Eur J Nutr 41 : 35–43 (2002)

ORIGINAL CONTRIBUTION

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Alcohol, cigarette smoking, dietary factors and the risk of colorectal adenomas and hyperplastic polyps – a case control study

Summary *Background & aims* Epidemiological studies on the association between lifestyle factors and the risk of colorectal polyps have led to conflicting results. The aim of the present study was to assess the relationship between alcohol consumption, dietary risk factors, cigarette smoking and colorectal adenomas or hyperplastic polyps, respectively. *Methods* Information on alcohol consumption, a detailed dietary history, cigarette smoking and intake of non-steroidal anti-inflammatory drugs was collected among 502 Caucasian subjects undergoing complete colonoscopy, 207 with colorectal adenomas, 71 with hyperplastic polyps and 224 controls with no polyps. *Results* Using univariate analysis significant risk factors for adenomas were age above 55 years, male sex, BMI > 24 (OR 1.91 [1.26–2.88]), an intake of ham + sausage > 15 g/day (OR 1.87 [1.12–3.11]) and smoking (OR 1.71 [1.17–2.5]). The association with alcohol intake > 7 g/day was not significant (OR 1.42 [0.97–2.07], p = 0.071). In the multiple logistic regression only age > 55 years (OR 2.97 [1.94–4.52]), male sex (OR 2.12 [1.54–3.6]) and smoking (OR 1.56 [1.01–2.39]) were significant risk factors for adenomas. Unexpectedly the mean consumption of alcohol, wine and beer, was significantly lower in subjects in whom adenomas were localized only in the rectum compared to those having adenomas in the sigmoid or in the proximal colon. Significant risk factors in subjects with hyperplastic polyps on univariate analysis were intake of > 15 g of ham and sausage/day (OR 3.70 [1.49–9.19]), smoking (OR 1.79 [1.04–3.06]) and male sex. In the multiple logistic regression only intake of > 15 g/day of ham + sausage and male sex were significant risk factors (OR 3.24 [1.23–140.8] and 1.83 [1.05–318], respectively). *Conclusion* When controlling for other potential risk factors, smoking was the only significant lifestyle risk factor for colorectal adenomas and the intake of ham and sausage > 15 g/day for hyperplastic polyps. The intake of alcohol, wine and beer were markedly higher in subjects with adenomas of the colon compared to those with adenomas in the rectum.

Key words Alcohol – colon cancer – colorectal adenomas – colorectal polyps – nutrition – diet

Received: 16 October 2001
Accepted: 16 January 2002

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Introduction

Cancer of the colon and rectum is the fourth most common cancer in the world [1]. Apart from genetic syndromes that markedly increase the risk of colorectal cancer these carcinomas are thought to have an important environmental etiology.

Colorectal adenomas are currently believed to be the precursors for most colorectal cancers [2, 3]. Since adenomas are intermediate steps in the pathway to colonic adeno-carcinomas they are especially attractive for

studying risk factors important in the early stages of colonic neoplasia.

Epidemiological and experimental evidence, supported by identification of mechanisms, suggests that dietary constituents markedly influence the risk of colorectal cancer. Diets high in total fat, especially high in saturated fat, and diets high in refined sugars are assumed to increase the risk, while certain components of a high-fiber diet are likely to lower the risk of colorectal carcinoma [1] although the association of dietary fiber and colorectal cancer has recently been questioned [4].

Previous studies have examined adenoma risk from alcohol consumption [5] and smoking [6, 7] or both [8, 9]. But most of these studies have been limited in their failure to simultaneously consider other risk factors, especially diet, that might have influenced adenoma risk. In contrast, in other studies examining dietary risk factors of colorectal adenomas alcohol consumption and/or cigarette smoking were not included [10–13].

Colorectal hyperplastic polyps are largely considered to be innocuous lesions and do not give rise to adenomas or carcinomas [14, 15]. However, some investigators have questioned the insignificance of hyperplastic polyps [16, 17]. Until now only two epidemiological studies from the United States have published results on the association of life style factors and the risk to develop hyperplastic polyps [18, 19].

To obtain more detailed information about factors which might influence the risk for colorectal adenomas and hyperplastic polyps, we conducted a case-control study that examined risks from alcohol consumption and cigarette smoking in addition to the influence of energy intake and several dietary factors.

Patients and methods

All adult patients reporting for colonoscopy at the Robert-Bosch Hospital because of occult blood in the stool were eligible for the study. The study was approved by the ethics committee of the Robert-Bosch Hospital and all subjects gave their informed consent to participate in the study.

