MEDICINA y SEGURIDAD del trabajo

Revisiones

Radon and its effects on the health of uranium mine workers

Radón y sus efectos en la salud en trabajadores de minas de uranio

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Abstract

Introduction: Radon is a gas that can be found underground, particularly in uranium mines, and which has consequences on health, namely lung cancer. It is the second cause of mortality for this disease in the United States. In spite of the strong causal relationship between both elements, there are no specific European regulations concerning miners.

Objectives: To identify the effect of radon and its derivatives on the health of uranium mine workers; to describe the association between exposure to radon and other minerals and health as well as the association between radon and tobacco consumption.

Methods: We perform a bibliographic review of the literature that has been published from 2007 to 2014 in different biomedical databases, using previously established inclusion and exclusion criteria.

Results: 32 articles were reviewed and a significant increase of lung cancer was observed (SMR: 2.03, 95% CI: 1.96-2.10) even for low doses (WLM: 300) as well as other types of cancer (laryngeal, gastric and hepatic cancer and leukemia) and cerebrovascular diseases, after adjusting for other confounding factors (tobacco consumption, silicosis, exposure to quartz and arsenic) in which no significant associations or synergies were found.

Conclusion: There is an association between exposure to radon and lung cancer in uranium mines, with an average latency period of 20 years, determined by the dose of radon and the time of exposure. We did not find risk of developing other types of tumors, and the studies that suggest this hypothesis are inconsistent.

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Keywords: *radon, occupational exposure, uranium mines.*

Resumen

Introducción: El radón es un gas presente en subsuelo, especialmente en minas de uranio, que produce consecuencias sobre la salud, entre las que destaca el cáncer de pulmón. En EEUU es la segunda causa de mortalidad por esta enfermedad. Pese a la fuerte relación causal no existe normativa específica europea de regulación en mineros.

Objetivos: Identificar el efecto del radón y sus derivados sobre la salud de los trabajadores de minas de uranio; describir la asociación entre exposición a radón y a otros minerales sobre la salud y asociación entre radón y consumo de tabaco.

Metodología: Realizamos una revisión bibliográfica de literatura publicada entre 2007 y 2014, en bases de datos biomédicas, utilizando los criterios de inclusión y exclusión previamente establecidos.

Resultados: Se revisan 32 artículos, encontrando un aumento significativo de cáncer pulmonar (SMR-2.03, IC95% 1.96-2.10), incluso a dosis bajas (300-WLM) así como otros cánceres (laringe, gástrico, hepático y leucemia) y enfermedades cerebrovasculares, controlando posibles factores de confusión (tabaco, silicosis, cuarzo y arsénico) no encontrando relación significativa ni sinergias.

Conclusión: Existe asociación entre la exposición al radón y cáncer pulmonar en minas de uranio, con un periodo medio de latencia de 20 años, determinado por la dosis de radón y el tiempo de exposición. No se ha demostrado riesgo de desarrollar otros tipos de tumores, y los estudios que lo sugieren son poco consistentes.

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Palabras clave: *radón, exposición ocupacional, minas de uranio.*

INTRODUCTION

Exposure to radon in uranium mines has been a subject of study due to the effects on health that have been observed in exposed workers. Exposure to this radioactive agent has mainly been linked to a higher incidence of lung cancer.

Radon is a radioactive, colorless, odorless gas, with a half-life of 3.8 days. It belongs to the decay chain of uranium-238, which can be found in the rocks and soil of different environments, such as uranium and coal mines, caves, metro stations and tunnels or underground parking lots, spas and wine cellars of houses. Radon is inert, and all the gas that is inhaled is exhaled afterwards. However, radon-222 decays to form short-lived solid radioisotopes which, when inhaled, enter the airways and act mainly on the lungs. Two of them, polonium-218 and polonium-214, emit alpha radiation, which is associated to a higher risk of lung cancer.

Since 1986, radon has been classified as a carcinogenic agent Group 1 by the World Health Organization (WHO) and, since 1988, by the International Agency for Research on Cancer (IARC). The main source of information on the risks of radon-induced lung cancer comes from the epidemiological studies carried out on underground miners from 1993 on by the International Commission of Radiological Protection (ICRP). More recent studies have provided data on the risks of developing lung cancer even at low levels of exposure[1] and it is estimated that exposure to this radioactive agent in the United States represents the second cause of lung cancer, which is in turn one of the main causes of death in the country.

