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Research Article

Nutrient-Based Dietary Patterns and Laryngeal Cancer: Evidence from an Exploratory Factor Analysis

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Abstract

Background: The issue of diet and laryngeal cancer has been rarely addressed considering the potential role of dietary patterns.

Methods: We examined this association using data from a case-control study carried out between 1992 and 2000. Cases were 460 histologically confirmed incident laryngeal cancers hospitalized in two Italian areas. Controls were 1,088 subjects hospitalized for acute nonneoplastic diseases unrelated to tobacco or alcohol consumption. Dietary habits were investigated through a 78-item food frequency questionnaire. A posteriori dietary patterns were identified through principal component factor analysis carried out on a selected set of 28 major nutrients. The internal reproducibility, robustness, and reliability of the identified patterns were evaluated. Odds ratios (OR) of laryngeal cancer and 95% confidence intervals (95% CI) were estimated using unconditional multiple logistic regression models on quartiles of factor scores.

Results: We identified five major dietary patterns named "animal products," "starch-rich," "vitamins and fiber," "vegetable unsaturated fatty acids," and "animal unsaturated fatty acids." The vitamins and fiber dietary pattern was inversely associated with laryngeal cancer (OR, 0.35; 95% CI, 0.24-0.52 for the highest versus the lowest score quartile), whereas the animal products (OR, 2.34; 95% CI, 1.59-3.45) and the animal unsaturated fatty acids (OR, 2.07; 95% CI, 1.42-3.01) patterns were directly associated with it. There was no significant association between the vegetable unsaturated fatty acids and the starch-rich patterns and laryngeal cancer risk.

Conclusion: These findings suggest that diets rich in animal products and animal fats are directly related, and those rich in fruit and vegetables inversely related, to laryngeal cancer risk. *Cancer Epidemiol Biomarkers Prev; 19(1); 18–27. ©2010 AACR.*

Introduction

Tobacco smoking and alcohol drinking are the two major risk factors for cancer of the larynx in Europe and other high-income countries (1, 2), showing a combined effect that may be multiplicative or greater than multiplicative (3-5).

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Among other factors, diet has been associated with laryngeal cancer risk. In particular, high intakes of nonstarchy vegetables, foods containing carotenoids, and fruit in general have been reported to be probably protective against laryngeal cancer (6). Dietary patterns have recently emerged as an intuitively practical tool to address the issues of collinearity of nutrients and interdependencies between foods and nutrients (7, 8).

In the current article, we apply exploratory principal component factor analysis (PCFA) to identify dietary patterns defined a posteriori in a multicentric case-control study conducted in Italy on cancer of the larynx. Previous analyses on single nutrients and laryngeal cancer risk on those data showed some direct relationships with energy intake, cholesterol, animal proteins, and vitamin D (9, 10), and inverse relationships with vegetable proteins, all types of fiber and most sources of total fiber, and several micronutrients such as vitamin C, carotene, folic acid, thiamin, and vitamin E (9-11).

Dietary patterns defined a priori were also identified for this population, looking at the specific role of diet diversity (12) and Mediterranean-type dietary profiles (13), which have been related to laryngeal cancer. The

Table 1. Factorability of the correlation matrix of the original nutrients: Bartlett's test of sphericity and measures of sampling adequacy

Bartlett's test of sphericity: *P*-value < 0.001	
Kaiser-Meyer-Olkin statistic - overall measure of sampling adequacy*: 0.80	
Individual measures of sampling adequacy*:	
<0.60	Linoleic acid, retinol
0.60-<0.70	Monounsaturated fatty acids, lycopene, vitamin D, vitamin E
0.70-<0.80	Other polyunsaturated fatty acids, starch, calcium, vitamin C, total fiber
0.80-<0.90	Animal protein, vegetable protein, cholesterol, saturated fatty acids, potassium, phosphorus, iron, thiamin, riboflavin, vitamin B6, total folate, niacin
≥0.90	Linolenic acid, soluble carbohydrates, sodium, zinc, beta-carotene equivalents

*Overall and individual measures of sampling adequacy range between 0 and 1, with values > 0.60 indicating a satisfactory size.

identification of dietary patterns defined a posteriori may allow integrating with new findings our assessment of the association between dietary patterns and laryngeal cancer in Italy.

