Pergamon

European Journal of Cancer Vol. 32A, No. 4, pp. 673–682, 1996

Printed in Great Britain
0959–8049/96 $15.00+0.00

0959-8049(95)00633-8

Original Paper

Dietary Risk Factors for Renal Cell Carcinoma in Denmark

A. Mellemgaard,[1] J.K. McLaughlin,[2] K. Overvad[3] and J.H. Olsen[1]

[1]Danish Cancer Society, Division of Cancer Epidemiology, Strandboulevarden 49, DK-2100 Copenhagen, Denmark; [2]International Epidemiology Institute, Rockville, Maryland, U.S.A.; [3]Institute of Epidemiology and Social Medicine, Aarhus University, Denmark

The role of diet in the aetiology of renal cell carcinoma was investigated in a population-based case-control study in Denmark. Cases were 20–79 years old, with a histologically verified diagnosis of renal cell carcinoma. Controls were sampled from the general population and were frequency-matched on age and sex. A total of 351 cases (73% of the eligible) and 340 controls (68% of the eligible) were included in the study. Dietary information was obtained in a self-administered food frequency questionaire and the information was confirmed in a subsequent interview performed by trained interviewers who also elicited information on other suspected risk factors such as smoking, occupation, medical history, education and reproductive history. Logistic regression models were used to calculate the odds ratios, and, both frequency of consumption of various food stuffs and computed nutrients were examined. A positive association was observed between risk of renal cell carcinoma and total energy intake (odds ratio, OR, for highest quartile compared to lowest: 1.7 (95% confidence interval, CI, 1.0–3.0) for men, and 3.5 (95% CI 1.6–6.5) for women), fat intake (OR for highest quartile compared to lowest: 1.9 (95% CI 1.1–3.5) for men, and 3.3 (95% CI 1.6–6.9) for women). For women, an effect was also seen for intake of carbohydrates (OR for highest quartile compared to lowest: 3.2 (95% CI 1.5–6.8), while no protective effect was seen for vegetables or fruit. Dairy products may be associated with risk of renal cell cancer (OR for women using thickly spread butter compared to thinly spread: 11.4 (95% CI 2.8–45), OR for women who drank more than one glass of milk with 3.5% fat content compared to never drink milk: 3.7 (95% CI 1.2–11). As expected, total energy intake, intake of fat, protein and carbohydrates were closely correlated making it difficult to identify one of the energy sources as more closely associated with risk of renal cell cancer than the other. Several energy sources have been identified as possible risk factors for renal cell carcinoma. It is possible that a high energy intake as such rather than the individual sources are responsible for the increased risk. Furthermore, dairy fats may be associated with renal cell carcinoma risk. The observed associations appeared stronger in women, and did not explain the association with obesity and low socio-economic status previously found in Denmark.

Key words: epidemiology, kidney, diet, renal cell carcinoma
Eur J Cancer, Vol. 32A, No. 4, pp. 673–682, 1996

INTRODUCTION

Previously identified risk factors for renal cell carcinoma (RCC) include cigarette smoking, history of hypertension and use of diuretics, occupational exposure to hydrocarbons, early menarche and first birth [1–5]. The role of diet remains unresolved, but two further observations could indicate a role for diet in the aetiology of RCC: the consistently found increase in risk among obese individuals, especially women, and the excess risk recently reported in Denmark among lower socio-economic subjects [2, 6]. Past correlation studies of dietary factors and RCC have found a positive association with animal protein [7, 8]. This association along with those for animal fat and dairy products have been examined in several case-control studies, but little or no association has been observed [9–14]. However, a recent large-scale case-control study reported a significant link with protein intake [15]. A protective effect of vegetables and fruits was observed

Correspondence to A. Mellemgaard.
Received 11 Jul. 1995; revised 9 Nov. 1995; accepted 15 Nov. 1995.

in a study from China [11], but this effect has not been seen in other studies [10, 12, 13, 15]. The present case-control study examines the role of diet in the aetiology of RCC in Denmark.

MATERIALS AND METHODS

The methods of this study have been described in detail previously [2]. Briefly, cases were identified from notifications to the Danish Cancer Registry as well as through repeated review of files in all pathology departments in Denmark. Histologically confirmed cases between 20 and 79 years of age who were born and living in Denmark were included. A total of 482 cases were identified but 44 (9.1%) died before they could be contacted, 26 (5.4%) were too ill, 33 (6.8%) refused to be interviewed, and we were unable to establish contact with 11 (2.3%). The remaining 368 were interviewed by trained interviewers in the subjects' homes, but 10 male and 7 female cases omitted major parts or all of the dietary questions and were excluded, leaving 351 cases for the analysis.

