1/FVC was negatively correlated (r=-0.489, r=-0.158, $p = 0.01$).

In multiple analyses, silica exposure ($p = 0.029$) and lung cancer development ($p = 0.002$) were significantly associated with survival time (Table 5). In contrast, no significant association was found with the variety of disease, additional occupational disease and history of tuberculosis ($p = 0.055$, $p = 0.957$, $p = 0.493$ and history of tuberculosis ($p = 0.055$, $p = 0.957$, $p = 0.493$, respectively).

Discussion

This study showed that exposure to silica dust and the development of lung cancer and pulmonary function parameters were associated with survival time in patients with pneumoconiosis. In the 10-year follow-up, the mortality rate of our patients was 2.5% and the mean overall survival time was 224 months. The others are that no significant relationship was found between total dust exposure duration and survival and no significant relationship was found between disease stage and age, dust type and total dust exposure duration.

Cohort studies in China, which have significantly contributed to the current literature in recent years thanks to the pneumoconiosis notification and control studies

Table 1 Demographic data and clinical characteristics of surviving patients and deceased patients

Characteristic	Surviving patients Mean (±) or Median [IQR] value	Deceased patients Mean (±) or Median [IQR] value
Age at first diagnosis (years)	42 [10]	45 [20]
Total exposure time (years)	16 [11]	15.5 [11.8]
	Surviving patients n (%)	**Deceased patients n (%)**
Gender		
Male	523 (94.7)	14 (2.5)
Female	2 (0.4)	0
Smoking status		
Never smokers	145 (27.6)	3 (21.4)
Former and current smokers	380 (72.4)	11 (78.6)
Comorbidity		
Yes	150 (27.8)	7 (1.3)
No	375 (69.6)	7 (1.3)
Attributed Sector		
Ceramic production	132 (24.5)	0 (0)
Dental technician	117 (21.7)	4 (0.7)
Coal mine	88 (16.3)	3 (0.6)
Quartz mine	79 (14.6)	3 (0.6)
Metal welding-casting	51 (9.5)	1 (0.1)
Metal mine	12 (2.3)	1 (0.1)
Brick production	5 (0.9)	0 (0)
Other	41 (7.6)	2 (0.4)
Workplace size		
Large	277 (51.4)	3 (0.5)
Medium	67 (12.4)	1 (0.2)
Small	24 (4.4)	2 (0.4)
Micro	15 (2.8)	0 (0)
Type of Dust		
Silica	474 (87.9)	9 (1.7)
Metal dust	112 (20.7)	5 (1)
Coal dust	91 (16.8)	3 (0.6)
Asbestos	11 (2)	0 (0)
Other	38 (7)	2 (0.4)
Type of Disease		
Silicosis	355 (65.8)	8 (1.5)
Mix dust pneumoconiosis	138 (25.6)	3 (0.6)
Coal worker pneumoconiosis	18 (3.3)	3 (0.6)
Asbestosis	1 (0.2)	0 (0)
Other	13 (2.4)	0 (0)
Stage		
Stage 0	41 (7.6)	1 (0.2)
Stage 1	350 (64.9)	9 (1.7)
Stage 2	119 (22)	2 (0.4)
Stage 3	15 (2.8)	2 (0.4)
Variety		
Simple pneumoconiosis	403 (74.7)	6 (1.2)
Complicated pneumoconiosis	122 (22.6)	8 (1.5)
Developed lung cancer		
Yes	2 (0.4)	1 (0.2)
History of tuberculosis		
No	412 (76.4)	7 (1.3)
Yes	112 (20.7)	7 (1.3)
Non-tuberculosis mycobacteria	1 (0.3)	0 (0)
Use of personal protective equipment		
Yes	370 (68.6)	7 (1.3)
No	162 (28.8)	7 (1.3)

Note: *Data presented as mean ± SD if normally distributed and median refers to Interquartile Range if not normally distributed. Categorical variables are presented as number (percentages of total). Column percentages are presented

Table 2 Characteristic features of patients and association with survival (univariate analysis) *

