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Silicosis and lung cancer among workers in North Carolina dusty trades

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In 1940—1983, 760 cases of silicosis were identified among male North Carolina (NC) workers in dusty trades. Vital status was ascertained through 1983 for 714 silicotics, and death certificates were obtained for 546 of the 550 decedents. The standardized mortality ratio (SMR) for lung cancer based on United States rates was 2.6 [95% confidence interval (95% CI) 1.8—3.6] for whites, 2.3 (95% CI 1.5—3.4) for whites unexposed to other known occupational carcinogens, and 2.4 (95% CI 1.5—3.6) for whites with no other exposure and diagnosed with silicosis while still employed in dusty trades. In addition, the age- and smoking-adjusted rate for silicotics was 3.9 times higher (95% CI 2.4—6.4) than that of nonsilicotic metal miners. This analysis effectively controlled for confounding by age, cigarette smoking, exposure to other occupational carcinogens, and detection bias. The results congrue with the hypothesis of an association between silicosis and lung cancer.

Key terms dusty trades, lung cancer, silicosis.

In 1987, the International Agency for Research on Cancer (1) concluded that there was sufficient evidence from animals and limited evidence from humans for the carcinogenicity of silica. Subsequently, McDonald (2) suggested that bias, confounding, and chance may explain the findings in humans.

By 1987, there existed a body of published evidence for increased lung cancer mortality among silicotics. However, this evidence was somewhat weakened by study shortcomings. Few studies of silica-exposed workers had employed reference groups of nonsilica-exposed workers, and few studies of silicotics had employed a nonsilicotic reference group defined within the same silica-exposed population. In most studies of silicotics, a definition of “compensable” silicosis was employed which differed between countries. A definition of silicosis based on a standardized radiographic classification was employed in only a few studies.

Detection bias was speculated to be the primary explanation of increased rate ratios for lung cancer mortality among silicotic cohorts, and it was not addressed in any studies before 1987. Detection bias was speculated to arise if the probability of detecting silicosis among lung cancer cases was greater than that among nonlung cancer cases.

In addition to these issues, confounding from cigarette smoking and occupational exposure to potential and known carcinogens such as radon, arsenic, and polycyclic aromatic hydrocarbons was generally not ruled out in most studies prior to 1987. In studies of underground metal and nonmetal miners, the association between silica, or silicosis, and lung cancer mortality was possibly con-

founded by exposure to radon and arsenic. Similarly, in studies of foundry workers, the association was likely confounded with a variety of potential carcinogens.

During 1983 to 1987, a collaborative study between the United States (US) National Institute for Occupational Safety and Health, the US National Cancer Institute, and the University of North Carolina at Chapel Hill was conducted to address some of the shortcomings of previous studies. In this collaborative study, we evaluated the mortality of 760 North Carolina (NC) workers who were employed in NC dusty trades and who were diagnosed with silicosis during 1940—1983. The results of this study were published during 1991 and 1992 (3, 4).

Data from our study have several advantages over investigations published prior to 1987. First, they represent silicotics in the NC dusty trades with occupational silica exposure. Second, the misclassification of silicosis was minimized because silicosis was defined radiographically. Third, individual data were available on cigarette smoking and employment history in order to adjust for potential confounding from cigarette smoking and exposure to other known occupational carcinogens. Fourth, workers who were examined as part of a voluntary examination conducted at their worksite could be distinguished from those examined as part of a self-initiated examination, often for compensation purposes. Thus detection bias among compensated workers could be minimized by excluding workers who were examined after leaving employment in NC dusty trades. Finally, data were available on a reference group of nonsilicotics with comparable risk factor information.

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The purpose of this paper is to summarize our methods and findings.

Methods

Since 1935, the state of North Carolina has conducted a voluntary program in which medical examinations are offered every one to two years to each worker in the NC dusty trades. The program defines dusty trades to include mining, foundries, quarrying, stone crushing, asbestos and silica manufacturing products, and construction.

Medical examinations are administered by the NC Industrial Commission at the worksite and consist of a posteroanterior chest radiograph and questionnaires on work history, medical symptoms, and, since 1964, cigarette smoking habits. Radiographs are classified for silicosis according to the 1930 Johannesburg Conference Report system.

Work history and cigarette-smoking habit data were abstracted from the NC Industrial Commission medical examination files for 760 silicotics. Vital status from 1940 through 1983 was verified for 714 (94%) of the 760 workers, and death certificates were obtained for 546 (99%) of the 550 deceased. The underlying cause of death was abstracted from the death certificates and coded according to the International Classification of Diseases, Adapted (5). Details of the program and the vital status follow-up have been documented elsewhere (3, 6).

Radiographs were available for 370 of the 760 silicotics. These films were reclassified for pneumoconiosis by three physicians who employed the classification of the International Labour Organisation (ILO) (7). The analysis focused primarily on whites, as there was only one lung cancer death among nonwhite subjects. Details of this reevaluation have also been published elsewhere (4).

The age-adjusted mortality rates of the silicotic cohort were compared to that of the US white male population and to that of a sample of white nonsilicotic metal miners (3). During 1959–1961, the US Public Health Service examined 12 258 metal miners as part of a cross-sectional study of silicosis. The vital status of this sample was ascertained as of 1975 (8). Each worker had been administered a chest radiograph and a questionnaire on work history, cigarette smoking habits, and respiratory symptoms. The chest radiographs were interpreted for pneumoconiosis according to the 1959 ILO classification. Data on 9543 nonsilicotic white males who were employed in nondiesel, nonuranium metal mines were used as a reference group for the NC cohort.