Materials and Methods

Design and Participants

A case-control study on cancer of the larynx was conducted from 1992 to 2000 in the provinces of Milan and Pordenone in northern Italy (14, 15). Cases were 460 subjects (415 men, 45 women; median age, 61 y; range, 30-80 y) admitted to major teaching and general hospitals in the study areas with incident, histologically confirmed squamous cell cancer of the larynx diagnosed no longer than 1 year before the interview and with no history of cancer at other sites. Laryngeal cancer cases included 248 cases of cancer of the glottis [International Classification of Diseases (ICD)-IX, 161.0], 90 of the supraglottis (ICD-IX, 161.1), 4 of the subglottis (ICD-IX, 161.2), 4 of the laryngeal cartilage (ICD-IX, 161.3), 3 of overlapping lesions of larynx (ICD-IX, 161.8), and 111 cases of cancer from unspecified sites of the larynx (ICD-IX, 161.9). Controls were 1,088 subjects (863 men, 225 women; median age, 61 y; range, 31-79 y) admitted to the same hospitals as cases for a wide spectrum of acute nonneoplastic conditions unrelated to smoking or alcohol consumption or to long-term modifications of diet. Controls were frequency matched with cases by age (5-y groups), sex, and area of residence. To compensate for the rarity of laryngeal cancer in women, a control-to-case ratio of ~5 was chosen for women as opposed to ~2 for men. Twenty-nine percent of the controls were admitted for traumas, 36% for other orthopedic disorders, 12% for acute surgical conditions, and 23% for miscellaneous other illnesses. Less than 5% of both cases and controls that were contacted refused to participate.

Food Frequency Questionnaire

Centrally trained interviewers administered a structured questionnaire to cases and controls during their hospital stay. The questionnaire included information on sociodemographic characteristics, anthropometric variables, lifestyle factors such as tobacco smoking and alcohol drinking, a problem-oriented personal medical history, family history of cancer, and, for women, menstrual and reproductive history.

Information on diet referred to the 2 years before diagnosis (or hospital admission for the controls) and was based on a food frequency questionnaire that was validated for nutrient intake and tested for reproducibility for specific nutrients and food items (16-18). The food frequency questionnaire presented 78 foods and food groups, including some of the most common Italian recipes, and various types of alcoholic beverages. Subjects were asked to indicate quantity and average weekly frequency of consumption for the period under investigation. Intakes reported at least once a month but less than once a week were coded as 0.5 per week. Other questions on fat-intake pattern, as well as portion size, were used to modulate the composition of recipes. Dietary supplements were not considered, given their rare consumption in this population. The study was approved by the local ethics committees.

Italian food composition tables (19, 20) were used to calculate intakes of total energy and various nutrients. Losses due to cooking were subtracted from the computation of the content of vitamins, when appropriate.

Statistical Analysis

Factorability of the Original Matrix. We conducted the analyses on a selected set of 28 major macronutrients and micronutrients. Nutrients were chosen to provide a comprehensive representation of the Italian diet and to assess their potential role in cancer risk. Moreover, we took into account existing relationships among nutrients to avoid overrepresentation of single nutrients and consequent artificially higher correlations. We preliminarily evaluated the correlation matrix to determine if it was factorable through visual inspection of the matrix and statistical procedures such as Bartlett's test of sphericity, Kaiser-Meyer-Olkin measure, and individual measures of sampling adequacy (21). Given the reassuring results that we obtained (see Results), we applied a factor analysis to derive the dietary patterns.

Identification of Dietary Patterns. Exploratory PCFA (22) was carried out on the correlation matrix of the overall original data to describe the variance-covariance structure among nutrients in terms of a few underlying unobservable and randomly varying factors that are generally known as dietary patterns. We chose the number of factors to retain based on the following criteria: factor eigenvalue >1; scree plot construction, looking for the optimal number of components to retain at the curve break point between factors with relatively large eigenvalues and factors with negligible eigenvalues; and factor interpretability (22). We applied a varimax rotation to the factor loading matrix to achieve a simpler loadings pattern. Nutrients having rotated factor loading greater than or equal to 0.63 on a given factor were used to name the factors and are indicated as "dominant nutrients" hereafter (23). We calculated factor scores following the weighted least squares method. They indicate the degree to which each subject's diet conforms to one of the identified patterns.

