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ORIGINAL CONTRIBUTION

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Diet, obesity and risk for renal cell carcinoma: Results from a case control-study in Germany

Ernährung, Übergewicht und Risiko eines Nierenzellkarzinoms: Ergebnisse einer Fall-Kontrollstudie in Deutschland

Summary Increasing incidence of renal cell carcinoma in Western countries raises particular attention to its etiology. Diet may be related to risk for renal cell carcinoma since obesity has been linked with this malignant condition.

A case-control study with 277 incident renal cell cancer patients (ICD 189.0) and 286 population controls was conducted in the Rhein-Neckar-Odenwald area, Germany, in the period of 1989 to 1991. The core study protocol included a face-to-face interview about demographical parameters, previous diseases, medication, tobacco smoking, occupational history, occupational exposures, beverage consumption, and obesity. In addition, study participants were asked to fill in a self-administered food frequency questionnaire with 122 food items to estimate overall food intake. Fifty-six % of the cases and 74 % of the controls participated in this part of the study (n = 155 cases and 212 controls). This was 47 % of the original cases (n = 328) and 56 % of the controls (n = 381). No selection bias could be identified with regard to age group, gender, educational status or recent BMI in the analyzed group compared with the eligible cases and controls.

Relative risk (RR) estimates for tertiles of consumption revealed a significantly increased risk with increasing intake of fat spread (RR of high intake compared to low intake: 1.90 (95 % CI 1.08–3.32)). Increased risk was also found for intake of meat and meat products (RR of high intake compared to low intake: 1.71 (95 % CI 0.96–3.04)) and energy adjusted fat (RR of high intake compared to low intake: 1.64 (95 % CI 0.95–2.83)). A decreased risk was seen with increasing intake of fruit (RR of high intake compared to low intake: 0.40 (95 % CI 0.23–0.69)) and of vitamin C (RR of high intake compared to low intake: 0.62 (95 % CI 0.37–1.05)). Beverage consumption, preparation of food and eating pattern were not linked with risk of renal cell cancer. The relative risk estimates of spreading fat (sauce and vitamin C intake were tested in two models, with and without including BMI as covariate. In both models significant associations of these nutritional variables with risk for renal cell cancer remained.

The current results indicate that specific food pattern associated with obesity explain differences in incidence of renal cell carcinoma in industrialized countries.

Zusammenfassung Der Anstieg der Inzidenz von Nierenzellkarzinomen in den westlichen Ländern erfordert eine besondere Beachtung der Ätiologie dieses Tumors. Ernährung und das Erkrankungsrisiko für ein Nierenzellkarzinom könnten assoziiert sein, da Übergewicht als Risikofaktor für diese Erkrankung in vielen Studien identifiziert werden konnte.

Eine Fall-Kontrollstudie mit 277 inzidenten Nierenkrebsfällen (ICD 189.0) und 286 bevölkerungsbezogenen Kontrollpersonen wurde im Rhein-Neckar-Odenwald-Raum, Deutschland, in der Zeit von 1989–1991 durchgeführt. Das Studienprotokoll umfaßte zunächst ein persönliches Interview über demographische Variablen, frühere Erkrankungen, Medikamenteneinnahme, Rau-

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chen, Berufshistorie, berufsbedingte Expositionen, Getränkeaufnahme und Übergewicht. Zusätzlich wurden alle Studienteilnehmer gefragt, ob sie einen selbstausfüllbaren Häufigkeitsfragebogen mit 122 Nahrungsmitteln ausfüllen würden, um die Nahrungsaufnahme abzuschätzen. 65 % der Fälle und 74 % der Kontrollpersonen beteiligten sich an diesem Studienteil (N = 155 Fälle und 212 Kontrollpersonen). Dies waren 47 % der studienrelevanten Fälle (N = 328) und 56 % der Kontrollpersonen (N = 381). Es konnte keine auffällige Auswahlverzerrung beobachtet werden in bezug auf Altersgruppe, Geschlecht, sozioökonomischen Status oder BMI bei der in diesen Studienteil einbezogenen Gruppe im Vergleich zu allen Fällen und Kontrollpersonen.