Exclusion criteria were any of the following: 1) previous colon resection because of other diseases; 2) previous polypectomy of a colon adenoma; 3) age > 80 years; 4) age < 30 years; 5) familial polyposis or history of familial non-polyposis colorectal carcinoma [20]; 6) incomplete examination (i. e., coecum not reached or unsatisfactory colon preparation); 7) colitis of any type (including ulcerative, Crohn's and infectious colitis); 8) any other type of disease that might influence lifestyle, dietary habits, smoking and/or alcohol consumption, such as diabetes, chronic heart failure, coronary heart disease, liver disease (chronic hepatitis, cirrhosis), renal insufficiency, malabsorption or recent weight loss > 3 kg. Subjects with criteria 1 and 2 were excluded to avoid biases that might arise from changes in lifestyle (dietary changes, reduction of alcohol consumption). Individuals belonging to the groups of criteria 4 and 5 were excluded to eliminate polyps known to be genetically mediated. Patients above of 80 years of age were excluded because of increasing difficulties of the patient cooperating in the computer assisted dietary history.

Colonoscopy was performed jointly by a staff gastroenterologist and an experienced endoscopy nurse, neither of whom was aware of the subjects alcohol consumption and dietary habits. The completeness of the colonoscopy was judged either by inspection of the ileocoecal valve or by fluoroscopy. Fluoroscopy was also used for the determination of the localization of the polyps whenever there was doubt regarding the exact position of the tip of the colonoscope. Larger polyps (diameter > 5 mm) were removed by snare. Smaller polyps or raised lesions were resected by biopsy forceps. Following each procedure the endoscopist completed a study report form that indicated size, shape and location of any polyp or suspected malignancy found. Polyps were classified as adenomatous or hyperplastic (= non-adenomatous). Histological assessment was performed routinely by 2 staff pathologists at the Department of Pathology, Robert-Bosch Hospital. International criteria were used for the histologic classification [21]. In this study two case series (case-group 1: adenomatous polyps, case-group 2: hyperplastic polyps) with the same control group were used in the analyses. Controls were defined as individuals with no adenomatous or hyperplastic polyps.

To assess risk factors, all patients were interviewed either before the colonoscopy or, if this was not possible, the day after the procedure was performed by a trained nutritionist using a computerized method of obtaining a diet history. The program of this method is based on the German Food and Nutrient Data Base (BLS). This data base includes 11,000 food items and recipes. For the diet history 300 foods are used that have been shown to contribute importantly to the intake of calories. To improve the estimation of their usual portion size for each item subjects were provided with pictures of small, medium or large serving sizes of the most frequently consumed foods. The method has been validated against data obtained from 7-day diet-records [22]. The patients were asked in detail about their frequency of alcohol consumption and serving size in terms of medium glasses or bottles of wine, 0.3 l cans or bottles of beer or shots of hard liquor. For calculation of mean daily alcohol consumption the following alcohol concentrations (v/v) were assumed: beer 4 %, wine 11 %, hard liquors 40 %. Subjects were classified according to the mean daily alcohol consumption into four subgroups: 1) < 10 g; 2) 10.1–30 g; 3) 30.1–50 g; 4) > 50 g.

All subjects were asked if they had ever smoked reg-

ularly more than two cigarettes per day for more than a year. Those who did were classified as 'smokers', those who did not as 'non-smokers'. Smokers were asked the number of cigarettes per day they were presently smoking, the age at which they started smoking and the average number of cigarettes they smoked during the entire period they smoked. Smokers were classified according to the average cigarettes per day as grade 1 (up to 10 cigarettes/day), grade 2 (11–20 cigarettes/day) and grade 3 (> 20 cigarettes/day). In addition, the subjects were asked regarding present or former frequent (> once per week) or regular intake of non-steroidal anti-inflammatory drugs (NSAID).

A total of 1,110 subjects were asked to participate between March 1995 and October 1997; 485 (43.5 %) were excluded because of one of the aforementioned exclusion criteria No. 1–8. The most common reasons for exclusion were any type of disease that might have influenced life style (criterion No. 8, 34 %), previous colon cancer or colon resection (No. 1, 29.5 %), previous adenoma (No. 2, 25.4 %) and colitis (No. 7, 11.1 %). In addition, 89 (7.9 %) patients refused to participate in the study. Furthermore, the data on 34 (3.1 %) patients with colorectal cancer are not reported because at least 14 of these patients had been symptomatic for two months or more which might have influenced their dietary habits and alcohol consumption. Two-hundred and seven cases with one or more adenomatous polyps and 71 cases with hyperplastic polyps and no adenomas were included. A total of 224 controls were identified. All subjects completed the interview but in one subject of both the control and the hyperplastic polyps groups data on some items were lacking (specified in the results section).

