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Indoor radon exposure and COPD in never smokers: a case–control study in a radon-prone area in Spain

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Abstract

Background Previous studies have linked radon exposure with mortality in patients with chronic obstructive pulmonary disease (COPD), but there is little data assessing the role of indoor radon exposure with the risk of COPD or its severity in never smokers. Objective: To explore whether indoor radon exposure is associated with the risk or severity of COPD in never smokers.

Methods Multicentric, hospital-based, case–control study, located in Northwest Spain. The study included 300 never-smokers with COPD (cases) and 462 never smoking controls. COPD cases and their severity were included following Global Initiative for Obstructive Lung Disease 2019 (GOLD) criteria for COPD diagnosis. Radon concentrations were measured in each participant's home using long-term (at least 3 months) alpha-track devices. Results were analyzed for cases and controls, and also for different lengths of residence in the last dwelling employing logistic regression. For cases, hospital admissions in the last 3 years due to COPD exacerbations and COPD severity were related to radon concentrations.

Results (1) Indoor radon exposure was similar in cases and controls, but radon exposure showed a statistically significant association with COPD when length of residence in the same dwelling was > 40 years. There was an odds ratio (OR) of 2.79 (1.06–7.40) for those with highest (> 300 Bq/m³) vs. lowest radon exposure (< 100 Bq/m³); (2) in cases, the severity of airflow obstruction increased with higher indoor radon exposure, and the proportion of COPD cases with radon exposure above 300 Bq/m³ was higher in GOLD 4 (50%) vs. GOLD 1 (9%).

Conclusions Although indoor radon exposure was not higher in cases compared to controls, the association increased for those with higher exposures who lived for longer periods in the same dwelling, reaching statistical significance when length of residence was higher than 40 years. In COPD cases, higher radon exposure was associated with more severe airflow limitation.

Keywords Chronic obstructive pulmonary disease, Indoor radon, Observational study, Never smokers, GOLD

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Introduction

Chronic obstructive pulmonary disease (COPD) is a major public health problem because of its high prevalence, its association with multimorbidity and its personal, familiar and social costs [1]. Tobacco smoking is the main environmental risk factor for COPD, but 30% of COPD patients worldwide have never smoked [2], indicating that other causes of COPD must be considered [3]. The International Agency for Research on Cancer recognized in 1988 that radon gas was a lung carcinogen [4]. Although the precise molecular mechanism underlying this association is not entirely known, there is a well-described exposure–response association for the induction of lung cancer by radon [5, 6]. Whether exposure to radon increases the risk and/or severity of COPD is controversial [7]. On the one hand, the Cancer Prevention Study showed a significant association between indoor radon exposure and COPD mortality [8]. However, more recent studies using individual radon measurements did not confirm this association, but their results might have been confounded by tobacco smoking [9]. Studies performed in miners occupationally exposed to radon did not observe a consistent association with mortality from respiratory diseases (other than lung cancer) and results were very heterogeneous between the different cohorts. The prevalence of smoking in those miners was very high, highlighting the need for studies in never smokers [10]. To date, no study has explored the relationship between indoor radon exposure and COPD occurrence and severity in never smokers. Radon exposure might be related to COPD incidence or prevalence. Previous studies have observed that some areas with high radon exposure seem to have higher COPD prevalence, though this is based on an ecological approach [11]. Nevertheless, to analyze if radon exposure is associated with COPD risk, we should analyze incident cases instead of prevalent cases. To date, there is only one case–control study on radon and COPD with individual radon measurements which included mainly prevalent cases [9] with no clear association observed.

Here, we investigated whether residential radon exposure in never smokers: (1) is related with COPD risk, (2) is associated with the severity of airflow obstruction and, (3) is associated with COPD exacerbations (ECOPD) and hospitalizations.