In 1973, the American National Standards Institute (ANSI) published the first consensus document on radiological protection in uranium mines, which established as one of its main standard measures the periodical measurement of the accumulated concentration of short-lived radon progeny per liter of air, expressed in WL; which is related to the concentration of alpha energy emitted by short-lived radon daughters. A working level month (WLM) is defined as the cumulative exposure from breathing an atmosphere at a concentration of 1 WL for a working month of 170 hours. The exposure can also be quantified in terms of concentration and exposure to the activity of radon gas in becquerels (Bq/m^3 and $Bq{\cdot}h/m^3$, respectively). The dose of radon is expressed in milisieverts (mSv), which represent the radiation absorbed by tissue. In November 2009, the ICRP issued the Statement on Radon[2] and to cohorts of underground miners exposed to relatively low levels of radon. The residential and miner epidemiological studies provide consistent estimates of the risk of lung cancer, with significant associations observed at average annual concentrations of approximately 200 Bq/m^3 and cumulative occupational levels of approximately 50 working level months (WLM, which included the new international recommendations.

With regard to the Spanish norm, protection against exposure to natural radiation is included in the Royal Decree 783/2001 of 6 July which approves the Health Protection Regulations against Ionizing Radiation (RPSRI). The Title VII of the text refers to the exposure of workers to natural sources of radiation, specifically to exposure to radon (radon-222) and its decay products. Afterwards, the Royal Decree 1439/2010 of 5 November added some changes to the previous text and, subsequently, the Royal Decree 1299/2006 marked a milestone when it included the table of occupational diseases and included radon as a carcinogenic agent, classified in Group 1.

The regulations of the RPSRI are complemented with the text of Instruction 33 (IS-33) of 21 December 2011 from the Spanish Nuclear Safety Council on the radiological criteria for protection against exposure to natural radiation. The document states that the threshold level for the protection of workers must be set at an average annual concentration of 600 Bq/m^3 during the working day, and that in case of concentrations above this level, protection measures have to be implemented. If the levels exceed 1000 Bq/m^3, it is considered inadequate to allow any kind of exposure.

Radon is included as a carcinogenic agent Group 1 in the WHO classification and also in the Spanish law; and uranium, as a source of radon emission, represents one of the main energy resources available whose extraction procedures employ a large number of workers who are potentially exposed to this agent and, consequently, to certain risks for their health. For this reason, this study wants to carry out a bibliographic review of the latest literature in search of scientific evidence as described by different authors on the possible effects of radon and its derivatives on the health of uranium mine workers, and also to describe a possible synergy between exposure to radon and to other materials, and to compile the main current measures of radiological protection for the prevention of possible pathologies.

METHODS

We carried out a bibliographic review of scientific literature published from 2007 to 2014 and collected from different biomedical databases, including MEDLINE-PubMed, Cochrane Library, Scopus, OVID, LILACS and IBECS. The results were completed with bibliography from the Scientific Electronic Library Online Repository (SciELO) and other sources.

To obtain the bibliographical references, different search strategies were defined with descriptors for the MeSH and DeCS thesauri, as well as some free terms that led to the search equations that can be seen in Table I.

Table I. Databases and Search equations

Database	Descriptors and Search equation
MEDLINE	«radon/adverse effects» AND «air pollutants, occupational» OR «occupational exposure/adverse effects» AND «uranium mine»
SCIELO	«radon/adverse effects» OR «radon/toxicity» AND «air pollutants, occupational» OR «occupational exposure»
SCOPUS	«radon» AND «occupational exposure» AND «uranium mine«
OVID	«radon« AND «occupational exposure» AND «uranium mine»
IBECS	«radon/adverse effects» OR «radon/toxicity» AND «air pollutants, occupational» OR «occupational exposure»
LILACS	«radon/adverse effects» OR «radon/toxicity» AND «air pollutants, occupational» OR «occupational exposure»
COCHRANE	«radon» AND «occupational exposure»

Inclusion and exclusion criteria were established according to the objectives of the study, and they are described in Tables II and III.