Die relative Risiken (RR) für verschiedene Aspekte der Nahrungsaufnahme zeigten ein signifikant erhöhtes Risiko mit einer erhöhten Aufnahme von Streichfetten/Soßen (RR der hohen Aufnahme im Vergleich zur niedrigen Aufnahme: 1.90 (95 % Konfidenzintervall (95 % KI) 1.08–3.32)). Ein erhöhtes RR wurde für die Aufnahme von Fleisch und Fleischwaren beobachtet (RR der hohen Aufnahme im Vergleich zur niedrigen Aufnahme 1.71 (95 % KI 0.96–3.04)) und für energieadjustierte Fettaufnahme (RR einer hohen Aufnahme im Vergleich zu einer niedrigen Aufnahme: 1.64 (95 % KI 0.95–2.83)). Ein vermindertes RR fand sich bei einer erhöhten Aufnahme von Obst (RR einer hohen Aufnahme im Vergleich zu einer niedrigen Aufnahme: 0.40 (95 % KI 0.23–0.96)) und der Vitamin-C-Aufnahme (RR einer hohen Aufnahme im Vergleich zu einer niedrigen Aufnahme 0.62 (95 % KI 0.37–1.05)). Die Aufnahme von Getränken, Zubereitungsmethoden und andere Angaben zum Ernährungsverhalten waren nicht mit dem Risiko des Nierenzellkarzinoms assoziiert. Die RR für den Verzehr von Streichfetten/Soßen und Vitamin C wurden in zwei Modellen getestet, mit und ohne BMI als Kovariable. In beiden Modellen ergaben sich signifikante Beziehungen zwischen den Ernährungsvariablen und dem Risiko eines Nierenzellkarzinom.

Diese Resultate geben Hinweise, daß bestimmte Ernährungsmuster in Verbindung mit Übergewicht herangezogen werden können, um das Auftreten von Nierenzellkarzinomen in industrialisierten Ländern zu erklären.

Key words Renal cell carcinoma – case-control study – fruit – vegetable – meat

Schlüsselwörter Nierenzellkarzinom – Fall-Kontrollstudie – Obst – Gemüse – Fleisch

Introduction

In industrialized countries, the incidence of renal cell carcinoma is slightly increasing. In Europe, high incidence rates can be found, especially in Scandinavian countries. In the USA, areas with a high proportion of Scandinavian or German immigrants exhibit comparatively high incidence rates (4, 10, 14). This increase lead to the question whether or not lifestyle factors are involved in the widely unknown etiology.

Recent epidemiological studies investigated several risk factors, such as smoking, occupation and occupational exposures, previous diseases, and medical drugs, mostly with inconsistent results (20). A consistently reported risk factor for the development of renal cell tumor is obesity measured by body mass index (19, 23, 27). However, the mechanisms for this effect are still unclear, as is the question of whether particular dietary patterns rather than obesity itself are related to increased risk in renal cell carcinoma. The particular research into dietary habits in connection with obesity may clarify etiologic mechanisms but also help to prevent obesity-related cancer risk.

In a population-based case-control study on risk factors for renal cell carcinoma a self-administered food frequency questionnaire had been applied in addition to an interview-based questionnaire about other possible risk factors. The latter questionnaire was used in a framework of an international multicenter study on renal cell cancer. The study included six centers (Australia, Denmark, Germany (Heidelberg and Berlin), Sweden and USA). As dietary patterns are country-specific and strongly associated with national nutritional habits, this article focuses only on the relation between obesity, dietary pattern and the risk for renal cell tumors in Germany.

Material and methods

Subject and material

In the Rhein-Neckar-Odenwald area, comprising about 1.3 million inhabitants, a population-based case-control study on renal cell cancer (ICD: 189.0) on adults (age 20 to 75) was conducted. During January 1989 to July 1991, we identified 328 incident cases, 212 men and 116 women, with histologically confirmed renal cell cancer in 10 urology departments covering the treatment of patients with renal cell carcinoma in the study area. All persons were of German ethnicity. Out of these, 185 men and 92 women participated in the study (84 % of 328), whereas nine cases (3 %) refused to do so and 42 persons (13 %) could not be interviewed for various reasons: 23 were not reported by the physicians within 6 months after diagnosis (one of the inclusion criteria), two patients presented with a secondary kidney tumor, six cases died

before the interview could be performed, two cases interrupted the interview at an early stage, and nine were too ill to be interviewed.