Methods

Study design and ethics

This multicentric, hospital-based, case–control study recruited participants between September 2020 and December 2023. The study was carried out in Northwestern Spain (Galicia), a well-recognized radon-prone area,

where half of the population lives in detached houses on the countryside [9]. Seven public hospitals located in Galicia (University Clinical Hospital of Santiago, Alvaro Cunqueiro Hospital, University Hospital Lucus Augusti, University Clinical Hospital of Ferrol, University Clinical Hospital of A Coruña and University Clinical Hospital of Ourense) and Asturias (Central University Hospital of Asturias) participated in the study. The study protocol was approved by the Ethics Committee of Santiago de Compostela-Lugo (ID 2019/521).

Study population: inclusion and exclusion criteria

All cases and controls were never smokers, defined as not having smoked more than 100 cigarettes during their lifetime or having smoked less than 1 cigarette per day (cig/day) for 6 months [12]. Only participants older than 35 years were recruited. To be included as a case, COPD patients had to fulfill the following characteristics simultaneously, according to GOLD 2019 (Global Initiative for Obstructive Lung Disease) guidelines: (1) Presence of airflow obstruction after bronchodilatation ($FEV_1/FVC < 0.7$), (2) Previous exposure to other recognized risk factors for COPD as per GOLD guidelines [1], including environmental tobacco smoke exposure, occupational exposure, biomass exposure and/or low birth weight/prematurity, and, (3) COPD symptomatology. Of note, GOLD criteria have changed, and new criteria have been proposed in 2025 [13]. Previous exposure, by definition, has to be at a different time than assessment of COPD symptoms and airflow obstruction during a clinic visit. All COPD cases were recruited at COPD specific clinics following a specific check before inclusion to confirm the presence of these characteristics. Participants already diagnosed with asthma were allowed to take part in the study. Fifty percent of included cases had a duration of COPD of 4 years or less. We admitted the inclusion of prevalent cases to enlarge our sample size provided that these cases continued living in the same home from at least 5 years before the diagnosis until the moment of the radon measurement. Controls were never smokers without known respiratory diseases/symptoms, attending the hospital for minor non-respiratory reasons (e.g., minor ambulatory surgery) who volunteered to participate in the study after being informed and made aware of its goals and design. Controls were recruited following a frequency-based matching on sex regarding cases to preserve comparability among these two groups. Controls were recruited by trained nursing staff at participating hospitals from non-respiratory clinics and from general population because of the difficulty of localizing never smokers, particularly among men. Informed consent forms were signed by all study participants, cases and controls.

Study variables

Clinical variables were recorded by trained personnel (pneumologists or nursing staff) using standardized questionnaires previously used in other investigations related to radon and lung cancer or COPD in smokers [5, 9]. These included demographics, educational level [classified as (1) having primary studies or less, (2) secondary studies or (3) university studies], lifestyle characteristics, exposure to environmental tobacco smoke, occupational history, previous respiratory diseases, birth weight/prematurity, and exposure to indoor biomass combustion. In COPD cases (not in controls), lung function was assessed by spirometry, before and after bronchodilation, following international recommendations [14]. Reference values used were those of the Global Lung Function Initiative (GLI) [15]. The severity of airflow obstruction was established following GOLD recommendations (GOLD grades: 1 or mild: $FEV_1 \geq 80\%$; 2 or moderate: $50\% \leq FEV_1 < 80\%$ predicted; 3 or severe: $30\% \leq FEV_1 < 50\%$ predicted and; 4 or very severe: $FEV_1 < 30\%$ predicted) [1].

Indoor radon exposure measurement

An alpha track radon detector (Radosys Inc, Hungary) was given to all participants (cases and controls), who were asked to place it in their bedroom for at least 3 months. Participants were instructed on the correct placement of the device, which was later checked by telephone, and provided with recommendations to follow if a radon concentration was higher than 300 Bq/m^3 . Radon measurements took place as cases and controls were being recruited. Since cases and controls were recruited simultaneously, no seasonal adjustment was performed given the season of the year where measurements took place was the same. The detectors were read and evaluated after they were received at the Galician Radon Laboratory (www.radon.gal). The laboratory, which is certified since 2019 by the Spanish National Accreditation Agency (ENAC), guarantees that radon measurements are of the highest quality regarding accuracy and reproducibility.

