

Silica dust and sarcoidosis in Swedish construction workers

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Background	The aetiology of sarcoidosis is not well established. In previous studies, smoking has been negatively associated with sarcoidosis and there are some indications of an association between exposure to silica dust and sarcoidosis.
Aims	To study the risk of sarcoidosis in relation to silica dust exposure.
Methods	A longitudinal cohort of construction workers linked with a registry of Swedish inpatient diagnoses. Workers were designated as exposed or unexposed to silica based on job titles in a job–exposure matrix. The relative risk (RR) was analysed with Poisson regression adjusting for age and smoking.
Results	We identified 371 cases of sarcoidosis among 297 917 male workers. There was an increased risk of sarcoidosis in the medium- to high-exposure group [RR 1.83 (95% confidence interval {CI} 1.14–2.95)]. A stratified analysis according to smoking showed that ever-smoking workers had an increased risk of sarcoidosis if highly exposed to silica dust [RR 2.44 (95% CI 1.37–4.33)] compared to non-exposed ever-smokers. The risk of non-smokers highly exposed to silica was not significantly increased [RR 1.07 (95% CI 0.72–1.58)] compared to non-exposed non-smokers.
Conclusions	The study indicates an increased risk of developing sarcoidosis in ever-smoking men exposed to silica.
Key words	Occupation; occupational health; sarcoidosis; silica; smoking.

Introduction

The prevalence of sarcoidosis is highest in the Nordic countries and among African-Americans [1,2]. While there are some indications that genetic predisposition may influence the risk of sarcoidosis, seasonal clustering to late winter and early spring supports a role for environmental factors as well [3,4]. Exposure to microbial aerosols has been suggested as a cause of sarcoidosis [5]. Some studies have also indicated that workers with occupational exposures, e.g. agricultural workers, fire/rescue workers and healthcare professionals such as dentists, and workers with heavy dust exposure have a higher risk [3,5]. A few studies of a possible relationship between exposure to silica dust and sarcoidosis show conflicting results [6–8]. We designed a longitudinal cohort study to investigate if silica dust exposure was a risk factor for sarcoidosis.

Methods

This is a longitudinal cohort study using data from The Swedish Construction Workers Cohort [9,10]. Construction workers in Sweden were offered free health examinations at intervals of 2–5 years from 1969 to early 1993. Results from the examinations were stored in a computerized register from 1971, which includes information on job title, year of birth, weight, height, smoking and lung function. Construction workers between the ages of 15 and 67 at their first examination, who had at least one health examination registered in The Swedish Construction Workers Cohort, were included. Using Swedish personal identification numbers, the participants were linked to data in the national Swedish inpatient care register to find the occurrence of sarcoidosis (ICD10: D86) from 1997 to 2010. Participants who had died or emigrated before 1997 were excluded and the

Key learning points

What is already known about this subject:

- Studies on the relationship between silica exposure and sarcoidosis are few and show conflicting results.
- Smoking has been suggested to reduce the risk of sarcoidosis.

What this study adds:

- An increased risk of developing sarcoidosis was observed in occupational groups highly exposed to silica dust in a large cohort of construction workers in Sweden.
- The risk of sarcoidosis seems to be higher among ever-smokers compared to never-smokers when exposed to silica dust, while non-exposed ever-smokers had a reduced risk of developing sarcoidosis compared to non-exposed never-smokers.

What impact this may have on practice or policy:

- Future studies on the relationship between sarcoidosis and silica exposure should consider the role of smoking in the development of disease.
- Additional importance should be placed on the need for smoking cessation in silica-exposed occupations.

restriction to 1997 was due to the change of classifications to ICD10 in 1997. Women were excluded, because there were few female workers in the cohort, and they were mainly office workers or had job titles which could not be assessed for silica exposure. Workers with unknown smoking status were also excluded. The total number of men included in the study was 297 917 (Figure 1).

Exposure to silica dust was evaluated by job title at the first examination using a job–exposure matrix intended to reflect the level of silica exposure [9]. There were three levels of exposure (no exposure, low exposure and medium–high exposure). Occupations regarded as exposed included, for example rock worker (medium–high), concrete worker (medium–high), brick layer (low), asphalt worker (low), machine operators as well as maintenance and repair workers in environments with exposure to silica dust (low).

