original article

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Fried foods, olive oil and colorectal cancer

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Background: The epidemiologic evidence for an etiologic role of fried foods and heterocyclic amines in colorectal carcinogenesis is inconsistent.

Patients and methods: We have investigated the relation between fried foods and colorectal cancer risk using data from a large, multicentric case–control study conducted in Italy and Switzerland between 1992 and 2000, with 1394 cases of colon cancer, 886 cases of rectal cancer and 4765 controls.

Results: After allowing for major relevant covariates, the multivariate odds ratios (ORs) for an increment of one portion per week of fried foods were 0.97 [95% confidence interval (CI) = 0.93–1.01] for colon cancer and 1.04 (95% CI = 1.00–1.09) for rectal cancer. When we analyzed the type of fats mainly used for frying, we found that olive oil, but not other types of oils, appeared to protect from colon cancer risk (OR = 0.89, 95% CI = 0.82–0.98).

Conclusions: Our results do not indicate a relevant role of fried foods on colorectal cancer risk. We found a possible favorable effect of (fried) olive oil on colon cancer risk but not on rectal cancer risk.

Key words: acrylamide, case–control study, colorectal cancer, fried foods, heterocyclic amines, olive oil

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introduction

Heterocyclic amines (HCAs), compounds formed in the cooking of certain foods, especially during the frying of protein-rich food such as meat, eggs and fish, have been shown to be bacterial mutagens and animal carcinogens [1]. In rats, these amines induce cancer specifically in organs such as breast, colon or pancreas, which are associated with Western-type diet [2]. Further, fried potatoes are an important dietary source of acrylamide, a substance that the International Agency for Research on Cancer classified in 1994 as 'probably carcinogenic to humans' (Group 2A), on the basis of sufficient evidence for carcinogenicity in experimental animals and mechanistic considerations [3].

It is therefore important to investigate whether fried foods are related to digestive tract cancers in humans, but the epidemiologic evidence for an etiologic role of fried foods and HCAs in colorectal carcinogenesis is inconsistent [4], whereas there is no evidence of a role of acrylamide from dietary sources [5, 6]. A Swedish case–control study found no association between total HCAs intake and colorectal cancer risk [7] and other studies found no relation between fried meat and colorectal cancer [8–11]. However, an American case–control study found a positive association between pan-fried red meat intake [odds ratio (OR) = 2.0, for the highest level of intake] and colon cancer risk [12], and other epidemiological studies found a direct relation with colorectal adenomas and cancer [13, 14]. In a cohort study on Swedish women, including 741 cases of colorectal cancer [15], there was no association between estimates of acrylamide intake and colorectal cancer. The OR was 0.90 for the highest quintile of intake [95% confidence interval (CI) = 0.6–1.4].

We have therefore investigated the possible relation between fried foods and colorectal cancer risk using data from a large, multicentric case–control study.

patients and methods

Data were derived from a multicentric case–control study of colorectal cancer conducted in Italy and Switzerland between 1992 and 2000. The study included 1394 cases of colon cancer (median age 62 years), 1225 from Italy and 169 from Switzerland; 886 cases of rectal cancer (median age 63 years), 728 from Italy and 158 from Switzerland and 4765 controls, 4154 from Italy and 611 from Switzerland (median age 58 years) [16, 17]. All cancer cases were incident and histologically confirmed. Controls were patients admitted to the same hospitals for acute, non-neoplastic conditions unrelated to digestive tract diseases (22% had non-alcohol-related traumas, mostly fractures and sprains; 28% non-traumatic orthopedic disorders; 24% acute surgical conditions and 26% miscellaneous other illnesses such as eye, ear or skin diseases). Trained interviewers questioned cases and controls during their hospital stay; the proportion

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of refusals was <5% for both cases and controls in all Italian centers and about 15% in Switzerland. The design was the same for the Italian and Swiss studies. Information was collected on sociodemographic factors, anthropometric variables, smoking, alcohol and other lifestyle habits, a problem-oriented medical history, physical activity and history of cancer in relatives. Information on diet referred to the previous 2 years and was based on a validated and reproducible food frequency questionnaire (FFQ) [18, 19] comprising 78 foods, food groups or recipes, and allowing the estimation of total energy intake. The FFQ was divided into six sections: (i) bread, cereals, first courses; (ii) second courses (i.e. meat, fish and other main dishes); (iii) side dishes (i.e. vegetables, fried/baked potatoes); (iv) fruits; (v) sweets, desserts and soft drinks and (vi) milk, hot beverages and sweeteners. At the end of each section, one or two open questions were used to include foods that were not in the questionnaire, but were eaten at least once per week. There were a few differences in the dietary items listed in the Italian and Swiss versions of the questionnaire, to account for different eating and drinking patterns, but these differences did not concern the fried food items and types of fat used to fry. Among the items in the FFQ, some questions referred specifically to consumption of fried foods, such as beef, fish, eggs and omelets and potatoes. The weekly frequency of consumption of fried foods, as well as their usual portion size, was investigated. An additional question aimed at assessing the type of fat used to fry (i.e. olive oil; specific-seed oils such as sunflowers, maize, peanut and soya; mixed-seed oils and butter and margarine) was included.