Controls were matched to cases on sex and age in 5-year intervals, and were drawn from the Central Population Register. Of the 500 identified controls, 72 (14.4%) refused to be interviewed, 20 (4.9%) were too ill, and we were unable to establish contact with 12 (2.4%). Among the remaining 396 controls, 40 male and 16 female controls omitted major parts or all of the dietary questions and were consequently excluded from the analysis leaving 340 for the analysis.

Dietary information was obtained by a structured interview using a validated food frequency questionnaire (FFQ) [16, 17]. The FFQ focused on usual adult consumption of foodstuffs, fruits, cakes and beverages. The FFQ was sent to the participants prior to the interview with information on how to fill out the FFQ. Later, the dietary information was checked by trained interviewers who also performed a face-to-face interview to obtain information on other known and suspected risk factors for RCC such as education, past and present occupation, use of medications, smoking history, weight history, reproductive history and medical history.

The dietary questionnaire included 92 food items and portions sizes which encompasses 81% of the average total supply of nutrients in Denmark, and allows reliable ranking of individuals with respect to their nutrient intake [16]. Nutrient intake was calculated by multiplying the frequency of consumption of specific foods by the nutrient content of standard portions for most food and individually indicated portion sizes for some foods (i.e. size of a serving of stew, steamed vegetables, boiled potatoes, or thickness of spreaded butter). Danish food tables and standard recipes were used for the calculation [18]. Missing values were assumed to be zero consumption in the analysis of the calculated nutrients, except for portion-sizes where a median portion size was assumed. Based on the distribution among controls, quartiles of the nutrients were calculated separately for men and women.

Unconditional logistic regression was used to calculate point estimates [odds ratios (OR)] and associated 95% confidence intervals (CI) [19]. All ORs were adjusted for age, and ORs for frequency of different types of main dishes or dairy products were additionally adjusted for cigarette smoking, body mass index (BMI) and socio-economic status (SES), which have previously been identified as possible risk factors in Denmark. For calculated nutrients, ORs were further adjusted for total energy intake [20]. Tests for trend were also used to evaluate the effect of the variables [19]. Trends tests was calculated in models including only the variable in question and age.

RESULTS

Table 1 presents the ORs for RCC by frequency of intake of different types of main dishes, and Table 2 presents the distribution of cases and controls with respect to the variables which were used to control for the effect of smoking, obesity and socio-economic status. In general, no associations were

Table 1. Odds ratio (OR) and 95% confidence intervals (CI) for renal cell carcinoma by frequency of different types of main dishes

	Men					Women				
	Cases	Controls	OR*	OR†	95% CI	Cases	Controls	OR*	OR†	95% CI
Meat										
less than once/week	8	9	1	1		11	14	1	1	
2–3 times/week	39	28	1.6	1.5	0.5–4.4	29	33	1.1	0.9	0.3–2.5
4–5 times/week	84	77	1.2	1.1	0.4–3.2	42	49	1.1	0.9	0.3–2.3
more than 5 times/week	85	83	1.2	1.0	0.4–2.9	53	47	1.4	1.1	0.4–2.9
test for trend, $P=$			0.56					0.33		
Fish										
rarely or never	75	91	1	1		48	55	1	1	
once/week	121	90	1.6	1.7	1.1–2.7	78	72	1.2	1.3	0.8–2.3
more than once/week	20	16	1.5	1.4	0.6–3.1	9	16	0.6	0.5	0.2–1.4
test for trend, $P=$			0.04					0.83		
Vegetarian‡										
rarely or never	158	126	1	1		76	83	1	1	
once/week	36	48	0.6	0.6	0.4–1.1	31	29	1.2	1.4	0.7–2.7
twice/week	14	11	1.0	1.2	0.5–2.8	15	16	1.0	1.1	0.5–2.5
more than twice/week	7	11	0.5	0.6	0.2–1.7	11	14	0.9	1.0	0.4–2.5
test for trend, $P=$			0.10					0.88		

*Adjusted for age. †Adjusted for age, smoking, body mass index and socio-economic status. ‡Some data missing.

