Lung Cancer in Women and Type of Dwelling in Relation to Radon Exposure

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ABSTRACT

A case-control study based on interviews with 210 incident female lung cancer patients, 209 age-matched population controls, and 191 hospital controls was carried out in Stockholm county, Sweden. Radon measurements made in a sample of 303 dwellings, in which the study subjects had lived, showed that dwellings with ground contact had an average concentration of approximately 160 Bq m\(^{-2}\), twice the average concentration of other dwellings. A cumulated radon exposure index was calculated for each subject based on data from the interviews and the measurements. For the total group of lung cancer a relative risk (RR) adjusted for smoking, age, and degree of urbanization, of 1.8 (95% confidence interval: 1.2–2.9) and 1.7 (0.9–3.3) associated with "intermediate" and "high" exposure to radon was found. There was also a significant trend to a positive dose-response relationship (P<0.03). For small cell cancer the corresponding figures for RRs were 1.9 (0.6–4.5) and 4.7 (1.5–14.2), respectively (P<0.01). There seemed to be a positive interaction between radon exposure and smoking in relation to lung cancer. The findings indicate that domestic radon may be of importance for the induction of lung cancer, particularly for some histological types.

INTRODUCTION

Experimental studies on animals show that alpha radiation from RnDs\(^3\) may induce cancer in the respiratory tract (1, 2), and epidemiological studies among miners indicate that such exposure increases the risk for cancer of the lung and bronchus (3–7). The radon levels in most homes are much lower than in the mines where increased lung cancer risks have been found, but in some dwellings Rn concentrations in the same range can occur (8, 9). There are some epidemiological studies suggesting increased lung cancer risks associated with domestic Rn exposure (10–14). Most of these studies are of limited size, and the exposure estimates are uncertain.

Human cancer risks associated with exposure to low levels of ionizing radiation are generally estimated from risks found at high levels, e.g., among survivors from nuclear bomb explosions, patients who have received therapeutic radiological treatment, and miners exposed to Rn. For Rn, the risk estimates derived from studies on miners may not be directly applicable to the general population. The radiation dose to the respiratory epithelium per unit exposure varies depending on the particle content of the atmosphere as well as on the breathing pattern (15), and interactions with other factors such as smoking may be of importance. It is therefore important to gain empirical knowledge of risks encountered in people primarily exposed to Rn in the home.

To investigate the roles of Rn and some other possible causative or protective factors in lung carcinogenesis, an epidemiological case-control study was performed among women living in Stockholm county, Sweden. This report focuses on risks associated with domestic exposure to Rn.

MATERIALS AND METHODS

The study consists of 210 incident female cases of lung cancer, 209 age-matched population controls, and 191 hospital controls. The aim was to interview all patients with a suspected or confirmed primary pulmonary carcinoma admitted to the three clinical departments of pulmonary medicine and the only clinical department of thoracic surgery in Stockholm county. Those patients, who subsequently were shown not to have lung cancer constituted the hospital control group. The population controls were selected at random from the population register of Stockholm county among women, who were born on the same day as a case.

The interviews of cases and hospital controls were conducted in the hospital wards during September 1983 to December 1985. The population controls were interviewed during a personal visit or on the telephone following identification of each of the cases. A structured questionnaire was used, in which detailed information was requested on smoking habits, exposure to environmental tobacco smoke, and on all dwellings in Sweden where the subject had lived for at least 2 years since birth or arrival to Sweden. A history of occupations and information on consumption of foodstuffs rich in carotenoids, vitamin A, and vitamin C were obtained as well. An extensive description of the study group and exposure data obtained is given elsewhere (16).

Estimation of Cumulated Rn Exposure. The assessment of exposure to Rn was based on data from two sources. Firstly, data on types of dwellings lived in by the study subjects were used as recorded in the questionnaires. Secondly, Rn measurements were made in a sample of dwellings in Stockholm county, where the subjects had lived.