Results

The standardized mortality ratios (SMR) based on US white rates were significantly increased for white male silicotics due to tuberculosis (SMR 30.7), cancer of the intestine (SMR 2.3), pneumonia (SMR 2.4), bronchitis (SMR 7.9), emphysema (SMR 3.6), pneumoconiosis and other respiratory diseases (SMR 32.9), and infectious kidney disease (SMR 6.5). Several SMR values were greater than 1.5, but they did not reach statistical significance, including cancers of the liver (SMR 2.3), prostate (SMR 1.9), and lymphatic and hematopoietic tissue (SMR 1.7), influenza (SMR 2.6), and asthma (SMR 3.1). The lung cancer SMR was also significantly increased for the white male silicotics, 2.6 [95% confidence interval (95% CI) 1.8–3.6], based on rates for US white males, and 3.0 (95% CI 2.0–4.2), based on rates for NC white males. The

SMR values for tuberculosis (SMR 20.5), ischemic heart disease (SMR 2.1), and pneumoconiosis and other respiratory diseases (SMR 56.4) were significantly increased for nonwhites. Because only one case of lung cancer occurred among the nonwhites (SMR 0.7), the remainder of the results presented are for whites only.

The lung cancer SMR values were 2.3 (95% CI 1.5–3.4) for silicotics who had no exposures to other known occupational carcinogens and 4.5 (95% CI 1.8–9.2) for those with other exposures (ie, previous employment in asbestos product manufacturing, olivine mining, talc mining, insulation work, or foundries). The lung cancer SMR was 3.4 (95% CI 2.0–5.3) for workers with a history of cigarette smoking and 1.7 (95% CI 0.5–3.9) for non-smokers.

In order to minimize the effect of detection bias on the rate ratio for lung cancer mortality, lung cancer SMR values were estimated separately for silicotics who were diagnosed with silicosis while employed in the dusty trades. In addition, lung cancer SMR values were estimated with control for years after silicosis diagnosis. The lung cancer SMR was 2.5 (95% CI 1.7–3.7) for silicotics who were diagnosed while employed and 2.9 (95% CI 0.9–6.8) for those diagnosed after leaving employment. Among those diagnosed while employed, the lung cancer SMR values were 3.8 (95% CI 1.5–7.8) for < 5 years after the silicosis diagnosis, 1.3 (95% CI 0.3–3.9) for 5–9 years, 2.4 (95% CI 1.2–4.5) for 10–19 years, and 2.8 (95% CI 1.2–5.6) for ≥ 20 years. The comparable figures for the silicotics diagnosed after leaving employment were 2.2 (95% CI 0.1–12.2) for < 5 years, 7.0 (95% CI 1.5–20.6) for 5–9 years, and 1.6 (95% CI 0.0–9.2) for 10–19 years (there were no lung cancer deaths for ≥ 20 years).

With the use of the metal miner reference group, the age-adjusted Mantel-Hansel incidence density rate ratios were 3.2 (95% CI 1.8–5.8) for cigarette smokers and 8.6 (95% CI 3.6–20.5) for those who had never smoked. The age and smoking-adjusted rate ratio was 3.9 (95% CI 2.4–6.4).

Among the 370 workers whose radiographs were available and were reclassified, 104 were reclassified as category 0, 160 as simple silicosis (category 1–3), 83 as progressive massive fibrosis, and 23 were unreadable (4).

The lung cancer SMR values for the silicotics whose radiographs were reclassified and who were never employed in a job with exposure to other known carcinogens were 1.2 (95% CI 0.2–4.4) for those whose radiographs were reclassified as category 0 and 2.4 (95% CI 1.0–5.0) for those reclassified as simple silicosis (4). The age-adjusted Mantel-Haenszel rate ratio for simple silicosis compared with category 0 was 1.5 (95% CI 0.4–5.8).

Discussion

The association between silicosis and lung cancer mortality did not appear to be explained by chance, misclassification of silicosis, confounding from cigarette smoking, confounding from exposure to other occupational carcinogens, or detection bias. Lung cancer mortality was significantly higher for white silicotics than for US white males, NC white males, and white male metal miners. The increased lung cancer mortality was not likely a chance finding for the silicotics.

After the silicotics were partitioned by the severity of the radiographic evidence of silicosis, lung cancer mortality was also higher for those reclassified with simple silicosis compared with

those reclassified with category 0. This procedure effectively controlled for the misclassification of silicosis.

Lung cancer mortality was significantly higher among the NC silicotics who had no other occupational exposure than among nonsilicotic metal miners after adjustment for cigarette smoking habits. This procedure effectively controlled for confounding from exposure to other known occupational carcinogens and cigarette smoking.

Finally, lung cancer mortality was increased among the silicotics who had been diagnosed as having silicosis at least 10 years prior to death or at the end of follow-up. In addition the lung cancer SMR was increased and the SMR for all cancers excluding the lung was not increased (0.9) among the silicotics diagnosed while employed in NC dusty trades. This finding suggests that detection bias is an unlikely explanation for the increased lung cancer mortality among NC silicotics.

Our results are consistent with the hypothesis of an association between silicosis and cancer. This evidence is relatively free of the major shortcomings common in previous studies, such as chance, misclassification of silicosis, confounding, and detection bias.

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