

A Population-Based Case-Control Study of Occupation and Renal Cell Carcinoma Risk in Iowa

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A case-control study involving 406 incident cases and 2434 controls was conducted in Iowa to examine the association between occupational exposures and renal cell carcinoma risk. After adjusting for major confounders, an increased risk was observed for men among mechanics and repairers (odds ratio [OR] 1.9, 95% confidence interval [CI] = 1.2–2.9); assemblers (OR 2.5, 95% CI = 0.8–7.6); automotive dealership and service station employees (OR 1.9, 95% CI = 0.9–3.9); wholesale traders of durable goods (OR 1.5, 95% CI = 0.7–3.2); farm product vendors (OR 4.4, 95% CI = 1.3–15.5); service organization managers (OR 2.2, 95% CI = 1.0–5.1); financial specialists (OR 2.7, 95% CI = 1.0–7.6); sales occupation supervisors (OR 1.8, 95% CI = 1.0–3.3); guards (OR 5.4, 95% CI = 1.4–20.7); and general farm workers (OR 1.9, 95% CI = 1.0–3.7). Among women, an increased risk was found for employees in depository institutions (OR 3.6, 95% CI = 1.1–11.3); colleges and universities (OR 7.6–95% CI = 2.3–25.6); and retail, including those in grocery stores (OR 2.2, 95% CI = 1.0–4.7). Our results indicate that occupational exposures may increase the risk of renal cell carcinoma. (J Occup Environ Med. 2004;46:235–240)

The incidence of renal cell carcinoma (RCC) has increased during the last several decades in the United States.¹ It was estimated that 29,000 new cases of RCC were diagnosed and 17,000 people died in the United States in the year 2002.² Improving diagnostic technology and better access to medical care are unlikely to be the only explanations for the observed increase.¹ Cigarette smoking, hypertension, and excess weight, established risk factors for RCC, can explain about 50% of cases.^{3,4} Thus, other risk factors remain to be identified.

Employment in several industries and occupations has been linked to RCC risk, including employment in asbestos-related industries,^{5–8} the oil refinery industry and gasoline-related occupations,^{9–12} trichloroethylene and perchloroethylene exposure-related occupations,^{13–16} and the printing and publishing industries.^{17–19} An increased risk of RCC has also been reported among truck drivers,^{20–22} coke oven workers,^{23,24} physicians,²⁵ architects,²⁶ firefighters,²⁷ pulp and paper mill workers,²⁸ pilots and navigators,²⁹ nickel alloys workers,³⁰ and dry cleaners.³¹ Results linking specific job titles or industries to risk of RCC, however, have been inconsistent. To further examine the association between occupational and industrial exposures and risk of RCC in both males and females, we analyzed data from a population-based case-control study of RCC in Iowa.

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Materials and Methods

Study Population

A detailed description of the study population has been published elsewhere.^{32,33} Briefly, a total of 463 histologically confirmed, incident RCC cases in subjects aged 40 to 85 were identified by the State Health Registry of Iowa as being diagnosed between July 1985 and December 1987. Eligible cases were residents of Iowa without previous diagnosis of a malignant neoplasm. Of the 463 eligible cases, 406 (88%) RCC cases participated (261 males and 145 females). These cases were part of a larger study that also included cancers of the bladder, kidney, brain, pancreas, colon, and rectum.

A total of 2434 population-based controls (1601 males and 833 females) was frequency-matched by sex and 5-year age group to all cases in the larger study. Controls under age 65 were randomly selected from computerized state driver's license records. Controls aged 65 years or over were randomly selected from U.S. Health Care Financing Administration listings. As with the cases, persons with a previous cancer diagnosis, other than nonmelanoma skin cancer, were excluded from consideration as controls. The participation rate was 82% for controls younger than 65 and 79% for those aged 65 or over.