Controls were randomly chosen from the compulsory population register of the study area and frequency matched to the cases for age and gender. They were invited by letter to participate in this study as a control. Of 381 controls approached, 286 (75 %) accepted to be interviewed.

First, an interview was carried out "face-to-face" by trained interviewers using a standardized questionnaire. The questionnaire included detailed questions about demographical parameters, such as marital status, religion, educational level, residential history, previous diseases, family history, drug intake, and questions about lifelong tobacco smoking, occupational history, occupational exposures, beverage consumption, and obesity. After this interview the interviewer handed out a self-administered food frequency questionnaire to each participant with a short introduction about how to fill in the questionnaire. Questionnaires were returned to the responsible person in the ward (for cases) or to the study center by using a prepaid envelope (for controls). Controls were reminded by the interviewer if the food frequency questionnaire had not be sent back. If a case or control person was unable to fill in the food frequency questionnaire, they were supported by the interviewer.

The participation rate for the dietary part of the study differed among the case and control group. The total number of returned questionnaires was 458. Eighty-eight % of the controls (n = 252) returned the questionnaire, but only 74 % of the cases (N = 206) did so. After a first inspection, 28 questionnaires from the case group and 22 from the control group were not included because complete pages had not been filled in.

Dietary data

The food frequency questionnaire was designed to estimate overall food intake. Data from a national food survey were used to identify food items relevant for Germany (11). The introduction section of the questionnaire informed the participants that the period 3 years before the interview had to be addressed.

The questionnaire included 122 different food items. For each of the items an estimate of the usual portion size (low, medium, high in relation to a given standard portion size) and the usual frequency of consumption was requested. Portion size and frequency information were used to calculate food intake of each participant. The quantitative figures for each food item were summarized to broader food groups (Table 1). Nutrient intake was calculated from the amount of individual food items by using a national food table (Bundeslebensmittelschlüssel, distributed by the Institute of Social Medicine and Epidemiology, Federal Health Office, Berlin). For specific food items fat content was asked separately. Additional questions were asked for other dietary habits such as preparations and food preferences (Table 1). Beverage consumption was not included in this dietary questionnaire because a complete history of beverage consumption was performed during the face-to-face interview. Therefore, in the analysis, beverage consumption was handled differently from the diet-questionnaire data and was not utilized for the calculation of energy intake.

Table 1 List of dietary variables included in the analysis

Food groups:	Bread, rice, noodles, vegetables, fruit, legumes, potatoes, milk and milk products, cheese, eggs, spreading fat sauce, fish, meat, meat products, cakes, sweet spreads, salty snacks, nuts, sweets
Nutrients:	Protein, fat, carbohydrates, carotene, vitamin C, calcium, magnesium, phosphate, monosaccharides, disaccharides, polysaccharides, saturated fat, monounsaturated fat, polyunsaturated fat, alcohol
Other dietary variables:	Energy, dietary fiber, cholesterol, percentage of energy from fat, percentage of energy from protein, percentage of energy from carbohydrates, residuals from regressing energy to fat intake, residuals from regressing energy to protein intake, residuals from regressing energy to carbohydrate intake
Dietary habits:	Cooking practices of meat (dark parts), eating dark broiled meat, cutting the fat from meat, eating preferences (low in meat, low in calories, low in salt, low in fat, low in carbohydrates, low in sweets, high in milk products, high in vitamin content, high in mineral content, high in dietary fiber, high in fruit and vegetable, high in meat, fresh products, no food additives, vegetarian diet, high in taste and appearence, normal cuisine, food to serve satiety, low-price foods)

According to preliminary analyses we assumed the current questionnaire's ability to rank participants according to their intake of food groups and nutrients to be similar to other food frequency questionnaires (16). An extended version of this questionnaire has been proofed for its validity and reliability (6).

The self-administration resulted in food frequency questionnaires of different quality. The major problems were missing values of the consumption of a specific food item, and over-estimation of food intake. Therefore algorithms had to be developed by which questionnaires of low quality could be identified and excluded from the total of 408 questionnaires.

