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SHORT COMMUNICATION

Diet diversity and the risk of oral and pharyngeal cancer

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Abstract *Background* Diet diversity has been recommended to achieve a healthy diet and prevent cancer. *Aim of the study* The relation between diet diversity (i.e., variety in food intake computed as the total number of foods consumed at least once per week) and the risk of oral and pharyngeal cancer was investigated using data from a multicentric case-control study carried out between 1991 and 2005 in Italy. *Methods* Cases were 805 patients with histologically confirmed incident cancers of the oral cavity and pharynx, and controls were 2,081 patients admitted for acute, non-neoplastic diseases, unrelated to tobacco or alcohol consumption. *Results* A significant inverse association was observed with total diet diversity. The multivariate odds ratio (OR), adjusted for education, tobacco and alcohol, was 0.78 (95% confidence interval, CI 0.61–0.98) for subjects in the highest tertile of diversity. Inverse relations were found also for diversity within vegetables (OR = 0.62; 95% CI 0.49–0.78) and fruits (OR = 0.67; 95% CI 0.53–0.86). *Conclusions* This study suggests that a more diversified, and particularly a diet varied in vegetables and fruit, is a favourable indicator of oral and pharyngeal cancer risk, independently from the major recognised risk factors, i.e. alcohol and tobacco consumption.

Key words case-control study – oral and pharyngeal neoplasm – diet

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Introduction

Oral and pharyngeal cancer is strongly related to smoking and alcohol consumption [8, 9], but a role of diet has been recognised, and dietary factors may account for about 25% of cases in Europe [14, 17]. Intake of fruit and vegetables has been inversely related to the risk of oral and pharyngeal cancer, whereas a poor nutritional status and an unbalanced diet have been related to an excess risk [16, 21, 22]. Only limited attention, however, has been paid to the definition of potential correlates of oral and pharyngeal cancer risk in terms of dietary patterns.

It has been suggested that diet diversity (i.e., a measure of the variety of diet) may reduce mortality and prevent cancer [12, 22]. Total mortality in relation to diet diversity has been considered in the first National Health and Nutrition Survey Epidemiologic Follow-up Study [10], which found a relative risk of 1.5 in the lowest quartile of diversity. Diet diversity was inversely related to the risk of stomach [13] and colorectal cancer [3, 4, 20]. The variety of vegetables consumed seems also to have a beneficial role on breast cancer, beyond the favorable effect of vegetable intake per se [6].

A case-control study conducted in Switzerland on 156 cases and 284 controls found a decreased risk of oral and pharyngeal cancer for subjects reporting higher total diet diversity (OR = 0.35 for the highest versus the lowest tertile), as well as vegetable (OR = 0.24) and fruit diversity (OR = 0.34) [15]. A multicenter case-control from Italy, including 512 cases of oral and pharyngeal cancer also found an inverse relation for vegetable (OR = 0.5 for the highest versus the lowest tertile) and fruit diversity (OR = 0.6) [5].

We analyzed the role of total and specific food group diversity on the risk of oral and pharyngeal cancer using the data from a larger dataset of the multicenter case-control study conducted in Italy.

Materials and methods

The present analysis is based on data from a case-control study of oral and pharyngeal cancer conducted in Italy between 1992 and 2005 in the greater Milan area, and in the provinces of Pordenone, Rome and Latina [5, 18]. Data collection started and ended later in Milan. However, the same questionnaire and selection criteria were used in all centres. Briefly, cases were 805 patients (659 men and 146 women; median age 58, range 22–78 years) admitted to major teaching and general hospitals in the study areas, with incident, histologically confirmed cancer of the oral cavity (406 cases) and pharynx (399 cases), diagnosed no longer than one year before the interview. Cancers of the lip, salivary glands and nasopharynx were not included. Controls were 2,081 subjects (1,302 men and 779 women; median age 58 years, range 19–79 years) admitted to the same hospitals as cases for a wide spectrum of acute, non-neoplastic conditions, unrelated to known risk factors for oral and pharyngeal cancer, and not associated with long-term dietary modifications. Controls were frequency-matched with cases according to study center, sex, and 5-year age groups. To compensate for the rarity of oral and pharyngeal cancer in women, a control-to-case ratio of ~5 was chosen for women, as opposed to ~2 for men. Twenty-five percent of controls were admitted for traumas, 30% for other orthopedic disorders, 19% for surgical conditions, and 26% for miscellaneous various other illnesses. Less than 5% of both cases and controls contacted refused to participate.