Table II. Inclusion criteria

Variables	Inclusion criteria
Study population	Workers in uranium mines of any kind (underground, surface). Workers who underwent at least one occupational medical checkup. Workers who had been working in a uranium mine for over one month.
Size of the sample	Works with a study population of no less than 150.
Type of design	Observational, analytic and experimental studies and meta-analysis.
Age range	18 to 65 years.
Period of study	2007-2014.
Languages	English, Spanish and Italian.

Table III. Exclusion criteria

Variables	Exclusion criteria
Exclusion criteria	Workers of uranium processing facilities. Workers with prior cancer. Environmental studies. Articles on genetic alterations caused by radon.
Duplicates	In different databases/author.

Once that the series of articles had been selected according to their title and abstract and based on the inclusion and exclusion criteria, a second double-blind analysis was carried out and all controversies were solved through joint review and agreement, in order to identify those works that for some reason may not be considered adequate for their inclusion in the study.

RESULTS

Based on the search strategies described for each database, 376 bibliographical references were recovered, 297 of which were ruled out because they did not fulfil some of the inclusion/exclusion criteria. Out of the remaining 79 references, and after the pertinence study, 47 of them were rejected because they were not considered adequate to the objectives of the study. Finally, 32 articles were selected (1 meta-analysis, 26 cohort/cohorts/nested cohort studies, 3 case-control studies and 2 reports/expert opinions).

Table IV shows the total number of articles recovered in each of the bibliographic databases.

Table IV. Results of the article selection

Database	Results obtained	No. Of articles after duplicate search and inclusion/exclusion criteria application
PUBMED	53	10
SCIELO	0	0
SCOPUS	259	18
OVIDS	23	2
IBECS	9	0
LILACS	31	2
COCHRANE	1	0
ARTICLE TOTAL	376	32

Out of the 43 articles that are part of our review study, 10 of them assess the association between lung cancer and exposure to radon, 11 analyze the association with different extrapulmonary neoplasms, 7 the relation with cardiovascular diseases and 6 its relation with tobacco and exposure to other minerals, such as silica. Some of these studies correlated between themselves.

Relation between exposure to radon and lung cancer

The following studies analyze the incidence and/or mortality of lung cancer in workers of uranium mines exposed to radon and its progeny. The most significant studies were carried out by Walsh L et al [3], Hunter N et al [4], Vacquier B et al [5] and Rachel S et al [6].

Walsh et al [7] carry out one of the most important cohorts studies due to its large population size which includes 59,000 workers in uranium mines from the Wismut company in Germany, who were hired from 1948 to 1989 and monitored in 5-year periods until the present, and which showed a significant increase of lung cancer (SMR: 2.03, 95% CI: 1.96-2.10).

Hunter et al [4] carry out a joint case-control study in 3 European countries (France, Czech Republic and Germany) with 73,969 workers in uranium mines in which they found an observed incidence of ERR/WLM of 0.0174, compared with an expected incidence of ERR/WLM of 0.008 (95% CI: 0.004-0.014). The study also analyzed the risk in populations exposed to low doses (50 WLM and 300 WLM) and it found a significant association at those levels as well.

Rachel et al [6] present a cohort of 55,284 workers of uranium mines in Eldorado, Canada, and they study the mortality in the general and the mining population, with a SMR: 0.97 (95% CI: 0.95-1.00) in the general population for all causes of death; and SMR: 1.31 (95% CI 1.21-1.42) in the mining population for lung cancer as the only cause of death. These same authors found that the incidence of lung cancer in the miners group was 7 times higher than in the general population, with significant confidence intervals (RR: 7.20, 95% CI: 4.84-10.68).

Vacquier et al [5] carried out a study in France in 2007 in which they found SMR: 1.03 (95% CI: 0.98-1.08) for all causes of death, SMR: 1.19 (95% CI: 1.09-1.29) for deaths caused by any kind of cancer and SMR: 1.43 (95% CI: 1.22-1.68) for deaths caused only by lung cancer. All the members of the sample had been exposed to radon and its derivatives.

