

Lung cancer among workers exposed to silica dust in Chinese refractory plants

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A retrospective cohort mortality study was conducted for lung cancer among silica and clay brick workers at 11 refractory plants in China. The cohort included 6266 male workers employed before 1962 and followed between 1963 and 1985. The standardized rate ratios (SRR) were obtained by comparing the mortality rates of the silica-exposed cohort with those of a population of 11 470 male steel workers. As expected, significant excesses were observed for all deaths, all cancers, lung cancer, cardiorespiratory diseases, pulmonary heart diseases, and pulmonary tuberculosis. The lung cancer SRR was 1.49 ($P < 0.01$) for the total cohort. The increased lung cancer risk was attributed to the silicotics (SRR 2.10; $P < 0.01$) in the cohort. Higher lung cancer risk was found with increasing latency and severity of silicosis; this finding suggests that the excess was possibly related to occupational exposure to silica dust. Among the silicotics, there was a twofold excess of lung cancer risk among both the nonsmokers and the smokers.

Key terms epidemiologic study, fire brick, refractories, silica exposure, time since first exposure, smoking.

Silicosis has been the most important occupational illness in China since 1951 when health examinations for occupational lung diseases were initiated. The number of newly detected cases per year over the last 20 years has declined sharply compared with the corresponding numbers of the 1950s, and the mean years of silica dust exposure at the time of certification of silicosis has increased. However, according to the bulletin announced by the Ministry of Public Health on 28 January 1991, in the metallurgical industry of China 820 949 workers were exposed to silica dust, and 30 574 workers were certified silicotics.

Goldsmith et al reviewed (1, 2) and compiled (3) studies related to silica exposure, silicosis and cancer; the results indicated that iron and steel foundry workers, nonuranium miners, and sand-blasters had an excess risk of lung cancer. The authors noted that several issues tend to question silica's etiologic role in the observed excesses of lung cancer. First, these workers, besides being exposed to silica, worked in complex environments containing carcinogens such as polycyclic aromatic hydrocarbons, metallic oxides, arsenic, asbestos, and radon. Excess lung cancer among the workers could have been confounded by exposure to these industrial carcinogens (2, 3). Second, smoking was unadjusted in many early studies (3). In addition, some studies reported either no association with silica exposure or a negative association (3, 4). For these reasons, the issue of silica exposure, silicosis, and cancer risk has continued to be controversial in industrial medicine research.

This study evaluated refractory brick plant workers to measure the risk from lung cancer among silica-exposed workers whose exposure to quartz was and remains relatively pure. In April 1988,

according to a directive of the Chinese Ministry of Metallurgical Industry, the Institute of Industrial Health of the Anshan Iron and Steel Corporation (AISC) initiated a retrospective study of 11 refractory plants.

Subjects and methods

The study population consisted of 6266 male refractory brick workers who were subjects of periodic health examinations for silicosis between 1 January 1963 and 31 December 1985. Entry to the study was restricted to those employed before 1962 in manufacturing silica or clay brick. Demographic and employment history was obtained through an interview and an examination of the personnel records of each plant. All deaths were determined from funeral allowance records at each plant. Information on the cause of death was obtained from certificates or from medical records. All causes of death were routinely coded according to the Chinese classification of diseases, injuries and causes of death, similar to the seventh revision of the International Classification of Diseases (ICD-7). The identification of silicotics was based on the 1963 diagnostic standard for pneumoconioses of the Chinese Ministry of Public Health.

The standardized rate ratios (SRR) were calculated (5) for selected causes of death by comparing age- and cause-specific observed numbers of death in the study cohort with expected numbers from a population of 11 470 male workers from 10 rough rolling steel mills. As a means of minimizing exposure to known occupational carcinogens, steel workers ever exposed to silica dust or other known occupational carcinogens were excluded. We evaluated the following: smoking, latency since first exposure,

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radiological status, silicosis, and employment in silica brick or clay brick manufacturing.