In Sweden the ground is the most important source of Rn, particularly in dwellings with the highest concentrations (17). The greatest variation in Rn concentration could thus be expected to occur among dwellings with ground contact, i.e., one-family houses or apartments on the ground floor in multifamily houses without basement. Based on information provided by the study subjects, the dwellings with ground contact were pinpointed on geological maps, and the ground, on which they were built, was classified into one of three risk categories ("high," "medium," or "low") by the Swedish Geological Company. The aim was to make Rn measurements in all dwellings with ground contact built on ground with high or medium risk of Rn emanation. In addition, a 10% random sample of dwellings with ground contact on low risk ground, and of apartments on the ground floor in multifamily houses with basement were selected for measurements as well as a 2% random sample of apartments above the ground floor.

According to the information obtained during the interviews, the 610 study subjects had lived in a total of 3,518 dwellings during 2 years or more. 384 of these (10.9%) were selected for measurements. The house owners refused measurements for 25 dwellings, and for 17 dwellings we failed to get in contact with the owner. In 39 dwellings measurements were not made for various reasons, e.g., because they were no longer used for residential purposes or because the buildings no longer existed or could not be located. Measurements were thus made in 303 dwellings, or 78.9% of the original sample.

The average Rn gas concentration during a 2-week period was measured with a TLD. The instrument is designed by the National Institute of Radiation Protection in Sweden (18). Dust and RnDs are filtered out, and moisture minimized by diffusion of the air through a silica gel. The relative standard deviation between different TLDs is estimated to be 5–6%. The instruments are calibrated yearly, and the SD of the mean of the calibration constants for different calibration.
periods is of the same order as between different instruments. For the ionization chamber used as primary standard the deviation from the true Rn concentration is in the order of 10% (1 SD).

The measurement program was started in 1985 and concluded in 1987. All measurements were made during the heating season. The TLDs were deployed by personnel from the National Institute for Building Research and the Swedish Geological Company. They were placed in the living room during 1 week and then for another week in a bedroom. The measurement crew recorded information on building materials, type of foundation, and type of ventilation. Measurements of $\gamma$ radiation were also made in order to investigate if aerated concrete based on alum shale had been used as building material. Such concrete has a high exhalation of Rn and was used extensively in Sweden from the 1940s until the mid-1970s. In 1975 approximately 10% of the residential buildings contained various amounts of this material (8).

Based on the information provided by the study subjects, each dwelling was classified as having ground contact or not. Each of the two categories was assigned the arithmetic mean of the Rn concentrations in dwellings measured in the category. A "cumulated exposure" was calculated for each subject for whom we had information on type of dwelling lived in during at least 75% of the lifetime up to 5 years prior to the interview (for population controls 5 years prior to the interview of the corresponding case). Exposure during the last 5 years was not included in the assessment. An occupancy factor of 0.8 was assumed. For subjects, with no information on type of dwelling during some time periods, the average exposure intensity during the years for which there was information, was used for the missing years.

Statistical Methods. Maximum-likelihood estimates of RRs and CIs were computed by multiple logistic regression analysis (19), in which indicator variables represented categories of age, smoking, and Rn exposure as shown in Tables 3 and 4 as well as degree of urbanization (city of Stockholm versus other municipalities in Stockholm county). All $P$ values for trend ($P_{\text{trend}}$) presented, were estimated from the regression models using a scoring of 1, 2, and 3 in the three Rn-exposure categories. Analyses were also performed using the estimated median cumulated Rn exposure in the three categories, but the results were only marginally affected.

The data presented were based on analyses with both control groups pooled and unconditional of the matching performed for the population controls. When the analysis was restricted to the cases and population controls, similar results were obtained with conditional and unconditional logistic regression analysis.