Table 2. Number of cases and controls by smoking, body mass index and socio-economic factors

	Men			Women	
	Cases	Controls		Cases	Controls
Smoking (cigarette packyears)					
Never smoked	24	26		51	65
<20	90	118		57	61
20–40	61	66		26	28
>40	49	23		6	4
Body mass index					
<23.1	52	63	<27.2	32	42
23.1–24.5	45	60	27.2–29.6	25	39
24.5–26.4	65	55	29.6–31.7	23	39
>26.4	63	59	>31.7	61	39
Socio-economic status					
I (highest)	16	25		7	22
II	25	40		25	38
III	63	68		55	49
IV	80	78		42	35
V (lowest)	40	25		12	14

Table 3. Odds ratio (OR) and 95% confidence intervals (CI) for renal cell carcinoma by frequency of intake of dairy products

	Men					Women				
	Cases	Controls	OR*	OR†	95% CI	Cases	Controls	OR*	OR†	95% CI
Cheese‡										
rarely or never	22	30	1	1		15	27	1	1	
1–2 servings/day	58	38	2.1	2.1	1.1–4.5	36	41	1.5	1.6	0.7–3.6
3–4 servings/day	63	67	1.3	1.2	0.6–2.5	57	47	2.2	1.9	0.9–4.0
5-6 servings/day	73	62	1.6	1.5	0.8–3.1	27	27	1.8	1.8	0.7–4.3
test for trend, $P=$			0.63					0.110		
Spreads butter‡										
thinly	18	9	1	1		12	29	1	1	
moderately	72	76	0.5	0.5	0.2–1.2	47	42	2.7	2.6	1.1–6.3
thickly	47	26	0.9	0.9	0.3–2.4	17	4	10.3	11.4	2.8–45
test for trend, $P=$			0.51					<.001		
Milk with 3.5% fat‡										
never	123	118	1	1		89	104	1	1	
<1 glass/day	37	39	0.9	0.9	0.5–1.6	13	20	0.8	0.8	0.4–1.8
1 glass/day	25	18	1.3	1.4	0.7–2.8	18	14	1.5	1.6	0.7–3.6
>1 glass/day	31	22	1.4	1.3	0.7–2.5	14	5	3.3	3.7	1.2–11
test for trend, $P=$			0.27					0.04		
Milk with 1.5% fat‡										
never	132	114	1	1		78	89	1	1	
<1 glass/day	31	35	0.8	0.8	0.4–1.4	22	22	1.1	1.0	0.5–2.1
1 glass/day	22	28	0.7	0.6	0.4–1.2	1.9	18	1.2	1.0	0.5–2.2
>1 glass/day	30	20	1.3	1.2	0.6–2.4	15	13	1.3	1.3	0.6–3.0
test for trend, $P=$			0.99					0.42		
Milk with 0.1% fat‡										
never	186	170	1	1		115	115	1	1	
<1 glass/day	9	13	0.6	0.7	0.3–1.8	7	9	0.8	0.7	0.2–2.1
1 glass/day	9	5	1.6	1.9	0.6–6.0	2	12	0.2	0.2	0.0–0.7
>1 glass/day	10	8	1.1	1.5	0.6–4.2	10	6	1.7	1.8	0.6–5.6
test for trend, $P=$			0.71					0.59		

*Adjusted for age. †Adjusted for age, smoking, body mass index and socio-economic status. ‡Some data missing.

Table 4. Odds ratio (OR) and 95% confidence intervals (CI) for renal cell carcinoma by intake of vegetables

	Men					Women				
	Cases	Controls	OR*	OR†	95% CI	Cases	Controls	OR*	OR†	95% CI
Cruciferous‡§										
rarely or never	36	17	1	1		8	12	1	1	
less than once/week	39	48	0.4	0.4	0.2–0.8	21	26	1.2	1.0	0.3–3.1
once/week	101	83	0.6	0.7	0.3–1.3	60	60	1.5	1.2	0.4–3.2
more than once/week	40	48	0.4	0.5	0.2–1.0	44	45	1.5	1.4	0.5–3.9
test for tend, $P=$			0.09					0.41		
Lettuce§										
rarely or never	50	46	1	1		30	24	1	1	
once/week or less	83	77	1.0	1.1	0.6–1.9	46	54	0.7	0.8	0.4–1.7
2–4 times/week	62	42	1.3	1.5	0.8–2.8	39	36	0.9	1.1	0.5–2.4
>4 times/week	20	32	0.6	0.7	0.3–1.4	20	29	0.6	0.6	0.3–1.5
test for trend, $P=$			0.51					0.30		
Potatoes§										
3 times/week or less	45	38	1	1		32	39	1		
4 times/week	31	38	0.7	0.7	0.4–1.3	19	23	1.0	1.3	0.6–2.9
5 times/week	42	35	1.0	1.0	0.5–1.9	24	30	1.0	1.2	0.5–2.6
6 times/week	45	39	1.0	1.0	0.5–2.0	28	22	1.6	1.8	0.8–3.9
7 times/week	51	47	0.9	0.9	0.5–1.8	32	29	1.3	1.5	0.5–3.1
test for trend, $P=$			0.86					0.23		
Fruit										
once/week or less	66	55	1	1		27	24	1	1	
1–2 times/week	113	104	0.9	1.0	0.6–1.5	53	72	0.7	0.6	0.3–1.3
2–3 times/week	24	20	1.0	1.0	0.5–2.0	33	25	1.2	1.3	0.6–2.9
>3 times/week	13	18	0.6	0.6	0.3–1.4	22	22	0.9	0.9	0.4–2.3
test for trend, $P=$			0.34					0.63		