Other studies analyzed some kind of relation between lung cancer and exposure to radon, and they found similar results. [2,8-12]

Table V. Incidence of lung cancer in cases exposed to radon

Author	Year	Design	Place	Monitoring period	Sample size	Association measure	95% CI
L. Walsh*	2014	COHORT	GERMANY	1946-2008	59,000	ERR/WLM 0.19	0.16-0.22
Tomasek, L.	2012	COHORT	CZECH REP	1948-2010	9,978	ERR/WLM 0.0097	0.0074-0.0127
Rachel S. D.	2010	COHORT	CANADA	1932-1999	17,660	ERR/WLM 0.55	0.37-0.78
Kreuzer, M.	2010	COHORT	GERMANY	1946-2003	58,987	ERR/WLM 0.19	0.17-0.22
B. Vacquier	2007	COHORT	FRANCE	1946-1999	5,086	ERR/WLM 0.71	0.29-1.35

ERR = excess relative risk.

Table VI. Mortality by lung cancer in cases exposed to radon

Author	Year	Design	Place	Monitoring period	Sample size	Association measure	95% CI
L. Walsh*	2014	COHORT	GERMANY	1946-2008	59,000	SMR 2.03	1.96-2.10
Tomasek, L.	2012	COHORT	CZECH REP	1948-2010	9,978	SMR 3.47	
M. Coggiola	2011	COHORT	ITALY	1946-1995	1,795	SMR 106.7	73.4-149.9
Rachel S. D.	2010	COHORT	CANADA	1932-1999	17,660	SMR 1.31	1.21-1.42
Taeger, D	2008	COHORT	GERMANY	1957-1990	8,066	SMR 2.86	2.72-3.01
Boice, Jr	2008	COHORT	NEW MEXICO	1955-2005	5,660	SMR 1.65	1.36-1.97
B. Vacquier	2007	COHORT	FRANCE	1946-1999	5,086	SMR 1.43	1.22-3.09

SMR: standardized mortality ratio.

Relation between radon exposure and extrapulmonary cancer

Kulich et al [13], through the study of a cohort of 22,816 workers of uranium mines, described the appearance of different types of cancer, and they found a general incidence of ERR/WLM: 0.88 (95% CI: 0.73-1.04), with a slight although not significant increase of malignant melanoma ERR/WLM 2.92 (95% CI: 0.91-9.42) and of gall bladder cancer ERR/WLM: 2.39 (95% CI: 0.42-10.58).

Zablotska et al [14] measured the incidence of leukemia, lymphoma and multiple myeloma through a cohort of 16,770 uranium miners in Canada, and they found SMR: 0.69 (95% CI: 0.48-0.97) for leukemia, which was significantly higher than the rest. However, multiple myeloma showed a higher incidence (SIR: 0.85, 95% CI: 0.40-1.01). This study showed an incidence of hematological cancer which was lower than in the general population.

Kreuzer et al [15], in a cohort based on the Wismut study, who were monitored from 1960 to 2003, found 24 different types of non-pulmonary cancers (RR: 1.02, 95% CI: 0.98-1.05); and they highlight a statistically significant increased incidence of digestive (RR: 1.15, 95% CI: 1.06-1.25) and hepatic neoplasms (RR: 1.26, 95% CI: 1.07-1.48). The global incidence of neoplasms was significantly higher when compared with the general population (RR: 1.03, 95% CI: 1.02-1.05).

These were the studies with the most significant results and the highest evidence levels, although other studies who added different data to this review were also assessed. [15-17]

