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Research Article

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Relationship between occupational sunlight exposure and the incidence of renal cancer

Hyun-Suk Jang [1], Jong-Han Leem [1,2], Seong Soo Jeon [3], Shin-Goo Park [1,2], Sangyoon Lee [1], Yangwon Kang [1], Go Choi [1], Hyung Doo Kim [1,4], Hyeonwoo Ju [1], Sung Wook Jang [1], Youna Won [1], Hwan-Cheol Kim [1,2*]

[1]Department of Occupational and Environmental Medicine, Inha University Hospital, Incheon, Korea
[2]Department of Occupational and Environmental Medicine, School of Medicine, Inha University, Incheon, Korea
[3]Department of Urology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
[4]Department of Environmental Health Sciences, Graduate School of Public Health, Seoul National University, Seoul, Korea

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***Correspondence:**
Hwan-Cheol Kim
Department of Occupational and Environmental Medicine, Inha University Hospital, and Department of Occupational and Environmental Medicine, School of Medicine, Inha University, 27 Inhang-ro, Jung-gu, Incheon 22332, Korea.
E-mail: carpediem@inha.ac.kr

ORCID iDs
Hyun-Suk Jang
https://orcid.org/0000-0002-8663-8608
Jong-Han Leem
https://orcid.org/0000-0003-3292-6492
Seong Soo Jeon
https://orcid.org/0000-0002-3265-6261
Shin-Goo Park
https://orcid.org/0000-0002-1544-4486
Sangyoon Lee
https://orcid.org/0000-0001-9175-9300
Yangwon Kang
https://orcid.org/0000-0002-7213-7474
Go Choi
https://orcid.org/0000-0001-8591-3025
Hyung Doo Kim
https://orcid.org/0000-0001-7478-8281

ABSTRACT

Background: The risk factors for renal cancer include smoking, obesity, hypertension, and exposure to trichloroethylene. Recent studies have shown that low sunlight exposure increases the risk of developing a range of cancers, including renal cancer. Given that most of the daytime is spent at work, a lack of occupational sunlight exposure can be a risk factor for renal cancer. Therefore, this study examined the relationship between occupational sunlight exposure and the incidence of renal cancer.
Methods: This was a university hospital-based case-control study on renal cancer. Of the 706 newly diagnosed patients with renal cell carcinoma (RCC), 633 cases were selected; 73 who had no occupational history were excluded. In addition, 633 controls were selected from the general population after 1:1 matching with respect to sex, age (within 5 years), and residential area (constituency-level). Information on sunlight exposure by the occupational group was referred to data from France. To estimate the association between occupational sunlight exposure and the RCC risk, the odds ratios (ORs) were calculated using conditional logistic regression analysis.
Results: Sunlight exposure was divided into quartiles and the risk of RCC was analyzed. The adjusted OR of RCC (OR: 0.664, 95% confidence interval: 0.449–0.983) was significantly lower for the Q4 group than Q1 group but the Q2 and Q3 groups did not show significant results. The risk of RCC tended to decrease with increasing exposure to sunlight (p for trend < 0.028).
Conclusions: Higher occupational sunlight exposure reduces the risk of RCC.

Keywords: Occupational sunlight exposure; Renal cancer; Renal cell carcinoma

BACKGROUND

In 2014, renal cancer was the 11th most common cancer in Korea; 4,471 new cases were diagnosed, and 944 deaths were recorded. The incidence of renal cancer per 100,000 people has increased from 3.0 in 1999 to 5.7 in 2014 [1]. Renal cancers are classified as

Hyeonwoo Ju
https://orcid.org/0000-0001-5296-2808
Sung Wook Jang
https://orcid.org/0000-0003-4747-1400
Youna Won
https://orcid.org/0000-0002-5924-2712
Hwan-Cheol Kim
https://orcid.org/0000-0002-3635-1297

Abbreviations

CI: confidence interval; KOCSS: Korean Occupational Cancer Surveillance System; ISCO-08: International Standard Classification of Occupations 2008; OR: odds ratio; RCC: renal cell carcinoma; SD: standard deviation; TCE: trichloroethylene; UV: ultraviolet; UVB: ultraviolet B.