Results

The distribution of year of first employment and the follow-up results for the vital status of 6266 members of the refractory brick cohort are shown in table 1. From 1963 to 1985, 871 (13.9%) members died, 5132 (81.9%) were alive, and 263 (4.2%) were lost to follow-up. There were 130 730 person-years of follow-up, 93 169 for the nonsilicotics, and 37 561 for the workers with silicosis. Table 2 shows the number and distribution of the study

Table 1. Results of the follow-up for vital status of 5132 Chinese silica brick workers from 1963 to 1985.

Year of 1st exposure	Alive	Dead		Lost to follow-up		Total
		N	%	N	%	
—1950	611	310	30.8	6	0.6	1007
1950—1954	1941	372	15.5	88	3.7	2401
1955—1959	2319	173	6.6	113	4.3	2905
1960—1962	181	16	6.9	56	22.1	253
Total	5132	871	13.9	263	4.2	6266

Table 2. Distribution of the study population by radiographic category of silicosis.

Radiographic categories of silicosis	Number	Percentage
0	2882	48.0
0—I	1294	21.6
I	1202	20.0
II	445	7.4
III	180	3.0
Total	6003	100.0

Table 3. The standardized rate ratios (SRR) for selected causes of death.

Causes of death	Nonsilicotics		Silicotics		Total	
	Observed (N)	SRR	Observed (N)	SRR	Observed (N)	SRR
All cancers	148	1.23*	73	1.05	221	1.16**
Esophageal cancer	12	1.31	11	1.62	23	1.44
Stomach cancer	28	1.33	8	0.62	36	1.07
Intestine cancer	6	0.68	—	—	6	0.45
Liver cancer	40	1.32	12	0.75	52	1.13
Lung cancer	30	1.11	35	2.10**	65	1.49**
Other cancers	32	0.98	7	0.41	39	0.77
Cardiorespiratory disease	111	0.96	144	1.65**	255	1.25
Pulmonary heart disease	21	0.74	71	3.08**	92	1.79**
Silicosis	—	—	33	∞	33	∞
Cerebrovascular disease	50	0.83	20	0.43	70	0.66
Coronary heart disease	18	1.12	8	0.73	26	0.97
Other cardiorespiratory disease	22	1.90**	12	1.48	34	1.73**
Pulmonary tuberculosis	15	1.38	222	31.31**	237	13.22**
Diseases of the digestive system	26	1.00	12	0.81	38	0.93
Cirrhosis of the liver	25	1.23	10	0.87	35	1.11
Accident or suicide	62	0.94	8	0.29	70	0.75
Other diseases	11	0.57	5	0.44	16	0.52
Unknown	17	1.04	17	1.47	34	1.22
All causes	390	1.04	481	2.10**	871	1.44**

** $P < 0.01$.

population (excluding those lost to follow-up) by radiographic categories of silicosis according to the 1963 standards of the Chinese Ministry of Public Health. The silicotics, including simple silicosis and silicotuberculosis, numbered 1827 men, and 4176 men were classified as nonsilicotics.

Table 3 shows the observed and expected deaths and the SRR values for selected causes of death by silicosis status. For the nonsilicotics, there were statistically significant excess SRR values for all cancers (SRR 1.23, $P < 0.05$) and diseases of the respiratory and circulatory system (SRR 1.90, $P < 0.01$). For the silicotics, statistically significant excesses were seen for all causes (SRR 2.10, $P < 0.01$), lung cancer (SRR 2.10, $P < 0.01$), diseases of the respiratory and circulatory system (SRR 1.65, $P < 0.01$), including pulmonary heart disease (SRR 3.08, $P < 0.01$), and pulmonary tuberculosis (SRR 31.31, $P < 0.01$). There were 33 deaths listing silicosis as the underlying cause of death, with zero expected. For the total cohort, there were significant excesses for all causes (SRR 1.44, $P < 0.01$), all cancers (SRR 1.16, $P < 0.01$), lung cancer (SRR 1.49, $P < 0.01$), pulmonary heart disease (SRR 1.79, $P < 0.01$), diseases of the respiratory and circulatory system (SRR 1.73, $P < 0.01$) and pulmonary tuberculosis (SRR 13.22, $P < 0.01$). There was a nonsignificant excess of 32—33% for both stomach and liver cancer among the nonsilicotics, while both sites showed a deficit among the men with silicosis. The SRR for lung cancer among all the refractory brick workers was 1.49 ($P < 0.01$). In this silica-exposed population, workers with silicosis appeared to be at the highest pulmonary cancer risk (and for several other conditions), while among the nonsilicotics there was no excess from lung cancer, SRR 1.11 ($P > 0.05$).