Table VII. Association between radon and extrapulmonary cancer

Author	Year	Design	Place	Monitoring period	Sample size	Type of cancer	Association measure	95% CI
Zablotska	2014	COHORT	CANADA	1969-1999	16,770	LEUKEMIA HODGKIN LYMPHOMA NHL MULTIPLE MYELOMA	SIR 0.79 SIR 0.93 SIR 0.89 SIR 0.65	(0.59-1.03) (0.51-1.57) (0.70-1.11) (0.40-1.01)
Kulich M	2011	NESTED COHORT	CZECH REP	1977-1996	22,816	EXTRAPULMONARY GASTRIC GALL BLADDER LARYNX MELANOMA	RR 0.88 RR 0.87 RR 2.39 RR 0.79 RR 2.92	(0.73-1.04) (0.69-1.09) (0.52-10.98) (0.38-1.64) (0.91-9.42)
Matthias Möhner	2010	CASE-CONTROL	GERMANY	1950-1989	1,357	LEUKEMIA	OR1.78	(1.09-2.91) 90%
Möhner, M.	2008	CASE-CONTROL	GERMANY		1,483	LARYNX	OR1.13	(0.75-1.70)
Kreuzer M.	2008	COHORT	GERMANY	1960-2003	57,199	EXTRAPULMONARY GASTRIC HEPATIC	RR 1.02 RR 1.15 RR 1.26	(0.98-1.05) (1.06-1.25) (1.07-1.48)
Boice, Jr	2008	COHORT	NEW MEXICO	1955-2001	5,660	GASTRIC RENAL LIVER NHL LEUKEMIA, CLL	SMR 0.99 SMR 1.11 SMR 1.7 SMR 0.75 SMR 1.36	(0.32-2.30) (0.41-2.42) (0.78-3.23) (0.28-1.64) (0.59-2.68)
B. Vacquier	2007	COHORT	FRANCE	1946-1999	5,086	GASTRIC LEUKEMIA LARYNX RENAL	SMR 1.16 SMR 1.20 SMR 1.24 SMR 1.09	0.76-170 0.67-1.98 0.83-1.78 0.98-1.22

Table VIII. Incidence between radon and extrapulmonary cancer

Author	Year	Design	Place	Monitoring period	Sample size	Type of cancer	Association measure Err/wlm	95% CI
L. Walsh*	2014	COHORT	GERMANY	1946-2008	59,000	EXTRAPULMONARY	0.014	(0.006-0.023)
						GASTRIC	0,022	(0,001-0,042)
						HEPATIC	0,04	(0.008-0.095)
						LEUKEMIA	0,005	(0.034-0.045)
Rachel S. D.	2010	COHORT	CANADA	1932-1999	17,660	GASTRIC	0.04	p 0.16
						LEUKEMIA	0.02	p 0.81
						OTHER CANCERS	0.06	p 0.51
Kreuzer, M.	2011	COHORT	GERMANY	1946-2003	58,987	EXTRAPULMONARY	0.014	0.006-0.023
						TRACHEA	0.062	0.002-0.121
						STOMACH	0.02	0.01-0.04
						LIVER	0.043	0.007-0.094
Kreuzer, M.	2008	COHORT	GERMANY	1946-2003	58,987	EXTRAPULMONARY	0.014	(0.006-0.023)

Relation between exposure to radon and cardiovascular diseases

Nusinovici et al [18] found, in a cohort in France with 5,086 miners and an average monitoring period of 30 years, 1,411 deaths, 319 of which were due to cardiovascular causes (SMR: 0.93, 95% CI: 0.83-1.04) and an incidence RR: 0.92 (95% CI: 0.72-1.19), with a higher tendency for cerebrovascular diseases (SMR: 1.00, 95% CI: 0.79-1.24; RR: 1.39, 95% CI: 0.81-2.38; and ERR/WLM: 0.49, 95% CI: 0.07-1.23).

Kreuzer et al [15] used the Wismut study with the same data set to identify the association with cardiovascular diseases, and out of 13,254 deaths they observed that 5,141 were caused by heart diseases and 1,742 by cerebrovascular diseases, with ERR/WLM: 0.0003% and ERR/WLM=0.0001%, respectively. Other studies showed similar results. [3,5,6,10,12]

