Residential Radon and Lung Cancer in a High Radon Area of Gansu Province, China

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Although studies of underground miners demonstrate convincingly that exposure to radioactive radon gas and its decay products increases the risk of lung cancer (*1*), direct demonstration of excess risks from residential radon is needed to confirm the risk for residential exposures and to affirm extrapolations from the miner data. To date, some case–control studies of residential radon find no risk with indoor radon exposure, while others are consistent with increasing risk with increasing indoor exposure. Meta-analyses report statistically significant excess risk from radon exposure.

Residential studies are hampered by low radon exposure, resulting in small risks, and uncertainties from imprecise reconstruction of historical exposures due to residential mobility and missing data (*2–5*). To address these limitations, we conducted a case–control study in an area of China where indoor radon concentrations are high and residential mobility is low (*6*).

Materials and Methods

The study was conducted in Pingliang and Qingyang, two rural prefectures in Gansu Province, China, where most residents live or have lived in underground dwellings, and where radon levels are high. Case subjects included all individuals between ages 30 and 75 years who were diagnosed with lung cancer between January 1994 and April 1998 at prefecture and county hospitals, anti-tuberculosis stations, or hospitals in large nearby cities. Based on clinical/radiological symptoms or pathological evidence and a review by an expert panel, we identified a total of 938 cases. Of those, 43 cases were not located, 6 cases were outside the age range and 3 cases moved from the area, leaving 886 cases (656 males, 230 females). Diagnoses of lung cancer were based on clinical/radiological criteria for 533 cases (60%) and pathological evidence for 353 cases (40%). Among the clinical/radiologically identified cases, 414 (78%) died prior to the end of the study period.

We randomly selected 1,968 controls from 1990 census lists and frequency-matched on age in 1995 to cases in 5-year age groups, within categories of sex and prefecture. The number of controls was based on twice the expected number of lung cancers. Among controls, 6 refused to be interviewed, 23 moved from the area, 62 were not located, 73 died before 1994, 4 became cases, and 35 were not interviewed for other reasons. The study enrolled 1,310 male and 455 female controls.

Questionnaires were administered by trained interviewers and included questions on smoking habits, occupational, residential and medical histories, and other factors. Next of kin, usually the spouse, provided information for 481 (54%) cases and 71 (4.0%) controls.

We defined reference age as age at diagnosis for a case and age at interview for a control and designated 5–30 years prior to the reference age as the time-relevant exposure period for lung cancer risk. Interviewers placed two 1-year α-particle track detectors, one in the living area and one in the sleeping area, in the current house and in all former houses within the study area occupied by the subject within the exposure window. For cases and controls, 87.5% and 94.6% had measurements within the exposure window, respectively, based on 1.9 and 1.6 mean eligible residences per subject.

We computed time-weighted average radon concentration within the exposure window in becquerels per cubic meter (Bq/m^3), using years resident as weights. Two control subjects were excluded due to extreme values (1,554 and 1,676 Bq/m^3) that were more than 40% greater than the next largest value. We imputed values for gaps in residential history from missing measurements or less than 2 years occupancy using mean radon for control houses within house type and prefecture (*7*). Alternative approaches, which adjust for imputation variance, were similar due to high coverage of the exposure window.

We computed odds ratios (ORs), adjusted for age, sex, prefecture, tobacco use, and, where appropriate, other factors using unconditional logistic regression (8). We calculated 95% Wald confidence intervals (CI) for category-specific ORs. We also fitted a linear model, $\mathrm{OR}(x) = 1 + \beta x$, where x was mean radon level and β was the excess OR (EOR) per Bq/m^3, and derived likelihood-based CIs for estimates of β.

We initiated a substudy to assess variation in radon within and between rooms, between dwellings, and over time to provide data to adjust for exposure uncertainty. We placed six 1-year α-particle track detectors in each room (two at the front, middle and back) of 55 houses in three consecutive years, starting July 1996. A total of 1,654 detectors were placed in one to five rooms in each house (mean 2.3 rooms/house).

Three important sources of error in radon exposure assessment were (1) measurement error of the detector, (2) use of contemporary measurements to estimate radon throughout the house and in prior years, and (3) missing radon values. Detector error was relatively small and was ignored. Estimation of radon induces classical error, while missing data induced Berkson error. For the error adjustment, we restricted data to subjects with 70% or greater coverage of the exposure window, thus minimizing Berkson error, so that classical error predominated. Based on a multiplicative error structure, we estimated the geometric standard deviation (GSD) for the error as 1.5 and used Monte Carlo methods to adjust the observed exposure–response relationship for this uncertainty.

