

Mining, lung cancer and smoking

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AXELSON, O. and SUNDELL, L. Mining, lung cancer and smoking. *Scand. j. work environ. & health* 4 (1977) 46—52. Several studies have shown an increased lung cancer mortality among Swedish metal and iron ore miners, as probably caused by exposure to radon and its daughters. An earlier study of zinc-lead miners has been updated. The results show a 16-fold increase in lung cancer mortality. Surprisingly, nonsmokers were more apt to develop lung cancer than smokers, but the induction-latency time was about nine years shorter on the average for the smokers. An explanation for these findings might be that smoking increases the thickness of the mucus layer and therefore protects the bronchial epithelium from alpha radiation, but it also promotes the development of cancer once induced by the radiation.

Key words: case-referent (case-control) design, lung cancer, mining, radon daughter exposure, smoking.

In 1971 a high mortality from lung cancer was reported in Swedish metal miners (zinc and lead) as probably caused by exposure to radon and radon daughters in the mine atmosphere (4, 5). Other reports followed that indicated a similarly increased mortality from lung cancer also in Swedish iron ore miners (9, 18). In a nationwide study, as yet unpublished, the average lung cancer mortality among Swedish miners (the great majority mining iron ore) was found to be about fivefold the normal. There seemed to be an exposure-effect relationship between the increased mortality from lung cancer and radon daughter concentrations as measured in the mines in the years around 1970. Earlier measurements were lacking, however. Table 1 is taken from the nationwide report to summarize some of the findings.

Lung cancer is strongly associated with smoking, and there are indications of a synergistic effect between smoking and occupational exposure, e.g., to asbestos (6). A similar effect has appeared with regard to radon daughters in studies of uranium miners (2). In the aforementioned primary study (4, 5) several of the lung cancer cases were nonsmokers, an observation requiring further evaluation, and therefore the present study was made to determine the relationships between mining and risk of lung cancer as modified by smoking habits. Furthermore, the original cohort study (1956 through 1970) is updated through 1976 by means of the case-referent technique (14).

MATERIAL AND METHODS

Source of subjects

The register of deaths and burials in the parish (Hammar, with about 4,000 inhabitants) around two adjacent and connected zinc-lead mines was used as the source of

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Table 1. Deaths from lung cancer in 1961–68 among underground and surface workers in mines classifiable with regard to probable radon daughter levels.^a

Approx. working levels ^b	Age group (years)			Number of workers 1960
	20–64	65–79	20–79	
< 0.3	12	14	26	5,947
0.3–1	24	13	37	5,001

^a Note: Half the worker population (in Swedish mines) might be considered as exposed. About 85 % of the lung cancer cases had experience in underground work.

^b One “working level” is any combination of short-lived radon daughters (through ²¹⁴polonium, RaC') leading to a total emission of 1.3×10^5 MeV of alpha energy per liter of air.

subjects for this case-referent study comprising the period 1956 through 1976 and dealing with men only.

The cases were those 29 subjects who died from lung cancer (ICD 162) in the parish during the period at issue. The referents were those three persons who were entered in the register before and after each case. The cause of death for the referents could be accident or any other disease but lung cancer. Thus, a sort of matching procedure was applied with regard to time of death in the selection of referents, of whom there were 174. Since there was no reason, however, to believe that time of death should be a confounding factor (13) (the method of selecting the referents having been applied for reasons of convenience only), the tuplets were not maintained in the analysis. It might be added that the register of deaths and burials seemed to contain fairly complete diagnoses from the death certificates, a result found in other similar Swedish studies.

Assessment of exposure

The lists of subjects were submitted to the mining company for the identification of those who had been employed and for the assessment of worktime under-

ground. From medical files and interviews with two former foremen (now retired), it was possible to obtain information about the smoking habits of the miners. In 10 out of 19 cases of lung cancer, independent information about smoking habits was available from different sources, and it was contradictory in 2 of the 10 cases. Therefore, the obtainable information about smoking seemed to be reasonably reliable. However, these two cases were considered smokers, as were also exsmokers and occasional smokers (pipe as well as cigarettes). Smoking data on two cases and three referents among the miners were not available and therefore these five men were disregarded in the evaluation of the effect of smoking (table 3). The two cases were also lost for the calculations of means and medians for the age at death and latency time for developing lung cancer among the smokers and nonsmokers (table 4).