Characteristic	Median [IQR]	*p*
Age at first diagnosis (years)	42 [10]	**0.024**
Total exposure time (years)	16 [11]	0.611
	N (%)	
Gender		
Male	537 (99.6)	0.880
Female	2 (0.4)	
Smoking status		
Never smokers	145 (27.6)	0,067
Former and current smokers	380 (72.4)	
Comorbidity		
Yes	157 (29.1)	0.089
Attributed Sector		
Ceramic production	132 (24.5)	0.137
Dental technician	121 (22.4)	
Coal mine	91 (16.9)	
Quartz mine	82 (15.2)	
Metal welding-casting	52 (9.6)	
Metal mine	13 (2.4)	
Brick production	5 (0.9)	
Other	43 (8)	
Workplace size		
Large	280 (51.9)	0.289
Medium	68 (12.6)	
Small	26 (4.8)	
Micro	15 (2.8)	
Type of Dust		**0.008**
Silica	483 (89.6)	
Metal dust	117 (21.7)	
Coal dust	94 (17.4)	
Asbestos	11 (2)	
Other	40 (7.4)	
Type of Disease		0.095
Silicosis	363 (67,3)	
Mix dust pneumoconiosis	141 (26.2)	
Coal worker pneumoconiosis	21 (3.9)	
Asbestosis	1 (0.2)	
Other	13 (2.4)	
Stage		0.172
Stage 0	42 (7.8)	
Stage 1	359 (66.6)	
Stage 2	121 (22.4)	
Stage 3	17 (3.2)	
Variety		**0.026**
Simple pneumoconiosis	409 (75.9)	
Complicated pneumoconiosis	130 (24.1)	
Developed lung cancer		**0.033**
Yes	3 (0.6)	
No		
History of tuberculosis		**0.037**
No	393 (72.9)	
Yes	146 (27.1)	
Non-tuberculosis mycobacteria	1 (0.2)	
Use of personal protective equipment		0.117
Yes	365 (67.7)	
No	162 (30.1)	

Note: *Data presented as mean ± SD if normally distributed and median refers to Interquartile Range if not normally distributed. Categorical variables are presented as number (percentages of total). Column percentages are presented

Table 3 Demographic and occupational characteristics according to stage of pneumoconiosis*

	Stage 0 and I *n* = 401	Stage II *n* = 121	Stage III *n* = 17	*p*
Age at first diagnosis				
≤44	279 (76.8%)	74 (20.4%)	10 (2.8%)	0.109
45–59	104 (70.7%)	37 (25.2%)	6 (4.1%)	
≥60	18 (62.1%)	10 (34.5%)	1 (3.4%)	
Type of disease				
Silicosis	268 (73.8%)	82 (22.6%)	13 (3.6%)	0.766
Mix dust pneumoconiosis	103 (73.1%)	34 (24.1%)	4 (2.8%)	
Coal worker pneumoconiosis	20 (95.2%)	1 (4.8%)	0	
Asbestosis	0	1	0	
Other	10 (76.9%)	3 (%23.1)	0	
Total Dust Exposure (Years)				
≤5	43 (71.7%)	16 (26.7%)	1 (1.7%)	0.852
6–14	116 (76.8%)	30 (19.9%)	5 (3.3%)	
≥15	242 (73.8%)	75 (22.9%)	11 (3.4%)	