To examine the robustness of the identified dietary patterns, we considered the following checks. First, we did a principal axis factor analysis, and we obtained results that were comparable with the ones from PCFA. Second, we calculated factor scores by applying the multiple regression method and standardizing the results (22). The

Table 2. Factor loading matrix and explained variances for the five major dietary patterns identified by factor analysis

Nutrient	Animal products	Starch-rich	Vitamins and fiber	VUFA	AUFA
Animal protein*	**0.76**	0.25	—	0.26	0.43
Vegetable protein	0.31	**0.82**	0.32	0.20	0.12
Cholesterol	**0.67**	0.28	—	0.25	0.43
Saturated fatty acids	**0.75**	0.23	0.12	0.42	0.18
Monounsaturated fatty acids	0.29	0.20	0.26	0.59	0.22
Linoleic acid	0.18	0.19	—	**0.84**	0.12
Linolenic acid	0.31	0.16	—	**0.80**	0.12
Other polyunsaturated fatty acids	0.18	0.22	0.10	0.18	**0.90**
Soluble carbohydrates	0.50	0.21	0.56	—	—
Starch	0.31	**0.86**	0.11	0.15	—
Sodium	0.60	**0.65**	—	0.15	0.12
Calcium	**0.89**	—	0.18	0.12	—
Potassium	0.52	0.41	0.55	0.24	0.25
Phosphorus	**0.82**	0.36	0.17	0.23	0.23
Iron	0.45	0.42	0.23	0.28	0.35
Zinc	**0.69**	0.48	0.15	0.27	0.33
Thiamin (vitamin B_1)	0.57	0.46	0.46	0.22	0.26
Riboflavin (vitamin B_2)	**0.82**	0.12	0.36	0.15	0.21
Vitamin B_6	0.53	0.42	0.49	0.27	0.36
Total folate	0.46	0.32	**0.65**	0.23	0.22
Niacin	0.37	0.47	0.30	0.29	0.59
Vitamin C	0.13	—	**0.87**	—	—
Retinol	0.38	−0.15	0.16	—	0.40
β-Carotene equivalents	—	—	**0.69**	0.31	—
Lycopene	—	0.55	0.19	0.25	0.18
Vitamin D	0.19	0.16	0.11	0.15	**0.86**
Vitamin E	0.14	0.20	0.39	**0.82**	0.17
Total fiber (Englyst)	0.19	0.39	**0.79**	0.15	—
Proportion of VAR explained (%)	24.75	14.97	14.87	12.69	11.72
Cumulative VAR explained (%)	24.75	39.72	54.59	67.28	79.00

NOTE: Estimates from a PCFA performed on 28 nutrients. The magnitude of each loading measures the importance of the corresponding nutrient to the factor.

Abbreviations: VUFA, vegetable unsaturated fatty acids; AUFA, animal unsaturated fatty acids; VAR, variances.

*Loadings ≥0.63 define the dominant nutrients for each factor and were shown in bold typeface; loadings <0.1 were suppressed.

Table 3. Standardized Cronbach's coefficient alpha for each factor and standardized Cronbach's *coefficient alpha when item deleted* for each factor and nutrient

	Animal products	Starch-rich	Vitamins and fiber	VUFA	AUFA
Standardized α when item deleted					
Animal protein	0.967	—	—	—	0.861
Vegetable protein	—	0.946	—	—	—
Cholesterol	0.969	—	—	—	0.864
Saturated fatty acids	0.968	—	—	0.886	—
Monounsaturated fatty acids	—	—	—	0.881	—
Linoleic acid	—	—	—	0.879	—
Linolenic acid	—	—	—	0.870	—
Other polyunsaturated fatty acids	—	—	—	—	0.858
Soluble carbohydrates	0.972	—	0.930	—	—
Starch	—	0.950	—	—	—
Sodium	0.969	0.950	—	—	—
Calcium	0.969	—	—	—	—
Potassium	0.967	0.946	0.916	—	—
Phosphorus	0.965	—	—	—	—
Iron	0.969	0.950	—	—	—
Zinc	0.966	0.945	—	—	—
Thiamin (vitamin B1)	0.967	0.946	0.919	—	—
Riboflavin (vitamin B2)	0.967	—	—	—	—
Vitamin B6	0.966	0.944	0.916	—	—
Total folate	0.969	—	0.917	—	—
Niacin	—	0.947	—	—	0.856
Vitamin C	—	—	0.930	—	—
Retinol	—	—	—	—	0.921
β-Carotene equivalents	—	—	0.942	—	—
Lycopene	—	0.962	—	—	—
Vitamin D	—	—	—	—	0.870
Vitamin E	—	—	—	0.841	—
Total fiber	—	—	0.918	—	—
Standardized α	0.970	0.954	0.933	0.895	0.892