Results

There were 768 cases (563 males and 205 females) and 1,659 controls (1,232 males and 427 females) with radon measurements and data on the primary adjustment factors. Most men smoked (92.3%), while most women did not (10.4%). Consistent with other studies in China, the OR for ever-smokers compared to never-smokers was low, OR = 1.69 (1.2, 2.4), and was similar for males and females, although it increased to 4.26 (2.4,7.4) for those who smoked 40 years or more or 20 cigarettes per day. Based on preliminary analysis, we adjusted ORs for socioeconomic factors, smoking rate, age, sex and prefecture.

Radon concentrations for the 3,188 measured houses were approximately log-normally distributed, with arithmetic mean (AM) 222.9 Bq/m^3, geometric mean (GM) 176.2 Bq/m^3, and GSD 2.08.

Mean concentrations for cases and controls were 230.4 and 222.2 Bq/m^3, respectively, with 81.6% of cases and 76.3% of controls at or above 150 Bq/m^3. ORs increased significantly with increasing concentration. Relative to $<$100 Bq/m^3, ORs and 95% confidence intervals for categories 100–149, 150–199, 200–249, 250–299 and 300+ Bq/m^3 were 1.00 (0.7,1.5), 1.42 (1.0, 2.0), 1.36 (1.0, 1.9), 1.28 (0.8, 1.9) and 1.58 (1.1, 2.3). The estimated EOR at 100 Bq/m^3 was 0.19 (95% CI: 0.05, 0.47).

Coverage of the exposure window ranged from 8% to 100%, with 76.7% (71.6% for cases and 79.1% for controls) mean coverage. Subjects with 70% or greater coverage (463 cases and 1,143 controls with 98.1% coverage), 90% or greater coverage (398 cases and 1,069 controls with 99.8% coverage), or 100% coverage (366 cases and 1,045 controls) had EORs at 100 Bq/m^3 of 0.22 (95% CI: 0.06, 0.54), 0.26 (95% CI: 0.08, 0.66), and 0.31 (95% CI: 0.10, 0.81), respectively.

Results were similar when data were restricted to histologically confirmed cases or were restricted to subject respondents, as opposed to surrogates. In addition, there was no significant variation in radon effects by age, sex, smoking status, previous diagnosis of pulmonary tubercu-

losis, indoor smokiness, or amount of coal use. There was heterogeneity in the EOR by type of house, with a significant trend in risk for those living in underground dwellings, but no trend for subjects living in standard above-ground dwellings or apartments. However, this heterogeneity disappeared with more detailed adjustment for smoking and with greater coverage of the exposure time window.

For subjects with 70% or greater coverage of the exposure window, the EORs at 100 Bq/m^3 adjusted for error GSDs of 1.25, 1.5 and 1.6 were 0.27 (95% CI: 0.03, 0.69), 0.32 (95% CI: 0.08, 1.37) and 0.59 (95% CI: 0.14, 2.73), respectively, in contrast to the unadjusted estimate 0.22 (95% CI: 0.06, 0.54). EOR estimates, as well as widths of the CIs, increased with the adjustments for exposure error.

Summary

Uncertainty in dosimetry can have an impact on estimates of radon effect. The estimated EOR increased after adjustment for our best estimate of exposure uncertainty by about 50%. This agrees with previous attempts at uncertainty adjustment of the EOR, which also increased estimates about 50–100% (*3, 5, 6*). In addition, three recent studies with enhanced exposure assessments found an increased risk of lung cancer (*2, 9, 10*), suggesting that radon risks may be higher than previously estimated.

In conclusion, radon concentrations in our study were high, exceeding most previous indoor studies, and the population was stable, suggesting improved accuracy in dosimetry. The overall EOR at 100 Bq/m^3 was 0.19 (0.05, 0.47). These results provide evidence that high levels of residential radon increased the risk of lung cancer and support findings from meta-analyses of indoor studies and from miners. In addition, our estimates suggest that the effects of residential radon may equal or exceed miner-based estimates, which are currently used for risk evaluation.

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