Statistical analysis

Distribution of categorical variables were presented using percentages and continuous variables using the median and interquartile range. To explore the relationship of indoor radon exposure with case/control status, we used logistic regression analysis with residential radon exposure as the main independent variable (stratified in 4 categories using the lowest exposure as the reference category: $< 100 \text{ Bq/m}^3$, $100\text{--}199 \text{ Bq/m}^3$, $200\text{--}299 \text{ Bq/m}^3$ and $\geq 300 \text{ Bq/m}^3$) and the case/control status as the dependent variable. All regression analyses were adjusted

for age (continuous), sex, educational level, and environmental tobacco smoke exposure (defined by having cohabited with a current smoker in the last 20 years) as a common set of adjustment variables. To explore the potential influence of length of residence in the same home on the risk of COPD (as a proxy for different lengths of radon exposure), three different logistic regression analyses were performed that included participants who resided in the same home for > 20 , > 30 or > 40 years, respectively. The results of the logistic regression analysis were expressed as an Odds Ratio (OR) and a 95% confidence interval (95% CI).

Exclusively for cases, to explore the relationship between indoor radon exposure and the severity of airflow obstruction or previous hospitalizations because of exacerbations of COPD (ECOPD), radon exposure was compared with the GOLD grade of airflow obstruction (1 to 4) and frequency of previous ECOPD in the last 3 years requiring hospitalization (0, 1 or 2 or more hospital admissions), based on the median values. For both comparisons we used the median test (two-tailed) [16]. The significance level for statistical tests was $\alpha = 0.05$, thus a $p < 0.05$ was considered to indicate a statistically significant result. All analyses were performed using SPSS v29.

Results

Clinical characteristics of the study population

The study included 300 never smoking COPD cases and 462 never smoking controls (Table 1). There were more females among both cases and controls. The median age of cases was 9 years higher than that of controls. The level of education was lower in cases than in controls. The proportion of cases and controls exposed to environmental tobacco smoke at home was similar. Among cases, airflow obstruction ranged from moderate to severe (median post bronchodilator FEV_1 value 63% reference (pct25-75: 50–77% reference)). Accordingly, most cases had GOLD 1 or 2 grades (Table 1). A 50.1% of COPD cases were diagnosed 4 years or earlier before inclusion. Regarding potential risk factors for COPD among participants, 3.9% of cases were born prematurely, 42.5% had asthma previously diagnosed, 11.6% had previously diagnosed tuberculosis, 25.4% had previously pneumonia, 15.1% had occupational exposures and 34.6% had been exposed to biomass smoke at home (of note, some cases may have more than 1 risk factor). Most cases (74%) did not require any hospitalization due to ECOPD in the prior 3 years.

Indoor radon exposure and COPD risk in never smokers

A total of 280 cases and 428 controls had indoor residential radon measurement and were therefore included in analyses involving radon exposure. The return rate of