NOTE: Cronbach's coefficient alpha values generally range between 0 and 1.
Abbreviations: VUFA, vegetable unsaturated fatty acids; AUFA, animal unsaturated fatty acids.

correlations between corresponding scores calculated with different methods were equal to 1 for all the comparisons. Third, we conducted stratified PCFA analyses by sex and study center. The identified dietary patterns were consistent with the ones obtained on the overall sample. Given the robustness in the patterns identified by these complementary checks, we calculated factor scores in all subsequent analyses by using results from the original overall PCFA and applying the weighted least squares method.

To assess reliability and refine the identified factors, we evaluated the internal consistency of those nutrients that load >0.40 on any factor using standardized Cronbach's coefficient alpha values (24). We calculated coefficient alpha values for each factor and "coefficient alpha when item deleted" for each factor and for each of the previous nutrients (21).

To confirm internal reproducibility of the identified patterns, individuals were randomly placed into one of two equally sized groups or split samples, and factor analysis was carried out separately in both split samples using the same approach of the main analysis. The procedure was repeated several times.

To improve interpretability of the identified dietary patterns, we calculated the values of the Spearman rank correlation coefficient between the continuous factor scores derived from our factor analysis and the weekly number of portions for 29 selected food groups defined on the same data.

Risk Estimates. For each factor, participants were grouped into four categories according to quartiles of factor scores among the controls.

We estimated the odds ratios (OR) and the corresponding 95% confidence intervals (95% CI) for each quartile category using unconditional multiple logistic regression models. We fitted both separate models for each factor and a composite model that included all the five factors simultaneously. Tests for linear trend were computed for all these models using the within-category medians calculated among the controls. We included in each model the same set of potential confounding variables and risk factors: age, sex, study center, education, body mass index (BMI), occupational physical activity, alcohol drinking, and tobacco smoking.

We carried out stratified analyses of risk by age, education, alcohol drinking, tobacco smoking, BMI, and anatomic subsite. In these analyses, we entered into the composite model categories built on tertiles of each dietary pattern, together with the relevant confounding and risk variables.

We performed most of the analyses using SAS software, version 9.1 (SAS Institute, Inc.). We referred to the open-source statistical computing environment R[9] (25) to do Bartlett's test of sphericity, to calculate factor scores through multiple regression method, and to evaluate internal reproducibility of the patterns through the split-half technique.

Results

The correlation matrix of the original nutrients resulted to be amenable to factor analysis. From visual inspection, it emerged that each nutrient showed at least 10 correlation coefficients that are >0.30 in absolute value (data not shown), thus allowing to perform the analyses on the entire set of selected nutrients. Table 1 reports on statistical procedures for matrix factorability. Bartlett's test of sphericity allowed rejecting the null hypothesis that the correlation matrix is an identity matrix ($P < 0.001$). The Kaiser-Meyer-Olkin statistic was equal to about 0.80, suggesting that we have a good sample size relative to the number of nutrients. The individual measures of sampling adequacy were generally very high, with 22 nutrients having measures >0.70, four in the 0.60s, and only two nutrients with measures <0.60. Overall, the correlations among the individual nutrients were strong enough to suggest that the correlation matrix was factorable.