Table 4 shows the results of the latency analysis and demonstrates that for all causes, all cancers, and lung cancer the risk rises with greater latency. When analyzed separately, the lung cancer risk rises with increasing latency for the silicotics (data not shown), but not for those without silicosis. As seen in table 4, the lung cancer and all cancer SRR increased with increasing latency, but

Table 4. Analysis by years since first employment (latency) for selected causes of death of the silica-exposed workers. (SRR = standardized rate ratio)

Cause of death	Duration of exposure									
	0—9 years		10—19 years		20—29 years		≥ 30 years		Total	
	Observed (N)	SRR	Observed (N)	SRR	Observed (N)	SRR	Observed (N)	SRR	Observed (N)	SRR
All causes	57	1.08	290	1.44**	351	1.44**	173	1.63**	871	1.44**
All cancers	12	0.74	63	0.92	101	1.31**	45	1.60**	221	1.16
Lung cancer	2	0.88	11	0.76	35	1.77**	17	2.39**	65	1.49**
Cardiorespiratory disease	13	1.67	66	1.22	106	1.15	70	1.41**	255	1.25**
Pulmonary heart disease	2	1.18	25	2.04**	39	1.67**	26	1.83**	92	1.79**
Cerebrovascular disease	3	0.81	14	0.51	35	0.73	18	0.69	70	0.66
Pulmonary tuberculosis	12	10.26**	98	18.56**	88	11.18*	39	10.77**	237	13.22**

** $P < 0.01$.**Table 5.** Lung cancer risk by smoking and silicosis status. (SRR = standardized rate ratio)

Group	Smokers		Nonsmokers		Unknown		Total	
	Observed (N)	SRR	Observed (N)	SRR	Observed (N)	SRR	Observed (N)	SRR
Nonsilicotics	21	1.20	7	0.85	2	1.49	30	1.10
Silicotics	21	2.34**	12	2.13*	2	1.09	35	2.10**
All deaths	42	1.58**	19	1.37	4	1.26	65	1.49**

* $P < 0.05$, ** $P < 0.01$.**Table 6.** Standardized rate ratio (SRR) from selected causes of death by radiological categories of silicosis.

Causes of death	Nonsilicotics		Silicotics by radiological categories							
			I		II		III		Total	
	Observed (N)	SRR	Observed (N)	SRR	Observed (N)	SRR	Observed (N)	SRR	Observed (N)	SRR
All causes	390	1.04	253	1.75**	144	2.30**	84	3.72**	481	2.10**
All cancers	148	1.23**	47	1.06	17	0.94	9	1.37	73	1.05
Lung cancer	30	1.11	21	1.97**	10	2.34*	4	2.55	35	2.10**
Cardiorespiratory	111	0.96	79	1.50**	42	1.65**	23	2.52**	144	1.65**
Pulmonary heart disease	21	0.74	39	2.85**	21	3.04**	11	4.45**	71	3.08**
Pulmonary tuberculosis	15	1.38	94	20.70**	77	40.96**	51	72.86**	222	31.21**

* $P < 0.05$, ** $P < 0.01$.

only became significantly elevated 20 or more years after exposure. The lung cancer SRR was < 1.00 for latency of less than 20 years, but rose to 1.77 for 20—29 years of exposure to silica and to 2.39 for a latency of ≥ 30 years of dust exposure. Cardiorespiratory diseases and pulmonary tuberculosis did not show positive gradients for latency.

The SRR values for lung cancer are presented in table 5 by smoking status. Among the silicotics, significant excess lung cancer risks appeared for both the smokers (SRR 2.34) and the nonsmokers (SRR 2.13). Although there was a 20% excess risk for the smoking workers who were nonsilicotics, there was an SRR of 0.85 for nonsmoking nonsilicotics.