*Adjusted for age. †Adjusted for age, smoking, body mass index and socio-economic status. ‡Cabbage, broccoli and cauliflower. §Some data missing.

observed, although men who ate fish at least once a week had an elevated risk of RCC (P for trend = 0.04), but there was no stepwise increase in risk and no association was seen for women. There was no clear association between intake of various dairy products and risk of RCC among men (Table 3). Among women, however, a high intake of 3.5% fat milk and use of thickly spread butter was associated with an increased risk, while intake of milk with a lower fat content did not confer an increase in risk. The OR for women who used thickly spread butter was approximately 11 (95% CI: 2.9–37). Neither intake of vegetables such as lettuce, potatoes or cruciferous vegetables, nor fruits was associated with risk of RCC, although a slightly lower but non-significant risk was observed for men who ate cruciferous vegetables at least once per week (P for trend = 0.09) (Table 4).

Tables 5–8 presents the findings for the analysis of the calculated nutrients. Total energy (joules) and fat intake was positively associated with risk of RCC in both men and women, although the association appeared stronger in women (Table 5). Intake of protein and carbohydrates was positively associated with risk of RCC in women. The associations were observed even after adjustment for body mass index, smoking and socio-economic status. Additional adjustment for other suspected risk factors such as reproductive and medical history and exposure to hydrocarbons also had no effect on the associations (data not shown). There was a high degree of correlation between intake of various energy sources (Pearson correlation coefficients for men/women respectively; fat–protein: 0.72/0.80, fat–carbohydrates: 0.60/0.72, protein–carbohydrates: 0.60/0.64) making it virtually impossible to separate the effect of one energy source from the other.

Further analysis revealed that the association with fat was restricted to associations with saturated and mono-unsaturated fats in both sexes, while poly-unsaturated fats appeared unrelated to risk of RCC. Cholesterol was not clearly associated with risk (Table 6). The findings for vitamins are shown in Table 7. For men, neither vitamin A, C, D, E nor total carotene was associated with risk of RCC. For women, an association with vitamins A, C and E disappeared after adjustment for total energy intake. Consumption of vitamin supplements during winter was frequent, with approximately half the respondents taking vitamins regularly. There was no relationship between intake of vitamins and risk of RCC, and adjustment for vitamin supplement use did not change the findings for vitamins from foodstuffs (data not shown). The same pattern seen for vitamins was seen for intake of minerals, with no association for men, while an initial association with sodium, potassium, calcium and magnesium among women disappeared after adjustment for total energy intake (Table 8). After adjustment for total energy intake, a negative association with intake of sodium and magnesium was observed in men, but this may reflect overadjustment.

DISCUSSION

We found a positive association between risk of RCC and intake of fat, protein and carbohydrates, indicating that total

Table 5. Odds ratio (OR) and 95% confidence intervals (CI) for renal cell carcinoma by intake of total energy, protein, fats and carbohydrates

	Men						Women				
	Cases	Controls	OR*	OR†	95%CI		Cases	Controls	OR*	OR†	95% CI
Total energy											
<7030 kJ	41	49	1	1		<4919 kJ	17	35	1	1	
7030–8487 kJ	48	49	1.2	1.2	0.7–2.2	4919–6081 kJ	28	36	1.6	1.6	0.7–3.74
8488–10206 kJ	55	49	1.3	1.4	0.8–2.6	6082–7446 kJ	34	36	1.9	2.1	0.9–4.61
>10206 kJ	72	50	1.7	1.7	1.0–3.0	>7446 kJ	56	36	3.2	3.5	1.6–6.5
test for trend, $P=$			0.04						0.001		
Protein											
<54 g	42	49	1	1		<41 g	20	35	1	1	
54–67 g	52	49	1.2	1.2	0.6–2.1	41–50 g	20	36	1.0	0.9	0.4–2.1
68–81 g	69	49	1.6	1.6	0.9–2.9	51–64 g	51	36	2.5	2.5	1.2–5.3
>82 g	53	50	1.2	1.3	0.7–2.3	>64 g	44	36	2.1	2.0	0.9–4.2
test for trend, $P=$			0.31						0.007		
Fat											
<64 g	35	49	1	1		<42 g	21	35	1	1	
64–82 g	50	49	1.4	1.5	0.8–2.7	42–55 g	22	36	1.0	1.1	0.5–2.5
83–105 g	63	49	1.8	1.8	1.0–3.2	56–72 g	30	36	1.4	1.5	0.7–3.2
>105 g	68	50	1.9	1.9	1.1–3.5	>72 g	62	36	2.9	3.3	1.6–6.9
test for trend, $P=$			0.02						<0.001		
Carbohydrate											
<174 g	47	49	1	1		<133 g	21	35	1	1	
174–211 g	53	49	1.1	1.2	0.6–2.1	133–162 g	19	36	0.9	0.7	0.4–2.2
212–255 g	46	49	1.0	1.0	0.6–1.9	163–203 g	35	36	1.6	1.7	0.8–3.7
>255 g	70	50	1.5	1.5	0.8–2.6	>203 g	60	36	2.8	3.2	1.5–6.8
test for trend, $P=$			0.23						<0.001		

