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The prevalence of stroke according to indoor radon concentration in South Koreans

Nationwide cross section study

Soo Han Kim, MD[a], Jeong Mee Park, MD, PhD[b], Hee Kim, OT, PhD[c,*]

Abstract

To investigate the relationship between indoor radon level and stroke, which is a major factor for background radiation.

This study combines 2 nationwide studies. Demographic characteristics and medical history of participants were obtained from Korean National Health and Nutrition Examination Survey (KNHANES) from 2007 to 2012. Participants over 40 years old and who completed the questionnaire were included in the study. Indoor radon concentration was analyzed using the mean value of winter housing radon concentration from 2012 to 2016 published by the National Institute of Environmental Research. The average values of each metropolitan city and province were assigned to the residence of the participant. To eliminate the potential confounding factors, participants' age, sex, hypertension, diabetes, dyslipidemia, ischemic heart disease, education level, occupation, smoking, drinking, exercise, and dietary intake were adjusted in multivariable logistic regression.

Total of 28,557 participants were included in this study. Indoor radon levels were significantly higher in the participants with stroke, and the prevalence of stroke increased as indoor radon levels increased ($P < .001$, P for linear trend $< .001$). Indoor radon level was associated with stroke even after adjusting potential confounding factors (OR: 1.004 [95CI: 1.001–1.007], $P = .010$) and high radon exposure (indoor radon over 100Bq/m3) was also associated with stroke (OR: 1.242 [95CI: 1.069–1.444], $P = .005$). Trend analysis showed linear correlation of increased odds between radon quartile and stroke (P for linear trend $< .001$). In subgroup analysis, elevated indoor radon was most strongly associated in participants with age over 76(OR: 1.872[95%CI:1.320–2.654], $P < .001$).

High indoor radon concentration may be associated with stroke. Specifically, elevated radon was associated with stroke in participants over 76 years old. In high-risk population, home modification to reduce indoor radon may help decreasing the risk of stroke.

Abbreviations: CI = confidence intervals, KNHANES = Korean National Health and Nutrition Examination Survey, OR = odds ratio.

Keywords: big data, nationwide, radon, stroke

1. Introduction

South Korea is one of the world's fastest aging country with more than 12.66% of elderly among total population.[1] As the elderly population grows, so does the stroke population. From 1995 to 2003, the annual increase of ischemic strokes was 7.18%.[2] Each year, 105,000 people develop initial or recurrent stroke in South Korea.[3] Among South Korean population over the age of 30, 795,000 people are diagnosed as stroke.[4]

Commonly known risk factors for stroke include hypertension, diabetes, hypercholesterolemia, smoking, and obesities. In Korean, the prevalence of most risk factors except hypertension and smoking are increasing over the last 10 years.[4] Most clinicians and scientists are mainly focusing on these risk factors and the environmental factors of stroke are barely noticed. Environmental factors like seasonal change and air pollution are validated as 2 main environmental factors and there may be others that affect the stroke incidence and prevalence.[5,6]

Radon is a radioactive isotope that is naturally formed through the collapse of uranium and thorium.[7] Radon releases alpha particles and decay into polonium-218 (218 Po) which also emits alpha particles and eventually decays into lead (214Pb).[7,8] These alpha particles and decay products are the main causes of tissue damage form radon.[9] Radon is the main source of ionizing radiation received by the general population in most countries.[8] The general level of radon on the outside air and water is very low.[7,10] However, people working or living in enclosed spaces, especially in underground working areas (such as miners or building workers) can be exposed to high concentrations of radon.[7,10] Since 1988, radon was classified as human carcinogen by The International Agency for Research on Cancer.[8]

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Various previous studies showed relationship between elevated radon and lung cancer and possible association with cardiovascular disease has also been mentioned.[8–13] However, no previous studies have reported the relationship between indoor radon concentration and stroke. This study was performed to investigate whether indoor radon concentration is associated with stroke.

2. Methods

In this study we used data from the Korea National Health and Nutrition Examination Survey (KNHANES) of South Korea from 2007 to 2012. KNHANES is a nationwide, cross-sectional survey carried out by the Korean Centers for Disease Control and Prevention. All participants were selected based on demographics such as gender, age, region, and residence type of stratified sampling which means the sample represents the total population of South Korea.[14] Several details of KNHANES may vary by their studied years. The Institutional Review Board of the Korean Centers for Disease Control and Prevention approved this study (IRB Number: 2010–02CON-21-C). All participants were notified and signed a written agreement on the use of health information for research. People under 40 years old or did not complete the questionnaires were excluded in this study.

