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ARTICLES

Reevaluation of Silicosis and Lung Cancer in North Carolina Dusty Trades Workers

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We previously reported on the lung cancer mortality through 1983 of 760 males who were diagnosed with silicosis during 1930–1983 by the State of North Carolina's medical examination program for dusty trades workers. The lung cancer SMR (95% confidence interval) was 2.6 (1.8–3.6) among 655 white members of this group. In this paper, we report the results of a reanalysis of mortality among a subgroup for whom chest radiographs were currently available for rereading.

Technically acceptable radiographs were available for 306 white males and were independently reclassified for pneumoconiosis by 3 "B" readers using the 1980 ILO Classification. Lung cancer SMRs were 1.7 (0.8–3.1) for the entire group of 306 white males, 2.5 (1.1–4.9) for 143 subjects reclassified as simple silicosis, and 1.0 (0.1–3.5) for 96 subjects whose radiographs were reclassified as ILO category 0. There were no lung cancer deaths among 67 subjects whose radiographs were reclassified as progressive massive fibrosis.

Corresponding lung cancer SMRs for subjects who had never been employed in a job with exposure to known occupational carcinogens were 1.2 (0.2–4.4) for those reclassified as category 0, and 2.4 (1.0–5.0) for those reclassified as having simple silicosis. The age-adjusted lung cancer rate ratio among subjects with simple silicosis compared to those with category 0 was 1.5 (0.4–5.8).

Our findings from this reanalysis, which effectively controls for misclassification of silicosis due to errors in radiograph interpretation by North Carolina program readers, offer additional evidence consistent with the hypothesis of an association between silicosis and lung cancer in this study group.

Key words: cancer, PMF, pneumoconiosis, dusty trades, silica exposures

INTRODUCTION

We previously reported [Amandus et al., 1991] on the mortality through 1983 of 760 males who were diagnosed as having silicosis during 1935–1983 as part of the

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state of North Carolina (NC) medical examination and dust sampling program for dusty trades workers. Age-adjusted lung cancer rates in the white members of this group were 2.6 times higher than those in U.S. white males, 1.5 times higher than those in a referent group of coal miners with coal workers' pneumoconiosis, and 2.4 times higher than those in a referent group of metal miners with no radiographic evidence of silicosis. The increase in lung cancer rates in NC silicotics was not explained by age, cigarette smoking, exposures to other known occupational carcinogens, time since diagnosis of silicosis, or detection bias (e.g., silicosis detected as the result of an examination for lung cancer).

The NC medical examinations administered at the work site have included miniature screening chest radiographs. These screening radiographs were interpreted by the same physician during 1935–1983 and, if any evidence of silicosis was observed, a standard 14 × 17 inch radiograph was taken. All standard size radiographs were evaluated for pneumoconiosis according to the procedure described in the 1930 Johannesburg Conference Report [Gardner et al., 1930] by the NC Advisory Medical Committee.

One possible limitation of our earlier report [Amandus et al., 1991], which relied on the NC program diagnosis to evaluate the relationship between silicosis and cancer, is possible misclassification of silicosis due to reader error. Diagnoses of silicosis were made by the NC Advisory Medical Committee, which was composed of three physicians. Membership, however, varied over time and could have introduced some variations in classification. To determine whether or not misclassification compromised our previous findings [Amandus et al., 1991], we reevaluated all available chest radiographs and recomputed lung cancer rates by radiographic category of silicosis.

MATERIALS AND METHODS

Vital status of the 760 silicotics diagnosed since 1935 was determined through 1983 and, for the deceased, certified cause of death was coded according to the International Classification of Diseases [NCHS, 1968]. Information on work history, including employment in jobs with possible exposure to other known occupational carcinogens, and on cigarette smoking habit were collected from medical examination records. For purposes of this analysis, cigarette smoking habit was categorized as ever or never smoked cigarettes, and exposure to other known occupational carcinogens was categorized based on employment in jobs with potential exposure (asbestos manufacturing, insulation work, olivine mining, talc, and foundry work). Details of these data have been described elsewhere [Amandus et al., 1991].