Data management and statistical analysis

The data were entered into a computerized database at the coordinating centre (University of Hohenheim). After closing of the database the data were transferred to the IMI for further data processing.

Non-normally distributed continuous variables are expressed as median and 10^{th}–90^{th} percentile range and compared between cases and controls using the Mann-Whitney U-test or the t-test of logarithmic transformed values. Discrete variables are expressed as numbers and percentage, and compared using Fisher's Exact Test. Data are presented with nominal two-tailed p-values (unadjusted for multiple comparisons). Because of the sex differences the descriptive results are reported separately for female and male groups. In the further analysis only variables of which the test comparing cases and controls showed p-values < 0.05 were selected to be statistically significant. Prior to the analysis the selected risk variables were tested in categories. The following variables were included: age (≤ 55, > 55 years), sex, body mass index (≤ 24, > 24), smoking (ever, never), intake of ham and sausage (≤ 15 g/day, ≥ 15 g/day), alcohol intake (≤ 7 g/day, > 7 g/day). All cut-off points were found in post hoc analysis. The Mantel-Haenszel method was used to estimate odds ratios and corresponding 95 percent confidence intervals for the risk factors (univariate analysis). A stepwise forward unconditional regression analysis was used to estimate odds ratios and corresponding 95 percent confidence intervals (multiple analysis). Patients without complete data were excluded from the multiple analysis. All tests were performed using SAS software (version 6.12.; SAS Institute, Cary, NC).

Results

The demographic characteristics of the study groups are shown in Table 1. Controls and patients with adenomas were comparable with respect to intake of energy, fat, protein, carbohydrates and alcohol. However, patients with adenomas had a higher body mass index (BMI) than controls, were older, were also likely to be male and smokers. Patients with hyperplastic polyps were not different from controls with respect to age, BMI and intake of energy, fat, protein and carbohydrates (Table 1). They drank more alcohol and were more likely to be male and smokers.

Table 1 Descriptive characteristics of the study population

	Control (n = 224)	Adenoma (n = 207)	Hyperplastic polyps (n = 71)
Age (yr)	55 (39–71)	62 (49–73)[u, 5]	58 (46–70)
Out-patients (%)	69.2	63.8	76.1
Men (%)	35.7	57.5[f, 3]	52.1[f, 2]
Body mass index	25.0 (21.0–29.7)	25.8 (21.9–30.5)[t, 3]	25.9 (21.9–30.3)
Energy intake (KJ/day)	9580 (6741–13214)	10027 (6730–14314)	10335 (7097–14811)
Fat intake (g/day)	94 (63–147)	101 (62–149)	98.6 (60.5–174.7)
Protein intake (g/day)	81.3 (56.6–119.8)	84.9 (56.4–117.6)	85.8 (62.7–142.4)
Carbohydrate intake (g/day)	238 (156–336)	242 (153–376)	236 (146–335)
Alcohol intake (g/day)	6.6 (0–41.2)	8.5 (0–55.7)	12.1 (0.5–55.2)[u, 4]
Present smoker (%)	14.8[a]	14.5	17.1[b]
Smoker or previous smoker (%)	39.9[a]	53.1[f, 3]	54.3[b, f, 1]

Data given as median, 10^{th}–90^{th} percentile range, unless otherwise noted
All tests compared to control:
[u] Mann-Whitney U test
[t] t-test of logarithmic transformed values
[f] Fisher's Exact Test
p-values: [1] p = 0.039, [2] p = 0.018, [3] p = 0.007, [4] p = 0.002, [5] p < 0.001
[a] n = 223
[b] n = 70 (missing values excluded)

Table 2 Intake of nutrients and alcohol and smoking habits in controls and subjects with adenomas according to sex