RESULTS

Radon Measurements. The distribution of Rn measurement values was approximately lognormal. In Table 1 the results are tabulated according to different classification criteria based on information recorded by the measurement crew. Dwellings with ground contact had a higher mean Rn concentration than others (163.5 Bqm\(^{-3}\) and 76.2 Bqm\(^{-3}\), respectively). Since inspections and measurements were made in only about 10% of all dwellings, where the subjects had lived, calculations of cumulated exposure were based on classification of types of dwellings as recorded in the questionnaires. This classification gave quite similar results:

$$\bar{x}_{\text{ground contact}} = 160.1 \text{ Bqm}^{-3}; \bar{x}_{\text{non-ground contact}} = 80.0 \text{ Bqm}^{-3}$$

Table 1 shows that dwellings, where aerated concrete based on alum shale was used, had higher Rn concentrations than others. However, this information could not be utilized for assessment of individual exposure experience, since the women themselves generally did not know whether this material had been used in the construction of the dwellings where they had lived.

There were no significant differences in Rn concentrations between dwellings with ground contact on different types of ground. However, only seven dwellings on low risk ground were measured, making the estimate in this category uncertain. Ex-

### Table 1 Results from measurements of $^{222}$Rn-concentration in 303 dwellings in Stockholm county

<table>
<thead>
<tr>
<th>Type of dwelling</th>
<th>Arithmetic mean ($\text{Bqm}^{-3}$)</th>
<th>Geometric mean ($\text{Bqm}^{-3}$)</th>
<th>Range ($\text{Bqm}^{-3}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ground contact</td>
<td>245</td>
<td>163.5</td>
<td>106.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-1350</td>
<td></td>
</tr>
<tr>
<td>One-family houses</td>
<td>239</td>
<td>161.1</td>
<td>105.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-1350</td>
<td></td>
</tr>
<tr>
<td>Ground floor without basement</td>
<td>6</td>
<td>258.3</td>
<td>194.7</td>
</tr>
<tr>
<td>Type of ground</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;High risk&quot;</td>
<td>50</td>
<td>145.6</td>
<td>98.7</td>
</tr>
<tr>
<td>&quot;Medium risk&quot;</td>
<td>188</td>
<td>165.7</td>
<td>107.5</td>
</tr>
<tr>
<td>&quot;Low risk&quot;</td>
<td>7</td>
<td>230.0</td>
<td>153.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>46-722</td>
<td></td>
</tr>
<tr>
<td>Not ground contact</td>
<td>58</td>
<td>76.2</td>
<td>60.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>16-300</td>
<td></td>
</tr>
<tr>
<td>Above ground floor</td>
<td>39</td>
<td>83.4</td>
<td>64.1</td>
</tr>
<tr>
<td>Ground floor with basement</td>
<td>19</td>
<td>61.5</td>
<td>53.9</td>
</tr>
</tbody>
</table>

### Table 2 RR and CI values for different histological types of lung cancer in relation to estimated cumulated $^{222}$Rn-exposure among women in Stockholm

<table>
<thead>
<tr>
<th>Type of Lung Cancer</th>
<th>RR (95% CI) N</th>
<th>RR (95% CI) N</th>
</tr>
</thead>
<tbody>
<tr>
<td>All lung cancer</td>
<td>1.7 (0.9-3.3)</td>
<td>74</td>
</tr>
<tr>
<td>Squamous cell</td>
<td>1.0 (0.5-2.0)</td>
<td>18</td>
</tr>
<tr>
<td>Small cell</td>
<td>0.9 (0.4-2.1)</td>
<td>15</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>0.8 (0.4-1.8)</td>
<td>29</td>
</tr>
<tr>
<td>Other types</td>
<td>1.1 (0.7-1.9)</td>
<td>12</td>
</tr>
</tbody>
</table>

### Table 2. The RRs for the total group of lung cancer were 1.8 (95% CI, 1.2-2.9) and 1.7 (0.9-3.3) in the intermediate and high categories of cumulated Rn exposure. There was also a conclusion of dwellings containing alum shale based concrete did not substantially affect the comparison between the categories (none of the seven dwellings on low risk type of ground contained alum shale).

Risk Estimates. After restricting the analyses to individuals for whom we had information regarding types of dwellings lived in for the required time period, there remained 187 cases (65 adenomatous cell, 48 squamous cell, 41 small cell, 14 undifferentiated, 11 large cell, and eight carcinomas of other histology) and 337 controls (177 population and 160 hospital controls). Complete residential histories were available for 170 subjects. For the remaining 354 study subjects the information in the questionnaire covered an average of 92.9% of the time period of interest.