Medical records from the NC dusty trades program on 760 silicotics who were part of our previous mortality study were reviewed. Chest radiographs which had been reported as showing evidence of silicosis were available for 370 of the silicotics. Radiographs could not be located for the other 390 silicotics. Silicotic radiographs were reclassified (see below) to determine the level of possible false-positives and to reanalyze the mortality data.

In addition, radiographs from 107 dusty trades workers who had been examined in the program and who had been determined to have no evidence of pneumoconiosis were also selected from the NC program medical files. These were reclassified (see below) to estimate the level of possible false-negatives.

Each of the 477 radiographs were independently classified by three "B" readers

TABLE I. Number of Reclassified Silicotic and Nonsilicotic Radiographs by Radiographic Category and Reader

	Silicotics				Nonsilicotics			
	Reader				Reader			
Radiographic category	1	2	3	Median	1	2	3	Median
Category 0	121	142	52	104	101	105	103	104
Simple silicosis	144	153	168	160	1	1	4	1
PMF	89	57	150	83	0	0	0	0
Unreadable[a]	16	18	0	23	5	1	0	2

[a]Either 2 readers found the radiographs unreadable or no median was calculated (e.g., one reader reported a radiograph as unreadable, one reported category 0, and one reported category 1–3 or PMF).

(Reader 1, Reader 2, and Reader 3) according to the 1980 ILO procedures [ILO, 1981]. Based on the median reading of the three readings, silicotics and nonsilicotics were subdivided into three groups for reanalysis. These groups were 1) category 0; 2) simple silicosis (small opacities of ILO profusion category 1, 2, or 3); and 3) progressive massive fibrosis (PMF) (large opacities of ILO category A, B, or C).

The age-adjusted lung cancer mortality rates in silicotics whose radiographs were reclassified as category 0, simple silicosis, or progressive massive fibrosis were compared to those in U.S. white males using a person-years analysis. Person-years of follow-up for the silicotic study group were tallied over 5-year intervals of age and time since diagnosis of silicosis. Standardized mortality ratios (SMRs) were estimated by dividing the total observed by the total expected (U.S. white male rates) number of lung cancer deaths. Finally, 95% confidence intervals were estimated assuming that the observed number of deaths followed a Poisson distribution [Bailar and Ederer, 1964].

The age-adjusted lung cancer rate in silicotics whose radiographs were reclassified as simple silicosis was compared to that in silicotics with radiographic category 0. Person-years and observed numbers of deaths were tallied by 10-year intervals of age. Mantel-Haenzel (MH) age-adjusted rate ratios for incidence density data and 95% test-based confidence intervals were calculated employing a continuity correction [Kleinbaum et al., 1982].

RESULTS

Reclassification of Chest Radiographs

Based on median readings, there were 104 silicotics whose radiographs were reclassified as category 0, 160 as simple silicosis, 83 as PMF, and 23 as unreadable (see footnote, Table I).

The proportion of the 370 silicotic radiographs reclassified as either simple silicosis or PMF was 63% by Reader 1, 57% by Reader 2, 86% by Reader 3, and 66% by median reading. In addition, 2 of the 3 readers reported evidence of rounded opacities in nearly all of the radiographs which they had reclassified as simple silicosis (99% from Reader 1 and 93% from Reader 2).

Based on median readings, there were 104 nonsilicotics whose radiographs were reclassified as category 0, one as simple silicosis, none as PMF, and two as unreadable (see footnote, Table I). The proportion of the 107 nonsilicotic radiographs

TABLE II. Observed and Expected Number of Lung Cancer Deaths in Whites, and SMR for the Entire Silicotic Cohort, for Those Whose Radiographs Were Reclassified by Radiographic Category, and for Those Whose Radiographs Were Unavailable

Radiographic category	Number of subjects	Person years	Observed deaths	Expected deaths	SMR	95% CI	
						L	U
Radiographs reclassified							
Category 0	96	1,350	2	2.0	1.0	0.1	3.5
Simple silicosis	143	2,306	8	3.2	2.5	1.1	4.9
PMF	67	620	0	0.6	—	—	—
Sub-total	306	4,276	10	5.8	1.7	0.8	3.1
Radiographs unavailable[a]	349	4,327	23	7.0	3.3	2.1	4.9
Total	655	8,603	33	12.9	2.6	1.8	3.6

[a]Subjects whose radiographs were either unavailable or technically unreadable (see Table I footnote).

which were reclassified as category 0 was 96% by Reader 1, 98% by Reader 2, 94% by Reader 3, and 97% by median reading.