Table 1 Characteristics of the study population

	Cases, n (%), unless otherwise specified 300	Controls, n (%), unless otherwise specified 462
Demographics		
Sex		
Women	186 (62.0)	301 (65.2)
Men	114 (38.0)	161 (34.8)
Age, years (median and pct 25–75)	74 (65–80)	65 (57–73)
Education achieved		
No primary studies completed	30 (10.0)	12 (2.6)
Primary studies	132 (44.0)	179 (38.7)
Secondary studies	35 (11.7)	120 (25.6)
Bachelor or higher studies	19 (6.3)	144 (31.2)
Missing data	84 (28.0)	7 (1.5)
Environmental tobacco smoke exposure at home*		
No	198 (66.0)	317 (68.6)
Yes	99 (33.0)	145 (31.4)
Missing data	3 (1.0)	–
COPD characteristics		
FEV ₁ post bd (% reference), median and pct 25–75	63 (50–77)	
FVC post bd (% reference), median and pct 25–75	86 (70–99)	
FEV ₁ /FVC post bd (%), median and pct 25–75	59.1 (51.0–64.5)	
GOLD grades of airflow obstruction		
1	63 (25)	
2	146 (57)	
3	44 (17)	
4	4 (2)	
Years since COPD diagnosis, median and pct 25–75	4.1 (1.2–8.7)	
COPD patients diagnosed up to 4 years before inclusion	134 (50.1)	
Exposures reported as possible causes of COPD **		
Premature birth	11 (3.9)	
Asthma	116 (42.5)	
Tuberculosis	34 (11.6)	
Pneumonia	75 (25.4)	
Occupational exposure	45 (15.1)	
Biomass exposure at home	104 (34.6)	
Hospital admissions because of exacerbation of COPD in the last 3 years		
0	212 (74)	
1	47 (16)	
> 1	29 (10)	
Indoor radon exposure	n = 280	n = 428
Radon concentration, median and pct 25–75 (Bq/m ³)	118 (65–207)	120 (67–224)
Number and percentage above 300 Bq/m ³	36 (12.5)	72 (16.6)
Years living in the same dwelling, median and pct 25–75	37 (18–50)	26 (15–40)

Pct percentile

* Measured as living with a smoker for more than 20 years

** Some cases can have one or more exposures. Calculated over valid cases for each variable

radon devices was very high and comparable between cases and controls (93.3% and 92.7%, respectively). The median and interquartile range of residential radon exposure (Bq/m^3) were similar for cases at 118 Bq/m^3 (pct 25–75: 65–207) and for controls at 120 Bq/m^3 (pct 25–75: 67–224) ($p=0.93$). Cases resided for more time in the same dwelling compared to controls (37 vs 26 years of median residence; $p<0.01$) (Table 1).

The results in Table 2 showed that neither the crude nor adjusted ORs from logistic regression identified a significant association between indoor radon exposure and COPD risk. However, when participants were restricted to specific lengths of residence in the same dwelling, we observed that the adjusted risk of COPD increases progressively from the lowest vs. the highest radon exposure categories with a longer length of residence in the same dwelling. For those living for more than 20 years in the same dwelling, the adjusted OR was 1.31 (95 CI%

0.65–2.63), for those living for more than 30 years, the OR was 1.66 (95 CI% 0.75–3.69), and, finally, for those who have lived more than 40 years in the same dwelling, the OR was 2.79 (95 CI% 1.06–7.40), with this last result showing statistical significance. The results of the sub analysis performed excluding COPD cases having a previous asthma diagnosis were similar, though in this case no result reached statistical significance.

Indoor radon exposure and COPD severity of cases

Figure 1 shows that both the median indoor radon exposure, both in absolute terms (Panel A) and as percentage above 300 Bq/m^3 (Panel B) were higher for GOLD 4 cases than GOLD 3 cases. Median indoor radon concentration for each GOLD grade of airflow obstruction was 107, 114, 148 and 333 Bq/m^3 for GOLD 1, 2, 3 and 4, respectively (p -value for the median comparison = 0.08). The percentage of COPD cases surpassing 300 Bq/m^3 per

Table 2 Logistic regression results (both crude and adjusted for age, sex, environmental tobacco exposure at home and educational level) of indoor radon exposure and risk of COPD in the total study population and selected by length of residence in the same dwelling