Data Collection

We collected information from subjects or next of kin using mailed questionnaires supplemented by telephone interviews. Of the 406 case respondents, 119 (29%) were proxies, and of the 2434 population-based controls, 243 (10%) respondents were proxies. We asked respondents to report all jobs held for at least 5 years since age 16. For each job reported, information was elicited about the job title, the type of business or industry, the year when each job began and ended, and the activities and duties associated with the job. Additionally, we asked respondents to report the usual occupa-

tion held during most of the subject's adult life and to describe the main activities and duties. We coded industries and job titles according to schemes of the 1987 edition of the Standard Industry Classification (SIC)³⁴ and the 1980 Standard Occupational Classification Manual (SOC).³⁵ We also collected information on demographic factors, smoking, past medical history, and first-degree family history of kidney and other cancers. Information on usual adult dietary intakes also was collected through mailed questionnaires.

Data Analysis

Odds ratios (ORs) for RCC associated with jobs held for at least 5 years were calculated separately for males and females using unconditional logistic regression models. ORs and 95% confidence intervals (95% CI) were calculated using SAS statistical software (SAS Institute; Cary, NC). ORs were calculated for all two-digit, three-digit, and four-digit SOC and SIC codes when there were at least five or more exposed cases in one of the sexes. We also evaluated the risk of RCC by duration of employment (<10 years and ≥10 years) in various SOC and SIC categories. The reference category was composed of subjects not employed in the occupation or industry of interest.

The following potential confounders, which showed an impact on the observed ORs, were included in the final regression models: age (40–54, 55–64, 65–74, 75–85 years), body mass index (<24, 24–26, >26 kg/m²), history of tobacco use (ever/never: “ever” included people who ever smoked cigarettes or cigar or pipe, or chewed tobacco products), type of respondent (self-report, proxy, unknown), self-report of a physician-diagnosed history of hypertension (yes/no), red meat intake (<299, 299–436, 437–637, >637 servings per year, unknown), fruit intake (<431, 431–588, 589–858, >858 servings per year, unknown), and

having a first-degree relative with kidney cancer (yes/no). Additional adjustment for education level and other types of cancer in first-degree relatives did not result in a material change in the observed associations. Therefore, these factors were not included in the final models.

Results

The distributions of selected characteristics for cases and controls are presented in Table 1. As described earlier, we frequency matched controls by age and sex to all cases in a larger study. Therefore the age distribution of controls differed from that of RCC cases. Compared with controls, both male and female cases were more likely to smoke, consume more red meat, and were less likely to eat fruits. A higher proportion of cases reported having high blood pressure during their lifetime and having a first-degree relative with kidney cancer among both males and females. Among females, cases were more likely than controls to have an elevated body mass index.

Table 2 presents associations where the 95% CI excludes the null value (1.0), either overall or in one of the duration categories, for RCC in males by industry and occupation using two-, three-, or four-digit SIC and SOC codes. An increased risk was observed among men who worked in meatpacking plants, wholesale trade in durable goods or farm products, automotive dealers and service stations, car dealers, and automotive repair shops. When we considered occupational title, we found an increased risk among men employed as service organization managers; accountants, auditors, and other financial specialists; marketing and sales occupation supervisors; guards; general farm workers; mechanics and repairers; assemblers; as well as garage and service station-related occupations. Risk was increased with increasing duration of employment for some of the industries or occupations. Men who were employed in the printing and pub-