None of the 107 nonsilicotic radiographs or the 104 silicotic radiographs reclassified as median category 0 had other abnormalities suggesting silica exposure (e.g., eggshell calcification of hilar nodes, nodular calcification, or coalescence of small opacities).

Lung Cancer Mortality

Only data from whites were analyzed because there were only 41 nonwhites whose radiographs were reclassified, and there were no lung cancer deaths among nonwhites. Lung cancer SMRs (Table II) were 1.7 (0.8–3.1) among 306 whites whose radiographs were reclassified and 3.3 (2.1–4.9) among 349 whites whose radiographs were either unavailable or available but technically unreadable. The apparent difference in lung cancer rates between these groups was not explained by cigarette smoking habit, age, or exposure to other known occupational carcinogens (Table III). More importantly, the SMR for lung cancer (Table II) was 1.0 (0.1–3.5) among whites whose radiographs were reclassified as category 0, but was 2.5 (1.1–4.9) among whites with radiographic evidence of simple silicosis. There were no lung cancer deaths among whites with PMF.

SMRs for lung cancer (Table IV) among whites who had no exposure to other known occupational carcinogens were 1.2 (0.2–4.4) for those with radiographic category 0 and 2.4 (1.0–5.0) for those with simple silicosis. The age-adjusted lung cancer rate among subjects who had no exposure to other known occupational carcinogens and who had radiographic evidence of simple silicosis was 1.5 (0.4–5.8) times higher than that among subjects with category 0.

DISCUSSION

In contrast to our previous report [Amandus et al., 1991], this analysis effectively partitions risk of lung cancer by severity of radiographic evidence of silicosis using current ILO guidelines. We previously reported that the age-adjusted lung cancer rate among whites in the total cohort of 760 silicotics (Table II) was 2.6 times

TABLE III. The Number of White Silicotics Whose Radiographs Were Reclassified and Whose Radiographs Were Unavailable by Cigarette Smoking Habit, Age at Hire, and Exposure Status

	Radiograph reclassified (306)		Radiograph unavailable (349)[a]	
	No.	%	No.	%
Cigarette smoking habit				
Yes	137	45	142	41
No	74	24	63	18
Unknown	95	31	144	41
Age at hire				
<20	122	40	114	33
20–29	122	40	149	43
30–39	48	16	59	17
40–49	9	3	16	5
50–59	5	2	8	2
60–69	0	0	3	1
Exposure status[b]				
Silica only	273	89	304	87
Silica and other	33	11	45	13

[a]See Table II footnote.
[b]Employment in job with potential exposure to silica and other known occupational carcinogens (see text).

higher than that among U.S. white males. In this analysis, the age-adjusted lung cancer rate among 306 whites with technically acceptable radiographs was also elevated (SMR = 1.7). The principal purpose of the current analysis, involving reclassifying radiographs, was to reduce possible misclassification of silicosis present in the data we previously analyzed. The expectation was that reduction of nondifferential misclassification of "exposure" (i.e., silicosis) would tend to increase the lung cancer rate ratio. We observed an SMR of 2.5 among white silicotics whose radiographs were reclassified as having simple silicosis, while those reclassified as category 0 had a rate similar to that among U.S. white males (SMR = 1.0).

It is not clear whether smoking is [Weiss, 1988] or is not [Blanc, 1989] associated with small radiographic opacities. However, even when a smoking-small opacity association has been observed in populations of workers exposed to dust which is known to cause small rounded opacities, the association has been restricted to small irregular opacities [Amandus et al., 1976; Thériault et al., 1974]. In nearly all the NC dusty trades radiographs reclassified as simple silicosis for our study, the small opacities were classified as having a rounded shape (characteristic of silicosis). Therefore, the observed chest radiographic abnormalities do not suggest that smoking affected the radiographic classifications.