Note: Row percentage is presented

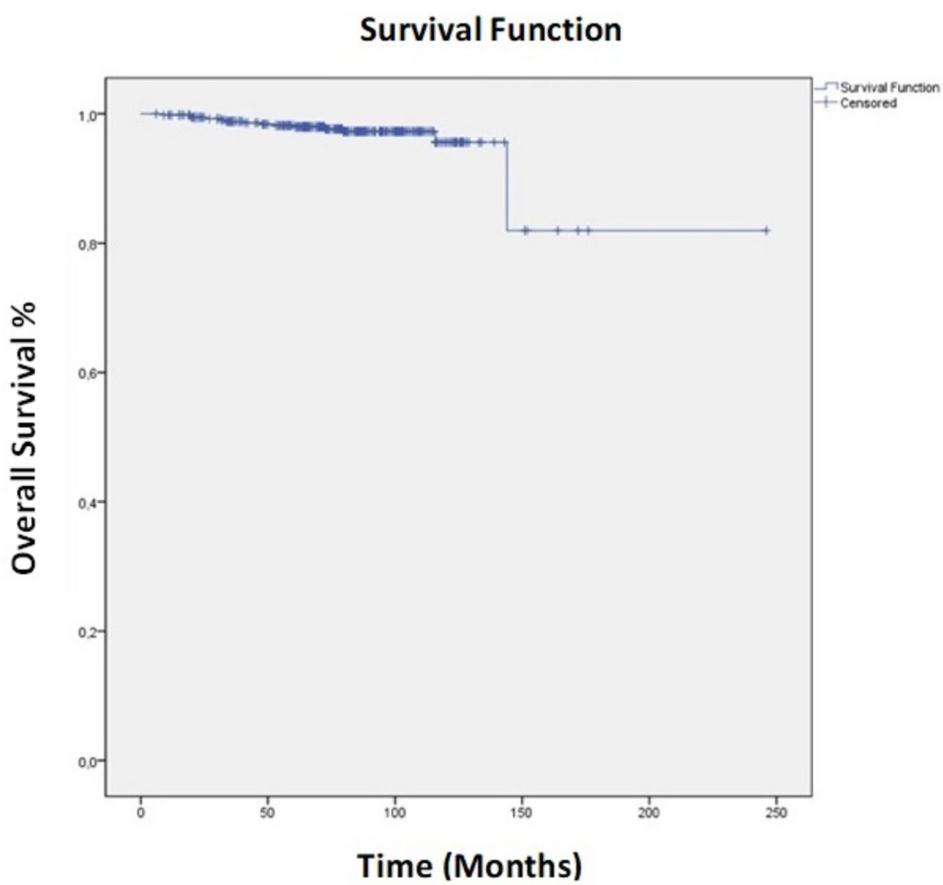

Fig. 1 Kaplan-Meier overall survival curve

carried out in China, report different rates. Song et al. reported a 19.89% mortality rate and survival time was stated as 14.74 ± 9.57 years. Another cohort performed by China found median survival times according to pneumoconiosis stage (1, 2, 3) were 18, 14 and 9 years, respectively. In a study of 936 patients, the mean survival time was 19.4 years. The 10, 20 and 30-year cumulative survival rates were 62.8%, 35.2% and 15.4%, respectively [20]. All studies highlighted the importance of early disease diagnosis and implementing measures to prevent disease progression [21, 22].