We decided to discard all questionnaires for which more than 10 food items with missing information were counted, and, in addition, those which showed a lower energy intake (< 0.97) than the estimated basal metabolic rate (BMR) calculated for this individual (3). This means that we only discarded those questionnaires in which the missing information probably seriously affected the estimates of food and nutrient intake. Forty questionnaires (22 cases and 18 controls) fell into this category and were not further processed. One questionnaire (case) was additionally discarded because the energy intake (without beverages) was more than twice as high as the energy requirements for a respective person with heavy physical activity, expressed in BMR cut points (4.20 times the BMR for men and 3.64 for women (3)). Finally, 155 questionnaires from the case group and 212 from the control group were used in the analysis. The different response rates among cases and controls lead to participation rates of 47 % for cases respectively 56 % for controls of the original study population (328 cases and 381 controls) and of 56 % respectively 74 % of those being successfully interviewed (277 cases and 286 controls). All algorithms of evaluation of the quality of the food frequency questionnaires were developed and applied before risk analysis.

Statistical methods

Data were analyzed by standard methods for case-control studies using unconditional logistic regression models (7). The relative risks (RR) were estimated from the odds ratio coefficients and corresponding 95 % confidence intervals (95 % CI). All relative risk estimates were adjusted for age, gender, educational status, tobacco smoking, and alcohol intake. The educational status was defined from education following the three ranks of graduation of the German school system and occupational training. The combination of education and occupational training was ranked into three levels (low, medium, high) (24). Persons with the lowest educational status level formed the reference group. Three smoking categories were defined: non-smokers (respectively a maximum of 100 cigarettes lifelong, reference category), ex-smokers (smoking stopped at least 5 years prior to the interview), and current smokers. Alcohol intake was categorized into tertiles (low, medium, high consumption). The cut points were derived from the controls. The values were calculated from the lifelong history of beer, wine, and spirit consumption multiplied with the average alcohol concentration in these beverages (0.04 for beer, 0.1 for wine, and 0.36 for spirits). For food and nutrient intake tertiles were used. The cut points for each tertile had been derived from the group of controls and then applied to the cases and controls respectively. Each tertile category reflected persons with low, medium and high exposure. Since food frequency questionnaires are primarily designed to rank subjects, no quantitative figures of the cut points will be given in order to avoid unjustified conclusions since systematic bias with respect to quantitative estimates cannot be ruled out for food frequency questionnaires. Body Mass Indices (BMI) were calculated as the most recent BMI-value at the beginning of the age decade before the disease. The BMI was calculated as weight/height^2 and subdivided into three categories (less than 25, 25 to 26, and 27 and more) for the analysis of the relative risk.

Results

Comparison of specific characteristics of the cases and controls who participated in the interview and of those who completed the self-administered questionnaire is shown in Table 2. There were no substantial differences with respect to gender, age group, educational status and BMI between those who provided adequate food frequency questionnaires and participants who were interviewed.

Relative risks for renal cell carcinoma were estimated for tertiles of food intake (Table 3). A significant inverse association was seen with the intake of fruit and a non significant one with the intake of vegetables. The intake of spreading fat/sauce was significantly associated with risk. Risk also increased, borderline significantly, with the consumption of meat and meat products.

Information of the lifelong intake of alcohol and specific beverages, selected from the interview, showed no significant associations with risk. The estimated relative risks for the highest consumption category for: tea, herbal tea, decaffeinated coffee, soft drinks, and liquor, adjusted for age, gender, educational status, tobacco smoking and for alcohol consumption (in case of non-alcoholic beverages), are: mineral water (RR = 1.30; 95 % CI 0.75–2.26); soft drinks (RR = 1.07; 95 % CI 0.59–1.93); coffee with caffeine (RR = 0.98; 95 % CI 0.56–1.71); coffee without caffeine (RR = 1.48; 95 % CI 0.92–2.40); tea (RR = 0.91; 95 % CI 0.58–1.43); herbal tea (RR = 1.12; 95 % CI 0.71–1.75); alcohol intake in total (RR = 0.90; 95 % CI 0.49–1.00); beer (RR = 1.01; 95 % CI 0.57–

Table 2 Characteristics of cases and controls of the study population participating in the direct interview and in the self-administered part (with complete food frequency questionnaires)