	Cases n (%)	Controls n (%)	Crude OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR excluding asthma cases (95% CI) *
Total study population					
Indoor radon exposure (Bq/m^3)					
< 100	116 (41.4)	176 (41.4)	1 (–)	1 (–)	1 (–)
100–199	93 (33.2)	129 (30.1)	1.10 (0.77–1.57)	1.16 (0.76–1.76)	1.31 (0.72–2.38)
200–299	35 (12.5)	51 (11.9)	1.02 (0.62–1.57)	0.84 (0.44–1.59)	1.53 (0.65–3.57)
> 300	36 (12.9)	72 (16.8)	0.76 (0.48–1.22)	0.84 (0.48–1.48)	1.14 (0.51–2.54)
TOTAL	280	428			
Length of residence in the same dwelling					
More than 20 years living in the same dwelling and indoor radon exposure (Bq/m^3)					
< 100	91 (44.8)	125 (44.6)	1 (–)	1 (–)	1 (–)
100–199	61 (30.0)	87 (31.1)	0.97 (0.64–1.49)	0.95 (0.56–1.61)	1.00 (0.47–2.14)
200–299	21 (10.3)	30 (10.7)	0.93 (0.49–1.73)	0.40 (0.15–1.05)	1.72 (0.19–2.70)
> 300	30 (14.8)	38 (13.6)	1.10 (0.63–1.90)	1.31 (0.65–2.63)	1.58 (0.59–4.23)
TOTAL	230	280			
More than 30 years living in the same dwelling and indoor radon exposure (Bq/m^3)					
< 100	75 (42.6)	80 (46.5)	1 (–)	1 (–)	1 (–)
100–199	54 (30.7)	56 (32.6)	1.04 (0.64–1.70)	1.07 (0.60–1.92)	0.02 (0.40–2.11)
200–299	21 (11.9)	17 (9.9)	1.27 (0.62–2.61)	0.49 (0.18–1.38)	0.76 (0.20–2.91)
> 300	26 (14.8)	19 (11.0)	1.48 (0.76–2.89)	1.66 (0.75–3.69)	1.49 (0.50–4.44)
TOTAL	176	172			
More than 40 years living in the same dwelling and indoor radon exposure (Bq/m^3)					
< 100	49 (38.6)	49 (44.1)	1 (–)	1 (–)	1 (–)
100–199	40 (31.5)	38 (34.2)	1.07 (0.59–1.95)	1.53 (0.74–3.14)	0.91 (0.34–2.41)
200–299	17 (13.4)	13 (11.7)	1.26 (0.55–2.89)	0.47 (0.13–1.69)	0.70 (0.14–3.47)
> 300	21 (16.5)	11 (9.9)	1.95 (0.85–4.47)	2.79 (1.06–7.40)	2.01 (0.54–7.53)
TOTAL	127	111			

Bq/m^3 Bequerels per cubic meter, CI Confidence Interval, OR odds ratio

* For the analysis excluding asthma cases, the number of cases included for each of the four analysis presented in the table are respectively 147, 107, 95, and 71