Statistical methods

The statistical analyses of the data were based on the Mantel-Haenszel procedures for the calculation of p values and for the estimation of the overall rate ratio (11). Stratification was made by a confounder score according to principles outlined by Miettinen (15), along with methods for determining the standardized rate ratios (12) and calculating the confidence interval of the rate ratio and the preventive fraction (14). Differences between smokers and nonsmokers in induction-latency time for developing lung cancer was tested by Student's *t* test.

RESULTS

The study included 29 cases and 174 referents. Twenty-one of the 29 cases were found to have been exposed to underground mining, i.e., 72 % in comparison to 19 out of 174 referents or 11 %. The crude rate ratio was consequently 21.5 for lung cancer among the underground workers in comparison to nonexposed individuals in the parish. There seemed to

Table 2. Exposure to zinc mining among cases of lung cancer and referents taken from the death records in the parish of Hammar, 1956–1976.

Age groups (years)	Nonexposed	Exposed underground
< 50		
Cases	0	1
Referents	6	1
50–59		
Cases	2	6
Referents	10	2
60–69		
Cases	3	7
Referents	27	4
70–79		
Cases	2	6
Referents	38	7
≥ 80		
Cases	1	1
Referents	74	5
Total		
Cases	8	21
Referents	155	19
Crude rate ratio		21.4
Standardized mortality ratio		16.4
Standardized rate ratio (unexposed as the standard)		16.3
Mantel-Haenszel rate ratio, Point estimate		16.6
90 % confidence interval (approx.)		7.8–35.3

be some confounding effect of age, and the standardized mortality ratio (SMR) was determined to be 16.4, as shown in table 2. The overmortality from lung cancer was highly significant, $\chi^2(1) = 37.5$; $p < 0.0001$.

Regarding miners only, table 3 shows the distribution of the subjects in dichotomized smoking categories. Among the referents 19 % were nonsmokers (i.e., never-smokers according to the previously mentioned criteria for classification) versus 47 % among the lung cancer cases. Thus, somewhat surprisingly, the risk of dying from lung cancer primarily seemed to be higher for nonsmokers than for smokers. When the information from tables 2 and 3 is combined, the crude rate ratio for smoking miners versus nonminers (smokers as well as nonsmokers) can be estimated to be 14.9 (and correspondingly one obtains 58.1 for nonsmoking miners), i.e., smoking miners have a much higher risk for developing lung cancer than might be expected from smoking alone (3).

Table 3. Distribution, into smoking categories, of lung cancer cases and referents among miners with known smoking habits.

Age	Exposed underground	
	Smokers	Nonsmokers
≤ 69 years		
Cases	9	3
Referents	6	1
≥ 70 years		
Cases	1	6
Referents	7	2
All ages		
Cases	10	9
Referents	13	3

Table 4. Distribution of lung cancer cases and referents among miners with known smoking habits from the Zinkgruvan mines into smoking categories. Stratification by means of a confounder score with smoking, age and underground work until eight years prior to death as independent variables.^a Two individuals with extreme scores have been excluded.

Confounder score	Underground exposure	
	Smokers	Nonsmokers
> 0.75		
Cases	7	6
Referents	1	1
< 0.75		
Cases	3	2
Referents	11	2
Total		
Cases	10	8
Referents	12	3
Crude rate ratio	0.31	(1.0)
Standardized mortality ratio	0.59	(1.0)
Mantel-Haenszel rate ratio		
Point estimate	0.49	(1.0)
90 % confidence interval (approx.)	0.11–2.2	

^a $YC/R = 2.918 + 0.145 \ln(\text{years underground}) - 0.622 \ln(\text{age}) - 0.292(\text{smoking})$.