Demographic information and formally known risk factors of stroke were obtained through medical questionnaires, physical examination and serologic tests. Hypertension was defined when the participant was taking blood pressure medications or systolic blood pressure was higher than 140 mm Hg or diastolic blood pressure was higher than 90 mm Hg. Diabetes was defined when the participant uses diabetic medication or fasting blood glucose was above 126 mg / dl. Dyslipidemia was defined when the participant was taking medications or fasting total cholesterol was above 240 mg/dl, fasting triglycerides was over 200 mg/dl, or fasting HDL cholesterol was less than 40 mg/dl. Exercise was defined when moderate physical activity is performed at least 3 times a week, at least 10 minutes at a time. Participants provided information on age, smoking status, drinking, and past medical history including stroke. The height and weight of participants were also measured by health professionals.

Indoor radon was measured with alpha track detector according to the indoor air quality process test standard (Korean Ministry of Environment Notice No. 2010–24).[15] In brief, radon concentration is measured by detecting microscopic damage to the plastic or cellulose film from the alpha particles that are released when the radon and radon decay products collapse into the detection film. LR-115 and CR-39 are the films used as detectors. Alpha track detectors are used in an appropriate container to eliminate external factors that could interfere with the measurement.[15,16] The sampling period of the Alpha track detectors was 90 days or more. When the sampling is completed, it was packed and stored in an airtight package and transported to the laboratory for analysis.[15] Calibration was performed at least once every 12 months to ensure accuracy of the radon detector, and was performed at 3 or more different radon concentrations.[15] The radon concentration in air is measured in Bq/m^3.

Radon concentrations were analyzed by using the values published in Korea Living Environment Information Center.[17] The average value of each major city or province from 2012 to winter 2016, which is the longest average value in the published data, was used in the analysis. The Radon level was used as a continuous variable and dividing by 4 quartiles of radon levels, and those exposed to high concentrations of radon were assigned according to WHO recommendations, indoor radon concentrations above 100 Bq/m^3.

For statistical analysis, Independent 2-sample *t* test and Chi-Squared (or Fisher exact) test were performed. For continuous variables, the data is stated as mean ± standard deviation. For categorical variables, the data is displayed as a count and percentage. To assess potential risk factors for stroke, separate univariable logistic regression models were created with each covariate as independent predictors and stroke as the outcome. To eliminate the potential confounding factors 2 multivariable model was designed. Model 1 was adjusted with age, sex, hypertension, diabetes, dyslipidemia, and ischemic heart disease. Model 2 was adjusted with all variables in model 1, education, occupation, smoking, drinking, exercise, and dietary intake. Results were reported as odds ratio (OR) and 95% confidence intervals (CI). We considered a *P* value of less than .05 as being statistically significant. Participants with partial missing data were included only in the statistical analyses that were unrelated to the missing items, but excluded from statistics containing the missing items. All statistical analyses were performed with SPSS Statistics 21.0 software (IBM SPSS Inc., Chicago, Ill., USA).

3. Result

The flow diagram of participants with inclusion and exclusion criteria is demonstrated in Figure 1. A total of 60,149 participants were surveyed in KNHANES from 2007 to 2012. Of these, 29,634 participants were excluded because they were under 40 years of age and 1958 participants were excluded due to the lack of information on medical questionnaire. Finally, 28,557 people were included in the study. Among the included participants, partial data was missing in 4 participants (0.01%) regarding renal failure, 5 participants (0.02%) related to liver cirrhosis (0.02%), 655 participants (2.3%) related to household income, and 91 participants (0.3%) in relation to the education level, 177 participants (0.6%) in occupation and 133 participants (0.5%) in exercise reports.

Participant's clinical characteristics and demographics are displayed in Table 1. Participants with stroke were relatively older, more males, and had a history of blood pressure, diabetes, hyperlipidemia, and ischemic heart disease. In addition, household income, education level, and employment level were relatively low when compared to non-stroke participants. Radon levels were also higher in participants with stroke.