Competing interests

The authors declare that they have no competing interest

Author contributions

Conceptualization: Jang HS, Jeon SS, Kim HC; Data curation: Kang Y, Choi G, Kim HD; Formal analysis: Jang HS, Jeon SS, Kim HC, Ju H, Jang SW, Won Y; Investigation: Jang HS, Jeon SS, Kim HC; Methodology: Jang HS, Jeon SS, Kim HC; Project administration: Jeon SS, Kim HC; Software: Jang HS, Jeon SS, Kim HC; Supervision: Leem JH, Park SG, Lee S; Validation: Jeon SS, Kim HC; Writing - original draft: Jang HS, Jeon SS, Kim HC; Writing - review & editing: Leem JH, Park SG, Lee S

tumors originating from the renal parenchyma or from the renal pelvis. The majority of tumors that originate from the renal parenchyma are primary tumors. Among them, renal cell carcinoma (RCC), which is a malignant tumor, accounts for approximately 85% [2]. Cigarette smoking, obesity, and hypertension have been reported to be risk factors of RCC, but their reported contributions are relatively small [3]. A number of epidemiological studies on the relationships between occupational exposure and the development of RCC have been conducted over the past 30 years. Epidemiological and animal studies conducted in Germany have shown that exposure to trichloroethylene (TCE) increases the risk of RCC development significantly [4-6]. In addition, many studies have recently been conducted on the relationship between sunlight exposure and the level of vitamin D in the body in relation to various types of cancer, including renal cancer [7-10].

Vitamin D is ingested in food or synthesized naturally from cholesterol in skin exposed to sunlight (ultraviolet B; UVB). Foods, such as milk, butter, and fish, are relatively rich in vitamin D, but people obtain most of their vitamin D through exposure to sunlight [11,12]. In vivo, vitamin D plays important roles in the metabolisms of calcium and phosphorus as well as in skeletal formation; osteoporosis, osteomalacia, or rickets can develop when its levels are insufficient [13]. Recent studies have shown that vitamin D reduces the risk of cardiovascular disease, metabolic syndrome, inflammatory disorders, and even malignancies [7,14]. Vitamin D interferes with carcinogenesis by inhibiting cell proliferation, promoting cell differentiation, and suppressing tumor invasiveness, angiogenesis, and metastasis [8,9,15].

Despite the important functions of vitamin D, recent studies have shown that adolescents and young adults are at risk of vitamin D deficiency. According to a report on vitamin D deficiency in Koreans released in 2013, only 34.2% of males and 22.4% of females had normal vitamin D levels, and that vitamin D deficiency was more serious in younger females [16]. Because skin exposure to sunlight is the main source of the vitamin [11], the cause of vitamin D deficiency in Koreans is likely to be associated with reduced outdoor activity. In a study based on data collected during The Korean National Health and Nutrition Examination Survey conducted in 2009–2013, a positive correlation was found between outdoor physical activity and the serum vitamin D levels [17,18]. Considering that most of the daylight hours on weekdays are spent at work, it is estimated that individual sunlight exposure is affected significantly by occupational sunlight exposure. Thus, a lack of occupational sunlight exposure may increase the risk of developing a range of cancers, including RCC. This study examined the relationship between occupational sunlight exposure and the incidence of RCC.

METHODS

Study population

This study was based on data collected from the Korean Occupational Cancer Surveillance System (KOCSS) for RCC [19,20]. The KOCSS aimed to identify the status and characteristics of various cancers, occupational factors related to its development, and preventive measures. The KOCSS was a university hospital-based case-control study on RCC in Seoul from April 2015 to December 2016. The cases included patients with newly diagnosed RCC (C64 according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems classification) and the total number of cases was 706:347 in 2015 and 359 in 2016. The survey was conducted through a questionnaire, which included sex, age, education, smoking history, alcohol history, exercise, hypertension, urinary stone,

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family history of renal cancer, and occupational history. Of the 706 patients, 633 cases were selected; 73 who had no occupational history were excluded. The controls had similar characteristics to the cases except that there was RCC and used community control living in the same area as the cases. Finally, 633 controls were selected after 1:1 matching with respect to sex, age (within 5 years), and residential area (constituency-level).

Exposure assessment

Data on sunlight exposure by occupation was unavailable in Korea; thus, the results of a study conducted in France were used. In that study, Boniol et al. examined occupational ultraviolet (UV) exposure in 889 workers aged from 25 to 69 [21]. The workers were selected by random digit dialing and interviewed by trained personnel using computer-assisted telephone interviews from May to June 2012. The collected data included information on their jobs over the past 5 years, the start and end times of work, and the daily total outdoor exposure times. Using the satellite's UV data, they calculated the daily standard UV dose, taking into consideration the exposure time and location. **Table 1** lists the samples classified by the International Labor Organization International Standard Classification of Occupations 2008 (ISCO-08) and shows the quartiles of sunlight exposure for each occupational group. In this study, the median sunlight exposure calculated in the above study was used for each ISCO-08 occupational group. After classifying the previous occupations of the cases and controls according to the ISCO-08 criteria, the weighted average was obtained by multiplying the occupational sunlight exposure and working period.