Table IX. Association between radon and cardiovascular disease

Author	Year	Design	Place	Monitoring period	Sample size	Type of cardiovascular disease	Association measure Err/wlm	95% CI
L. Walsh*	2014	COHORT	GERMANY	1946-2008	59,000	CORONARY	0.0003	
						CARDIOVASCULAR	0.001	
M. Coggiola	2011	COHORT	ITALY	1946-1995	1,795	CARDIOVASCULAR	SMR: 91.8	78.8 -106.4
Kreuzer M.	2010	COHORT	GERMANY	1946-2003	58,987	CARDIOVASCULAR	0.001%	P'0.05
						CORONARY	0.0003%	P'0.05
						CEREBROVASCULAR	0.001%	P'0.05
						AMI	0.008%	P 0.114
Nusinovici S	2010	COHORT	FRANCE	1946-1999	5,086	CARDIOVASCULAR	0.102%	P 0.18
						AMI	0.013%	P'0.5
						CEREBROVASCULAR	0.49%	P 0.02
Rachel S. D.	2010	COHORT	CANADA	1932-1999	17,660	AMI	-0.01	p 0.18
						CEREBROVASCULAR	-0.04	p 0.012
						OTHER CARDIOVASCULAR	-0.02	p 0.49
Boice, Jr	2008	COHORT	NEW MEXICO	1955-2005	5,660	CARDIOVASCULAR	SMR 0.93	0.81-1.93
						CEREBROVASCULAR	SMR 0.95	0.64-1.36
BVacquier	2007	COHORT	FRANCE	1946-1999	5,086	CARDIOVASCULAR	1.05	P 0.15

Lung cancer and exposure to radon, associated to tobacco, arsenic, quartz and silica

Taeger et al [19] analyze exposure to silica, quartz and arsenic as confounding factors, and they found SMR: 2.86 (95% CI 2.72-3.01) with confounding factors, SMR: 2.37 (95% CI 2.17-2.59) in silicotic cases associated to confounding factors and SMR: 3.17 (95% CI: 2.99-3.37) in non-silicotic cases without these factors.

Schnelzer et al [20] used a nested case-control study and showed that the mortality risk for lung cancer increases in parallel with exposure to radon in smoking and non-smoking workers (ERR/WLM: 0.23, 95% CI: 0.11-0.46; and ERR/WLM: 0.25, 95% CI: 0.13-0.46, respectively).

Leuraud et al [21], in a case-control study carried out in France, found that after controlling exposure to tobacco consumption, mortality for lung cancer was the same in smoking and non-smoking cases (RR: 3.32, 95% CI: 1,32-8.35 vs. RR 3.04, 95% CI: 1.20-7.70).

Amabile et al [22] carried out a multifactorial analysis in France which revealed a significant association between the relative risk for lung cancer and silicosis (OR: 3.6, 95% CI: 1.4-8.9). However, the relation between radon and lung cancer remains present after adjusting for tobacco consumption and silicotic state (ERR/WLM: 1.0%, 95% CI: 0.1-3.5%).

These tables summarize the results obtained: studies that analyze the association between radon and lung cancer (Table V and VI), studies that analyze the relation between radon and extrapulmonary cancer (Table VII and VIII), studies on the scientific evidence of cardiovascular risk associated to exposure to radon (Table IX) and studies that analyze confounding factors [1,23] (Table X).

Table X. Association between radon and possible confounding factors

Author	Year	Design	Place	Monitoring period	Sample size	Confounding factor type	Association measure	95% CI
Tomasek, L.	2013	NESTED COHORT	CZECH REP	1946-2010	11,842	NON SMOKER SMOKER RADON WITHOUT TOBACCO MEASUREMENT	ERR/WLM: 0.049 ERR/WLM: 0.010 ERR/WLM: 0.013	0.010-0.179 0.006-0.017 0.007-0.019
Tomasek, L.	2011	NESTED COHORT	CZECH REP		2,782	NON SMOKER EX - SMOKER SMOKER RADON WITHOUT TOBACCO MEASUREMENT	ERR/WLM: 0.044 ERR/WLM: 0.01114; ERR/WLM.: 0.015	0.015-0.240 0.004-0.045 0.006-0.022
Schnelzer, M.	2010	NESTED COHORT	GERMANY	1946-1989	59,000	RADON RADON + TOBACCO	ERR/WLM: 0.25 ERR/WLM: 0.23	(0.13-0.46) (0.11-0.46)
Taeger, D.	2008	COHORT	GERMANY	1957-1990	8,066	ARSENIC QUARTZ RADON	AVERAGE (SD) 100.09 AVERAGE (SD): 16.95 AVERAGE (SD) 756.57	
Leuraud, K.	2007	NESTED COHORT	FRANCE	1946-1994	5,098	RADON RADON + TOBACCO	ERR/WLM 0.98 ERR/WLM 0.85	(0.18-3.08) (0.18-2.79)
Amabile, J. C.	2007	CASE-CONTROL	FRANCE	1946-1999	5,098	RADON TOBACCO SILICOSIS RADON + SILICOSIS SILICOSIS+TOBACCO RADON+SILICOSIS+ TOBACCO	OR 0.011 OR 2.8 OR 3.57 OR 2.54 OR 8.31` OR 8.59	0.003-0.025 1.23-6.34 1.42-8.94 1.10-5.75 0.96-6.71 1.91-36.23 1.8-40.98