TABLE 1
Renal Cell Carcinoma Cases and Controls by Selected Characteristics

Factor	Men		Women	
	Case (%)	Control (%)	Case (%)	Control (%)
Age (years)				
40–54	48 (18.4)	149 (9.3)	25 (17.2)	93 (11.2)
55–64	84 (32.2)	358 (22.4)	39 (26.9)	190 (22.8)
65–74	89 (34.1)	629 (39.3)	58 (40.0)	276 (33.1)
75–85	40 (15.3)	465 (29.0)	23 (15.9)	274 (32.9)
Body mass index (kg/m ²)				
<24	61 (23.4)	366 (22.9)	46 (31.7)	307 (36.9)
24–26	75 (28.7)	545 (34.0)	24 (16.6)	196 (23.5)
>26	100 (38.3)	581 (36.3)	66 (45.5)	240 (28.8)
Unknown	25 (9.6)	109 (6.8)	9 (6.2)	90 (10.8)
Red meat intake (servings/year)				
<299	31 (11.9)	283 (17.7)	34 (23.5)	229 (27.5)
299–436	58 (22.2)	313 (19.5)	35 (24.1)	175 (21.0)
437–637	61 (23.4)	337 (21.1)	28 (19.3)	155 (18.6)
>637	72 (27.6)	371 (23.2)	33 (22.8)	104 (12.5)
Unknown	39 (14.9)	297 (18.5)	15 (10.3)	170 (20.4)
Fruit intake (servings/year)				
<431	78 (29.9)	345 (21.6)	38 (26.2)	101 (12.1)
431–588	61 (23.4)	338 (21.1)	26 (17.9)	141 (16.9)
589–858	46 (17.6)	295 (18.4)	30 (20.7)	195 (23.4)
>858	30 (11.5)	287 (17.9)	33 (22.8)	216 (25.9)
Unknown	46 (17.6)	336 (21.0)	18 (12.4)	180 (21.6)
Smoking				
Never	42 (16.1)	445 (27.8)	92 (63.5)	574 (68.9)
Ever	219 (83.9)	1156 (72.2)	53 (36.5)	259 (31.1)
First-degree relatives with kidney cancer				
No	237 (90.8)	1,498 (93.6)	123 (84.8)	787 (94.5)
Yes	7 (2.7)	20 (1.2)	7 (4.8)	13 (1.5)
Unknown	17 (6.5)	83 (5.2)	15 (10.3)	33 (4.0)
History of hypertension				
No	129 (49.4)	996 (62.2)	65 (44.8)	437 (52.5)
Yes	105 (40.2)	502 (31.4)	74 (51.0)	315 (37.8)
Missing	27 (10.4)	103 (6.4)	6 (4.1)	81 (9.7)

lishing industry, the transportation equipment industry, and railroad transportation also experienced increased risk; however, the 95% CI included the null value (data not shown).

Table 3 presents statistically significant associations (or OR >2.5) either overall or in one of the duration categories by industry and occupation for females. A significantly increased risk of RCC was found among women employed in food stores, grocery stores, depository institutions, and colleges and universities, as well as those who were employed as sales workers. Women who worked in nursing and personal care facilities and who had miscellaneous administrative support occu-

pations also experienced an increased risk of RCC. Further analyses that excluded proxy respondents showed similar results to those reported above.

Discussion

We found an increased risk of RCC for mechanics and repairers among men, especially for vehicle and mobile equipment, and automobile mechanics and repairers. Men employed in automotive repair shops and automotive dealers and service stations and those who had garage and service station-related occupations also experienced increased risk. Among automobile mechanics, risk associated with long-term employment (≥ 10 years) was greater than

for shorter periods; however, in the broader group of all mechanics, risk was higher among shorter-term workers. Mechanics have been linked to an increased risk of RCC²⁰ and bladder cancer^{36–38} in previous epidemiological studies. Mechanics may be exposed to solvents, gasoline vapors,^{3,39} and mineral oils, which contain additives and contaminants, including polycyclic aromatic hydrocarbons, nitrosamines, chlorinated paraffins, long-chain aliphatics, sulfur, *N*-phenyl-2-naphthylamine, and formaldehyde.⁴⁰ Some of these compounds have been shown to increase RCC risk.^{9–12,23,24}

Two recent large population-based case-control studies from Canada⁴¹ and Germany⁴² also reported an increased risk of RCC from exposure to benzene. The study by Hu et al.,⁴¹ which involved 1279 RCC cases (691 male and 588 female) and 5370 controls, showed that a two times increased risk of RCC associated with occupational exposure to benzene among men. The study by Pesch et al.⁴² from Germany, which involved 935 RCC cases and 4298 controls, also reported that occupational exposure to polycyclic aromatic hydrocarbons was associated with 30% to 50% increased risk of RCC.