Table 2 presents the factor loading matrix for the five retained factors. The magnitude of each loading measures the importance of the corresponding nutrient to the factor. These factors explained 79% of the total variance in the original data set. The first factor, named "animal products," had the greatest loadings on calcium, phosphorus, riboflavin, animal protein, saturated fatty acids, zinc, and cholesterol. The second factor, named "starch-rich," was characterized by the greatest loadings on starch, vegetable protein, and sodium. The third factor, named "vitamins and fiber," had the greatest loadings on vitamin C and total fiber, β-carotene equivalents, and total folate. The fourth factor, named "vegetable unsaturated fatty acids," had the greatest loadings on linoleic acid, vitamin E, and linolenic acid. The fifth factor, named "animal unsaturated fatty acids," had the greatest loadings on other polyunsaturated fatty acids and vitamin D. All the examined nutrients showed at least one loading >0.40 on any factor, thus proving to be good candidates for the original set of nutrients even from the statistical standpoint.

Table 3 reports the values of standardized Cronbach's coefficient alpha for each factor and standardized Cronbach's coefficient alpha when item deleted for each factor and nutrient. Standardized coefficient alpha values for each factor were very high. Almost all the standardized coefficient alpha values when item deleted were lower than the corresponding overall standardized coefficient alpha for the same factor, although the differences were small. These findings indicate that most of the nutrients are contributing to high reliability and, in general, justify the original list of nutrients from the statistical standpoint. The internal reproducibility of the sets of patterns identified in the two split samples is reassuring. Factor loading matrices and communalities obtained from the two factor analyses on the split samples were almost identical (data not shown).

Table 4 gives the values of the Spearman rank correlation coefficient between the continuous factor scores derived from our factor analysis based on nutrient intakes and the weekly number of portions for 29 selected food groups on the same data. For the animal products pattern, the highest values of the Spearman rank correlation coefficient were with cheese, milk, eggs, sugar and candies, red meat, cakes and desserts, and liver; for the starch-rich pattern, the highest values were with bread, pasta and rice, and red meat; for the vitamins and fiber pattern, the highest values were with other fruits, citrus fruits, fruiting vegetables, other vegetables, olive oil, cruciferous vegetables, leafy vegetables, and pulses; for the vegetable unsaturated fatty acids pattern, the highest values were with unspecified seed oils and red meat; and for the "animal unsaturated fatty acids" pattern, the highest values were with fish, liver, red meat, white meat, and unspecified seed oils.

Table 5 gives the ORs and corresponding 95% CIs for laryngeal cancer by quartiles of factor scores for the retained dietary patterns. Results refer to the composite model that included all the five factors simultaneously, together with the relevant confounding and risk variables. High intakes of the dominant nutrients for the animal products dietary pattern were directly related to laryngeal cancer risk (OR, 2.34; 95% CI, 1.59-3.45 for the highest versus the lowest score quartile; P for trend <0.001). There was no clear association between the starch-rich factor in dietary pattern and laryngeal cancer (OR, 1.43; 95% CI, 0.97-2.10; P for trend = 0.021), although an indication of risk seemed to emerge. In contrast, the vitamins and fiber dietary pattern was inversely

[9] R Development Core Team: a language and environment for statistical computing. R Foundation for Statistical Computing. Vienna, Austria, 2009. Available from: http://www.R-project.org.

Table 4. Spearman rank correlation coefficients between continuous factor scores derived from factor analysis on nutrient intakes and weekly number of portions for 29 selected food groups defined on the same data

Food group	Animal products	Starch-rich	Vitamins and fiber	VUFA	AUFA
Milk*	**0.47**	−0.17	0.19	−0.11	—
Coffee	0.10	0.10	—	—	—
Tea and decaffeinated coffee	—	—	0.11	—	—
Bread	0.19	**0.67**	—	—	—
Pasta and rice	—	**0.37**	0.10	—	0.11
Soup	0.20	—	—	—	—
Eggs	**0.32**	—	—	0.11	0.22
White meat	—	—	—	0.19	**0.27**
Red meat	**0.29**	**0.25**	—	**0.28**	**0.33**
Liver	**0.27**	−0.13	0.12	—	**0.38**
Processed meat	0.21	0.18	—	—	0.21
Fish	—	—	0.12	—	**0.65**
Cheese	**0.62**	—	—	0.14	—
Potatoes	0.17	0.14	—	0.19	—
Pulses	—	—	**0.27**	—	—
Leafy vegetables	—	—	**0.27**	0.22	—
Fruiting vegetables	—	—	**0.43**	0.12	—
Root vegetables	—	—	—	—	—
Cruciferous vegetables	—	—	**0.30**	—	0.19
Other vegetables	—	—	**0.38**	0.16	—
Citrus fruit	—	—	**0.59**	−0.14	—
Other fruit	—	—	**0.72**	—	—
Soft drinks and fruit juice	0.22	—	—	—	—
Desserts	**0.28**	0.13	0.13	—	—
Sugar and candies	**0.29**	0.14	—	—	—
Butter and margarine	0.19	—	—	0.19	—
Specified seed oils	—	—	—	0.16	—
Unspecified seed oils	0.18	—	−0.13	**0.41**	**0.25**
Olive oil	—	—	**0.31**	0.14	0.15