Cases and controls were interviewed during their hospital stay by trained interviewers using a structured questionnaire. This included information on socio-demographic characteristics, lifestyle habits, such as tobacco smoking and alcohol drinking, anthropometric measures, personal medical history, and family history of cancer. Information about the frequency of consumption per week of 78 foods, food groups, or recipes during the 2 years prior to cancer diagnosis or hospital admission (for controls) was collected using a satisfactorily reproducible [7] and valid [2] food-frequency questionnaire.

Total diversity was computed as the total number of different foods consumed at least once per week [13]. Our definition of diversity did not include portion size nor frequency of consumption. It is therefore a simple indicator of a varied diet, independent from frequency and quantity. Since the variety of some foods can be more important than total variety, we also computed the diversity within four food groups: first courses, including pasta or rice, bread, polenta; second courses, including beef and veal, poultry, fish, processed meats, cheese and eggs; vegetables, including various raw and cooked vegetables, pulses and potatoes; fruits, including citrus, other fresh and cooked fruits and unsweetened juices. Subjects were subdivided into approximate tertiles of total diversity and specific food group diversity based on the control distribution.

ORs of oral and pharyngeal cancer and the corresponding 95% confidence intervals (CI) according to various measures of diet diversity were derived from unconditional multiple logistic regression models [1]. Allowance was made for age, sex, study centre, year of interview, years of education, tobacco smoking and alcohol drinking.

Results

Table 1 gives the distribution of 805 cases and 2,081 controls according to sex, age, and selected other covariates. By design, the proportion of women was higher in controls than in cases, and the age distribution was similar in cases and controls. Cases were slightly less educated, and reported a significant higher tobacco and alcohol consumption.

The ORs of oral and pharyngeal cancer according to tertile of intake of total, first course, second course, vegetable and fruit diversity are shown in Table 2. Compared with subjects in the lowest tertile, the ORs were 0.78 (95% CI 0.61–0.98) for subjects in the highest tertile of total diversity, 0.62 (95% CI 0.49–0.78) for vegetable diversity and 0.67 (95% CI 0.53–0.86) for fruit diversity, with significant inverse trends in risk. No material association emerged for first course (OR = 0.99) and second course (OR = 1.07) diversity. Consequently, the inverse association with total diet diversity was mainly due to vegetable and fruit. Further allowance for other covariates, including total energy intake or body mass index, did not modify the association observed. The inverse relation with total, vegetable and fruit diversity was consistent in strata of sex, age, education, tobacco smoking and alcohol drinking.

Table 1 Distribution of 805 oral cavity and pharyngeal cancer cases and 2,081 controls according to sex, age and selected other covariates. Italy, 1992–2005

	Cases (%)	Controls (%)
Sex		
Male	659 (81.9)	1,302 (62.6)
Female	146 (18.1)	779 (37.4)
Age (years)		
<50	164 (20.4)	502 (24.1)
50–59	270 (33.5)	630 (30.3)
60–69	286 (35.5)	698 (33.5)
70–79	85 (10.6)	251 (12.1)
Education (years)[a]		
<7	496 (61.6)	1,152 (55.4)
7–11	215 (26.7)	590 (28.4)
≥12	89 (11.1)	338 (16.3)
Smoking habit[a]		
Never smoker	102 (12.7)	881 (42.3)
Ex-smoker	220 (27.3)	646 (31.0)
Current smoker		
1–19 cigarettes/day	222 (27.6)	334 (16.0)
≥20 cigarettes/day	260 (32.3)	217 (10.4)
Alcohol consumption (drinks/day)[a]		
<4	264 (32.8)	1,482 (71.2)
4– < 9	247 (30.7)	484 (23.3)
≥9	290 (36.0)	110 (5.3)

[a]The sum does not add up to the total because of some missing values

Discussion

This study, based on a large dataset, suggests that total diet, and particularly vegetable and fruit diversity are inversely related to the risk of oral and pharyngeal cancer. Diet diversity (especially diversity within vegetables) has also been linked to a decreased risk for gastric [13], breast [6] and colorectal cancer [3, 4, 20], with specific reference to plant foods. Our results are consistent with the findings reported in a previous study from Switzerland [15], as well as in a preliminary analysis of the Italian dataset [5].