Smoking status was based on workers reporting ever having smoked at the first health examination, dividing them into two groups: ever-smokers and never-smokers.

Statistical analyses were undertaken using Statistical Analysis Software (SAS) version 9.3. We performed a Poisson regression analysis taking first recorded diagnosis of sarcoidosis during the follow-up period as our outcome. Person-years were calculated for 10-year age groups, and were accumulated up to the earliest of first diagnosis of sarcoidosis, death, emigration or the end of the follow-up period. Silica exposure and smoking were assessed in the same regression model, adjusting for each other and for age. Silica exposure was also assessed in an analysis stratified by smoking status.

Ethical approval was granted by the Regional Ethical Review Board at Umeå University (2013-113-32M).

Results

The mean age at inclusion was 34 years in the silica-exposed group and 32 years in the unexposed group. In total, 17% ($n = 51\,688$) of the men were exposed to silica dust and 55% ($n = 164\,137$) were ever-smokers. A total of 373 cases of sarcoidosis were identified in the

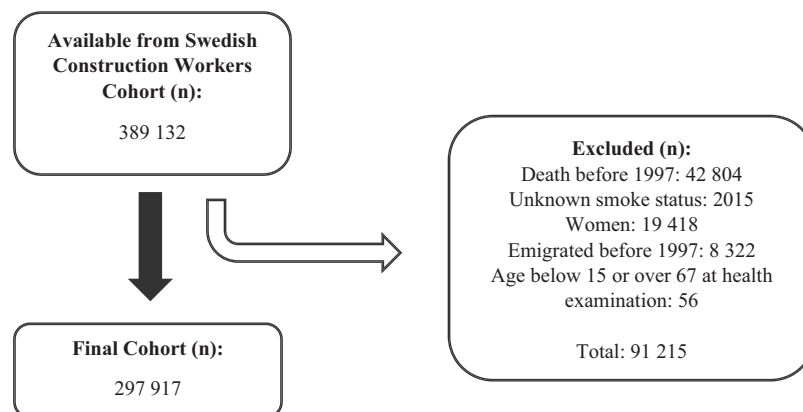


Figure 1. Total number of people in the cohort, number excluded within each group and total number included in the study (n = number of people).

cohort, of which 371 could be assessed for both exposure to silica and smoking status. Out of these, 152 men were ever-smokers and 70 men were exposed to silica (Tables 1 and 2).

The relative risk (RR) of sarcoidosis for a worker exposed to any level of silica dust (low to high) was 1.15 [95% confidence interval (CI) 0.89–1.50] compared to non-exposed workers (Table 1). The RR of sarcoidosis for workers in jobs with the highest exposure (medium to high) was higher and significantly increased [RR 1.83 (95% CI 1.14–2.95)] compared to non-exposed workers. An analysis stratified by smoking status showed an even higher risk among highly exposed ever-smokers [RR 2.44 (95% CI 1.37–4.33)] and a lower risk among highly exposed never-smokers [RR 1.07 (95% CI 0.72–1.58)] (Table 2). Among workers not exposed to silica dust, ever smoking was negatively associated with sarcoidosis [RR 0.54 (95% CI 0.42–0.69)].

Discussion

Our study indicated an increased risk of sarcoidosis in workers with medium to high exposure to silica dust and smoking seemed to modify the risk.

The main strength of our study is the large sample size, with close to 300 000 workers included and 371 cases of sarcoidosis identified, a considerable contribution to the number of cases reported in previously published studies. Furthermore, using a longitudinal cohort design, exposure was determined independently

from diagnosis, eliminating the risk of information bias. Assessing exposure based on a job–exposure matrix may not give as accurate results as having actual measurements from the industries or individual assessment, which could lead to exposure misclassification and thereby an underestimation of the risk. Silica exposure is common in the construction industry and the group classified as non-exposed may have had some exposure, also leading to a possible underestimation of the risk. However, we consider the groups designated as medium or highly exposed as occupations where a substantial exposure is very likely compared to those groups designated as having low exposure.