	Cases				Controls			
	Direct Interview		Self-administered FFQ		Direct Interview		Self-administered FFQ	
	n	%	n	%	n	%	n	%
Total	277	100	155	100	286	100	212	100
Gender								
men	185	67	106	68	192	67	148	70
women	92	33	49	32	94	33	64	30
Age groups								
< 55 years	82	30	54	34	79	28	56	26
55–64 years	94	34	53	34	94	33	79	37
> 65 years	101	36	48	31	113	39	77	36
educational status								
high	33	12	18	12	51	18	43	20
medium	191	69	108	70	180	63	132	62
low	53	19	29	19	55	19	37	18
Recent BMI								
≤ 25 BMI	88	32	43	28	121	42	95	45
25 – ≤ 27 BMI	59	21	37	24	70	24	50	24
> 27 BMI	112	40	67	43	89	31	62	30
BMI missing	18	7	8	5	6	2	5	2

1.80); wine (RR = 0.72; 95 % CI 0.41–1.26); liquor (RR = 0.79; 95 % CI 0.51–1.24).

A detailed analysis of the association between nutrients and other food compounds with renal cell carcinoma was performed. Energy intake (excluding alcohol) had no effect on risk. A non significant increased relative risk compared to the first intake tertile was found for the different fat variables. The association was comparatively strong for energy adjusted fat (II. tertile RR = 1.54 (95 % CI 0.89–2.67), III. tertile 1.64 (95 % CI 0.95–2.83), p-value for trend = 0.085) and for percent of energy from fat (II. tertile RR = 1.08 (95 % CI 0.62–1.88), III. tertile 1.53 (95 % CI 0.89–2.62), p-value for trend = 0.109). This tentative abundance of fat intake among cases was counterbalanced by a decreased intake of carbohydrates (energy adjusted carbohydrates: II. tertile RR = 0.72 (95 % CI 0.43–1.19), III. tertile RR = 0.66 (95 % CI 0.39–1.10), p-value for trend = 0.103). Among vitamins, vitamin C (II. tertile RR = 0.82 (95 % CI 0.49–1.36), III. tertile RR = 0.62 (95 % CI 0.37–1.05), p-value for trend = 0.074) as well as carotene intake (II. tertile RR = 1.06 (95 % CI 0.64–1.76), III. tertile 0.64 (95 % CI 0.37–1.10), p-value for trend = 0.119) showed an inverse effect (borderline significant) on risk for the highest tertile of intake. There was no trend in risk among categories for other nutrients or compounds.

The pattern of food consumption identified in this study, and nutrient intake associated with renal cell carcinoma support previous observations from other studies that obesity is linked with this disease. We analyzed whether the observed associations of food and nutrients with risk of renal cell carcinoma are independent from each other and also independent from obesity as indicated by BMI. Table 4 shows the result of two different models that we used to proof this hypothesis. Model I shows that the adjustment of the two variables, "spreading fat/sauce consumption" and "vitamin C intake" by each other did not alter the risk with renal cell carcinoma substantially. The inclusion of obesity, expressed as BMI categories (Model II), had also no influence on risk for renal cell carcinoma by intake of spreading fat/sauce or vitamin C. A significant association existed between BMI and risk of renal cell carcinoma, simultaneously adjusted to the dietary and educational variables. Compared to the reference category of BMI < 25, BMI-category 25 to 26 was associated with a relative risk of 1.70 (95 % CI 0.95 to 3.05), and the BMI-category 27 and more with 2.29 (95 % CI 1.34 to 3.92). The dietary variables being used in the analysis have probably statistically independent effects from BMI status.

The influence of food preparations and food preferences in respect to the risk for renal cell cancer were also investigated with no particular success. Several questions concerning preparation of the consumption of meat (avoid roasted meat, discard dark parts, cat dark parts), or cutting the fat from meat did not show significant associations. The estimation of the relative risk of 19 food preferences (see Table 1) revealed that only one

Table 3 Estimated relative risk* for renal cell carcinoma by intake of food groups based on 155 cases and 212 controls

Food groups	Consumption tertiles			
	I = low**	II = medium	III = high	p-value for trend
	RR	RR (95 % CI)	RR (95 % CI)	
cereals (bread, rice, noodles, salty snacks)	1	1.08 (0.63–1.85)	1.41 (0.82–2.41)	0.212
sweet food items (cakes, sweets, deserts, marmelade, honey)	1	0.70 (0.41–1.20)	0.94 (0.56–1.57)	0.818
milk, milk products, eggs, cheese	1	2.03 (1.17–3.51)	1.31 (0.75–2.33)	0.432
potatoes	1	1.24 (0.75–2.06)	0.68 (0.39–1.18)	0.195
legumes	1	0.79 (0.46–1.35)	1.06 (0.64–1.76)	0.797
vegetables	1	0.95 (0.57–1.58)	0.75 (0.44–1.27)	0.285
fruit	1	0.78 (0.47–1.27)	0.40 (0.23–0.69)	0.001
fish	1	1.29 (0.77–2.17)	1.00 (0.58–1.72)	1.000
fats (spreading fat, sauce)	1	1.59 (0.91–2.78)	1.90 (1.08–3.32)	0.028
meat and meat products	1	1.33 (0.75–2.35)	1.71 (0.96–3.04)	0.064