DISCUSSION AND CONCLUSIONS

Several studies, such as those by Walsh et al [3], Kreuzer et al [8], Hunter et al [4], Tomasek et al [1], Vacquier et al [5], among other authors [2,6,7,9-12,24] and to cohorts of underground miners exposed to relatively low levels of radon. The residential and miner epidemiological studies provide consistent estimates of the risk of lung cancer, with significant associations observed at average annual concentrations of approximately 200 Bq/m³ and cumulative occupational levels of approximately 50 working level months (WLM in different countries such as the United States, Canada, France and Italy, have found a statistically significant increased association between exposure to radon and lung cancer. In underground sites, exposure to radon entails a high risk for health, and particularly with regard to this kind of tumor, especially when there are high concentrations of radon inside the mine, an extended time of exposure and when the exposure has been recent. The studies by Hunter et al [4] seem to prove that restricting the time of exposure to less than 300 WLM reduces the risk, and this finding matches those by other authors [6,8]. It has been proven that ERR/WLM is higher in workers who have been exposed recently, 5-24 years ago, than in those who were exposed more than 25 years ago. In this last case, the risk of lung cancer is reduced by up to 47%, although this difference is not associated with age at first exposure or average time of occupational exposure. [1,10]

Although most authors found a statistically significant association between exposure to radon and the appearance of lung cancer, such a relation could not be found for other types of neoplasms (Darby et al 1995; NRC, 1999; UNSCEAR, 2009). Some studies have suggested some type of relation, but failed to show any consistent pattern that could be reproduced. Recent studies in the Czech Republic revealed an association with the incidence of chronic lymphocytic leukemia (CLL) (Rericha et al, 2006), but this finding was not confirmed by other studies on the same population (Tomasek and Malátova, 2006), or in Germany, by Möhner et al [16]. Other studies suggest a higher presence of larynx cancer, although this relation has not been confirmed (Möhner et al [17]), or an increase of other tumors, such as non-Hodgkin lymphoma (NHL), multiple myeloma, and kidney, liver and stomach cancer (Vacquier et al [5]; Kreuzer et al [15]; Schubauer-Berigan et al [11]), but they were not confirmed by subsequent studies either.

With regard to leukemia-associated mortality, Kreuzer [15] and Walsh [3] did not find an increased risk in relation to radon exposure from the calculation of SMR and ERR. Möhner et al [16] expanded the study with exposure to ionizing radiations derived from the medical-occupational monitoring and the organ dose in the bone marrow, with statistically significant results only in the highest dose category for CLL and non-CLL (OR: 1.75, 95% CI: 1.09-2.91, assuming a latency of 15 years and OR: 2.62, 90% CI 1.6-4.35 for a latency of 20 years). This analysis suggests that an accumulated exposure throughout the years contributes to the risk of leukemia. Also, the results showed that the latency for leukemia associated to exposure to ionizing exposure may be longer than what was assumed until now.