	Men (n = 199)		Women (n = 232)	
	Control (n = 80)	Adenoma (n = 119)	Control (n = 144)	Adenoma (n = 88)
Age (yr)	54.5 (36.5–71.5)	61 (49–72)[u]	55.5 (40–71)	66 (52–73)[u]
Body mass index	25.7 (22.1–30.3)	26.1 (22.6–30.8)[t]	24.5 (20.4–30.1)	25.1 (20.8–30.5)
Alcohol intake (g/day)	19.8 (1.0–58.7)	19.2 (0.3–62.8)	2.9 (0–22.2)	2.7 (0–21.6)
Beer intake (ml/day)	214 (0–990)	214 (0–1000)	0 (0–200)	0 (0–143)
Wine intake (ml/day)	71 (0–397)	57 (0–400)	10 (0–146)	17.5 (0–250)
Present smoker (%)	19.0[a]	17.7	12.5	10.2
Ever smoked (%)	57.0[a]	68.1	30.6	33.0
Energy intake (KJ/day)	10978 (8290–14818)	11117 (7809–14820)	8366 (6524–12098)	8818 (5839–12056)
Fat intake (g/day)	106 (77–150)	113 (70–154)	83 (60–129)	89 (51–127)
Protein intake (g/day)	96.9 (68.1–135.4)	92.2 (62.4–124.7)	74.7 (55.0–108.3)	77 (50.6–104.9)
Carbohydrate intake (g/day)	258 (184–358)	258 (157–390)	224 (147–322)	225 (138–325)
Fiber intake (g/day)	26.6 (16.5–37.2)	24.9 (14.5–40.0)	24.4 (14.6–34.8)	22.0 (15.5–33.7)
Sausage and ham intake (g/day)	63.5 (14.5–145.0)	63 (14–155)	33.5 (4–90)	37.5 (7–83)
Vitamin C intake (mg/day)	116 (65–185)	114 (62–232)	126 (68–225)	120 (64–234)
β-Carotene intake (mg/day)	3.2 (1.8–6.7)	3.1 (1.6–5.8)	3.5 (1.9–5.9)	3.4 (1.8–5.3)
Iron intake (mg/day)	16.8 (12.0–23.2)	15.8 (11.3–23.0)	13.3 (9.9–18.6)	13.1 (8.8–18.8)

Data given as median, 10^{th}–90^{th} percentile range, unless otherwise noted
All tests compared to control:
[u] Mann-Whitney U test: $p \leq 0.001$
[t] t-test of logarithmic transformed values: $p = 0.041$, all other tests: $p > 0.05$
[a] n = 79

The median of daily alcohol consumption in the adenoma group was 29 % higher than in the controls but the difference was not significant (Table 1). The higher values of alcohol consumption in the adenoma group is likely to be due to the higher alcohol consumption by males (Table 2) and the predominance of male sex in the adenoma group (Table 1). No significant differences in the mean consumption of alcohol, beer or wine between controls and the adenoma group were found when the data were calculated for both sexes separately (Table 2). Adenomas were not associated with the categorized consumption of alcohol, wine, beer or hard liquors (Table 3). In individuals with hyperplastic polyps, the median daily alcohol intake was 83 % higher compared to that in the controls ($p = 0.002$; Table 1). In parallel to the situation in the adenoma group (Table 2), this difference is explained by the higher alcohol consumption in the males (Table 4).

In the total group, adenomas were not associated with present smoking (Table 1). The percentage of subjects who smoked or were previous smokers was higher in the adenoma group ($p = 0.007$) and in the group with hyperplastic polyps ($p = 0.039$) compared to the controls (Table 1). Again this difference was not significant when the data were analyzed separately for men and women (Tables 2 and 4). There was also no significant relationship between adenomas and the mean number of cigarettes smoked per day (data not shown).

Male sex was associated with a significantly higher intake of alcohol, beer and wine, and smoking compared to females (Table 2; for all differences $p < 0.015$). These differences were found for both the control and the adenoma group. Male sex was also associated with higher intake of energy and fat in both the control and the adenoma group (Table 2). Similar differences between males and females were found for the same variables in the group with hyperplastic polyps (Table 4).

The fiber intake was similar in the subjects with both groups of polyps compared to the controls of both sexes (Tables 2 and 4).

Furthermore, the prevalence of subjects taking

Table 3 Consumption of alcohol, wine and beer in the three study groups

	Controls (n = 224) abs.[a] (%)	Adenoma (n = 207) abs. (%)	Hyperplastic polyps (n = 71) abs. (%)
Alcohol intake per day (g)			
< 10 g	135 (60.3)	108 (52.2)	31 (43.7)
10–29.9	53 (23.7)	54 (26.1)	20 (28.2)
30–49.9	21 (9.4)	21 (10.1)	9 (12.7)
> 50 g	15 (6.7)	24 (11.6)	11 (15.5)
Wine intake per day (l)			
< 0.2	187 (83.5)	165 (79.7)	52 (73.2)
0.2–0.499	28 (12.5)	32 (15.5)	14 (19.7)
> 0.5	9 (4.0)	10 (4.8)	5 (7)
Beer intake per day (l)			
< 0.3	185 (82.6)	161 (77.8)	54 (76.1)
0.3–0.999	29 (15.9)	33 (15.9)	13 (18.3)
≥1	10 (4.5)	14 (6.8)	9 (5.6)
Hard liquor intake per day (ml)			
0	190 (84.8)	162 (78.3)	57 (80.3)
1–3	21 (9.4)	20 (9.7)	8 (11.3)
≥4	13 (5.8)	25 (12.1)	6 (13.6)