Small numbers in the current analysis prevented adjusting rate ratios for cigarette smoking habit. Of the 10 lung cancer deaths which occurred among those whose radiographs were reclassified, six (five simple silicosis and one category 0) had smoked cigarettes, one had never smoked cigarettes (category 0), the one (simple silicosis) had no information available on smoking history. There were no lung cancer cases among silicotics who had never smoked. Lung cancer SMRs were 3.4 (1.1–7.9)

TABLE IV. Lung Cancer Rates and Age-Adjusted Rate Ratios in Silicotics Whose Radiographs Were Reclassified and Who Were Never Employed in a Job With Exposure to Other Known Carcinogens*

	Age at follow-up				
Radiographic category	<50	50–59	60–69	≥70	Total
Category 0					
O	0	0	1	1	2
PY	251	366	341	179	1,137
Rate	0	0	293	559	176
E	.05	.31	.72	.57	1.65
SMR	0	0	2.0	1.8	1.2
95% CI	1	—	(.1–10.9)	(.0–9.7)	(.2–4.4)
Simple silicosis					
O	0	1	4	2	7
PY	494	678	633	253	2,058
Rate	0	147	632	791	340
E	.09	.59	1.33	.86	2.87
SMR	—	2.6	3.0	2.3	2.4
95% CI	—	(.1–14.2)	(.8–7.7)	(.3–8.4)	(1.0–5.0)
Unadjusted MH rate ratio[a]	—	—	2.2 (.3–18.3)	1.4 (.1–15.4)	1.9 (.4–9.1)
Age-adjusted MH rate ratio[a]					1.5 (.4–5.8)

*Those with PMF were excluded. O = Observed no. of deaths; PY = person-years; Rate = rate per 100,000 PY; E = expected no. of deaths (U.S. white male rates); CI = confidence interval.
[a]Ratio of lung cancer rate in those with simple silicosis to that in those with category 0. The age-adjusted rate ratio was 1.8 (.4–7.3) after combining subjects into three age groups (<60, 60–69, ≥70), and was 1.8 (.4–8.8) after combining subjects into two age groups (<70, ≥70).

among silicotic smokers and 1.3 (0.03–7.1) among smokers reclassified as category 0. Complete data on duration and intensity of cigarette smoking were unavailable.

Confounding from cigarette smoking is an unlikely explanation for this 2–3-fold cancer rate ratio. The proportion who had smoked cigarettes was 50.6% (81/160) among those whose radiographs were reclassified as having silicosis and 44.2% (46/104) among those reclassified as category 0. This difference would not explain a 2–3-fold difference, as Finkelstein et al. [1987] indicated that a 15% difference in proportion of smokers would increase the lung cancer rate ratio by only 20%.

For these reasons, it is unlikely that the observed increased lung cancer rate associated with simple silicosis can be explained by smoking alone. This is consistent with our earlier results, where adjusting for smoking had little effect on risk estimates for lung cancer [Amandus et al., 1991].

As in our previous report, exposure to other known occupational carcinogens did not explain the increased lung cancer rate in silicotics. The age-adjusted lung cancer mortality rate in silicotics whose radiographs were reclassified as showing evidence of simple silicosis and who had no exposure to other known occupational carcinogens was 2.4 times higher than that in U.S. white males, and 1.6 times higher than that in silicotics whose radiographs were reclassified as category 0.

An explanation as to why the age-adjusted lung cancer mortality rate among silicotics whose radiographs were reclassified (SMR = 1.7) was lower than that among those whose radiographs were unavailable (SMR = 3.3) could not be determined. Differences in cigarette smoking habit, age, and exposure to other known occupational lung carcinogens do not appear to explain this difference.

CONCLUSIONS

Lung cancer rates appear to be increased in NC silicotics. This increase in not explained by differences between silicotics and nonsilicotic referent groups in age, exposure to other occupational carcinogens, detection bias, or smoking habits. Our findings from this mortality analysis based upon a reevaluation of available radiographs for silicosis offer additional evidence in NC dusty trades workers consistent with the hypothesis of an association between silicosis and lung cancer. Small numbers of lung cancer deaths in non-silicotics, no lung cancer deaths in silicotics who had never smoked, and lack of complete data on duration and intensity of smoking prevented estimation of the contribution to lung cancer risk of silicosis separately from that due to smoking.

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