Among men, we also found an increased risk of RCC for assemblers with risk increasing with duration of employment. Studies from Germany and the United States (ie, Arizona)^{16,39} have reported an increased risk of RCC for those in metal-related occupations. The studies by Hu et al.⁴¹ from Canada and Pesch et al.⁴² from Germany also showed an increased risk of RCC associated with occupational exposure to cadmium and lead. Exposure to metal dust and various organic solvents may be associated with the development of RCC in assemblers. We found a significantly increased risk of RCC among general farm workers. Two studies from Italy reported an excess risk of RCC among farmers.^{43,44}

TABLE 2

Renal Cell Carcinoma Risk by Duration of Employment for Selected Industry/Occupation in Men (based on 5 or more exposed cases)

Industry/occupation	All		10 years		≥10 years	
	Ca/Co†	OR* (95% CI)	Ca/Co†	OR* (95% CI)	Ca/Co†	OR* (95% CI)
Industry (SIC code)						
Meat packing plants (2011)	11/43	1.5 (0.7–3.1)	5/4	8.7 (1.9–38.7)	6/39	0.9 (0.4–2.3)
Wholesale trade: durable goods (50)	10/41	1.5 (0.7–3.2)	1/14	0.4 (0.0–3.0)	9/27	2.3 (1.0–5.4)
Wholesale trade: farm products (515)	5/8	4.4 (1.3–15.5)	0/1		5/7	5.2 (1.4–19.2)
Automotive dealers and service stations (55)	12/43	1.9 (0.9–3.9)	2/14	1.2 (0.3–5.8)	10/29	2.2 (1.0–4.9)
New and used car dealers (5511)	6/18	3.0 (1.1–8.3)	2/5	5.0 (0.9–26.8)	4/13	2.4 (0.7–8.3)
Automotive repair shops (753)	9/23	2.2 (0.9–5.3)	5/6	5.0 (1.3–19.7)	4/17	1.43 (0.4–4.4)
General automotive repair shops (7538)	7/9	4.0 (1.3–12.2)	5/3	14.4 (2.6–79.0)	2/6	1.3 (0.2–7.0)
Occupation (SOC code)						
Managers; service organizations (135)	10/25	2.2 (1.0–5.1)	5/8	3.1 (0.9–11.1)	5/17	1.8 (0.6–5.3)
Accountants, auditors, and other financial specialists (141)	6/22	2.7 (1.0–7.6)	0/6		6/16	3.7 (1.3–10.7)
Supervisors; marketing and sales occupations (40)	22/103	1.6 (0.9–2.7)	1/24	0.4 (0.1–3.2)	21/79	1.9 (1.1–3.3)
Supervisors; sales occupations, retail (403)	18/70	1.8 (1.0–3.3)	2/16	1.3 (0.3–5.8)	16/54	2.0 (1.0–3.7)
Guards (514)	5/7	5.4 (1.4–20.7)	2/3	3.7 (0.5–29.1)	3/4	7.0 (1.2–40.9)
General farm workers (5612)	15/57	1.9 (1.0–3.7)	8/27	2.2 (0.9–5.4)	7/30	1.6 (0.6–4.2)
Mechanics and repairers (61)	37/118	1.9 (1.2–2.9)	8/25	1.8 (0.7–4.5)	29/93	1.9 (1.2–3.1)
Vehicle and mobile equipment mechanics and repairers (611)	22/61	2.0 (1.1–3.5)	7/10	3.6 (1.2–10.7)	15/51	1.6 (0.8–3.1)
Automobile mechanics (6111)	17/35	2.9 (1.5–5.8)	3/8	2.0 (0.4–9.1)	14/27	3.2 (1.5–6.8)
Assemblers (772)	5/17	2.5 (0.8–7.6)	1/8	0.8 (0.1–8.0)	4/9	4.2 (1.2–15.3)
Garage and service station related occupations (873)	6/20	1.6 (0.6–4.4)	0/8		6/12	3.1 (1.0–9.1)

* Adjusted for age, body mass index, smoking, type of respondent, red meat intake, fruit intake, history of hypertension, and first-degree relative with kidney cancer.

† Cases/controls.

OR, odds ratio; CI, confidence interval.