We examined the risk differences between silica brick workers and clay brick workers (table not included). For both types of brick workers, there were elevated risks from lung cancer, but the risk was significant only for the silicotics. The same was true for diseases of the cardiorespiratory system, pulmonary heart disease, and pulmonary tuberculosis. With the exception of mortality from all cancers, there were no significant disease excesses for the nonsilicotic clay brick workers.

Table 6 shows the SRR value for selected causes by categories of silicosis. There were clear gradients for all causes of death, lung cancer, diseases of the cardiorespiratory system, pulmonary heart disease, and tuberculosis. The SRR values for lung cancer rose from 1.11 for nonsilicotics to 1.97 for category I, to 2.34 for category II, to 2.55 for category III for silicosis in table 6. We evaluated the lung cancer risk among silicotics by time since first employment and showed that there were positive gradients by latency periods within all three categories of silicosis. Employment of < 20 years showed an SRR of 0.87, while ≥ 30 years had an SRR of 3.78 (tables are not included). Furthermore, when silicotuberculosis was evaluated separately, it had an SRR of 2.24 for lung cancer (11 observed, 4.91 expected, $P < 0.05$), a finding similar to the SRR of 2.08 for simple silicosis (24 observed, 11.54 expected, $P < 0.01$).

Discussion

The associations between silica exposures, silicosis, and lung cancer are under dispute. The epidemiologic substance of the controversy mainly focuses on the following points: (i) the possibility of

confounding by other industrial carcinogens and smoking, (ii) the differential lung cancer risk among silica-exposed workers and those with silicosis, and (iii) uncertainty concerning the severity of silicosis and the risk of lung cancer.

The results of this study show that there was a significant excess risk from lung cancer (SRR 1.49) in the population exposed only to silica dust in the refractory brick and clay industry. For the silicotics, there was a significant excess risk from lung cancer (SRR 2.10, $P < 0.01$), but for nonsilicotics there was none (SRR 1.11). The 49% excess of lung cancer of the silica brick worker population was attributed to the excess of lung cancer among silicotics, even though in our study we observed a doubling of lung cancer risk for nonsmoking silicotics (SRR 2.13, $P < 0.05$). This study supports work by others who showed lung cancer risk ratios between 1.4 and 5.0 for silicotics, as summarized by Goldsmith (3). Our results also support the excess lung cancer risks found by other investigators among firebrick workers (6–8) and smelting furnace repairmen (9–10).

As shown by Zhong et al (this issue) silicosis is an occupational disease with high mortality in China. As seen in table 3, pulmonary tuberculosis plus pulmonary heart diseases (cor pulmonale) accounted for 69.9% of all causes of death. Because silicotics prematurely died of these diseases, the excess of lung cancer may have been underestimated. We observed that 46% of the patients with pulmonary silicotuberculosis died before 20 years of latency or exposure, but 88% of the lung cancer cases died after 20 years of latency; therefore, in this cohort, pulmonary tuberculosis and cor pulmonale may, as causes of death, be competing with lung cancer. Patients with silicosis have damaged pulmonary tissues, and impaired lung clearance. Thus, as duration of exposure increases, neoplasia arises in fibrotic pulmonary tissue. However, nonsilicotics do not have such damage, and risk is less.

Concluding remarks

This study of silica brick and clay workers confirmed significantly high mortality risks for all causes of death, all cancers, lung cancer, cardiopulmonary diseases (cor pulmonale, silicosis, and other respiratory diseases), and tuberculosis. The lung cancer risk in this

population was a modest SRR of 1.49. Statistically significant excesses were confined to silicotics only, and this finding held true for both silica brick and silica clay workers. When analyzed by years since first exposure, excess risk paralleled latency, a trend found for the silicotics and the whole cohort only. Among the silicotics, excess lung cancer risk was observed for the non-smokers and smokers, and the excess increased with latency. For the nonsilicotics, regardless of smoking status, no significant pulmonary cancer risk was shown. We observed striking excesses from cor pulmonale and tuberculosis that increased with the severity of silicosis.

Additional surveillance of these workers will enable us to determine whether excess mortality risks remain in this industry. Furthermore, more research would determine if these workers have elevated risks for other cancers such as lymphatic and gastric malignancies and for other diseases, including autoimmune conditions and renal diseases.

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