Abbreviations: VUFA, vegetable unsaturated fatty acids; AUFA, animal unsaturated fatty acids.
*Correlations ≥0.25 (in absolute value) were shown in bold typeface; correlations <0.1 (in absolute value) were suppressed.

associated with laryngeal cancer; the OR was 0.35 (95% CI, 0.24-0.52; P for trend < 0.001) for subjects consuming the highest intakes of the dominant nutrients for this factor. There was no significant association between the vegetable unsaturated fatty acids factor in dietary pattern and laryngeal cancer risk (OR, 0.83; 95% CI, 0.57-1.22; P for trend = 0.148). The animal unsaturated fatty acids pattern was directly related to laryngeal cancer risk: the OR was 2.07 (95% CI, 1.42-3.01; P for trend < 0.001) for subjects consuming the highest intakes of the dominant nutrients for this factor. Consistent results were observed for the five models that included each factor separately.

Table 6 shows the ORs of laryngeal cancer and the corresponding 95% CIs for the identified dietary patterns in strata of anatomic subsite. For the starch-rich, vitamins and fiber, and animal unsaturated fatty acids patterns, we observed similar ORs in the supraglottis and glottis sites and in a third category that we named other/unspecified site. The overall risk associated with the animal products pattern emerged as being mainly accounted for by the supraglottis and glottis subsites. We observed an increase of borderline significance in risk in both the categories of the "vegetable unsaturared fatty acids" pattern only for the supraglottic site of laryngeal cancer. Stratified analyses by age, education, alcohol drinking, tobacco smoking, and BMI did not reveal any significant heterogeneity in risk across strata of covariates, except for the absence of the protective effect of the vitamins and fiber pattern for subjects older than 60 years (data not shown).

Discussion

The present analysis identified five major dietary patterns that explained about 80% of the total variance in the nutrient intakes of this Italian population. They were named animal products, starch-rich, vitamins and fiber, vegetable unsaturated fatty acids, and animal unsaturated fatty acids. The animal products and the animal unsaturated fatty acids patterns were directly related to laryngeal cancer, whereas the vitamins and fiber pattern was inversely associated with it. There was no significant association between the starch-rich and the vegetable unsaturated fatty acids patterns and laryngeal cancer.

In the following, we discuss the identified associations also in terms of the list of food items in the food frequency questionnaire. The animal products pattern emerged as mainly based on foods of animal origin, including cheese and milk, roasted or boiled chicken, steaks and lean ground beef, and boiled, grilled, or roasted fish. The animal unsaturated fatty acids pattern emerged as mainly composed by boiled, grilled or roasted fish, steaks and lean ground beef, tinned tuna and sardines, pasta and rice with meat sauce, and fried eggs and omelettes. Although no clear indication of risk/protection emerged for milk and dairy products, meat, poultry, fish, eggs, and laryngeal cancer (6), there are suggestions that foods of animal origin and animal fats may have a detrimental effect on cancers of the upper aerodigestive tract (26-28).

Plant foods are among the components of the Mediterranean diet having a beneficial effect on cancers of the upper aerodigestive tract (6). Their consumption leads to higher intakes of micronutrients with known antioxidant and anticarcinogenic properties, including carotenoids, vitamins C and E, flavonoids, phytosterols, folates, and dietary fibers. The consistent protective effect of the vitamins and fiber pattern, which is mainly based on fruit and vegetables (see, for instance, Table 4), adds further evidence in this direction, witnessing the role of interdependencies among nutrients in the assessment of cancer risk.

