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Short Communication

Gastric Cancer Risk Factors in Subjects with Family History[1]

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Abstract

Until now, it has been unclear whether there are differences in various risk factor profiles for familial gastric cancer, *i.e.*, gastric cancer among subjects with a family history of the disease. A total of 722 gastric cancer patients and 2024 controls were admitted between 1985 and 1992 to a network of hospitals in the Greater Milan area. Of these, 88 cases and 103 controls who reported a family history of gastric cancer in first degree relatives were considered in the present analysis. There was no relationship between gastric cancer risk and tobacco smoking or alcohol drinking. Shorter duration of electrical refrigerator use was related to a nonsignificant increased risk and a high daily meal frequency was associated with an increased gastric cancer risk. Significant direct trends of risk were observed for pasta (odds ratio, OR = 4.20 for the highest *versus* the lowest tertile), bread (OR, 2.86), red meat (OR, 3.38), and preserved meat (OR, 1.90). Inverse associations were observed for increasing consumption of selected vegetables and fruits, chiefly peppers (OR = 0.31), total fruits (OR, 0.47), and citrus fruits (OR, 0.38). With reference to selected micronutrients, a significant inverse trend in risk with increasing consumption for β-carotene (OR, 0.27) and ascorbic acid (OR, 0.20) was observed. These results suggest that dietary risk factors for subjects with a family history of gastric cancer in first-degree relatives are not appreciably different from well-established risk factors of the disease in the general population.

Introduction

Risk factors for gastric cancer have been widely considered over the last few years. Studies conducted in Italy (1–4) and Greece (5), as well as North America (6, 7) and in developing countries (8–10), have indicated that a diet poor in fresh fruits and vegetables, and hence possibly in selected micronutrients such as ascorbic acid or β-carotene, is associated with increased risk. In contrast, various indicators of a poorer diet, such as bean, traditional soup, and canned and preserved meat consumption have also been associated with increased gastric cancer risk (11, 12). Other potential determinants of gastric carcinogenesis are salt intake, unavailability of refrigerators, and more in general, indicators of unfavorable socioeconomic level (13, 14).

It is also known that a family history of gastric cancer in first degree relatives is associated with approximately a 2-fold increased risk of the disease (15–17). It is, however, unclear whether there are differences in various risk factors profile for familial gastric cancer, *i.e.*, gastric cancer among subjects with a family history of the disease. Thus, we have analyzed data from a case-control study conducted in Northern Italy.

Patients and Methods

The data were derived from a case-control study of digestive tract cancers conducted in Northern Italy, based on a network of teaching and general hospitals in the Greater Milan area. Recruitment of gastric cases and controls began in January 1985, and this work is based on data collected up to December 1992. The general design of this investigation has been described previously (1, 2).

Briefly, trained interviewers identified and questioned cases and controls using a structured questionnaire, including information on sociodemographic factors, personal characteristics, and lifestyle habits (such as smoking, alcohol, and coffee and other methylxantine-containing beverage consumption), a problem-oriented medical history, and history of digestive tract cancers in first-degree relatives but not age at diagnosis. Furthermore, information on the weekly frequency of consumption or intake scores of 36 indicator foods was collected. These included major sources of β-carotene, retinol, ascorbic acid, vitamins D and E, folate, methionine, calcium, nitrites, and nitrates in the Italian diet. All information referred to the year before diagnosis or interview.

Cases were patients below age 75 years with histologically confirmed incident (*i.e.*, diagnosed within the year before interview) gastric cancer. They were admitted to the National Cancer Institute in Milan, to the Ospedale Maggiore of Milan, which includes the four largest teaching and general hospitals in Milan, and to selected specialized university wards.

The comparison group included subjects younger than 75 years admitted for a wide spectrum of acute, nonneoplastic, nondigestive tract, nonhormone-related disorders to the same network of hospitals where cases had been recruited. About 80% of cases and controls resided in the same region, Lombardy, and more than 90% came from Northern Italy. Less than 3% of subjects approached (cases and controls) refused to be

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Table 1 Distribution of 88 stomach cancer cases and 103 controls with history of the disease in first-degree relatives according to education and selected lifestyle factors, Italy, 1985–1992

	Cases with family history	Controls with family history	OR[a]	95% CI	OR for nonfamilial subjects
Education					
<6	61	60	1[b]		
7–11	19	30	0.69	0.34–1.42	0.74
≥12	8	13	0.73	0.27–1.98	0.50
Alcohol consumption					
<1	26	38	1[b]		
1–3	31	31	0.61	0.34–1.42	1.06
≥4	31	34	0.73	0.27–1.98	1.10
Use of the refrigerator					
≥30 years	37	51	1[b]		
≤29 years	51	52	1.27	0.69–2.35	1.15
Daily meal frequency					
0–2	54	81	1[b]		
≥3	34	22	2.32	1.18–4.54	1.82

[a] Estimates from logistic regression equations including terms for sex, age, area of residence, and education.
[b] Reference category.

interviewed. All of the data were collected by direct interview during hospital stay.