*Adjusted for age. †Adjusted for age, smoking, body mass index and socio-economic status.

Table 6. Odds ratio (OR) and 95% confidence intervals (CI) for renal cell carcinoma by intake of fats

	Men						Women				
	Cases	Controls	OR*	OR†	95% CI		Cases	Controls	OR*	OR†	95% CI
Saturated fat											
<26 g	33	49	1	1		<18 g	20	35	1	1	
26–34 g	46	49	1.4	1.4	0.7–2.8	18–23 g	26	36	1.3	1.3	0.5–3.4
35–45 g	66	49	2.0	2.1	1.0–4.4	24–31 g	25	36	1.2	1.4	0.5–4.2
>45 g	71	50	2.1	2.4	1.0–5.4	>31 g	64	36	3.1	3.0	0.9–9.9
test for trend, $P=$			0.005						<0.001		
Mono-unsaturated fat											
<21 g	35	49	1	1		<13 g	19	35	1	1	
21–26 g	53	49	1.5	1.4	0.7–2.8	13–17 g	25	36	1.3	1.3	0.5–3.5
27–33 g	62	49	1.8	1.5	0.7–3.1	18–22 g	30	36	1.5	2.0	0.6–6.2
>33 g	66	50	1.9	1.4	0.6–3.4	>22 g	61	36	3.1	3.9	1.0–14
test for trend, $P=$			0.04						<0.001		
Poly-unsaturated fat											
<9 g	55	49	1	1		<6 g	25	35	1	1	
9–12 g	38	49	0.7	0.6	0.3–1.0	6–8 g	23	36	0.9	0.6	0.2–1.5
13–16 g	69	49	1.3	0.9	0.5–1.6	9–12 g	43	36	1.7	1.0	0.4–2.4
>16 g	54	50	1.0	0.5	0.3–1.1	>12 g	44	36	1.7	0.7	0.3–2.1
test for trend, $P=$			0.61						0.04		
Cholesterol											
<231 mg	38	49	1	1		<166 mg	26	35	1	1	
231–302 mg	59	49	1.6	1.5	0.8–2.7	166–213 mg	15	36	0.6	0.4	0.2–1.0
303–387 mg	53	49	1.4	1.1	0.5–2.1	214–272 mg	25	36	0.9	0.7	0.3–1.6
>387 mg	66	50	1.7	1.2	0.6–2.5	>272 mg	69	36	2.6	1.8	0.7–4.5
test for trend, $P=$			0.11						<0.001		

*Adjusted for age. †Adjusted for age, total energy intake, smoking, body mass index and socio-economic status.

Table 7. Odds ratio (OR) and 95% confidence intervals (CI) for renal cell carcinoma by intake of vitamins A, C, D and E