TABLE 3

Risk of Renal Cell Carcinoma by Duration of Employment for Selected Industry/Occupation in Women (based on 5 or more exposed cases)

Industry/occupation	All		<10 years		≥10 years	
	Ca/Co†	OR* (95% CI)	Ca/Co†	OR* (95% CI)	Ca/Co†	OR* (95% CI)
Industry (SIC code)						
Food stores (54)	6/13	2.9 (1.0–9.0)	5/4	8.4 (1.9–38.1)	1/9	0.6 (0.1–5.7)
Grocery stores (5411)	5/10	3.2 (0.9–11.0)	4/3	8.0 (1.6–41.5)	1/7	0.7 (0.1–8.3)
Depository institutions (60)	5/13	3.6 (1.1–11.3)	3/2	18.8 (2.6–134.4)	2/11	1.5 (0.3–7.5)
Nursing and personal care facilities (805)	5/20	1.2 (0.4–3.8)	4/6	4.0 (0.8–18.8)	1/14	0.3 (0.0–2.6)
Colleges and Universities (8221)	6/8	7.6 (2.3–25.6)	2/2	4.2 (0.5–34.4)	4/5	10.3 (2.4–44.1)
Occupation (SOC code)						
Sales occupations, retail (43)	12/36	2.2 (1.0–4.7)	7/12	3.0 (1.0–9.0)	5/24	1.7 (0.6–5.0)
Sales occupations, other (436)	5/14	3.1 (1.0–9.6)	4/4	8.7 (1.9–38.9)	1/10	0.8 (0.1–7.0)
Miscellaneous administrative support occupations (479)	6/21	2.2 (0.8–6.0)	3/8	3.4 (0.8–15.1)	3/13	1.6 (0.4–6.2)

* Adjusted for age, body mass index, smoking, type of respondent, red meat intake, fruit intake, history of hypertension, and first-degree relative with kidney cancer.

† Cases/controls.

OR, odds ratio; CI, confidence interval.

Somewhat increased risks were observed for workers in various transportation-related occupations, consistent with previous studies.^{20–22} These workers may be exposed to exhaust gas, which contains hydrocarbons that have been associ-

ated with RCC.³ An increased risk of RCC among workers in the printing and publishing industry is consistent with earlier studies.^{17–19,42} There are a number of exposures including printing ink, paper dust, lubricating oil and solvents, sodium carbonate

and hypochlorite, which are used in craft recovery and bleaching processes, as well as asbestos that are related to this industry.

Strengths and limitations of this study should be considered in interpreting results. Chance cannot be

entirely ruled out as a possible explanation for some associations, in view of the small number of exposed cases for several observations. A potential limitation of this study is that multiple statistical comparisons were made by occupation (>160 categories) and by industries (>150 categories). Thus, some increased risks would be expected based on chance alone. However, the results linking RCC risk to working as mechanics and repairers, assemblers with longer duration of employment, and subjects who employed in various transportation-related occupations were consistent with earlier epidemiological studies, suggesting that chance may not be the only explanation for the observed associations.

Potential bias stemming from different proportions of proxy respondents among cases and controls is an unlikely explanation for observed associations. Previous studies have shown that the industries and occupations reported by study subjects or their next-of-kin were in good agreement with industry records.^{45–49} Use of mailed questionnaire instead of face-to-face interview to collect information on job history might introduce misclassification of exposure. The potential exposure misclassification, however, is likely to be nondifferential because the study subjects were not informed of the specific study hypothesis, and non-differential misclassification of exposure would result in an underestimation of the association. The consistency of our study findings involving mechanics and repairers, transportation-related occupations, metal-related occupations, and employment in printing and publishing industries with previous reports also lends confidence to the validity of this study. The population-based study design and relatively high response rates from both cases and controls minimized a potential selection bias. Another strength of this study is that all RCC cases were histologically confirmed, thereby reducing misclassification of disease. Potential informa-

tion bias from proxy respondents is a concern. However, results from additional analyses restricted to direct respondents were similar to findings from the larger study population.

Confounding is an unlikely explanation for the observed associations, since detailed information on lifetime job exposure history and major potential confounding factors suggested by previous studies were collected and controlled in this study.

In conclusion, in this population-based case-control study we observed an increased risk of RCC among mechanics and repairers, employment in automotive dealerships and service stations, assemblers, general farm workers, as well as those in various sales occupations and managers and supervisors. In addition, we also observed an increased risk of RCC for transportation-related occupations, and workers in the printing and publishing industries. Because chance alone cannot be entirely ruled out, these associations warrant further investigation.

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