Statistical analysis

All data were analyzed using SPSS (ver. 19.0; IBM, Armonk, NY, USA) after encoding had been completed. The characteristics of the participants (cases and controls) were compared using a χ^2 test. The participants were divided into quartiles according to occupational sunlight exposure and compared using a χ^2 test. The mean sunlight exposure of the case and control groups was compared using a 2-sample t-test. To minimize bias, conditional logistic regression was used, matching sex, age, and residential area by 1:1, and the odds ratio (OR) and 95% confidence interval (95% CI) were calculated. Confounders included the smoking history, hypertension, which were associated with RCC in previous studies, and education, alcohol history, exercise, and urinary stones, which were significantly higher in the case group according to univariate analysis. Simple conditional logistic regression and multiple conditional logistic regression analysis were conducted before and after adjusting for confounders, respectively. The OR and 95% CI of the Q2, Q3, and Q4 groups were obtained by a comparison with Q1, the lowest dose group, and the trend of the OR changes was calculated using the *p*-value for the trend.

Table 1. Occupational solar exposure in France in 2012[a]

ISCO-08	Number	Minimum	Lower quartile	Median	Upper quartile	Maximum
1. Managers	24	0.04	0.32	0.50	0.98	1.55
2. Professionals	132	0.04	0.22	0.57	1.09	1.85
3. Technical and associate professional	148	0.02	0.40	0.70	1.08	1.79
4. Clerical support workers	83	0	0.47	0.73	1.08	1.46
5. Services and sales workers	113	0.03	0.31	0.51	0.83	1.60
6. Skilled agricultural, forestry and fishery workers	107	0.07	0.70	0.94	1.15	1.81
7. Craft and related trades workers	126	0.02	0.73	1.08	1.27	1.77
8. Plant and machine operators and assemblers	58	0.18	0.56	0.91	1.16	1.72
9. Elementary occupations	69	0.10	0.40	0.83	1.13	1.67
10. Armed forces occupations	29	0.17	0.47	0.84	1.28	1.57

ISCO-08: International Standard Classification of Occupations 2008.
[a]Expressed as average daily erythemal ultraviolet dose (in kJ/m^2) by major groups of ISCO-08 classification of occupations.

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Ethics statement

The Institutional Review Board of Inha University Hospital and Samsung Medical Center approved the study protocol.

RESULTS

The cases and controls were compared according to sex, age, education, smoking history, alcohol history, exercise, hypertension, urinary stone, and family history of renal cancer (**Table 2**). The incidence of RCC was similar regardless of age and family history of renal cancer. On the other hand, there were significant differences in the incidence of RCC between the case group and control group in relation to education, smoking history, alcohol history, exercise, hypertension, and urinary stone.

The mean sunlight exposure of the case and control groups was 0.728 kJ/m^2 (standard deviation [SD]: 0.153) and 0.757 kJ/m^2 (SD: 0.173), respectively. This indicates that the case group had significantly lower mean sunlight exposure than the control group (**Table 3**).

Table 2. Sociodemographic factors and renal cancer

Variables	Renal cell carcinoma		*p*-value[a]
	Cases (n = 633)	Controls (n = 633)	
Sex			1.000
Male	492 (50.0)	492 (50.0)	
Female	141 (50.0)	141 (50.0)	
Age			0.184
< 50	198 (54.0)	169 (46.0)	
50–60	238 (47.8)	260 (52.2)	
≥ 60	197 (49.1)	204 (50.9)	
Education			0.001
Middle school or lower	89 (44.5)	111 (55.5)	
High school	218 (45.6)	260 (54.4)	
College or higher	326 (55.4)	262 (44.6)	
Smoking history (pack-year)			0.011
Never	216 (49.1)	224 (50.9)	
< 10	53 (40.8)	77 (59.2)	
10–20	97 (46.4)	112 (53.6)	
20–30	103 (50.2)	102 (49.8)	
≥ 30	164 (58.2)	118 (41.8)	
Alcohol history (unit/wk)			0.002
0	176 (50.3)	174 (49.7)	
0.1–7.0	269 (46.5)	309 (53.5)	
7.1–14.0	135 (51.5)	127 (48.5)	
> 14.0	53 (69.7)	23 (30.3)	
Exercise			0.003
No	395 (53.6)	342 (46.4)	
Yes	238 (45.0)	291 (55.0)	
Hypertension			<0.001
No	459 (46.7)	524 (53.3)	
Yes	174 (61.5)	109 (38.5)	
Urinary stone			0.022
No	560 (49.0)	584 (51.0)	
Yes	73 (59.8)	49 (40.2)	
Family history of renal cancer			0.166
No	537 (49.2)	554 (50.8)	
Yes	96 (54.9)	79 (45.1)	