[a] *abs.* absolute

Table 4 Intake of nutrients, alcohol and smoking habits in controls and subjects with hyperplastic polyps according to sex

	Men (n = 117)		Women (n = 178)	
	Control (n = 80)	Hyperplastic polyps (n = 37)	Control (n = 144)	Hyperplastic polyps (n = 34)
Age (yr)	54.5 (36.5–71.5)	58 (46–69)	55.5 (40–71)	59.5 (48–72)
Body mass index	25.7 (22.1–30.3)	25.9 (23.1–30.3)	24.5 (20.4–30.1)	25.5 (20.9–30.4)
Alcohol intake (g/day)	19.8 (1.0–58.7)	29.2 (1.5–60.5)	2.9 (0–22.2)	6.1 (0.1–29.6)
Beer intake (ml/day)	214 (0–990)	107 (0–1000)	0 (0–200)	0 (0–286)
Wine intake (ml/day)	71 (0–397)	107 (0–500)	10 (0–146)	43.5 (0–343)
Present smoker (%)	19.0[a]	16.2	12.5	18.2[b]
Ever smoked (%)	57.0[a]	75.7	30.6	30.3[b]
Energy intake (KJ/day)	10978 (8290–14818)	10282 (8114–15704)	8366 (6524–12098)	8491 (6508–11698)
Fat intake (g/day)	106 (77–150)	108 (69–175)	83 (60–129)	85 (55–120)
Protein intake (g/day)	96.9 (68.1–135.4)	96.2 (65.5–158.3)	74.7 (55.0–108.3)	74.5 (60.3–109.8)
Carbohydrate intake (g/day)	258 (184–358)	215 (187–371)	224 (147–322)	207 (120–318)
Fiber intake (g/day)	26.6 (16.5–37.2)	26.1 (16.7–41.7)	24.4 (14.6–34.8)	21.5 (13.8–31.8)
Sausage and ham intake (g/day)	63.5 (14.5–145.0)	72 (17–173)	33.5 (4–90)	49.5 (23–96)[u]
Vitamin C intake (mg/day)	116 (65–185)	109 (69–172)	126 (68–225)	97.5 (56–201)[t]
β-Carotene intake (mg/day)	3.2 (1.8–6.7)	3.4 (1.7–7.4)	3.5 (1.9–5.9)	2.6 (1.8–4.8)
Iron intake (mg/day)	16.8 (12.0–23.2)	16.2 (11.1–25.0)	13.3 (9.9–18.6)	12.8 (10.2–17.9)

Data given as median, 10th–90th percentile range, unless otherwise noted
All tests compared to control:
[u] Mann-Whitney U test: p = 0.03
[t] t-test of logarithmic transformed values: p = 0.02, all other tests: p > 0.05
[a] n = 79
[b] n = 33

NSAID in the group with adenoma (13.1 %) was not significantly different from that of the control group (9.4 %)

Using univariate analysis, the risk for adenomas was increased (OR 1.91) in subjects with BMI values above normal (> 24) and in those with regular intake of > 15 g of sausage and ham per day (Table 5). There was also an increased risk of colorectal adenomas for those subjects who drank more than 7 g alcohol/day (OR 1.42); however, the difference was not significant (p = 0.071; Table 5). Furthermore, an increased adenoma risk was also found for subjects who smoked (OR 1.71; p = 0.006).

In the stepwise multiple logistic regression earlier or present smoking remained as the only significant risk factor for adenomatous polyps (age and sex-adjusted OR: 1.56, Table 5). No other interactions between the explanatory variables in the final model were found.

When the intake of alcoholic beverages and the smoking habits in the patients with adenomas were analyzed with respect to the location of the polyps, subjects with one or more adenomas localized only in the rectum exhibited pronounced differences compared to subjects who had polyps in the more proximal parts of the large bowel (Table 6). The consumption of alcohol,