Alcohol and dietary factors are in direct contact with supraglottis site and, hence, more strongly associated with cancer of the supraglottis as compared with cancer of the glottis or other sites (29-32). In our study, there was no systematic difference in risk, but the vegetable unsaturated fatty acids pattern emerged to be related to cancer of the supraglottis only.

Factor analysis is the main statistical method used today to derive dietary patterns defined a posteriori in studies assessing the association between diet and cancer. A suitable use of this technique allows entering in the same regression model different aspects of the overall diet without suffering from severe multicollinearity. Because, for instance, people who consume large amounts of meat and processed meats tend to consume less poultry, fish, and vegetables, and vice versa, the apparent effect of meat and processed meat could possibly be due, at least in part, to low intakes of these other foods (6). Factor analysis may take care of this kind of problems in a more elaborate way than traditional approaches and may eventually offer advantages over simultaneous statistical adjustment for food groups used as independent exploratory covariates (33). However, subjective decisions are involved at each stage of this process, starting from the very first one concerning applying factor analysis or not, and including several other decisions about which data matrix to work on, the number of factors to retain, the opportunity of a factor rotation and which rotation to choose, and the identification of criteria for labeling the factors and of methods for calculating factor scores (34, 35). In this article, we propose the use of visual inspection and statistics for an assessment of the factorability of the correlation matrix. This avoids proceeding with a factor analysis in situations wherein it would be inappropriate. Moreover, we stress the importance of doing a series of separate robustness analyses to evaluate the impact of all the decisions taken during the analysis. For instance, we checked the solution method using different approaches; we considered two different methods for calculating factor scores and applied factor analysis separately in subgroups of subjects. Only after a complete series of checks, a given data reduction solution is

Table 5. ORs of laryngeal cancer and corresponding 95% CIs on quartiles of factor scores from a PCFA

Dietary pattern	Quartile category, OR (95% CI)				P_{trend}*
	I†	II	III	IV	
Animal products	1	1.09 (0.72-1.66)	1.59 (1.06-2.36)	2.34 (1.59-3.45)	<0.001
Starch-rich	1	0.93 (0.62-1.39)	1.46 (1.00-2.15)	1.43 (0.97-2.10)	0.021
Vitamins and fiber	1	0.62 (0.44-0.86)	0.47 (0.32-0.67)	0.35 (0.24-0.52)	<0.001
VUFA	1	1.23 (0.85-1.78)	1.09 (0.74-1.59)	0.83 (0.57-1.22)	0.148
AUFA	1	1.44 (0.97-2.14)	1.49 (1.00-2.21)	2.07 (1.42-3.01)	<0.001

NOTE: Estimates from a multiple logistic regression model adjusted for age, sex, study center, education, BMI, occupational physical activity, tobacco smoking, and alcohol drinking. Results refer to the composite model including all the five factors simultaneously.

Abbreviations: VUFA, vegetable unsaturated fatty acids; AUFA, animal unsaturated fatty acids.

**P* for linear trend.

†Reference category.

Table 6. ORs of laryngeal cancer and corresponding 95% CIs on tertiles of factor scores in strata of anatomic subsite

Dietary pattern	Tertile	OR (95% CI)		
		Supraglottis* 90:1,088†	Glottis* 248:1,088†	Other/unspecified site* 122:1,088†
Animal products	I‡	1	1	1
	II	1.17 (0.57-2.40)	1.32 (0.84-2.08)	0.88 (0.49-1.57)
	III	2.03 (1.07-3.84)	2.30 (1.51-3.49)	1.60 (0.93-2.74)
Starch-rich	I‡	1	1	1
	II	1.09 (0.56-2.12)	1.13 (0.74-1.71)	0.97 (0.55-1.73)
	III	1.35 (0.71-2.57)	1.34 (0.90-2.01)	1.15 (0.66-1.99)
Vitamins and fiber	I‡	1	1	1
	II	0.25 (0.03-2.09)	0.68 (0.25-1.85)	0.26 (0.03-2.05)
	III	0.47 (0.25-0.86)	0.57 (0.39-0.84)	0.45 (0.26-0.77)
VUFA	I‡	1	1	1
	II	2.03 (1.01-4.08)	0.96 (0.65-1.43)	1.07 (0.63-1.82)
	III	1.98 (1.00-3.92)	0.79 (0.53-1.18)	0.90 (0.51-1.58)
AUFA	I‡	1	1	1
	II	1.04 (0.53-2.06)	1.32 (0.86-2.00)	1.13 (0.63-2.02)
	III	2.05 (1.10-3.81)	2.02 (1.36-3.01)	2.00 (1.16-3.46)

NOTE: Estimates from multiple logistic regression models adjusted for age, sex, study center, education, BMI, occupational physical activity, tobacco smoking, and alcohol drinking. Results refer to the composite models including all the five factors simultaneously.