Values are presented as number of subject (%).
[a]Obtained by a χ^2 test.

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Table 3. Sunlight exposure and renal cancer

Variables	Renal cell carcinoma		p-value
	Cases (n = 633)	Controls (n = 633)	
Sunlight exposure			< 0.001[a]
Q1	154 (50.0)	154 (50.0)	
Q2	168 (57.3)	125 (42.7)	
Q3	185 (52.6)	167 (47.4)	
Q4	126 (40.3)	187 (59.7)	
Daily erythemal ultraviolet dose (kJ/m^2)	0.728 ± 0.153	0.757 ± 0.173	0.002[b]

Values are presented as number of subject (%).
[a]Obtained by a χ^2 test; [b]Obtained by 2-sample t-test.

Table 4. RCC risk according to occupational sunlight exposure

Quartile of sunlight exposure	Unadjusted[a]		Adjusted[b]	
	OR	95% CI	OR	95% CI
Q1	1	-	1	-
Q2	1.354	0.964–1.902	1.396	0.952–2.048
Q3	1.106	0.811–1.508	1.046	0.740–1.481
Q4	0.667	0.478–0.931	0.664	0.449–0.983
p for trend	0.007		0.028	

RCC: renal cell carcinoma; OR: odds ratio; CI: confidence interval.
[a]Obtained by simple conditional logistic regression analysis; [b]Obtained by multiple conditional logistic regression analysis after adjusting for education, smoking history, alcohol history, exercise, hypertension, and urinary stone.

Table 4 lists the changes in the risk of RCC according to occupational sunlight exposure. After dividing the sunlight exposure by quartile, the RCC risk for each quartile compared to the first quartile was shown before and after adjusting for education, smoking history, alcohol history, exercise, hypertension, and urinary stone. Compared to the first quartile, the RCC risk was higher in the second and third quartiles, but the difference was not statistically significant. The RCC risk was significantly lower only in the fourth quartile. The p for trend, which indicates the tendency for a change in the risk of RCC in each quartile, showed that the risk of RCC tends to decrease with increasing sunlight exposure.

DISCUSSION

Many studies have reported an association between sunlight exposure and renal cancer. Karami et al. [22] conducted a hospital-based case-control study on the relationship between occupational exposure to sunlight and the incidence of RCC. They reported that RCC has significant linear inverse associations with occupational exposure to sunlight among males. Boscoe and Schymura [23] conducted regression analysis of more than 3 million incident cancer cases against the daily satellite-measured solar UVB levels in the continental United States. They observed an inverse association between solar UVB exposure and cancer incidence for 10 sites (bladder, colon, Hodgkin lymphoma, myeloma, other biliary, prostate, rectum, stomach, uterus, and vulva). Mohr et al. [24] examined the association of UVB exposure, cloud cover, and intake of calories from animal sources with the incidence of renal cancer using multiple regression in 139 countries. They reported that the UVB irradiance was inversely associated with the incidence of renal cancer, whereas cloud cover and intake of calories from animal sources showed an independent positive association. Many other studies have explained the relationship between sunlight exposure and the incidence of renal cancer.