data analysis

ORs and the corresponding 95% CIs were derived from unconditional multiple logistic regression models, including terms for age, study center, sex, education (<7, 7 to <12 and ≥12 years), body mass index (in quartiles), tobacco smoking (never, ex, current smokers of <15, 15 to <25 and ≥25 cigarettes per day), alcohol drinking (≤1, >1 to ≤3 and >3 glasses per day, plus a term for non-drinkers and ex-drinkers), non-alcohol energy intake (in quintiles), family history of colorectal cancer, physical activity and red meat intake.

results

Table 1 reports the ORs of colorectal cancer according to levels of intake of various fried foods and, separately for colon and rectum, of total fried foods, after adjustment for several potential confounding factors. The ORs of colorectal cancer for the highest level of intake (≥ 1 portion per week) were 0.93 (95% CI = 0.79–1.07) for fried beef, 0.87 (95% CI = 0.75–1.01) for fried fish, 0.98 (95% CI = 0.86–1.11) for fried eggs and 0.95

Table 1. OR and corresponding 95% CI according to total fried foods consumption among 1394 cases of colon cancer, 886 cases of rectum cancer and 4765 controls (Italy and Switzerland, 1992–2000)

	Level of intake[a]			Continuous OR[b]
	1 (lowest)	2	3 (highest)	
Fried food (colon and rectum)				
Beef/veal				
OR[c] (95% CI)	1[d]	0.98 (0.87–1.12)	0.93 (0.79–1.07)	0.98 (0.88–1.09)
Ca : Co[e]	1316 : 2744	581 : 1184	382 : 836	
Fish/shellfish				
OR[c] (95% CI)	1[d]	0.97 (0.85–1.11)	0.87 (0.75–1.01)	0.92 (0.82–1.03)
Ca : Co	1422 : 3000	505 : 1021	353 : 744	
Eggs/omelettes				
OR[c] (95% CI)	1[d]	0.95 (0.83–1.10)	0.98 (0.86–1.11)	1.04 (0.98–1.09)
Ca : Co	980 : 2110	468 : 1011	832 : 1644	
Potatoes				
OR[c] (95% CI)	1[d]	1.00 (0.87–1.15)	0.95 (0.83–1.08)	1.01 (0.95–1.08)
Ca : Co	887 : 1870	513 : 1069	880 : 1826	
Total fried foods				
Colon				
OR[c] (95% CI)	1[d]	0.93 (0.78–1.11)	0.83 (0.70–0.98)	0.97 (0.93–1.01)
Ca : Co[e]	400 : 1268	348 : 1177	646 : 2319	
Rectum				
OR[c] (95% CI)	1[d]	1.07 (0.87–1.32)	0.91 (0.74–1.12)	1.04 (1.00–1.09)
Ca : Co[e]	212 : 1268	226 : 1177	447 : 2319	
Colorectum				
OR[c] (95% CI)	1[d]	0.97 (0.85–1.14)	0.86 (0.74–0.98)	1.00 (0.97–1.03)
Ca : Co[e]	612 : 1268	574 : 1177	1093 : 2319	

[a]For each fried food, the first level of intake was <0.5 portion per week, the second level was 0.5 to <1 portion per week the third level was ≥1 portions per week. For total fried foods, the first level of intake was <1 portion per week, the second level was 1 to <2 portions per week, the third level was ≥2 portions per week.
[b]For an increment of one portion per week.
[c]Estimates from unconditional logistic regression adjusted for age, center, sex, education, body mass index, tobacco smoking, alcohol drinking, non-alcohol energy intake, family history, physical activity and red meat intake.
[d]Reference category.
[e]The sum does not add up to the total because of two missing values.
OR, odds ratio; CI, confidence interval; Ca : Co, cases : controls.

(95% CI = 0.83–1.08) for fried/baked potatoes. Corresponding values for total fried foods were 0.83 (95% CI = 0.70–0.98) for colon, 0.91 (95% CI = 0.74–1.12) for rectum and 0.86 (95% CI = 0.74–0.98) for colorectum. When we restricted the analysis to the Italian data set, the OR for colorectal cancer for the highest tertile of total fried food intake was 0.84 (95% CI = 0.72–0.97), whereas in the Swiss data set the corresponding value was 1.22 (95% CI = 0.75–3.05). The ORs were borderline heterogeneous across strata of country ($P = 0.047$). The ORs for an increment of one portion of fried foods per week were 0.97 (95% CI = 0.93–1.01) for colon cancer, 1.04 (95% CI = 1.00–1.09) for rectal cancer and 1.00 (95% CI = 0.97–1.03) for both cancers together.