Table 5 Analysis of risk factors for colonic adenomatous and hyperplastic polyps

	Univariate odds ratio M			Multivariate odds ratio L		
Risk factor	OR	95 % CI	p	OR	95 % CI	p
Adenomatous polyps						
Age > 55 yrs	2.59	1.74–3.84	0.001	2.97	1.94–4.52	0.001
Male sex	2.43	1.65–3.59	0.001	2.12	1.54–3.60	0.001
BMI > 24	1.91	1.26–2.88	0.002	–	–	–
Intake of ham and sausage > 15 g/day	1.87	1.12–3.11	0.016	–	–	–
Smoker or previous smoker	1.71	1.17–2.50	0.006	1.56	1.01–2.39	0.043
Alcohol intake > 7 g/day	1.42	0.97–2.07	0.071	–	–	–
Hyperplastic polyps						
Age > 55 yrs	1.72	1.00–2.96	0.051	–	–	–
Male sex	1.96	1.15–3.35	0.014	1.83	1.05–3.18	0.032
BMI > 24	1.39	0.79–2.46	0.260	–	–	–
Intake of ham and sausage > 15 g/day	3.70	1.49–9.19	0.005	3.24	1.23–140.8	0.018
Smoker or previous smoker	1.79	1.04–3.06	0.035	–	–	–
Alcohol intake > 7 g/day	1.42	0.97–2.07	0.071	–	–	–

M OR and 95 % CI estimated by Mantel-Haenszel method, p-value of Cochran-Mantel-Haenszel test
L OR and 95 % CI estimated by Stepwise Forward Logistic Regression, p-value of Wald Chi-Square test

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Table 6 Adenoma localization; data on age, sex, BMI, alcohol intake and smoking habits

	Rectum (n = 23)	Sigma plus descending colon (n = 73)	Colon proximal of splenic flexure (n = 43)
Age (yr)	59 (48–71)	61 (50–72)	66 (48–75)
Women :Men	12 :11	31 : 42	18 : 25
Body mass index	26.4 (22.4–29.4)	25.4 (22.4–30.5)	26.3 (21.7–31.3)
Alcohol intake (g/day)	1.4 (0–12.5)	12 (0.1–58.2)[u, 4]	8.2 (0–44)[u, 1]
Wine intake (ml/day)	0 (0–107)	71 (0–400)[u, 1]	36 (0–400)
Beer intake (ml/day)	0 (0–71)	43 (0–858)[u, 3]	29 (0–600)[u, 2]
Hard liquor intake (ml/day)	0 (0–1)	0 (0–6)	0 (0–4)
Present smoker (%)	80.7	9.6	4.7
Ever smoked (%)	43.5	53.4	51.2

Data given as median, 10th–90th percentile range, unless otherwise noted
All test compared to rectum:
[u] Mann-Whitney U test
[t] t-test of logarithmic transformed values
p-values: [1] p = 0.02, [2] p = 0.004, [3] p = 0.002, [4] p < 0.001

wine and beer was significantly lower in those subjects in whom adenomas were localized only in the rectum compared to patients having adenomas in the sigma and descending colon or the colon proximal of the splenic flexure (Table 6). The same differences were observed when the data were calculated as mean values ± SEM (Fig. 1) instead of median and 10th–90th percentile. The consumption of alcohol in the subjects in whom adenomas were localized only in the rectum was also significantly lower when the calculation was performed for both sexes separately (men p = 0.003, woman p = 0.02). Since in the group with hyperplastic polyps 94.3 % of the lesions were localized in the rectum and distal part of the sigmoid, no attempt was made to analyze the influence of the location in this group.

The size of the adenoma, or of the largest adenoma if more than one polyp was present, was up to 5 mm in 74 cases and more than 5 mm in 127 cases. In 32 of the latter group the diameter of the polyp was over 20 mm. There was no association between the size of the adenoma and the variables mentioned in Tables 1 and 2. There was also no significant association between the histologic type of the adenoma and these variables. In most cases the adenoma were of tubular type (60.4 %), 35.8 % were tubulo-villous and 3.8 % were villous.

There was no association between intake of various micronutrients, such as vitamin C, beta-carotene and iron (Table 2), alpha-tocopherol, the B-vitamins, zinc, magnesium and calcium and adenomas or hyperplastic polyps (data not shown).

Using univariate analysis the risk for hyperplastic polyps was markedly increased in subjects with regular intake of > 15 g of sausage and ham per day (OR 3.70; Table 5). There was also an increased risk of hyperplastic polyps for those subjects who drank more than 7 g alcohol/day (OR 1.93) and in those who smoked (OR 1.79; Table 5). BMI, present smoking and the three types of alcoholic beverages were not significantly associated with the risk of hyperplastic polyps in univariate analysis but male sex was a significant risk factor (Table 5).

In the stepwise multiple logistic regression only intake of ham and sausage > 15 g/day and male sex remained significant risk factors for hyperplastic polyps (OR 3.24 and 1.83, respectively; Table 5).