Further analysis of the data showed, however, that smokers had a shorter effective exposure time, i.e., 18 years on the average (SD = 12.3) for smokers versus 35 years (SD = 14.2) for nonsmokers, when both cases and referents were included and the time of employment, i.e., exposure time, during the last eight years prior to

death was disregarded as ineffective in cancer induction. This eight-year limit for effective exposure was somewhat arbitrarily chosen but might correspond to about half or less of the induction-latency time observed in studies of occupational cancer. Obviously then, years of employment fulfill the criteria for a confounding factor related to both smoking and outcome. For the handling of both age and effective exposure time, stratification by a multivariate confounder score was undertaken and resulted in table 4, in which two subjects have been excluded due to extreme score values outside the range of good comparability. The stratification was optimized through the maximization of the SMR (when less than unity as here), but it was confined to only two strata due to the scanty data at hand.

This further analysis reduced the difference between smokers and nonsmokers, but still there seemed to be a higher lifetime risk of lung cancer among the non-smoking than the smoking miners. Although the (approximate) 90 % confidence interval reached 2.2, the observation is nevertheless inconsistent with general experience of, say, at least about a fivefold increase in the risk of lung cancer among smokers versus nonsmokers, and the so-called preventive fraction due to smoking can be estimated to be about 28 % (i.e., a relative prevention).

The induction-latency time for lung cancer to develop in these miners appears in table 5, which shows that smokers died from lung cancer approximately 11 years earlier than nonsmokers and that the induction-latency time was correspondingly shorter. However, the induction-latency time might have been somewhat overestimated since some of the miners probably started their career in surface work and the exact point in time when they entered underground work is not known. There is no reason to think, however, that there should be a difference among smokers and nonsmokers in this respect.

In conclusion the study showed a high incidence rate for lung cancer among miners, i.e., about 16 times the normal. Among these miners, nonsmokers seem to be more apt to develop lung cancer than smokers, whereas after induction lung cancer develops more quickly among smokers.

DISCUSSION

The previous study (4, 5) of lung cancer mortality among zinc miners resulted in an estimate of a 13-fold rate for active miners in comparison to the expected rate based on the average Swedish mortality from lung cancer. Since rural areas in Sweden, such as the parish under study,

Table 5. Age at death and latency time for lung cancer in 19 Swedish zinc miners with known smoking habits.

	Nonsmokers (n = 9)	Smokers (n = 10)	Difference between the groups
Age at death (years)			
Mean	70.4	59.3	11.1
Median	73	59	14
Range	59—81 (60—81) ^b	34—77 (53—77) ^b	
Latency time (years) ^a			
Mean	43.4	34	9.4 ^c
Median	49	37	12
Range	6—59 (31—59) ^b	4—52 (32—52) ^b	

^a n = 9 for smokers due to incomplete data for one individual.

^b One individual excluded from the group.

^c p = 0.016 (one-tailed).

have a lower mortality from lung cancer than the average for the country, it is reasonable that a case-referent study, utilizing the local population as the referent, should give a somewhat higher rate ratio than the cohort approach.

The high mortality from lung cancer among nonsmokers was unexpected. Lung cancer in uranium miners has been particularly observed among smokers (2), and the current view is, consequently, that radiation-induced lung cancer tends to affect miners who smoke (16). The question should be considered therefore of whether the information on smoking habits in this study could be incorrect. The difference in induction-latency time for the development of lung cancer among smokers and nonsmokers supports a (reasonably) correct classification as to smoking, however, since a misclassification would tend to eliminate the difference found. Moreover, it seems rather appealing that smokers should have a shorter latency time than nonsmokers, as found before (2).