A total of 722 cases and 2024 controls had been interviewed. Among them, 88 cases (median age, 62 years) and 103 controls (median age, 57 years) reported a family history of gastric cancer in first degree relatives. These were included in the present analysis. Of controls, 7% were admitted for traumatic diseases, 20% had nontraumatic orthopedic disorders, 19% had acute surgical conditions, and 14% had other miscellaneous diseases, such as ear, nose and throat; skin; eye; or dental disorders.

Nutrient intakes were computed using standard composition tables (18). Subjects were categorized by approximate tertiles of intake based on the distribution of controls, whenever possible.

Data Analysis. ORs,[3] as estimators of relative risks of familial gastric cancer, together with the corresponding 95% CIs, were derived from unconditional multiple logistic regression equations, fitted by the method of maximum likelihood (19). The variables included in the regression equations were gender, age in decades, area of residence and education, plus estimated total energy intake, when specified.

Results

Table 1 gives the distribution of gastric cancer cases and controls with family history according to education and selected lifestyle factors. More educated subjects showed a nonsignificant reduced risk. No apparent increase in risk was observed among alcohol drinkers. Subjects reporting refrigerator use for less than 30 years had some nonsignificant excess risk (OR, 1.27). Gastric cancer was significantly associated with higher daily meal frequency (≥3 meals/day; OR, 2.32). ORs for nonfamilial subjects are also given in the table for comparative purposes.

Selected food items are listed in Table 2. Significant positive trends of increasing risk with more frequent consumption were observed for pasta (OR, 4.20 for the highest *versus* the lowest tertile of intake), bread (OR, 2.86), red meat (OR, 3.38), canned meat (OR, 1.90), butter (OR, 1.88), and margarine (OR, 2.42). Significant inverse associations were observed for consumption of peppers (sweet green, red, and yellow; OR, 0.31), total fruits (OR, 0.47), and particularly citrus fruits (OR, 0.38). Consumption of other vegetables (cabbages and carrots) and whole-grain foods were also related to reduced (nonsignificant) risk. These results were not materially altered when the regression equations included terms for total energy intake (data not shown).

Selected micronutrients are considered in Table 3. There were no apparent trends in risk for retinol, calcium, vitamin D, vitamin E, folate, methionine, and nitrites. Significant inverse trends in risk with consumption for β-carotene (OR, 0.27 for the highest *versus* the lowest tertile), ascorbic acid (OR, 0.20), and nitrates (OR, 0.35) was observed. Nonsignificant direct associations were observed for methionine and nitrites, and an inverse association for folates. ORs for nonfamilial cases showed generally similar pattern of risks, and in several cases, the associations were less strong.

Discussion

This study suggests that the risk factors for gastric cancer among subjects with family history of the disease share several similarities with the same recognized risk factors in the general Italian population (1–4). If anything, several associations were stronger in familial cases.

This indicates that familial factors, which include genetic factors, would have a role in gastric carcinogenesis independent from the major recognized environmental factors and is consistent with the observation that the relative risk of gastric cancer associated with the family history of the disease does not appreciably change after allowance for major identified risk factors (4, 15–17). Similar findings emerged from a companion study on colorectal cancer.[4]

The results for several risk factors taken separately are, however, not significant and remain, therefore, open to discus-

[3] The abbreviations used are: OR, odds ratio; CI, confidence interval.

[4] E. Fernandez, C. La Vecchia, B. D'Avanzo, E. Negri, and S. Franceschi. Risk factors for colorectal cancer in subjects with family history of the disease, Br. J. Cancer, in press, 1997.

Table 2 Distribution of 88 cases with familial gastric cancer and 103 controls according to frequency of intake of selected food items, Italy 1985–1992[a]