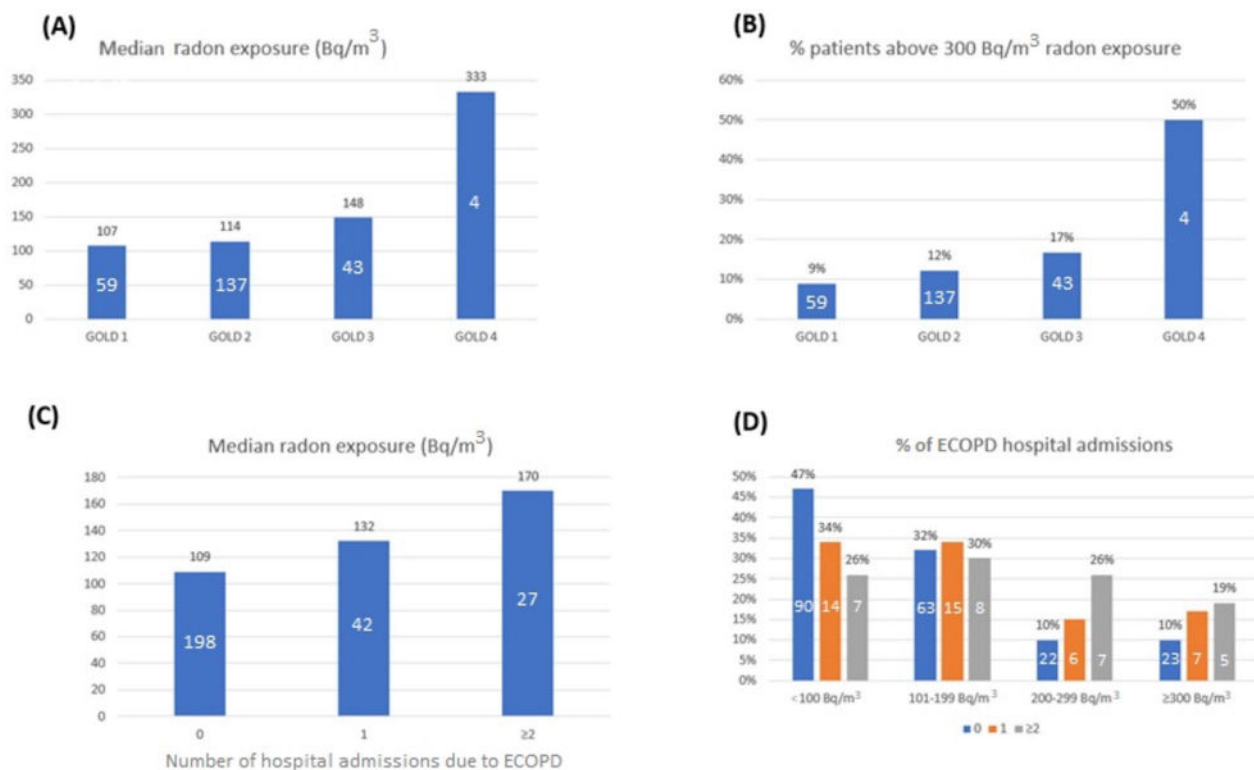


Fig. 1 Indoor radon exposure and its association with GOLD grades of airflow obstruction and history of previous hospitalizations because of ECOPD. Panel **A** shows median radon exposure for different GOLD categories; Panel **B** shows the percentage of patients above 300 Bq/m³ for each GOLD category; Panel **C** shows median radon concentration broken down by the number of hospitalizations due to ECOPD in the last 3 years and, Panel **D** shows the percentage of patients who were hospitalized in the previous 3 years (each group of 3 bars represents 0, 1 or 2 or more hospital admissions) for each radon category of exposure. In each panel, the number included inside the bar refers to the absolute number of cases

GOLD grade was 8.9%, 12.1%, 16.7% and 50% for GOLD 1, 2, 3 and 4, respectively.

Likewise, the median indoor radon exposures (Panel C) were higher for cases having had more ECOPD hospitalizations in the previous 3 years, as was the percentage of cases for radon exposures above 300 Bq/m³ (Panel D), but the differences were not statistically significant. Median radon exposure (Bq/m³) for COPD cases with 0, 1 or 2 or more admissions for ECOPD in the previous 3 years was 109, 132 and 170 Bq/m³, respectively (median test $p=0.137$).

Discussion

In this study, we have observed that the risk of COPD seems to increase with length of residence in the same dwelling for those exposed to more than 300 Bq/m³ versus less than 100 Bq/m³, reaching statistical significance for those living more than 40 years in the same dwelling. A higher radon exposure was associated (albeit not statistically significant) with more severe airflow limitation and previous ECOPD hospitalizations

among COPD cases. Collectively, these observations suggest that indoor radon exposure may be associated with COPD in never smokers.

An alternative explanation for observing an increased risk only among individuals who had lived in the measured dwelling for more than 40 years is the possibility of a genuine causal relationship between radon lifetime exposure (i.e., long-term exposure over approximately the last 50 years) and COPD, which may only become detectable when long-term exposure is adequately assessed. Participants who had resided in the same dwelling for more than 40 years had a substantial proportion of their lifetime radon exposure captured, whereas those who had lived there for a shorter period had only a small fraction of their exposure assessed. In the latter group, the causal effect may remain undetectable, especially considering that previous residences may have had different radon concentrations and different durations of residence (and participants may even have lived longer in their previous homes).