The method of assessing the amount of sunlight exposure is important in terms of the accuracy of the study. In Karami et al.'s study [22], interviewers surveyed the participants' occupations and tasks, and industrial hygienists or occupational health professionals categorized them and estimated the relative sunlight exposure between occupations. This study has limited accuracy in that it estimates and applies the relative difference in sunlight exposure between occupations. Boscoe and Schymura [23] used local UV doses measured by satellites in their study. They surveyed the residences of the participants diagnosed with cancer and used the UV data for the region, measured by satellites. Mohr et al. [24] analyzed the incidence of cancer according to latitude with the idea that sunlight exposure would decrease with increasing latitude. Their study also has a limitation in ignoring the individual differences and applying the amount of sunlight exposure in the area of residence collectively. On the other hand, this study surveyed the participants' past occupations and working periods. In addition, the sunlight exposure data were applied for each occupational group studied in France [21] and the weighted average occupational sunlight exposure was calculated considering the working period. Previous studies have estimated sunlight exposure by experts, or applied it equally according to the residential area or latitude. In contrast, although indirect, the present study used the UV data measured by satellites. On the other hand, because the referenced sunlight exposure was investigated according to the occupational group, the actual sunlight exposure within the same occupational group differed depending on individual occupations. Although the median of occupational sunlight exposure was used to reduce the deviation, this study also lacked accuracy.

The inverse correlation between sunlight exposure and RCC incidence is likely to have been affected by the lack of vitamin D in the body. Because most of the vitamin D in the body is produced by sunlight exposure of the skin, a lack of sunlight exposure causes a deficiency of vitamin D in the body [12,25]. Vitamin D, which is produced by food intake or by sunlight exposure on the skin, is converted to the active form (1,25-hydroxy vitamin D) through the metabolism in the liver and kidney [26]. The activated vitamin D works through 2 pathways in the target organs: one is a fast pathway to activate the voltage-dependent calcium channels through the non-genomic action; the other is a slow pathway that causes genomic action by binding to the vitamin D receptor [27]. Vitamin D receptors are found in most human tissues, in addition to the organs of vitamin D known previously, such as bones, gut, and kidneys [28]. Activated vitamin D also binds to the Vitamin D receptor of cancer tissues, differentiates cells through gene regulation, induces the apoptosis of tumor cells, and inhibits angiogenesis and the proliferation and metastasis of tumor cells [29,30]. Therefore, a vitamin D deficiency due to a decrease in sunlight exposure has not promoted apoptosis and inhibited the growth of tumor cells, thereby increasing the risk of RCC.

This study tested the hypothesis that the risk of RCC is lower in people with high sunlight exposure occupations. The Q4 group's OR for the Q1 group and p for trend supported the hypothesis of this study, but the Q2 and Q3 groups' OR showed no significant results. This study might have incomplete results due to some limitations. First, sunlight exposure through leisure activities, not work, was not considered. To evaluate the individual's exposure to sunlight more accurately, it is necessary to investigate and reflect the outdoor activity time on holidays as well as the commuting methods and time. Second, inaccuracy in exposure assessment may lead to misclassification bias. The difference in exposure to sunlight by different occupations in the same occupational group was not reflected. In the classification according to ISCO-08, the occupational classification of welders and sewing workers is bound to the same occupational group as No. 7 (craft and related trades workers), but the level of sunlight exposure will be significantly different in those who perform welding work outdoors and those who perform sewing work in a factory. Therefore, a future study will need to reduce the errors in exposure assessments with more detailed occupational classifications. Third, sunlight exposure data from France were used because there are no domestic data on sunlight exposure in the occupational groups. The use of domestically measured sunlight exposure data will provide results that are more accurate. Fourth, it does not reflect some personal risk factors and hazardous substances that affect the incidence of RCC. In RCC, smoking, obesity, and hypertension are known as personal risk factors, and TCE is known as an occupational risk factor [3-6]. Smoking and hypertension were adjusted but obesity and occupational TCE exposure. The risk factors above were overlooked because the participants were not investigated directly but used the data surveyed from other studies. The lack of adjusting the 2 risk factors is a weakness of this study. Fifth, it is possible that memory decay bias and no-response bias influenced the results of the study. The average age of the participants was approximately 55, so it can be difficult to remember exactly 30 years of occupational history. In particular, in the case of non-regular workers or day laborers, the survey on the occupational history may have been inaccurate due to frequent turnover. In addition, jobs with low social prestige may have either refused to participate in the survey or intentionally missed some of their occupational history. In particular, because the survey was conducted through a questionnaire, the accuracy might have been lower than that of the interview.

Despite these limitations, this study is meaningful in that it analyzed the relationship between occupational sunlight exposure and the incidence of RCC in Koreans and found a partial but significant inverse correlation. Future studies need to use occupational sunlight exposure measured in Korea, refine the occupational group, and reflect sunlight exposure in daily life to obtain more reliable results.

CONCLUSIONS

Higher occupational sunlight exposure tends to reduce the risk of developing RCC. Therefore, people who work indoors or have less occupational exposure to sunlight should be exposed to more sunlight through outdoor activities.

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