The RRs for different histological types of lung cancer in relation to estimated cumulated Rn exposure are shown in Table 2. The RRs for the total group of lung cancer were 1.8 (95% CI, 1.2-2.9) and 1.7 (0.9-3.3) in the intermediate and high categories of cumulated Rn exposure. There was also a
statistically significant trend ($P_{\text{trend}} = 0.03$). The association was strongest for small cell carcinoma, which also showed a statistically significant trend ($P_{\text{trend}} = 0.01$). The lowest risks were found for adenocarcinoma. When squamous cell and small cell cancers were grouped together, the RRs were 2.3 (1.2–4.3) and 3.1 (1.3–7.5) in the intermediate and high exposure categories, respectively, and the trend was highly significant ($P_{\text{trend}} = 0.005$).

Table 3 shows the dose-response relationships within different age strata. The highest risks seem to occur in the oldest age stratum with RRs of 8.3 (95% CI, 2.4–28.5) and 5.4 (1.4–21.3) in the intermediate and high exposure categories, respectively, for the total group of lung cancer. The trend was significant as well ($P_{\text{trend}} = 0.03$). The differences in mean age between cases and controls within each age stratum was less than one year (not shown in table).

Table 4 shows the dose-response relationships within smoking strata. The greatest risks are seen for the smokers of up to 10 cig/d with RRs of 2.2 (95% CI, 1.0–4.6) and 3.1 (1.0–9.4) in the intermediate and high exposure categories, respectively, and the trend was significant ($P_{\text{trend}} = 0.03$). Most of the exsmokers (those who had stopped smoking more than 2 years before the interview) belonged to this smoking category, and those in particular showed the greatest risks. No clear increases in risk are seen for never smokers. The estimates are uncertain, however, because of small numbers.

The interaction between smoking and estimated cumulated Rn exposure is elucidated in Table 5. There seems to be a positive interaction between the two exposures. In the highest stratum of radon exposure there were relative risks of 6.5 (1.6–27.1) and 15.9 (4.0–62.9) among smokers of up to 10 cigarettes a day or more, respectively, in relation to nonsmokers in the low radon exposure stratum. As would be expected the trend in lung cancer risk was stronger for smoking than for estimated Rn exposure.

As mentioned previously, all risk analyses presented were made with pooled control groups. Calculations with each control group separately showed similar results, but the risk estimates tended to be higher, when population controls were used. This was accounted for by differences in distribution of age and smoking habits between the control groups. In conjunction with the observed differences in RR in different age and smoking categories, this resulted in different overall risk estimates (compare Tables 3 and 4). In an analysis with hospital controls simulating cases and population controls in the noncase series, the “risk” estimates associated with Rn exposure were 1.3 and 1.0 for the intermediate and high exposure categories, respectively.

**DISCUSSION**

The main finding of this study was the association between lung cancer and estimated cumulated Rn exposure. This association was strongest for small cell carcinoma. In studies on miners elevated risks associated with Rn exposure have consistently been shown for small cell and squamous cell cancers (4–6), and the risk estimates have been highest for small cell carcinoma. A significantly increased risk for radon miners has been noted among U. S. but not among Czechoslovak uranium miners.

Several potential confounding factors need to be considered in the interpretation of the results. Confounding by smoking and age was controlled in the analysis. Residual positive confounding by smoking is unlikely since smoking was negatively correlated to having lived in dwellings with ground contact, a reflection of the fact that smoking is more common in urbanized areas, where one-family houses are rare and most apartments in multifamily houses do not have ground contact. Neither is residual confounding by age a likely explanation to the results. The mean ages for cases and controls differed by less than a year within each age stratum.