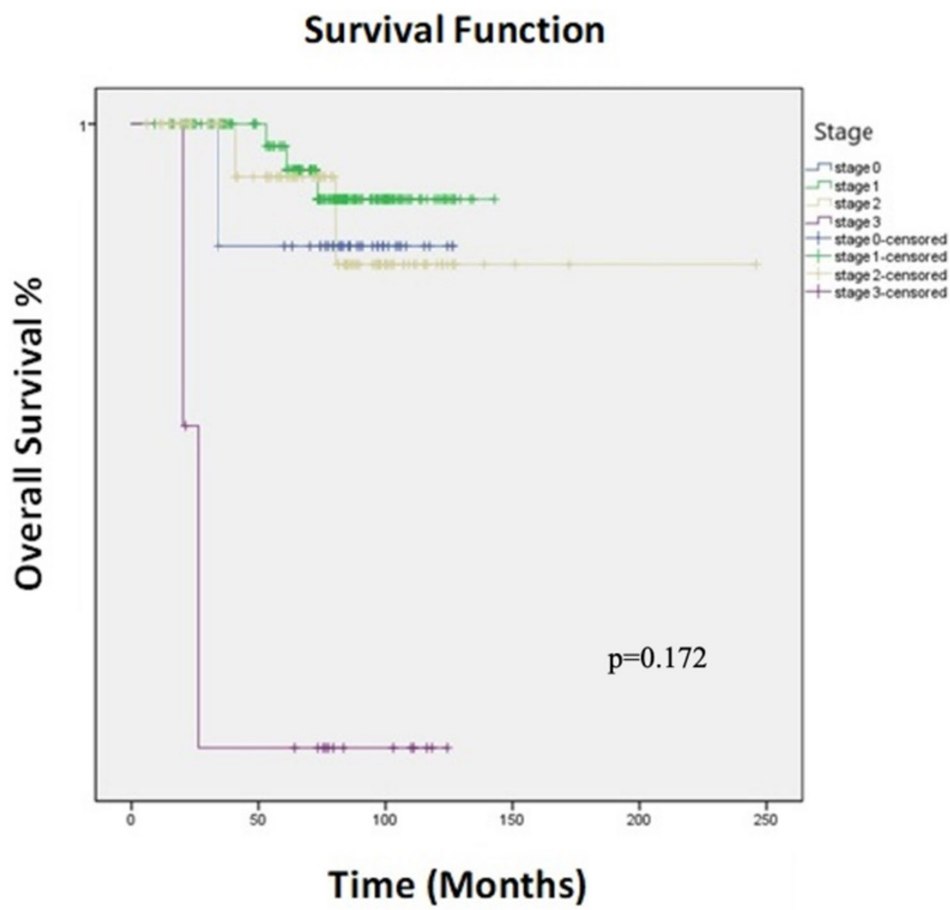

Fig. 2 Kaplan-Meier overall survival curve according to stage

Table 4 Association of pulmonary function test parameters with survival (Univariate Analysis)*

Variables	Mean (±) or Median value [IQR]	Surviving patients	Deceased patients	*p*
FEV1 (ml)	3242 (±752)	3261 (±742)	2177 (±554)	**0.001**
FEV1 (%)	86 [20]	86 [19]	67 [45]	**0.001**
FVC (ml)	4077 (±876)	4108 (±846)	2546 (±1010)	**0.001**
FVC (%)	90 [19]	90 [19]	69 [17]	**0.001**
FEV1/FVC	79 [10]	79 [10]	71 [23]	**0.002**
DLCO	80 [34]	-	-	-

Note: FEV1 Forced Expiratory Volume 1, FVC Forced Vital Capacity, DLCO Diffusion Lung Capacity for Carbon Monoxide

*Data presented as mean ± SD if normally distributed and median refers to Interquartile Range if not normally distributed

An analysis of the underlying causes of death of 43,366 deceased persons diagnosed with pneumoconiosis in the USA between 1999 and 2018 showed that pneumoconiosis was the cause of death in 40.5% of cases. However, unlike our study, this study reports more asbestosis cases [7]. The pneumoconiosis diagnosis reporting systems in different countries significantly affect this difference.

Studies frequently investigate the relationship between disease stage and life expectancy. As expected, life expectancy decreases as the stage of the disease progresses. A Chinese study evaluated risk factors for premature death and progressive massive fibrosis (PMF). It showed that 3.2% of patients with simple pneumoconiosis developed PMF during the follow-up period (mean 8 years). Patients who developed PMF exhibited higher age-specific mortality rates than those who remained in a simple state of pneumoconiosis (SMR: 3.42; $P < 0.01$). It was concluded that early death was associated with PMF and tuberculosis complications [23]. In our study, complicated disease (PMF) was found to be significant for survival time in univariate analyses but not in multivariate analyses ($p = 0.55$). This is likely due to the unequal distribution of simple and complex cases.

Table 5 Investigation of variables affecting survival by multivariate analysis

Variables	Overall Survival	
	HR (%95 CI)	**P value**
Silica exposure (Type of Dust) (yes/no)	3.56 (1.14–11.11)	**0.029**
Variety (simple/complicated)	0.34 (0.11–1.02)	0.055
Developed lung cancer (yes/no)	33.20 (3.47-317.55)	**0.002**
Additional occupational disease (yes/no)	0.00 (0.00-2.19)	0.957
History of tuberculosis (yes/no)	1.48 (0.48–4.57)	0.493

Note: Multivariate model was adjusted for Silica exposure, Additional occupational disease, Variety, Developed lung cancer, History of tuberculosis. HR: Hazard ratio, CI: Confidence interval

In a Chinese study with very similar results to the patient distribution in our study, 15,402 patients with pneumoconiosis, 80% of patients were initially diagnosed at stage 1, 15.5% at stage 2 and 4.5% at stage 3. The overall mean survival time was 14.74 ± 9.57 years, life expectancy reached 34.32 years and the overall mortality rate of patients with pneumoconiosis was 19.89%. The risk of death increased as the disease stage progressed and the duration of dust exposure increased [21].

