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Multifactorial study of the risk of lung cancer among French uranium miners: radon, smoking and silicosis

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Objectives

The aim of this study is to estimate the risk of lung cancer death related to silicosis in uranium miners and assess the impact of taking account of silicotic status on the relation between radon exposure and lung cancer adjusted on smoking

Materials and Methods

Data taken from a recent case-control study nested in the French cohort of uranium miners, which assessed the combined effect of radon exposure and smoking on the risk of death from lung cancer was added to by seeking information relative to silicosis for the individuals studied

o Population:

- The cohort: 5,098 miners employed at least 1 year in the CEA-COGEMA group between 1945-1990 and followed from 1946 to 1994
- 100 cases (miners deceased of lung cancer between 1980-1994 among the cohort) and 500 controls (5 controls randomly matched per case on 5-year birth period and attained age at the time of death of the corresponding case)

o Radon exposure in the mines: cumulated radon exposure expressed in Working Level Months (WLM) reconstructed for each of the 100 cases and 500 controls

o Smoking status: determined from complementary sources: occupational medical files and smoking questionnaire applied through face-to-face or phone interviews or postal mailing

o Silicotic status:

- A blind research on silicosis cases among the individuals included in the case-control study was carried out, without knowing whether the miner was a case or a control
- Main sources of information were: occupational health records, lists of suspected cases of silicosis found in the medical archives, information provided by the regional miners' social security funds, and related causes of death shown on the death certificates of the 100 cases

o Statistical methods:

- Conditional logistic regression based on a linear excess relative risk (ERR) model for radon
- Multiplicative model between radon, smoking and silicosis

$$OR = \exp(\theta x) \cdot (1 + \beta w)$$

where OR is the Odds-Ratio for lung cancer, x is an adjustment variable vector, w is the cumulative radon exposure (continuous) in WLM (with a latent period of five years) and parameter β is an estimate of the ERR per WLM

- To assess the impact of missing data, for each combination of risk factors, analysis was systematically carried out on the individuals with available information for the combination considered and on sample of individuals with complete information for radon, smoking and silicosis (minimum sample)
- To test the role played by each of the risk factors studied on the risk of lung cancer, we compared the adjustment between different nested models using the likelihood ratio test

Results

o Silicotic status was established for 80% of studied miners

o Risk of death from lung cancer relative to cumulative radon exposure, smoking status and/or silicotic status:

Model	Sample size	Risk estimate ^a [95%CI] ^b	Risk estimate ^a [95%CI] obtained from the minimal sample ^c	<i>p</i> ^d
M1: Radon	600	0.011 [0.003-0.025]	0.013 [0.003-0.044]	
M2: Smoking	287	2.80 [1.23-6.34]	4.24 [1.44-12.51]	
M3: Silicosis	393	3.57 [1.42-8.94]	6.68 [1.66-26.92]	
M4: Radon + Smoking				
Radon	287	0.007 [0.001-0.024]	0.011 [0.002-0.039]	Compared with M1: 0.008
Smoking		2.51 [1.10-5.75]	3.74 [1.25-11.19]	Compared with M2: 0.005
M5: Radon + Silicosis				
Radon	393	0.007 [0.001-0.021]	0.012 [0.002-0.040]	Compared with M1: 0.006
Silicosis		2.54 [0.96-6.71]	6.71 [1.62-27.82]	Compared with M3: 0.002
M6: Smoking + Silicosis				
Smoking	209	4.87 [1.56-15.21]	4.87 [1.56-15.21]	Compared with M2: 0.003
Silicosis		8.31 [1.91-36.23]	8.31 [1.91-36.23]	Compared with M3: 0.001
M7: Radon + Smoking + Silicosis				
Radon	209	0.010 [0.001-0.035]	0.010 [0.001-0.035]	Compared with M4: 0.004
Smoking		4.08 [1.33-12.52]	4.08 [1.33-12.52]	Compared with M5: 0.005
Silicosis		8.59 [1.80-40.98]	8.59 [1.80-40.98]	Compared with M6: 0.008

^a Excess of relative risk per Working Level Month for radon and Odds Ratio for silicosis and smoking

^b 95% confidence interval

^c Sample of individuals with complete information for the three factors (radon, smoking, silicosis) and not lost for conditional likelihood regression (209 individuals)

^d *p*-value of a two-sided likelihood ratio test between the current and the cited models

Discussion

o Diagnosing silicosis for the purposes of this study was based on appraisals, cross-referencing different sources of information

o We have shown that each of the three exposure factors systematically improves estimates of the risk of lung cancer

o In our study, it was not possible to test the interactions between radon, smoking and silicotic status due to the limited number of cases and controls

Conclusions and Prospects

o This study has revealed a significant relation between the relative risk of lung cancer and silicosis

o Furthermore, we have shown that the relation between radon and lung cancer persists after adjusting for smoking and silicosis with an ERR that is consistent to ERRs given in the literature

o Our results serve to remind us of the importance of and the complexity involved in assessing occupational risks within the context of multiple forms of exposure