Previous studies

Only a few previous studies have investigated the relationship between indoor radon exposure and COPD, and all were confounded by the inclusion of smokers (the main risk factor for COPD) and the lack of individual indoor radon measurements (exposures were estimated from county averages) [8, 9, 11, 17]. In fact, a systematic review could not reach a definitive conclusion between radon exposure and COPD risk, though most ecological studies have observed an association [18]. To our knowledge, this is the first study to investigate the relationship between indoor radon exposure (measured directly in each participant's home) and COPD in never smokers.

We need to specifically mention that there is only another case–control study on radon and COPD with individual placement of radon devices. While this study did not observe any association between radon exposure and COPD risk (practically all COPD cases were ever-smokers), this study observed that radon might modify (increase) the risk of COPD due to tobacco consumption, with smokers with higher radon concentration, with higher COPD risks compared to smokers with lower exposures. Furthermore, when analyzing never smokers or light smokers (less than 10 pack-years), it was observed that the six cases included had a radon concentration higher than controls (285 vs. 176 Bq/m³) [9].

Interpretation of findings

Tobacco smoking is the main environmental risk factor for COPD. Yet, about 30% of COPD patients around the world are never smokers [2], clearly indicating that there must be other still poorly characterized risk factors [1, 3, 19]. We hypothesized that the α -radiation of radon exposure might have some pro-inflammatory effect that could eventually contribute to increasing the risk of COPD in never smokers, as demonstrated in different studies [20–23]. The lung is a moderately radiosensitive organ, and radiation-induced lung injury attributable to ionizing radiation coming from residential radon decay products may result in molecular alterations or increased respiratory symptoms [24]. It has been observed in animal and in vitro experiments that radon may result in up-regulation of interleukin-6, bronchoalveolar lavage (BAL) fluid inflammation, and increased oxidative stress biomarkers in human fibroblasts, and up-regulation of gene pathways that include inflammatory and respiratory diseases [25, 26].

A sustained proinflammatory effect from α -radiation resulting from indoor radon decay may be associated with a higher probability of COPD when such exposure is present for years. Therefore, hypothetically, the higher the length of exposure, the higher the probability of COPD, similar to what occurs with tobacco and

COPD risk, where there is a long latency period (usually decades) between smoking and COPD [27]. Indirect evidence supporting the need of a long duration of exposure to radon to cause COPD may be related with the observation that higher indoor radon exposure was found in COPD cases with more severe airflow obstruction. Nevertheless, the hypothesis of radon being a risk factor for COPD requires validation in future studies that include other functional, biomarker and/or imaging markers.

Of note, a complementary explanation to the inflammatory pathway is that, in never smokers, mucus production is lower than in smokers with COPD. Therefore, never smokers might have a higher impact of alpha particles in the cell lining of the lungs compared to smokers [28], partially explaining a potentially differential COPD risk from different radiation exposure between smokers and never smokers.

It is well known that tobacco use causes COPD, following an induction period. In the case of radon and COPD, we observed that radon exposure might increase the risk of COPD when exposure is longer than 40 years (i.e. participants living for 40 years or more in the same dwelling). To some extent, this induction period would be similar to tobacco smoking exposure, as has been shown in recent cross-sectional and representative study where the risk of COPD due to tobacco consumption starts to increase from 30 years of smoking. This is something logical since smoking usually starts between ages 10 to 20 years old but the incidence of COPD usually occurs decades later [29]. The fact that in this study we had a significant number of participants who have lived for more than 40 years in a certain dwelling is important information allowing to analyze the possible induction period but also reflects indirectly the quality of the exposure assessment for such a long period.

The available evidence is very limited regarding the hypothetical role of radon on COPD severity. A recent study performed in COPD cases has observed that indoor radon might increase symptomatology in these patients, mainly cough and phlegm, and overall symptomatology measured through the Saint George Questionnaire [23]. Another study has observed an association between indoor radon exposure and a reduction in FEV₁ and FVC [22].