Ambient air pollution also seems unlikely as a positive confounder, since dwellings with ground contact are more common outside the urbanized areas. To some extent this should have been controlled in our analysis, which included a correlate of degree of urbanization (living in the city of Stockholm). Whether differences in dietary habits between rural and urbanized populations may influence the risk for lung cancer is not known, but in general rural populations have a lower incidence of cancer than urbanized even after control of smoking habits (20, 21). Furthermore, adjustment for carrot consumption did
not have a noticeable impact on the observed risk associations between living in dwellings with ground contact and lung cancer (16).

An adequate selection of study subjects, i.e., cases and controls, is another prerequisite for obtaining unbiased estimates of the relative risks. There are indications that the cases in our study constituted a biased sample of all cases diagnosed in Stockholm county with regard to age and living in the city of Stockholm (16). A comparison with the regional cancer register showed that the cases included in the study were on an average younger and more often living outside the city of Stockholm than cases not included. Since both age and living in the city of Stockholm are correlates of our measure of cumulated radon exposure, it was necessary to control these two factors in the analysis, particularly in relation to the use of the population controls.

The differences between RRs observed when using population and hospital controls separately, were largely due to differences in distribution over age and smoking strata. Both types of control groups have potential strengths and weaknesses (22). The hospital controls were interviewed under conditions very similar to those of the cases, which intuitively makes it more likely that the quality of the obtained information may be similar to that of the cases. On the other hand, there may be an association, direct or indirect, between the exposure(s) under study and the reason to their hospitalization. In view of the diagnoses of the hospital controls (16), this does not seem to be important taking the group as a whole.

The risk of selection bias among the population controls would be low since the response rate was comparatively high. On the other hand, there may be differences in the quality of information, since the interviews were made under different circumstances than for the cases. However, empirical data indicate that the quality of information obtained from population and hospital controls may be similar (22).

The Rn concentration was monitored with TLDs during a 2-week period only. A previous investigation based on 91 of the 303 dwellings measured in this study showed a high correlation between TLD measurements during 2 weeks and α track detectors deployed for 6 months or 1 year (23), indicating that the TLD measurements can be used for estimation of yearly Rn exposure. The increased average Rn concentration found in dwellings with ground contact confirms earlier data (8).

Although the biologically important radiation dose to the lungs and bronchi is delivered by the RnDs (24), measurements of indoor Rn gas concentration may be better suited for retrospectively estimating radiation exposure than direct measurements of the daughters. The concentration of airborne RnDs increases with increasing aerosol content of the atmosphere (15, 25). It is thereby influenced by lifestyle factors like smoking habits of the dwellers, which may differ markedly between time periods and dwellers.

The exposure classification for Rn in this study was based on information regarding ground contact of the dwellings. No usable data were available on building materials with high exhalation of Rn, although such materials have been widely used in Sweden (8). In order to increase the precision of the exposure estimates, an extended Rn measurement program for the dwellings of the study subjects is currently under way.

Cumulated Rn exposure would be difficult to estimate on the individual level, even if good quality measurements of today's radon concentrations were available for all dwellings of the study subjects. Previous measurements indicate that the mean Rn concentration in Swedish homes has increased over the last decades (17), but there are probably great individual variations. In addition, personal life-style is of importance, e.g., ventilation habits and hours spent in the home.

There were some indications of a positive interaction between smoking and Rn exposure as estimated in our study. A multiplicative interaction between smoking and Rn exposure has been indicated in some studies on miners (26, 27) but not in another (28). It is important to shed further light on the interaction between domestic Rn exposure and smoking, both for the understanding of the mechanisms of cancer induction and as a basis for optimising preventive measures.

Conclusion

An association was observed between lung cancer and years lived in dwellings with ground contact, which were shown to have about twice the Rn concentrations of other dwellings. The association was particularly strong for small cell carcinoma. Exposure to Rn seems to be the most plausible explanation to the findings. More precise exposure data are needed for a detailed quantitative assessment of dose-response relationships.

ACKNOWLEDGMENTS

We want to thank the Swedish Geological Company and the National Institute for Building Research for assistance in the classification of the ground and the measurement program, as well as Gunilla Hedqvist and Eva-Britt Gustafsson for help in the data collection.

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