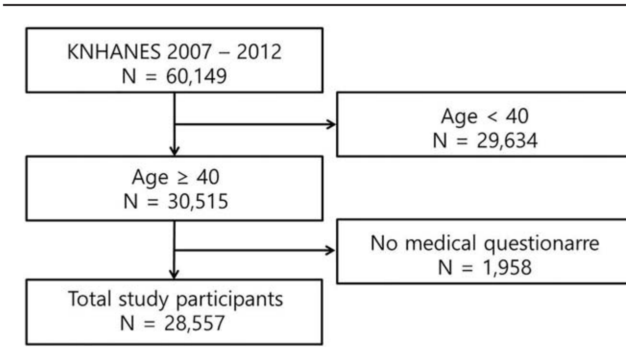

Figure 1. . Flow diagram of participants with inclusion and exclusion criteria.

Table 1

Clinical characteristics and demographics study participants.

	Total participants (N=28,557)	Non-stroke (N=27631)	Stroke (N=926)	*P* value
Age	58.7±12.0	58.4±11.9	67.9±9.4	<.001*
Sex (Male)	12154 (42.6%)	11690 (42.3%)	464 (50.1%)	<.001*
Hypertension	8822 (30.9%)	8198 (29.7%)	624 (67.4%)	<.001*
Diabetes	3308 (11.6%)	3066 (11.1%)	242 (26.1%)	<.001*
Dyslipidemia	12675 (44.4%)	12174 (44.1%)	501 (54.1%)	<.001*
IHD	1091 (3.8%)	1004 (3.6%)	87 (9.4%)	<.001*
Renal failure	166 (0.6%)	159 (0.6%)	7 (0.8%)	.504
Liver cirrhosis	106 (0.6%)	104 (0.4%)	2 (0.2%)	.588
Lung cancer	47 (0.2%)	46 (0.2%)	1 (0.1%)	1.000
BMI	23.97±3.15	23.96±3.15	24.27±3.19	<.001*
House income				<.001*
Very Low	7465 (26.8%)	7022 (26.0%)	443 (49.2%)	
Low	7100 (25.4%)	6872 (25.5%)	228 (25.3%)	
Moderate	6461 (23.2%)	6340 (23.5%)	121 (13.4%)	
High	6876 (24.6%)	6767 (25.1%)	109 (12.1%)	
Education				<.001*
Middle School	15918 (55.9%)	15197 (55.5%)	721 (78.0%)	
High School	12548 (44.1%)	12345 (44.8%)	203 (22.2%)	
Smoking				<.001*
Non-smoker	16897 (59.2%)	16428 (59.5%)	469 (50.6%)	
Former-Smoker	2875 (10.1%)	2754 (10.0%)	121 (13.1%)	
Current-Smoker	8785 (30.8%)	8449 (30.6%)	336 (36.3%)	
Alcohol				<.001*
None	9909 (36.5%)	9909 (35.8%)	526 (56.8%)	
1=< week	11662 (41.8%)	11662 (42.2%)	268 (28.9%)	
1>week	6068 (21.7%)	6068 (22.0%)	132 (14.3%)	
Exercise	8692 (30.6%)	8483 (30.8%)	209 (22.7%)	<.001*
Protein intake (g)	62.89±34.0	62.20±34.13	53.86±29.63	<.001*
Fat intake (g)	30.13±25.3	30.36±25.29	23.50±23.70	<.001*
CHO intake (g)	312.16±120.5	312.76±120.49	294.95±119.59	<.001*
Radon	103.1±22.0	103.0±22.0	106.5±21.9	<.001*

* $P<.05$.
BMI = body mass index; CHO = carbohydrate; IHD = ischemic heart disease.

Table 2 shows the prevalence of strokes among all participants and in different age groups over 4 quartiles of radon concentration. As the radon concentration increased, an increase in stroke prevalence was observed with linear trend ($P<.001$).

Table 3 shows the relationship between various confounding factors and risk of stroke. Prior to adjustment, increased age, male sex, hypertension, diabetes, dyslipidemia, ischemic heart disease, increased BMI, low household income, low education status, occupation, smoking, alcohol consumption, lack of exercise, dietary intake, and radon exposure level were all associated with stroke. To analyze the risk of stroke, medical and physical parameters were adjusted (Model 1). There was a significant difference in the radon level after the correction of the parameters (OR: 1.004 [95CI: 1.001–1.007], $P=.007$). Further adjustments were made in Model 2 to eliminate the potential confusion of socio-economic and behavioral effects. The concentration of radon still showed a significant correlation after the correction of additional parameters (OR: 1.004 [95CI: 1.001–1.007], $P=.010$). In order to evaluate dose dependent relationship with increase of radon, we investigated the prevalence of stroke according to quartile of radon using full adjusted model (Model 2) (Fig. 2). In all groups, the prevalence of stroke was found to increase with the increase of radon quartile, and linear trend was also observed.