Food item[b]	Cases	Controls	OR[c]	95% CI	χ^2_{1trend}	OR for nonfamilial subjects
Pasta						
≤4	11	32	1[d]			
5–7	51	52	3.15	1.38–7.17	8.54[e]	1.46
≥8	26	19	4.20	1.58–11.14		1.83
Bread						
≤9	26	41	1[d]			
10–14	39	45	1.57	0.78–3.15	5.43[e]	1.18
≥15	23	17	2.86	1.16–7.03		1.21
Polenta						
<1	19	37	1[d]			
≥1	69	66	1.82	0.93–3.57	3.14	1.28
Whole-grain foods (score)						
Low	75	81	1[d]			
Intermediate/high	13	22	0.63	0.28–1.40	1.30	0.77
Red meat						
≤2	29	46	1[d]			
3–4	35	42	1.62	0.81–3.26	7.82[e]	0.98
≥5	24	15	3.38	1.42–8.04		1.81
Canned meat						
0	41	65	1[d]			
≥1	47	38	1.90	1.04–3.47	4.35[e]	1.32
Vegetables, total						
≤6	42	31	1[d]			
7	25	38	0.50	0.24–1.05	3.79	0.64
≥8	21	34	0.47	0.22–1.03		0.46
Peppers						
0	34	20	1[d]			
1	44	63	0.42	0.21–0.86	6.93[e]	0.65
≥2	10	20	0.31	0.12–0.83		0.74
Fruit, total						
≤5	25	23	1[d]			
6–10	37	33	0.94	0.43–2.08	4.08[e]	0.72
≥11	26	47	0.47	0.21–1.05		0.57
Citrus fruits						
≤2	49	33	1[d]			
3–5	23	39	0.43	0.21–0.88	7.04[e]	0.81
≥6	16	31	0.38	0.17–0.83		0.58
Butter (score)						
Low	37	60	1[d]			
Intermediate/high	51	43	1.88	1.03–3.44	4.23[e]	1.45
Margarine (score)						
Low	66	92	1[d]			
Intermediate/high	22	11	2.42	1.06–5.51	4.63[e]	1.34

[a] Information was also collected on weekly frequency consumption of pastries, poultry, fish, liver, ham, raw ham, salami and other sausages, milk, cheese, cabbages, carrots, potatoes, beans, eggs, spinach, tomatoes, green salad, apples, melon, olive oil, seed oils, salt, and sugar. Because no meaningful association was observed, they have not been included in the table.
[b] Average number of weekly portions (or similar).
[c] Estimates from logistic regression equations including terms for sex, age, area of residence, and education.
[d] Reference category.
[e] $P < 0.05$.

sion. The low absolute number of cases and controls, moreover, did not allow meaningful analyses in separate strata of sex, age, or other covariates of potential interest. Furthermore, we have simply defined family history on the basis of the presence of gastric cancer among first-degree relatives. Thus, familial cases and controls include both genetically related cases and those attributable to shared environmental factors or the play of chance (14).

Other potential limitations and strengths of the present study are typical of hospital-based case-control studies (19). Problems with specific reference to the dietary questionnaire, which was not validated and included only a limited number of food items, have already been considered (1, 2, 14). In particular, the estimated nutrient intakes in this study were consistent with the recommended intakes of the Italian population (18). With reference to selection bias, patients with chronic neoplastic, metabolic, or digestive tract conditions were excluded from the control group. The comparable catchment area of cases and controls, together with their almost complete participation, are also reassuring against selection bias. Cases and controls were directly interviewed in the same setting, thus allowing us to obtain reasonably comparable information (20). With reference to confounding, the results were not substantially modified after allowance for several covariates, including years of schooling and total energy intake.

In conclusion, the major interest of this study is in pro-

Table 3 Distribution of 88 cases with familial gastric cancer and 103 controls according to estimated intake of selected nutrients, Italy 1985–1992[a]

Micronutrient	Cases	Controls	OR[b]	95% CI	χ^2_{1trend}	OR for nonfamilial subjects
β-carotene						
Low	42	34	1[c]			
Intermediate	25	35	0.46	0.21–1.01	9.36[d]	0.59
High	21	34	0.27	0.11–0.65		0.38
Ascorbic acid						
Low	41	34	1[c]			
Intermediate	34	35	0.62	0.29–1.34	11.89[d]	0.59
High	13	34	0.20	0.08–0.51		0.44
Folate						
Low	31	34	1[c]			
Intermediate	23	34	0.40	0.17–0.95	0.99	0.76
High	34	35	0.63	0.26–1.51		0.57
Methionine						
Low	15	34	1[c]			
Intermediate	25	34	1.02	0.40–2.62	1.65	1.21
High	48	35	1.75	0.65–4.41		1.65
Nitrites						
Low	22	34	1[c]			
Intermediate	25	34	1.12	0.48–2.59	1.47	1.09
High	41	35	1.62	0.71–3.69		1.30
Nitrates						
Low	34	34	1[c]			
Intermediate	35	34	0.66	0.30–1.47	5.62[d]	0.53
High	19	35	0.35	0.15–0.85		0.49

[a] Information were also obtained on intake of retinol, calcium, vitamin D, and vitamin E. Because no meaningful associations were observed, they have not been included in the table.
[b] Estimates from logistic regression equations including terms for sex, age, area of residence, education, and estimated total energy intake.
[c] Reference category.
[d] $P < 0.05$.

viding information of the pattern of risk factors of gastric cancer among subjects with family history of the disease, *i.e.*, an issue on which little was known previously.

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