* adjusted for age, gender, educational status, tobacco smoking and alcohol consumption
** ref category

aspect, the use of low-priced purchases was significantly related to the risk for renal cell cancer (RR 2.17, 95 % CI 1.26 to 3.75). These results were adjusted for age, gender, educational status, smoking and alcohol intake.

Discussion

Renal cell cancer occurrence is relatively rare, but the increase in incidence and mortality in some countries deserve nevertheless particular attention regarding the etiology. However, similar to other cancer sites with a low incidence, results from epidemiological studies are not easy to interpret, in particular when mass phenomena such as obesity or dietary practices are potentially involved.

This study identified for a German population a pattern of dietary intake composed of high fat and low carbohydrates and antioxidants to be associated with risk for renal cell carcinoma. Variables such as protein intake, liquid consumption or the use of dark broiled meat did not appear to be associated with risk of renal cell carcinoma.

A particular problem of this study is the use of a self-administered dietary questionnaire in combination with a time-consuming face-to-face interview. This strategy allowed to study possibly important nutrition co-factors in the etiology of specific cancer sites. However, some particular problems occurred during the study such as differences in refusals of the self-administered and interview part of the study between groups and low data quality of some individuals. Low data quality was addressed according to "ad hoc"-generated procedures before risk analysis. Also, in other studies using self-administered questionnaires data quality seems to be a problem (27). In future studies of this kind efforts should be made to assure complete questionnaires. In this study

Table 4 Estimated relative risk* for renal cell carcinoma by nutrient intake and recent BMI, adjusted by each other and confounder variables

	Model I		Model II	
	RR* (95 % CI)	p-value for trend	RR* (95 % CI)	p-value for trend
Consumption of spreading fat/sauce (tertile)				
low	1	0.016	1	0.027
medium	1.59 (0.90–2.79)		1.57 (0.88–2.79)	
high	2.01 (1.14–3.54)		1.93 (1.08–3.44)	
Vitamin C intake (tertile)				
low	1	0.047	1	0.050
medium	0.80 (0.48–1.34)		0.84 (0.50–1.43)	
high	0.58 (0.34–0.99)		0.58 (0.33–1.00)	
Recent BMI				
> 25	–		1	0.004
25 – < 27	–		1.70 (0.94–3.01)	
> 27	–		2.22 (1.29–3.81)	

* simultaneously adjusted for age, gender, educational status, tobacco smoking and alcohol consumption

Table 5 Recent results regarding nutritional habits and risk for renal cell carcinoma

Author	Type of study (no. of cases/no. of controls)	Meat	Fish	Vegetables	Fruit	Energy	Animal protein	Fat
Chow et al. 1994 (8)	case-control (670/707)	+	+/-	+/-	+/-	+/-	+	+/-
Kreiger et al. 1993 (12)	case-control (518/1381)	+/-	+/-	na	na	na	na	na
McLaughlin et al. 1992 (21)	case-control (154/157)	+ (men) +/- (women)	+/-	- (men) +/- (women)	- (men)	na	na	na
Maclure and Willett 1990 (17)	case-control (203/207 and 605)	+/-	+/-	+/-	+/-	+/-	+	+
Talamini et al. 1990 (24)	case-control (240/665)	+/-	+/-	+/- - (carrots)	+/-	na	na	na
McCredie et al. 1988 (18)	case-control (360/985)	+/-	+/-	na	na	na	na	na
Yu et al. 1986 (30)	case-control (160/160)	+/-	na	+/-	+/-	na	na	na
McLaughlin et al. 1984 (22)	case-control (495/697)	+/-	na	+/-	+/-	na	na	na
Wolk et al. 1997 (29)	case-control (1185/1526)	+/-	+/-	+/-	+/-	+	+/-	+/-

na = not presented; +/- = no significant relationship; - = significant inverse relationship; + = significant positive relationship

recontacts to the cases were restricted because of legal reasons. The comparison of the sub-population having filled in the dietary questionnaire with the original study population interviewed, however, did not show particular differences in terms of socio-demographic variables or obesity status. Therefore there was no indication of a serious selection bias. The ability to detect existing association with risk is reduced by measurement errors that are expected to be similar to other studies. Only strong associations will be identified with certainty.