To assess the risk of stroke due to increased indoor radon (over 100Bq) in all subjects and different age groups, further analysis was performed (Table 4). Increased indoor radon was strongly associated with stroke in the whole participants (OR: 1.242

Table 2

Difference in prevalence of stroke in all participants and in different age groups according to radon level.

	1st Q ~83.4	2nd Q 83.5–100.7	3rd Q 100.8–111.6	4th Q 111.7 ~	*P* value	*P* for linear trend
All age	199 (1.7%)	295 (1.8%)	144 (3.0%)	297 (3.0%)	<.001*	<.001*
Age < 64	66 (1.3%)	108 (1.5%)	40 (1.8%)	90 (2.1%)	.012*	.001*
Age 65-75	93 (5.8%)	125 (5.0%)	60 (7.0%)	136 (6.4%)	.087	.143
Age over 76	37 (6.5%)	62 (6.7%)	40 (11.3%)	49 (8.4%)	.028*	.061

* $P<.05$.
Q = quartile.

Table 3

Logistic regression analysis of stroke with demographic and clinical factors using various models.

	Crude		Model 1		Model 2	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age	1.070 (1.063–1.076)	<.001*	1.057 (1.050–1.064)	<.001*	1.028 (1.019–1.037)	<.001*
Sex (ref Male)	0.730 (0.641–0.832)	<.001*	0.657 (0.573–0.753)	<.001*	0.446 (0.355–0.562)	<.001*
Hypertension	4.898 (4.259–5.633)	<.001*	2.938 (2.520–3.426)	<.001*	2.977 (2.526–3.509)	<.001*
Diabetes	2.835 (2.437–3.298)	<.001*	1.595 (1.360–1.871)	<.001*	1.437 (1.212–1.704)	<.001*
Dyslipidemia	1.497 (1.312–1.707)	<.001*	1.130 (0.984–1.298)	.084	1.120 (0.965–1.299)	.135
IHD	2.750 (2.186–3.460)	<.001*	1.417 (1.113–1.803)	.005	1.373 (1.065–1.769)	.014
Renal Failure	1.316 (0.616–2.813)	.479	0.718 (0.331–1.557)	.401	0.616 (0.282–1.345)	.224
Liver cirrhosis	0.573 (0.141–2.324)	.436	0.451 (0.109–1.856)	.270	0.374 (0.090–1.559)	.177
Lung Cancer	0.648 (0.089–4.705)	.668	0.497 (0.067–3.694)	.494	0.000	.998
BMI	1.030 (1.09–1.051)	.005*	1.011 (0.989–1.033)	.344	1.017 (0.994–1.041)	.145
House income						
Very low	1 (reference)		1 (reference)		1 (reference)	
Low	0.526 (0.447–0.619)	<.0001*	0.795 (0.669–0.944)	.009	0.851 (0.710–1.021)	.082
Moderate	0.303 (0.247–0.371)	<.0001*	0.619 (0.497–0.770)	<.001*	0.753 (0.598–0.947)	.015
High	0.255 (0.207–0.316)	<.001*	0.577 (0.459–0.725)	<.001*	0.722 (0.562–0.927)	.011
Education						
Middle School	1 (reference)		1 (reference)		1 (reference)	
High School	0.347 (0.296–0.406)	<.001*	0.602 (0.503–0.720)	<.001*	0.650 (0.531–0.795)	<.001*
Occupation						
Non-employed	1 (reference)		1 (reference)		1 (reference)	
Office worker	0.160 (0.111–0.230)	<.001*	0.359 (0.244–0.529)	<.001*	0.464 (0.301–0.714)	<.001*
Service and Sales	0.274 (0.205–0.368)	<.001*	0.630 (0.642–0.861)	.004	0.695 (0.496–0.974)	.035
Manual worker	0.397 (0.338–0.466)	<.001*	0.555 (0.467–0.661)	<.001*	0.591 (0.492–0.711)	<.001*
Smoking						
Non-smoker	1 (reference)		1 (reference)		1 (reference)	
Former-smoker	1.539 (1.255–1.887)	<.001*	0.986 (0.759–1.280)	.913	1.018 (0.771–1.345)	.898
Current-smoker	1.393 (1.208–1.606)	<.001*	1.248 (1.017–1.531)	.034	1.280 (1.026–1.598)	.029
Alcohol						
None	1 (reference)		1 (reference)		1 (reference)	
1=< week	0.433 (0.372–0.502)	<.001*	0.651 (0.554–0.765)	<.001*	0.686 (0.578–0.813)	<.001*
1>week	0.409 (0.337–0.497)	<.001*	0.442 (0.355–0.550)	<.001*	0.444 (0.351–0.562)	<.001*
Exercise	0.659 (0.564–0.771)	<.001*	0.787 (0.670–0.926)	.004	0.893 (0.753–1.060)	.196
Protein intake (g)	0.990 (0.987–0.992)	<.001*	0.995 (0.992–0.998)	<.001*	0.998 (0.994–1.003)	.425
Fat intake (g)	0.985 (0.981–0.988)	<.001*	0.995 (0.991–0.999)	.010	1.001 (0.996–1.006)	.792
CHO intake (g)**	0.999 (0.998–0.999)	<.001*	0.999 (0.999–1.000)	.025	1.000 (0.999–1.001)	.680
Indoor Radon	1.007 (1.004–1.010)	<.001*	1.004 (1.001–1.007)	.010	1.004 (1.001–1.007)	.010