There are also more special subgroups of silicosis. For example, the mortality rate was found to be higher in sandblasters compared to our study's results because this special group has rapid radiological and clinical progression even in short-term exposures. Due to these devastating effects, our country has banned sandblasting since 2009 [24].

As another example, in a longitudinal study conducted in our country, 165 ceramic workers were followed up for an average of 3.7 years and radiological progression was found in 37.5% of the patients. The study found a significant relationship between radiological progression and ILO category at the first visit in multivariate analyses. Although radiological progression was not analysed in our study, the finding of a relationship with survival in our results, which we analysed according to the first visit stages (determined according to ILO category) by the mentioned study, may be relative evidence of progression [25].

Liu et al. demonstrated that a history of tuberculosis, along with the stage of the disease and the type of dust, increased the hazard ratio (HR) by 1.4 times [18]. In our study, age at diagnosis ($p = 0.024$), type of dust ($p = 0.008$), simple/complicated ($p = 0.026$), developed lung cancer ($p = 0.033$), history of tuberculosis ($p = 0.037$) and additional occupational disease diagnosis ($p = 0.008$) were found to be significantly associated with survival in univariate analyses. Tuberculosis is still very common in our country and the incidence of tuberculosis in our country was 14.6 per 100,000 [26]. In our study, a very high prevalence of tuberculosis was observed. It appeared to be an important factor affecting survival in univariate analyses, but its effect could not be demonstrated in multivariate analyses.

Although it is known that the risk of tuberculosis increases up to 30 times, especially in silicosis. In fact, in a study of 244 coal workers with pneumoconiosis, latent tuberculosis infection was found at a high rate of 66.4% [27].

The fact that pulmonary function test parameters are preserved until the advanced stages of the patients makes their interpretation difficult in survival analyses. Hatman et al. conducted a study in workers with pneumoconiosis, it was found that both decreased lung function and large opacities on chest films were associated with early death. In our study, FEV1, FVC ($p = 0.001$) and FEV1/FVC ($p = 0.002$) values were found to be associated with survival [28]. In 219 jeans sandblasting workers study, approximately half of the patients had silicosis, while the other half had only exposure. In both groups, low FEV1 and FVC were found to be associated with mortality ($p = 0.001$ for both), as in our article [29].

In a cohort study conducted in China, 5641 patients were followed up for two years. No significant association was found between pneumoconiosis subtypes and stages at diagnosis and survival. However, 25 years or more of dust exposure made a significant difference in survival ($P < 0.05$). While the total YLL value for 2360 male patients who died in this study was 4,203.72 and the average YLL was 1.78, the total YLL value for 14 male patients who died in our study was 31.8 year and the average YLL was 27.2. The reason why our YLL values were higher may be that we included all deaths since we did not know the causes of death and it was made according to premature death values. The authors thought that this result was due to the fact that the number of stage 3 patients was lower than the others [22].

This study has several limitations, the most important of which are the lack of access to causes of death and the fact that it is based on premature deaths. The study's cross-sectional design prevented us from determining whether the causes of death were definitively linked to pneumoconiosis. Furthermore, our country's lack of a nationwide surveillance system may have introduced biases in data standardization. To make more precise expressions about survival in patients with pneumoconiosis, it is a fact that a larger series of studies in which occupations, workplaces and exposure conditions such as dust levels are evaluated more comprehensively are needed. For this purpose, nationwide multicentre prospective studies should be designed.

Conclusions

The results of our study showed that the development of lung cancer and exposure to silica compared to other dust types affected life expectancy. The fact that exposed silica dust has a higher mortality effect than other dust types shows that the full implementation of the occupational health control hierarchy is the strongest step in occupational disease prevention policies. In addition, lung cancer screening and surveillance programs can be planned to be carried out in pneumoconiosis patients. Studies with larger case numbers, more homogeneous distribution and a prospective design are needed to support our results.

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Data availability
The datasets analysed during the current study are not publicly available due national policy restriction but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Ethical approval was obtained from Dokuz Eylül University ethics committee (No 8300-GOA, No 2023/41 – 08). The research was conducted in accordance with the Declaration of Helsinki. Written informed and verbal consent was obtained from all participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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