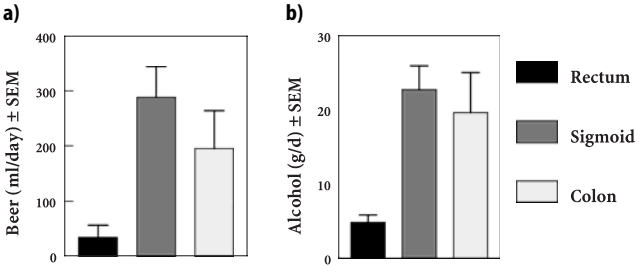

Fig. 1 Mean consumption of beer (**a**) and total alcohol intake (**b**) in subjects in whom adenomas were exclusively found in the rectum (n = 23) compared to subjects in whom adenomas were localized in the sigmoid + descending colon (sigmoid; n = 73) or in the colon proximal the splenic flexure (colon; n = 43). Mean values ± SEM.

Discussion

The association between alcohol consumption and colorectal cancer has been investigated in many studies [reviewed in 1, 23]. It was concluded that high alcohol consumption probably increases the risk of cancers of the colon and rectum. The effect seems to be related to total ethanol intake irrespective of the type of alcoholic beverages. In some studies alcohol intake, especially intake of beer, was directly related to the risk of rectal carcinoma with only a weak or no association between alcohol consumption and carcinoma of the colon [23–25].

The published data on the association between alcohol consumption and the risk of colorectal adenomas are less homogeneous. Alcohol consumption has been

shown to be a significant risk factor for colorectal adenomas in some studies [5, 9, 27]. In other studies no significant association between alcohol consumption and the risk of colorectal adenomas was observed [11, 28] or only one type of alcoholic beverage (beer [8] and hard liquor [29]) was a risk factor but not total alcohol intake. Some of the studies have been limited in their failure to simultaneously consider other factors, such as diet [5, 8] or smoking [11, 28] that might have influenced adenoma risk. The results of additional studies might have been influenced by the fact that the information was restricted to patients who underwent sigmoidoscopy [30] or that sigmoidoscopy or coloscopy were alternatively performed [28]. In two studies in which the data were analyzed separately according to sex, alcohol was found to be a significant risk factor of colorectal adenomas in males but not in females [8, 30].

In the present study alcohol consumption was only a 'borderline' significant risk factor for colorectal adenomas when univariate analysis was applied. When controlling for sex, age, smoking and dietary variables that afford to influence colon cancer susceptibility [1], total alcohol intake was no longer a risk factor. When the type of alcoholic beverage was evaluated separately there was also no significant association with adenoma risk.

Regarding the only borderline association between alcohol consumption and adenoma risk several factors may be considered. First, there is the opportunity for underestimation of consumption. Since drinking may be considered socially unacceptable the latter can not be ruled out with certainty. The fact that the percentage of patients in the present study consuming larger amounts of alcohol regularly (> 50 g/day) is well within the range estimated for the general adult population of Germany (8–10 %; [31]) supports the assumption that the data obtained on alcohol consumption do not markedly deviate from the real values. In addition, the interview technique used to estimate alcohol intake was judged to be reliable in earlier studies [22, 32]. Second, in a given population both the average daily consumption and the percentage of subjects drinking more than 'moderate' amounts of alcohol (30–40 g/day) might be important whether or not alcohol consumption influences the risk of colorectal adenomas. In two studies in which information regarding the latter points is given, the mean daily alcohol consumption [5] and the percentage of the subjects drinking more than 30 g alcohol/day [5, 30] are similar to the data of the present study. In one of these two studies alcohol consumption was found to be a risk factor for colorectal adenomas [5], while in the other study no significant association was seen [30]. In the majority of published series, information regarding average daily alcohol consumption and the percentage of subjects drinking more than 30–40 g of alcohol/day is lacking [8, 9, 11, 28, 29].

For several types of alcohol-induced organ injury, such as alcoholic liver disease and alcoholic pancreatitis, significant correlations between the average alcohol intake and the incidence of disease have been found [33]. The assumption that mainly the consumption of large quantities of alcohol (more than 80 g/day) may be a risk factor for colorectal adenomas is supported by the results of two studies [9, 34]. If only chronic alcohol abuse (more than 80 g/day) is a risk factor for colorectal adenomas, the number of subjects in the present study might be too small to detect a significant association (β error).