Strengths and limitations

The strengths of this study are that we studied never smokers with radon measurements done at each participant home by an accredited laboratory; that the study included individuals with long periods of residence in the same dwelling, with a population that lives in a well-known radon-prone area, and that it was a multicentric study which adds representativeness and external validity

to the results. Finally, the use of incidence instead of mortality might also be considered a strength.

Among potential limitations we acknowledge that the number of GOLD 3 ($n=42$) or GOLD 4 ($n=4$) COPD cases limited our analysis, and that we mixed incident and prevalent cases (though, in the latter, median time since diagnosis was only 4 years). We have observed differences between the median age of cases and controls and also on the education level. We think that these differences did not affect the findings because results were adjusted by them and also because a lower socioeconomic status has been classically associated with a higher risk of COPD [30]. Unfortunately, we do not have information on potential confounders such as possible asthma becoming fixed obstruction or therapies or eosinophil counts. Finally, approximately 40% of COPD cases had a previous diagnosis of asthma, which is often difficult to differentiate from COPD. Nevertheless, in the sensitivity analysis performed, global results were very similar to those observed excluding COPD cases with asthma, which gives consistency to our findings. A further limitation is the possibility that some controls may present COPD, since we did not perform a spirometry on this population. Nevertheless, since only never smokers were included, the possibility of controls presenting COPD is very low, though cannot be disregarded in a very small number. A final limitation could be that we placed detectors for at least 3 months instead of a complete year. This could have increased the uncertainty of radon results. Nevertheless, we do not think that the overall results have been affected since this uncertainty is similar for both cases and controls.

Conclusions

We have identified a pattern of an increase in the risk of COPD in never smokers related with the longer length of residence in the same dwelling, reaching statistical significance for those living more than 40 years in the same dwelling comparing the most exposed (≥ 300 Bq/m³) vs. the least exposed (<100 Bq/m³). These results suggest an association between radon exposure and COPD risk in never smokers who lived for extended periods (>40 years) in the same dwelling. Higher indoor radon exposures were also associated with more severe airflow obstruction and previous hospitalizations due to ECOPD. Altogether, these findings call for future research in never smokers' COPD patients assessing potential molecular pathways and higher sample size, particularly for severe cases of COPD. As a final message, individuals living in radon-priority areas should measure their dwellings and mitigate radon concentrations where necessary following available guidelines.

Acknowledgements

Authors want to thank the volunteers participating in the study for their willingness to contribute to medical research.

Author contributions

Carlota Rodríguez García: Conceptualization; Methodology; Formal Analysis; Writing – Original Draft; Writing – Review and Editing. Alberto Ruano Ravina: Conceptualization; Methodology; Formal Analysis; Writing – Original Draft; Writing – Review and Editing; Supervision; Funding Acquisition. Alvar Agustí: Writing—Review and Editing; Visualization. Cristina Represas Represas: Writing – Review and Editing. Rafael Golpe: Writing – Review and Editing. Karl Kelsey: Writing – Review and Editing. Ana Pando Sandoval: Writing – Review and Editing. Angélica Consuegra Vanegas: Writing – Review and Editing. Cecilia Mouronte Roibás: Writing – Review and Editing. Tara Pereiro Brea: Writing – Review and Editing. Cristina Candal Pedreira: Writing – Review and Editing. Guadalupe García: Writing – Review and Editing. Raquel Dacal-Quintas: Writing – Review and Editing. Julia Rey Brandariz: Writing – Review and Editing. Luis Valdés: Writing – Review and Editing. Alberto Fernández Villar: Writing – Review and Editing. Lucía Martín-Gisbert: Writing – Review and Editing.

Funding

This study has been funded by Instituto de Salud Carlos III (ISCIII) through the project PI20/00476 and co-funded by the European Union. The funding source was not involved in the execution, analysis, interpretation of the data or writing of this study. This article is part of the PhD research conducted to obtain the PhD degree of Carlota Rodríguez García.

Data availability

Data will be available upon request to the corresponding author.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Santiago de Compostela-Lugo (ID 2019/521).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Received: 16 June 2025 Accepted: 7 February 2026
Published online: 17 February 2026

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