	Men					Women				
	Cases	Controls	OR*	OR†	95% CI	Cases	Controls	OR*	OR†	95% CI
Vitamin A										
<1043 RE	52	49	1	1		<774 RE	29	35	1	1	
1043–1391 RE	50	49	1.0	0.9	0.5–1.6	774–1017 RE	12	36	0.4	0.3	0.1–0.8
1392–1897 RE	69	49	1.3	1.2	0.7–2.2	1018–1452 RE	37	36	1.2	1.0	0.5–2.2
>1897 RE	45	50	0.8	0.6	0.3–1.2	>1452 RE	57	36	1.9	1.4	0.6–3.0
test for trend, $P=$			0.91						0.005	
Total carotene										
<1558 fg	57	49	1	1		<1448 fg	24	35	1	1	
1558–2561 fg	56	49	1.0	0.9	0.5–1.7	1448–2651 fg	49	36	2.0	2.3	1.1–4.9
2562–3768 fg	40	49	0.7	0.7	0.4–1.2	2652–4241 fg	29	36	1.2	1.2	0.6–2.8
>3768 fg	63	50	1.1	1.1	0.6–2.0	>4241 fg	33	36	1.3	1.3	0.6–2.8
test for trend, $P=$			0.84						0.009	
Vitamin C										
<42 mg	51	49	1	1		<45 mg	20	35	1	1	
42–66 mg	60	49	1.2	1.2	0.7–2.1	45–73 mg	39	36	1.9	1.4	0.6–3.1
67–102 mg	52	49	1.0	0.9	0.5–1.7	74–113 mg	26	36	1.3	1.1	0.5–2.4
>102 mg	53	50	1.0	0.8	0.5–1.5	>113 mg	50	36	2.4	1.7	0.8–3.8
test for trend, $P=$			0.91						0.04	
Vitamin D										
<1.6 fg	37	49	1	1		<1.3 mg	35	35	1	1	
1.6–2.3 fg	55	49	1.5	1.5	0.8–2.8	1.3–1.7 mg	19	36	0.5	0.5	0.2–1.1
2.4–3.3 fg	63	49	1.7	1.5	0.8–2.9	1.8–2.6 mg	43	36	1.2	0.8	0.4–1.4
>3.3 fg	61	50	1.6	1.2	0.6–2.4	>2.6 mg	38	36	1.1	0.6	0.3–1.3
test for trend, $P=$			0.10						0.41	
Vitamin E										
<4.2 TE	56	49	1	1		<3.3 TE	22	35	1	1	
4.2–5.3 TE	45	49	0.8	0.7	0.4–1.2	3.3–4.4 TE	27	36	1.2	0.9	0.4–2.1
5.4–7.3 TE	63	49	1.1	0.8	0.5–1.6	4.5–5.9 TE	35	36	1.6	1.0	0.4–2.4
>7.3 TE	52	50	0.9	0.5	0.2–1.0	>5.7 TE	51	36	2.3	1.1	0.4–3.0
test for trend, $P=$			0.96						0.010	

RE, retinoid equivalents; TE, tocoferol equivalents. *Adjusted for age. †Adjusted for age, total energy intake, smoking, body mass index and socio-economic status.

Table 8. Odds ratio (OR) and 95% confidence intervals (CI) for renal cell carcinoma by intake of sodium, potassium, calcium, magnesium and cholesterol

	Men						Women				
	Cases	Controls	OR*	OR†	95% CI		Cases	Controls	OR*	OR†	95% CI
Sodium											
<1.9 g	60	49	1	1		<1.4 g	23	35	1	1	
1.9–2.4 g	38	49	0.6	0.5	0.2–0.9	1.4–1.6 g	23	36	1.0	0.7	0.3–1.6
2.5–3.1 g	63	49	1.0	0.6	0.3–1.3	1.7–2.0 g	24	36	1.0	0.7	0.3–1.9
>3.1 g	55	50	0.9	0.4	0.2–0.9	>2.0 g	65	36	2.7	1.6	0.6–4.8
test for trend, $P=$			0.89						<0.001		
Potassium											
<2.5 g	49	49	1	1		<2.0 g	25	35	1	1	
2.5–3.1 g	63	49	1.3	1.0	0.6–1.9	2.0–2.5 g	25	36	1.0	0.5	0.2–1.3
3.2–3.7 g	47	49	1.0	0.6	0.3–1.1	2.6–3.0 g	31	36	1.2	0.6	0.2–1.3
>3.7 g	57	50	1.1	0.6	0.3–1.3	>3.0 g	54	36	2.1	0.9	0.4–2.3
test for trend, $P=$			0.92						0.02		
Calcium											
<0.7 g	42	49	1	1		<0.6 g	18	35	1	1	
0.7–1.0 g	54	49	1.3	1.2	0.7–2.4	0.6–0.8 g	26	36	1.4	0.8	0.3–2.0
1.1–1.4 g	61	49	1.4	1.3	0.6–2.5	0.9–1.2 g	45	36	2.4	1.6	0.4–3.8
>1.4 g	59	50	1.4	1.1	0.5–2.4	>1.2 g	46	36	2.5	1.2	0.5–3.1
test for trend, $P=$			0.24						0.005		
Magnesium											
<0.24 g	53	49	1	1		<0.18 g	21	35	1	1	
0.24–0.30 g	58	49	1.1	0.8	0.4–1.5	0.18–0.21 g	26	36	1.2	0.8	0.3–2.0
0.31–0.34 g	49	49	0.9	0.4	0.2–0.9	0.22–0.27 g	42	36	1.9	1.1	0.4–2.6
>0.34 g	56	50	1.0	0.3	0.1–0.8	>0.27 g	46	36	2.1	1.0	0.4–2.8
test for trend, $P=$			0.95						0.01		