In the present study, subjects in whom exclusively rectal adenomas were found, the mean alcohol intake was significantly lower compared to control groups in which adenomas were localized in the colon (Table 6; Fig. 1). The difference was predominantly due to a lower mean intake of beer and wine. This is an unexpected finding since data from some studies on the association between alcohol consumption and carcinoma in the colon and rectum gave support to a closer association between alcohol consumption, especially the consumption of beer, and rectal carcinoma [23–26]. The reverse situation has, however, also been reported with a significant association between alcohol intake and colon carcinoma without increase in rectal carcinoma [34]. To the best of our knowledge the association of alcohol consumption and localization of adenomas in different parts of the large bowel has not specifically been studied before.

In the adenoma group of the present study, the percentage of smokers or previous smokers was higher compared to the controls. The association between smoking and adenoma risk observed in the present study on univariate analysis was also significant when the data were evaluated by stepwise logistic regression. This finding is in accordance with the results of most earlier studies in which patients with colorectal adenomas were more likely to have been smokers compared with controls [5–8, 28, 29, 35, 36]. However, most of these studies did not control for co-variates [5–8, 35, 36] In a few other studies no association between cigarette smoking and adenoma risk was found [9, 27]. An association between smoking and colorectal cancer occurrence has been extensively studied in both cohort and case control studies but the evidence remains inconclusive, and no definite conclusion can be drawn until now [15, 16, 37–39] More recently it has been assumed that the association between cigarette smoking and risk of colorectal cancer may have been masked by inclusion of subjects with adenoma in the control group [40].

For the manifold positive and negative associations which have been reported for dietary factors and colorectal adenomas [4, 10–13, 27], none was significant in the present study when the data were analyzed by multivariate analysis. On univariate analysis the only positive association with adenomas was found for subjects

who consumed on average more than 15 g of ham and sausages per day. The intake of ham and sausages was selected as a measure of red meat in the present analysis of the dietary habits because these items lead to a better separation from other types of meat in the population under investigation. The advantage of this selection is underlined by the fact that in a coincident case-control study on lifestyle risk factors for colorectal adenomas from Germany [29] the average consumption of red meat was determined to be markedly lower (24 ± 16 g/day in controls, 28 ± 20 g in cases) than the mean intake of ham and sausage in the present study (Tables 2 and 4). Our own results are in agreement with those of an earlier nation-wide study on food intake in Germany [41]. The consumption of red meat and processed meat has been judged to probably increase the risk of colorectal cancer, although it remains unclear whether the specific mechanisms involve processing and cooking methods, animal fat or other factors [1].

In several earlier case-control studies, a low intake of fiber [10, 11, 19, 27] and a low intake of vegetables [17, 19] among adenoma-bearing individuals were reported. This reverse association between intake of fiber and/or vegetables was not confirmed in the present study. Our results are in accordance with those of two recently published studies [4, 42].

Colorectal hyperplastic polyps are predominantly considered to be benign lesions [14, 43]. However, some investigators have suggested that hyperplastic distal polyps are markers of proximal cancers of the large bowel [17, 44] or even to be pre-malignant [44], especially if hyperplastic polyps are large [45]. However, epidemiological studies with adequate control groups failed to confirm the association of hyperplastic polyps with cancer in the proximal colon [16, 46]. In the present study the results obtained in the subjects with hyperplastic polyps suggest that high intake of ham and sausage is a relevant risk factor for developing this type of polyp. Alcohol consumption and smoking were significant risk factors only on univariate analysis but no longer when multiple analysis was applied. The association between various lifestyle factors and colorectal hyperplastic polyps has been examined in two previous studies [18, 19]. In both studies alcohol consumption and smoking were found to be significant risk factors. In a study by Martinez et al. [18] the risk for hyperplastic polyps was found to be increased for individuals in the upper vs. the lower quartile for total fat and BMI and an inverse association for dietary fiber. There is no obvious explanation for the different results. The fact that more than 50 % of the subjects in the latter study [18] underwent only a sigmoidoscopy is unlikely to be the cause of the dissimilar results since in our study more than 90 % of the hyperplastic polyps were located in the rectum plus sigmoid, a figure very similar to that in the earlier study [18].

In conclusion, in the present study the only persistent risk factor after control of other known risk factors for adenomas was smoking. Surprisingly subjects in whom adenomas were localized only in the rectum had significantly lower intake of alcohol, beer and wine compared to those with adenomas in the colon. According to the results of this study hyperplastic polyps share some lifestyle risk factors with adenomas but on multiple regression analysis high intake of ham and sausage remained the only significant risk factors.

Acknowledgment The authors thank Dr. P. Fritz and Dr. V. Voudouri, Department of Pathology, Robert-Bosch Hospital for performing the histological assessment. Supported in part by a Grant (to Dr. C. B) from the 'Mildred-Scheel-Stiftung', Bonn, Germany.

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