There are also some other data supporting this study. According to a preliminary study of iron ore miners in northern Sweden (19), there were 26 % of nonsmokers among the lung cancer cases who had died before the age of 65. Between the ages of 65 and 84, 47 % of the lung cancer cases were found to be nonsmokers, i.e., a distribution of lung cancers among smokers and nonsmokers which is similar to the findings in this report. The reason why a similarly high frequency of nonsmokers have not been observed among the lung cancer cases of American uranium miners could be that the elapsed time from the start of large-scale uranium mining is by now not much more than 20–30 years, which might be an insufficient induction-latency time for the development of lung cancer among nonsmokers. Moreover, the alpha-radiation dose rate might be of importance as being higher for the American uranium miners than for their colleagues in Swedish metal and iron ore mines.

With regard to the increased mortality risk from lung cancer among nonsmokers in comparison to smokers, one might also discuss the possibility of an improper reference entity in this study, i.e., there might be fewer nonsmokers among the re-

ferents than is to be expected. However, in an urban/rural sample on a 50/50 % basis and ranging in age from 18 to 69 years, 23.2 % were found to be persons who had never smoked, whereas the corresponding figure was 18.3 % for residents in the three biggest cities (7). This figure is in fairly close agreement with the 18.8 % of nonsmokers obtained for miners in our study. The total death rate ratio between smokers and nonsmokers in the age range 18–69 was 1.3 in the study referred to (7), which means that one should expect only a slight overestimation of the smoking frequency among the referents in the lower age range of this study, because of the tendency for smokers to die earlier than nonsmokers, e.g., from cardiovascular disease. This phenomenon also appears in the data, but it is not strong enough to explain the relatively low lung cancer mortality among smokers. Nor can an explanation be obtained from the assumption of competition between causes of death, since the relative prevention is greater than might result from such a mechanism.

As to a pathogenetic explanation of the findings, one can first consider some calculations of the alpha radiation dose to the tumor-producing cells in the respiratory tract. Altshuler et al. (1) emphasized that the distance from the sensitive epithelial basal cells to the mucus surface is critical because it is approximately of the same magnitude as the tissue ranges of alpha radiation. Thus the alpha particles from the radon daughters, RaA ($^{218}\text{polonium}$) and RaC' ($^{214}\text{polonium}$) is supposed to reach about 47 and 71 microns, respectively, into the tissue. Since the mucus sheath in the critical region of segmental and subsegmental bronchi has been estimated to be even as much as about 20 microns (8) and since the minimal distance from the surface of the mucus layer to the critical region of the basal cells might be at least about 36 microns (1), it is reasonable to believe that effective, tumor-producing alpha radiation would be strongly influenced by an increase in the thickness of the mucus sheath. Since smokers tend to have more productive cough than nonsmokers, it is credible that the mucus sheath covering their bronchial surfaces should be thicker than that of nonsmokers, and the dose therefore cor-

respondingly reduced. It is also of interest in this context that chronic bronchitis has been found to be more prevalent among smoking miners than among nonsmoking colleagues (17). The general underground aerial pollution was assumed to be an etiological factor in combination with smoking. Similar results have been obtained in a Swedish study of workers in a mine where diesel-driven vehicles were used to a considerable extent (10); however, this was not the situation in the mines of our present study.

As summarized by Walsh (20), different evaluations of the alpha-radiation dose to the critical basal cells indicate that an increase of the thickness of the mucus sheath might considerably reduce the effect of RaA and RaC' alpha particles; e.g., increasing the distance to the basal cells, say, from 36 to 46 microns would reduce the dose by about one-half. If a reasonably linear dose-response relationship is assumed, it seems rather credible that dying from lung cancer among nonsmoking miners should exceed that of smoking miners due to the differences in the thickness of the mucus layer and effective radiation dose. The shortening of the induction-latency time in smokers might well be explained by a promoting effect of tobacco smoke after the radiogenic induction of the carcinogenic process, just as suggested before (2).

There are no data available with regard to the exposure levels of these Swedish zinc-lead miners, but based on measurements during the 70s (the mechanical ventilation was even turned off in one of the mines for one month during the vacation period), it seems as if about one working level (see table 1) could be a reasonable estimate. Further studies are obviously desirable, however, to confirm or reject the conclusions set forth on the basis of these rather scanty data and to evaluate more precisely the lung cancer hazard in different mining populations.

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