*Adjusted for age. †Adjusted for age, total energy intake, smoking, body mass index and socio-economic status.

energy intake rather than individual energy sources is a risk factor. Saturated and mono-unsaturated fat but not poly-unsaturated fat increase the risk of RCC, and dairy fats may in particular play a role in the aetiology of RCC. There was little evidence of a protective effect of vegetables or fruit, and the observed associations were either restricted, or appeared stronger, in women. In multivariate models, these dietary findings do not explain the increased RCC risk among obese individuals nor among lower socio-economic subjects in Denmark.

In the analysis of nutrients, we have presented ORs adjusted for total energy intake, although this may introduce overadjustment. We therefore caution against overinterpretation of the energy-adjusted risk estimates [20]. The main limitation of this study is the potential for recall bias. We have not attempted to validate the information from the cases and controls. A study of long-term dietary recall among cancer cases and controls found that, although there were no major differences between the two groups, cases tended to have a poorer recall of their previous diet. In the same study, education had no effect on quality of dietary recall [21].

An association between intake of dairy products (milk or dairy fat) and risk of RCC ws first suggested by Wynder and associates [7], based on a correlation study of per capita consumption and RCC mortality rates. This observation has been replicated in several succeeding analytical studies [10, 12, 13, 22] while others have found no association [9, 14, 15]. We found a strong association among women which were restricted to dairy products with a high fat content.

In Denmark, as in many other countries with a high incidence of RCC, the average intake of dairy products is relatively high and continues in adulthood [23, 24]. During this century, the consumption of milk in Denmark has been rather stable while consumption of butter fluctuated dramatically during World War II when export of butter, and import of oils for margarine were restricted leading to a transient increase in national consumption. Intake of cheese has been slowly increasing [23]. The steep increase in incidence of RCC which took place in 1960–1970, may possibly result in part from the increased intake of butter in the 1940s, although this coincides with an increase in tobacco consumption, especially cigarettes [25, 26]. Saturated fat was found in one study to be more strongly associated with risk of RCC than other forms of fat [13]. Furthermore, it has been proposed that cholesterol deposits in the kidney, which are also seen in some non-malignant kidney diseases, may play a role in the aetiology of RCC [27]. Both these proposed associations receive some support from the findings in the present study, although further research is clearly needed.

A positive association between intake of protein and risk of RCC has been observed in a number of case-control studies [10–14]. Recently, a significant association was seen in a population based case-control study in Minnesota [15]. Our results are consistent with an increased risk associated with protein intake.

A protective effect of fruits and vegetables, which has been found to reduce risk in studies of cancers other than kidney, has not been convincingly demonstrated by this or other studies of RCC [28]. One Italian study did, however, find a protective effect for carrot consumption [12].

In conclusion, we found that diet may influence the risk of RCC. A high-energy diet from all sources, and more specifically, dairy products, saturated and mono-unsaturated fat increases the risk of RCC, especially among women. We found no associations between risk of RCC and intake of vitamins or minerals. The observed associations with dietary factors do not explain the excess risk observed in obese individuals or among lower socio-economic subjects in Denmark. It is unlikely that the exact nature of the relationship between diet and RCC can be determined in retrospective studies, suggesting the need for large-scale prospective studies in future investigations of this relationship.