On the other hand, a study on a Canadian cohort [6] described that the incidence of CLL showed a positive association, with ERR/Sv: 7.28, in contrast to the incidence of non-CLL, which revealed a negative estimation. Nevertheless, none of these observations was statistically significant. This last study was expanded in 2014 and it observed that workers showed lower mortality rates and incidence of hematological cancer after adjusting odds ratios for age and calendar year than the male Canadian population, a healthy worker effect. However, with regard to radiation, there were some suggestions, although statistically insignificant, of an increased risk of CLL, as well as higher incidence and mortality rates of HL and NHL with an increased radiation dose. [14]

With regard to the mortality risk for prostate cancer in connection with underground work, Gishilck had noticed that underground mining could act as a protective factor against this kind of cancer, but none of the studies managed to find a higher risk for the disease associated to exposure. [25] This point was further explored with an analysis of monitoring data since 1970, with 263 deaths caused by prostate cancer related to the number of days of underground work.[20] A linear model adjusted for years of work, intense physical activity and number of days of underground work reveals a statistically significant elevated ERR compared with the basal linear model (p: 0.039) and for the days of underground work (p: 0.0096), with a small protective effect of -5.59 (95% CI: -9.81 to -1.396 (x10^{-5})). However, additional calculations revealed that the results for prostate cancer might have been biased because of the selection effect or the healthy worker survivor effect.[3]

Another important association was established with larynx cancer, and it was reviewed by Vacquier[5], who observed a SMR of 1.26, similar to the results shown by Möhner[17], and established a strong association between short-term exposure to radon and larynx cancer.

Kreuzer[15] found a statistically significant relation between exposure to accumulated radon and extra-thoracic cancer of the airways and the trachea. It is not clear whether this relation is causal or not, because the analysis showed a linear growth when the exposure increased until 1,000 WLM and the levels decreased in the highest exposure levels. There are several explanations for this reduction, such as the healthy worker survivor effect, forcing variables that had not been considered or confounding factors such as alcohol consumption. Kreuzer[8] obtained some results on the relation of radon with larynx cancer and neoplasms of the oral cavity, which were higher-risk locations. In the first works on this subject, carried out by Darby on 11 studies on grouped miners, no relation was found between larynx cancer and exposure to an accumulative dose of radon, which matches the findings by Vacquier in the French cohort.[5] Even though Kulich[13] found a larger number of cases, the study was made on a small sample without control group, and no epidemiological monitoring was implemented.

With regard to renal cancer, Vacquier[5] observed a high amount of deaths due to this pathology which had not appeared in the previous analysis. Possible confounding factors were taken into account, as well as the period of previous occupations. In spite of this fact, no association was found between accumulated exposure to radon and this kind of cancer.

Different authors[3,10,13,14,16,20,26] have studied a potential association between exposure to radon in miners and different malignant extrapulmonary tumors. With regard to tumor pathologies, no author managed to find a significant relation.

With regard to the potential association between exposure to radon and cardiovascular pathologies, the study by Vacquier[5] is the only one that suggests an association between mortality due to cerebrovascular diseases and accumulative exposure to radon. This is the first studied cohort of uranium miners in which such an association has been observed. An important advantage of this cohort is the quality of the assessment of exposure to radon, because the intense physical activity that the work entails has been considered as a modifying factor.

Similarly, potential confounding factors such as tobacco consumption or joint exposure to radon and silica, quartz, arsenic and other types of dust were taken into account. Some studies[1,4] reveal that the risk for lung cancer is higher in non-smokers than in smokers, although without statistical significance. This would mean that the different morphology and lung capacity of non-smokers, which is larger than that of smokers, would lead to higher amounts of radon derivatives in this location, and subsequently a higher risk of cancer; in contrast with several studies[3,20,21,24] which reveal that tobacco does not act as a confounding factor.

Amabile et al[22] proved that the relation between lung cancer and exposure to radon is the same after adjusting for tobacco consumption and silicotic state (ERR/WLM: 1.0, 95% CI: 0.1-3.5%). In contrast, other authors[5,11] did find a significant association between radon and silicosis. However, we must take into account the fact that between 1956 and 1982, it was environmental measurements that were taken into account, and that only from 1983 an individual dosimeter was used, which might alter the final results.

Finally, new results are expected with regard to other diseases related to radon exposure as the monitoring provides more accurate results to estimate the risk of pulmonary cancer according to the exposure levels and the calculation of the organ dose, based on what was established in the European research project. It is expected that these results will be useful in future considerations on radiological protection and occupational safety.

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