* $P<.05$.

Model 1: Adjusted with Age, Sex, Hypertension, Diabetes, Dyslipidemia, Ischemic heart disease, BMI.

Model 2: All factors in Model 1 and House Income, Education, Occupation, Smoking Alcohol, Exercise, and Dietary intake.

BMI = body mass index; CHO = carbohydrate; CI = confidence intervals; IHD = ischemic heart disease; OR = odd ratio.

[95CI: 1.069–1.444], $P=.005$). Participants with age over 76 showed strong correlation even after adjusting for physical and socioeconomic variables (OR: 1.872[95%CI:1.320–2.254], $P<.001$). Analysis by age group showed no significant correlation between increased indoor radon and stroke prevalence in subjects under 64 years of age and between 65 and 75 years of age.

4. Discussion

Several investigations have been conducted on the risk of radon,[8–13] but the association between radon and stroke has not been reported. To our knowledge, this study is the first to investigate the association between indoor radon and stroke in a nationwide scale. Indoor radon level was associated with stroke even after adjusting potential confounding factors (OR: 1.004 [95CI: 1.001–1.007], $P=.010$) and high radon exposure (indoor radon over 100Bq/ m^3) was also associated with stroke (OR: 1.242 [95CI: 1.069–1.444], $P=.005$), especially in participants with age over 76 (OR: 1.872[95%CI:1.320–2.654], $P<.001$). This analysis used data from national representative samples of the Korean population and adjusted for multiple potential confounding variables, so our result supports the hypothesis that increased indoor radon exposure is associated to stroke.

The exact mechanism how indoor radon causes stroke is not identified and it requires further studies. The authors assume that radon may have directly affected the blood vessels. Radon can enter the body through inhalation and dissolve into bloodstream during gas exchange, entering systemic circulation.[18,19] Sakoda et al[18] reported that radon was detected in the blood, vein, artery and various tissues including the brain even when the radon was inhaled. Since the radiation from radon is strong enough to cause cell damage,[9] it is plausible that radon in the blood stream and vascular tissue causes vascular damage resulting in thromboembolic diseases such as stroke.[20] Sun et al[12] also reported increased thrombosis was associated with accumulation of radon exposure in animal model. Johnson and Duport[21] also speculated that increased radon might be associated with cardiovascular disease due to similar pathophysiology. Another