1. McLaughlin JK, Mellemgaard A, Lindblad P, *et al.* International renal cancer study. I. Tobacco use. *Int J Cancer* 1995, **60**, 194–198.
2. Mellemgaard A, Engholm G, McLaughlin JK, Olsen JH. Risk factors for renal cell carcinoma in Denmark. I. Role of socioeconomic status, tobacco use, beverages, and family history. *Cancer Causes Control* 1994, **5**, 105–113.
3. Mellemgaard A, Niwa S, Mehl ES, Engholm G, McLaughlin JK, Olsen JH. Risk factors for renal cell carcinoma in Denmark: role of medication and medical history. *Int J Epidemiol* 1994, **23**, 923–30.
4. Mellemgaard A, Engholm G, McLaughlin JK, Olsen JH. Risk factors for renal cell carcinoma in Denmark. III: Role of weight, physical activity, and reproductive factors. *Int J Cancer* 1994, **56**, 66–71.
5. Mellemgaard A, Engholm G, McLaughlin JK, Olsen JH. Occupational risk factors for renal cell carcinoma in Denmark. *Scand J Work Environ Health* 1994, **20**, 160–165.
6. Mellemgaard A, Lindblad P, Schlehofer B, *et al.* International renal cell cancer study. III. Role of weight, height, physical activity, and use of amphetamines. *Int J Cancer* 1995, **60**, 350–54.
7. Wynder EL, Mabuchi K, Whitmore WF. Epidemiology of adenocarcinoma of the kidney. *J Natl Cancer Inst* 1974, **53**, 1619–1634.
8. Armstrong B, Doll R. Environmental factors and cancer incidence and mortality in different countries with special reference to dietary practices. *Int J Cancer* 1975, **15**, 617–622.
9. Armstrong B, Garrod A, Doll R. A retrospective study of renal cancer with special reference to coffee and animal protein consumption. *Br J Cancer* 1976, **33**, 127–136.
10. McLaughlin JK, Mandel JS, Blot WJ, Schuman LM, Mehl ES, Fraumeni JF Jr. A population based case-control study of renal cell carcinoma. *J Natl Cancer Inst* 1984, **72**, 275–284.
11. McLaughlin JK, Gao YT, Gao RN, *et al.* Risk factors for renal cell cancer in Shanghai, China. *Int J Cancer* 1992, **52**, 562–65.
12. Talami R, Baron AE, Barra S, *et al.* A case-control study of risk factors for renal cell cancer in northern Italy. *Cancer Causes Control* 1990, **1**, 125–131.
13. Maclure M, Willett W. A case-control study of diet and risk of renal adenocarcinoma. *Epidemiology* 1990, **1**, 430–440.
14. Krieger N, Marrett LD, Dodds L, Hilditek S, Darlington DA. Risk factors for renal cell carcinoma: results of a population-based case-control study. *Cancer Causes Control* 1993, 4, 101–110.
15. Chow WH, Gridley G, McLaughlin JK, *et al.* Protein intake and risk of renal cell cancer. *J Natl Cancer Inst* 1994, **86**, 1131–1139.
16. Tjønneland A, Overvad K, Haraldsdottir J, Bang S, Ewertz M, Jensen OM. Validation of a semiquantitative food frequency questionaire developed in Denmark. *Int J Epidemiol* 1991, **20**, 906–912.
17. Overvad K, Tjønneland A, Haraldsdottir J, Ewertz M, Jensen OM. Development of a semiquantitative food frequency questionaire to assess food, energy and nutrient intake in Denmark. *Int J Epidemiol* 1991, **20**, 900–905.
18. Haraldsdottir J, Holm L, Jensen JH, Møller A. Dietary habits in Denmark 1985. I. Main results. Publication no 136. Danish National Food Agency, Copenhagen, 1986 (in Danish with an English summary).
19. Breslow NE, Day NE. *Statistical Methods in Cancer Research, Vol I. The Design and Analysis of Case-control Studies.* Lyon, International Agency for Research on Cancer (IARC), 1980.
20. Willet W. Nutritional epidemiology. *Monographs in Epidemiology and Biostatistics, Vol. 15.* New York, Oxford University Press, 1990.

21. Wilkins LR, Hankin JH, Yoshizawa CN, Kolonel LN, Lee J. Comparison of long-term dietary recall between cancer cases and controls. *Am J Epidemiol* 1992, **136**, 825–35.
22. McCredie M, Ford JM, Stewart JH. Risk factors for cancer of the renal parenchyma. *Int J Cancer* 1988, **42**, 13–16.
23. International Dairy Federation. Bulletin of the International Dairy Federation. Consumption statistics for milk and milk products. Brussels, 1994.
24. Muir C, Waterhouse J, Mack T, Powell J, Whelan S, eds. *Cancer Incidence in Five Continents, Vol V.* IARC scientific publications No. 88. Lyon, International Agency for Research on Cancer, 1987.
25. Mellemgaard A, Carstensen B, Norgard N, Knudsen JB, Olsen JH. Trends in the incidence of cancer of the kidney, pelvis, ureter, and bladder in Denmark 1943–88. *Scand J Urol Nephrol* 1993, **27**, 327–332.
26. Nielsen PE, Krarup NB. Consumption of tobacco in Denmark in the period 1920–1975. (Orig in Danish). *Ugeskr Læg* 1976, **41**, 2511–2516.
27. Leary T. Chrystaline ester cholesterol deposits and adult cortical renal tumors. *Arch Pathol* 1950, **50**, 151–178.
28. Steinmetz KA, Potter JD. Vegetables, fruit, and cancer. I. Epidemiology. *Cancer Causes Control* 1991, **2**, 325–357.