A possible explanation for the observed protective effect of a more varied diet on oral and pharyngeal cancer risk is that individuals eating more varied foods are more likely to consume a larger number (and quantity) of beneficial dietary components. It is possible that an increase in dietary diversity explain the effect of fruit and vegetable intake on the reduction of oral and pharyngeal cancer risk [11, 22]. A more heterogeneous diet, however, may simply be an indicator of a richer diet and of more favourable lifestyle correlates of oral and pharyngeal cancer.

Table 2 Odds ratios (OR) and corresponding 95% confidence intervals (CI) among 805 oral cavity and pharyngeal cancer cases and 2,081 controls according to diversity of intake of selected food groups. Italy, 1992–2005

Diet diversity[a]	Cases (%)	Controls (%)	OR (95% CI)[b]
Total			
<27	319 (39.63)	658 (31.62)	1[c]
27–33	273 (33.91)	734 (35.27)	0.81 (0.65–1.01)
≥34	213 (26.46)	689 (33.11)	0.78 (0.61–0.98)
P-value for trend			0.03
First course			
<6	211 (26.21)	586 (28.16)	1[c]
6–7	360 (44.72)	888 (42.67)	1.00 (0.80–1.26)
≥8	234 (29.07)	607 (29.17)	0.99 (0.77–1.27)
P-value for trend			0.95
Second course			
<7	272 (33.79)	750 (36.04)	1[c]
7–8	238 (29.57)	627 (30.13)	1.06 (0.84–1.33)
≥9	295 (36.65)	704 (33.83)	1.07 (0.85–1.33)
P-value for trend			0.58
Vegetable			
<5	315 (39.13)	587 (28.21)	1[c]
5–7	272 (33.79)	723 (34.74)	0.77 (0.62–0.97)
≥8	218 (27.08)	771 (37.05)	0.62 (0.49–0.78)
P-value for trend			<0.0001
Fruit			
<4	345 (42.86)	611 (29.36)	1[c]
4–5	289 (35.90)	839 (40.32)	0.71 (0.57–0.88)
≥6	171 (21.24)	631 (30.32)	0.67 (0.53–0.86)
P-value for trend			0.001

[a]Number of items consumed at least weekly
[b]Estimates from multiple logistic regression equations including terms for age, sex, study centre, year of interview, education, tobacco smoking and alcohol drinking
[c]Reference category

This study has some of the potential limitations of hospital-based case-control studies. To reduce information bias, the questionnaire was administered to both cases and controls by the same interviewers, under similar conditions. Bias in the recall of food intake should be limited in this not particularly health conscious population, and given the comparability between cases and controls in hospital-based settings. Moreover, we used a reproducible and valid FFQ questionnaire [2, 7], including a large number of common food items consumed in Italy. Non differential under- or over-reporting by cases and controls would, if anything, lead to an underestimation of the real association [1]. Controls were selected among patients with admission diagnosis not related to tobacco smoking, alcohol drinking and diet modifications. The high participation rate of cases and controls, the comparable catchment areas of study subjects, the adjustment for major risk factors for oral and pharyngeal cancer are among other strengths of the study. In fact, we were able to allow for major identified potential confounding factors, including indicators of socio-economic status, alcohol and tobacco, and the inverse relations with diet diversity were consistent across strata of these factors.

The present findings provide support to the dietary guidelines recommending a more varied diet (particular in terms of fruit and vegetables) [12, 19], and its impact on the risk of various digestive tract neoplasms, including oral and pharyngeal cancer. Studies analysing eating patterns that may favourably influence oral and pharyngeal cancer risk are useful, in addition to the analysis of individual foods and nutrients.

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