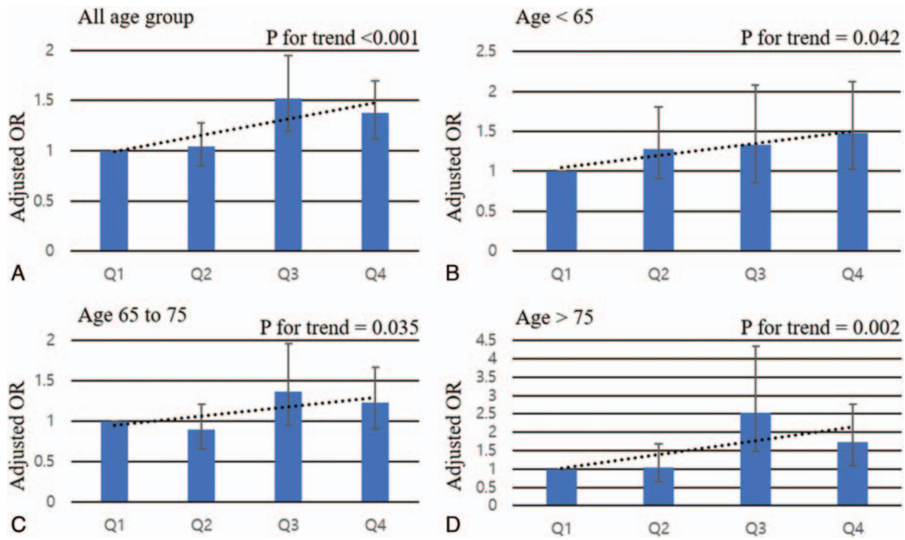

Figure 2. . Risk of stroke in all participants and in different age groups according to quartile of radon. 1st Quartile < 83.4 Bq/m^3, 2nd Quartile 83.5–100.7 Bq/m^3, 3rd Quartile 100.8–111.6 Bq/m^3, 4th Quartile < 111.7 Bq/m^3. (Adjusted with Age, Sex, Hypertension, Diabetes, Dyslipidemia, Ischemic heart disease, BMI, House Income, Education, Occupation, Smoking, Alcohol, Exercise and Dietary intake.).

Table 4

Risk of stroke due to increased indoor radon exposure.

	Crude Model		Model 1		Model 2	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
All	1.353 (1.181–1.550)	<.001*	1.207 (1.049–1.388)	.008*	1.242 (1.069–1.444)	.005*
Age < 65	1.225 (0.972–1.543)	.085	1.121 (0.885–1.421)	.342	1.051 (0.814–1.357)	.704
65-75	1.129 (0.920–1.385)	.246	1.110 (0.902–1.366)	.326	1.192 (0.952–1.491)	.125
Age > 75	1.666 (1.217–2.280)	.001*	1.680 (1.219–2.316)	.002	1.872 (1.320–2.654)	<.001*

* $P < .05$.
Model 1: Adjusted with Age, Sex, Hypertension, Diabetes, Dyslipidemia, Ischemic heart disease, BMI.
Model 2: All factors in Model 1 and House Income, Education, Occupation, Smoking Alcohol, Exercise, and Dietary intake.
CI = confidence intervals; OR = odd ratio.

possible explanation between radon and stroke could be from chronic irritation to lung parenchyma. Several studies have shown that chronic dust exposure is associated with cardiovascular diseases and stroke.[22,23] Chronic irritation of pulmonary parenchyma causes oxidative stress and inflammatory responses[24,25] which also increases the possibility of thrombosis.[26]

Unlike other risk factors of stroke such as hypertension and diabetes, indoor radon concentration is modifiable. Active Soil Depressurization is one way to reduce indoor radon.[2] It is performed by installing a pipe with a fan to the foundation of the house, which actively pulls and ejects the radon containing gas to outside of the house.[27] Sealing soil contact surface may also help in reducing indoor radon.[2,28] If the structure of the house itself is difficult to change, indoor radon concentrations can also be reduced through frequent ventilation.[2,29]

There are some limitations to this study. First, there is no investigation of whether stroke is ischemic or hemorrhagic. Therefore, we cannot confirm whether indoor radon is associated with hemorrhagic or ischemic stroke. Second, this study has limitations in evaluating causality due to its cross-sectional nature. Third, this is a study performed in a single ethnic population and there may be restrictions on applying the results directly to other ethnic groups. Forth, this study used winter indoor radon levels from 2012 to 2016 which is the longest average value in the published data. The authors use this value because it is the longest data, but there is also a part where the indoor radon concentration is measured to be the highest because of the reduction of ventilation in winter. Therefore, there is a difference between the value used in this study and the actual patient exposed value over time. Fifth, the medical history was obtained by questionnaire. Thus, reporting errors could possibly happen from recall bias and faking. Despite these limitations, this study was conducted on a large number of samples representing all Korean populations, and indoor radon levels were measured by national accredited agencies. Therefore, the authors believe that the results presented in this study are reliable.

In conclusion, authors suggest that the Indoor radon concentration may be associated with stroke. Specifically, elevated radon was associated with stroke in participants over 76 years old. In high-risk population, home modification to reduce indoor radon may help decreasing the risk of stroke. Due to, previous mentioned limitations, further investigation with larger sample and different ethnicities is required. Also, further research is needed to determine the exact pathophysiology of radon in stroke.

Author contributions

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