Table 2 gives the continuous ORs for colon, rectal and colorectal cancers according to the type of oil mainly used for frying. The ORs for an increment of one portion of fried foods per week for colon, rectal and both cancers together were, respectively, 0.89 (95% CI = 0.82–0.98), 0.97 and 0.93 for use of olive oil; 1.00, 1.06 and 1.02 for specific-seed oils and 0.98, 1.03 and 1.00 for mixed-seed oils used.

discussion

Our results do not indicate a relevant role of fried foods on colorectal cancer risk. These inconsistent findings may be explained by a relatively moderate consumption of fried foods in Italy (median value in our study: 1.8 portions per week) and/or by the large intake of vegetables, fruits and fiber-containing foods, typical of Mediterranean populations, which could be responsible for their comparably lower incidence of colorectal cancer. When we evaluated the fat used for frying, we found that olive oil, but not other types of oils, appeared to protect from colon cancer, confirming its possible favorable effect on colorectal and other cancers [20–24]. However, previous studies considered the overall dietary consumption of olive and other oils, whereas this investigation provided indications that fried olive oil may also reduce the risk for colon cancer.

The favorable effect of olive oil has been proposed on the basis of animal experiments and of its fatty acid composition (mainly oleic acid, a monounsaturated fatty acid) or of the content of specific micronutrients and antioxidants (including vitamin E) [20, 25]. Further, previous studies found that the formation of HCAs during cooking is decreased by the addition of pure antioxidants or food containing antioxidants [26, 27]. As in our population >24% of the subjects interviewed declared they used olive oil for frying, this may be another interpretation for the null relation found between fried foods and colorectal cancer. This was further supported by the higher risks observed in the Swiss than in the Italian data set, as use of olive oil for frying was uncommon (3%) in Switzerland as compared with 27% in Italy. The behavior of virgin olive oil, that presents a lower degree of unsaturation than vegetable shortening [28] during repeated frying operations, indicates that this oil is more stable in comparison with other vegetable oils and also for this reason the use of olive oil is suggested for deep-frying [29, 30].

In order to reduce potential information bias, in this study the questionnaire was administered by the same interviewers, under similar conditions, to both cases and controls, and controls were selected among patients with admission diagnoses not related to diet modifications. Bias in the recall of consumption of fried foods should be limited in this population, also given the satisfactory validity and reproducibility of the FFQ [18, 19] and the comparability between cases and controls in hospital-based settings [31]. Findings from companion case–control studies of the upper aero-digestive tract, where a positive association with fried foods was observed [32, 33], provide indirect evidence that the absence of association appears to be real, since both the upper and lower digestive tract cancer studies were conducted on similar populations and using similar study designs.

Other main strengths of this case–control study are its large size and the low percentage of refusals of the subjects contacted. With reference to confounding, the findings were consistent after inclusion in the regression models of several lifestyle and dietary covariates such as physical activity, energy, fruit and vegetable intake and red meat intake.

Table 2. Continuous OR[a] and corresponding 95% CI for colon and rectal cancer according to fried foods consumption in strata of fat mainly used for frying (Italy and Switzerland, 1992–2000)

Total fried food	Type of oil		
	Olive oil	Specific-seed oils[b]	Mixed-seed oils
Colon	0.89	1.00	0.98
OR (95% CI)	(0.82–0.98)	(0.93–1.07)	(0.90–1.06)
Ca : Co[c]	331 : 1008	548 : 1857	315 : 1330
Rectum	0.97	1.06	1.03
OR (95% CI)	(0.87–1.08)	(0.98–1.14)	(0.96–1.11)
Ca : Co[c]	202 : 1008	333 : 1857	254 : 1330
Colorectum	0.93	1.02	1.00
OR (95% CI)	(0.86–1.00)	(0.96–1.07)	(0.95–1.06)
Ca : Co[c]	533 : 1008	881 : 1857	569 : 1330

[a]Estimates from unconditional logistic regression adjusted for age, center, sex, education, body mass index, tobacco smoking, alcohol drinking, non-alcohol energy intake, family history, physical activity and red meat intake. OR for an increment of one portion per week.

[b]Sunflower, maize, peanut or soya.

[c]The sum does not add up to the total because some subjects used other types of fat for frying or had missing values.

OR, odds ratio; CI, confidence interval and Ca : Co, cases : controls.

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