In the literature, ecological correlations revealed that the incidence of kidney cell carcinoma is positively related to the intake of sugar, meat, milk, fats and oils, calories, animal protein, total protein, total fat, and total energy. Negative correlations were found for cereals, pulses, and vegetables (1). The results of recent case-control studies were shown in Table 5. This table reveals that until now no strong consistent pattern of nutritional habits could be attributed to risk for renal cell carcinoma. Evidence exists for a positive relation of energy/meat/fat/animal protein consumption and risk for renal cell carcinoma and an inverse relation of intake of fruit and vegetables (17, 21), which is in concordance with our findings. All other studies were not able to demonstrate significant results for the listed variables. Our finding that the intake of alcoholic beverages is not related with risk for renal cell carcinoma is supported by other studies (2).

Nearly all studies (20) found that obesity is positively related with risk for renal cell carcinoma. Obesity and dietary pattern are linked together (15). Obesity is also known to interfere with estimates of dietary intake as well as with the well-known phenomenon that obese people tend to underestimate their dietary intake (3). This was particularly observed in methodological studies for recording methods but also assumed for food frequency questionnaires (3). In the current data, BMI and energy intake were not directly correlated (Pearson correlation coefficient $r = .05$, $p = 0.32$) despite that the energy requirement of obese persons need to be higher on average than of non-obese persons (3). In contrast, for the highest BMI category, lower energy intake was reported on average. Mean energy intake were found to be for the lowest BMI category 9.3 MJ, for the second BMI-category 9.1 MJ, and for the highest BMI-category 8.2 MJ when adjusted for gender, age, education, tobacco smoking and alcohol intake. Recently Kuller (13) emphasized that nutritional epidemiology need to develop measurement techniques of nutritional habits which are unaffected by obesity status when the relation between obesity, nutritional factors, and risk for chronic diseases will be investigated. Therefore it cannot be ruled out that – like in other studies – methodological effects influence our conclusion regarding diet and renal cell carcinoma.

In addition to the methodological considerations regarding dietary estimates in groups with different BMI status the differences in eating pattern between obese and non-obese subjects are not well described in the literature. There seems to be the tendency that obesity results from a nutrient composition favoring fat (5) independent of total energy intake. Other research into food patterns revealed that negative correlations exist between a diet rich in fat and intake of fruit and vegetables or vitamin C (26). This may explain why groups with different BMI distributions are positively associated with diets rich in fat and negatively associated with diets rich in fruit and vegetable. However, the etiologic question remains of whether obesity or obesity related food pattern is related to risk for renal cell carcinoma. The answer to this question could not be given within this epidemiological study because various methodological considerations such as misclassification related to BMI status, long induction periods, eating behavior and obesity in young ages will not allow to set up sophisticated statistical models to sort out the variables with the highest prediction. Three options with respect to underlying biological effects need to be realistically considered according to this study: a) The effect of obesity independent of diet, i.e. hormones, b) diet affluent in fat, and c) diet low in fruit and vegetables. The current biological evidence for all three options is small or non existing. Therefore, we need more experimental studies in respect to nutrition and renal cell carcinoma in order to clarify mechanistic aspects (e.g. Clinton et al. (9)).

In addition we have to consider that these nutritional phenomena proposed to be linked with risk for renal cell carcinoma are widespread in Western populations. Therefore, other risk factors beside nutritional factors may be involved in the genesis of renal cell carcinoma. Dietary components seem to be only one risk factor in the etiology of renal cell carcinoma in connection with more specific factors for this disease. The results of this and other studies can be used as guidelines for further experimental research approaches. This study also shows the limitation of nutritional epidemiological approaches using questionnaire data. However the question is raised whether obesity or nutritional factors are causally involved in the pathogenesis of renal cell carcinoma.

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