Furthermore, the outcome in our study was hospital admission during follow-up. We have no information on whether the workers were free from sarcoidosis before follow-up. Indeed, onset of sarcoidosis before onset of exposure cannot be ruled out. However, the same lack of information on hospital admission exists in the non-silica-exposed groups and we do not believe that being exposed affects the probability of being admitted to a hospital if sarcoidosis already existed. Our results have been adjusted for 10-year age groups when admitted for sarcoidosis, death or emigration (Table 1). In a separate analysis, we also adjusted for 10-year birth year groups, with virtually identical results (data not shown). Such an analysis was not possible in the smoking-stratified cohorts (Table 2) because of relatively small sample sizes in some strata.

The association between exposure to silica dust and sarcoidosis is supported by some small studies. Vihlborg

Table 1. Mean age at inclusion and entry to follow-up, smoking status and RR of sarcoidosis for silica-exposed workers compared with non-silica-exposed workers (adjusted for age and smoking)

Level of exposure to silica	None	Low	Medium–high	Low–high
<i>N</i>	246 229	42 915	8773	51 688
Age at health examination	31.6	33.1	35.7	33.6
Age at entry to follow-up	49.0	51.3	55.0	52.0
Non-smokers	113 982	16 881	2917	19 798
Ever-smokers	132 247	26 034	5856	31 890
Sarcoidosis (<i>N</i>)	301	52	18	70
RR of sarcoidosis (95% CI)	1	1.03 (0.77–1.38)	1.83 (1.14–2.95)	1.15 (0.89–1.50)

Table 2. RR of sarcoidosis for silica-exposed workers compared with non-silica-exposed workers stratified for smoking habits and adjusted for age

Smoking habits	Non-smokers			Ever-smokers		
	None	Low	Medium–high	None	Low	Medium–high
<i>N</i>	113 982	16 881	2917	132 247	26 034	5856
Sarcoidosis (<i>N</i>)	185	29	5	116	23	13
RR of sarcoidosis (95% CI)	1	1.08 (0.45–2.64)	1.07 (0.72–1.58)	1 (ref.)	0.98 (0.62–1.53)	2.44 (1.37–4.33)

et al. [8] identified seven cases of sarcoidosis in a longitudinal cohort, and found a significantly increased risk [RR 3.94 (95% CI 1.07–10.08)]. The analysis was not adjusted for smoking habits. Rafnsson *et al.* [7] found an increased risk based on eight cases of sarcoidosis in a case referent study, six of which had been exposed to silica (odds ratio 13.2; 95% CI 2.0–140.9). However, Calvert *et al.* [6] did not find a significantly increased risk in a case referent study from the USA including 2036 exposed cases. However, the RRs increased from the lowest to the highest exposed groups and the analysis was not adjusted for smoking habits.

While it is well known that inhalation of silica may cause silicosis, silica exposure has also been associated with, for example, rheumatoid arthritis and scleroderma [6,11]. The association between silica exposure and autoimmune diseases [12] is interesting because, in sarcoidosis, the immune system reacts to an unidentified antigen and immune granulomas are formed in the target organs [2,11].

The effect of smoking on the risk of sarcoidosis has been assessed in multiple studies previously, including a study based on the same cohort as the present study, showing a negative association between smoking and sarcoidosis [13–17], although there are also reports of no negative association between smoking and sarcoidosis [18]. This finding has been suggested to be related to, for example, increased clearance of inhaled particles in smokers or smoking-related immune system interaction [13–15,19]. It is notable, however, that participants in our study with combined exposure to smoking and silica had a higher risk of developing sarcoidosis compared to silica-exposed never-smokers, suggesting an interaction between tobacco smoke and silica. Another possibility could be that smokers are more often admitted to hospital because of smoking-associated diseases, and sarcoidosis may therefore have been identified to a greater extent in smokers, since in-house diagnoses of sarcoidosis from the national registry were used as the outcome variable. These findings should be interpreted cautiously since the number of subjects for this analysis was low.

In conclusion, our study identified an increased risk of sarcoidosis associated with silica dust exposure in the highest exposed groups. While the risk of developing sarcoidosis was lower among ever-smokers compared to never-smokers, the findings indicate a higher risk among silica-exposed smokers compared to silica-exposed non-smokers.

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Competing interests

None declared.

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