Abbreviations: VUFA, vegetable unsaturated fatty acids; AUFA, animal unsaturated fatty acids.

*Subsites were defined according to the ICD-IX: glottic cancer, ICD-IX 161.0; supraglottic cancer, ICD-IX, 161.1; and other/unspecified laryngeal cancer, ICD-IX 161.2-161.9.

†Cases:controls.

‡Reference category.

likely to be independent from the specific statistical procedure used to derive it. Independence from the originating food frequency questionnaire, from the list of food groups or nutrients used as input, and from other study-specific or country-specific aspects is still a concern in dietary pattern analyses and deserves more attention in future analyses.

These concerns are shared with the definition of scores following the a priori approach for the identification of dietary patterns. This approach is also fraught with other uncertainties and difficulties inherent to score construction or, if it is the case, to selection and interpretation of guidelines. Difficulties include the definition of weightings for the components, of scoring criteria for each component, and of cutoff points for consumption of various foods/food groups incorporated in the score (36, 37). Moreover, although index scores are multidimensional in design, they still end up in a number that may provide little information about single contributing components, obliging researchers to report results from the individual components as well. Nonetheless, dietary patterns defined a priori still remain a very intuitive and practical tool to develop overall descriptors of dietary habits.

This study has some limitations but also several strengths of hospital-based case-control investigations. The high participation and the comparable catchment areas of cases and controls have likely avoided substantial selection biases, and comparison of cases with major diagnostic categories of controls led to similar results. The comparability of the recall between cases and controls was improved by interviewing all the subjects in a hospital setting (38). Information on alcohol, tobacco, and diet were satisfactorily reproducible (39, 40). Subjects with admission diagnosis related to tobacco smoking, alcohol drinking, and diet modifications were not considered as eligible controls. Bias in the recall of food intake by cases should be small, given the limited knowledge and attention paid in this population to the possible relationship between diet and laryngeal cancer.

In the only other study applying PCFA to assess the role of dietary patterns on laryngeal cancer risk, a hospital-based case-control study conducted in Uruguay (29), six dietary patterns were identified a posteriori. Among those, a "drinker" pattern, based on beer, wine, and hard liquors, and a "Western" pattern, based on fried meat, barbecued meat, processed meat, and fried eggs, were directly associated with laryngeal cancer. No significant associations were found for the other patterns, including a "healthy" and a "high-fat" pattern, after adjustment for main confounding and risk variables. The cumulative percentage of total variance explained by the six patterns was ~40%, of which ~11% was explained by the two patterns significantly associated with risk. A priori dietary patterns were identified for this (13) and for a larger set of data, including a companion study conducted in Switzerland (12). These articles pointed to a general protective effect of a Mediterranean dietary pattern (13) and of diversity within vegetable and fruit consumption, whereas a direct association with laryngeal cancer was found for the consumption of different types of meat (12).

We did not identify something similar to a so-called "drinker" pattern (29). We decided to exclude alcohol intake from our original list of variables and to favor its role of major risk factor for laryngeal cancer. At the same time, from visual inspection of the correlation matrix, we realized that the correlations between alcohol and other dietary nutrients were generally weak. One can get the same message looking at the "drinker" pattern identified in the Uruguayan study, wherein loadings of food groups not involving alcohol consumption all looked very weak on this pattern. In agreement with previous studies, our study highlights a protective effect of a diet rich in fruit and vegetables, expressed in the form of a vitamins and fiber pattern, and a detrimental effect of a diet based on large amounts of different foods of animal origin and animal fats, expressed in the form of animal products and animal unsaturated fatty acids patterns. These findings are consistent with a previous analysis on food groups in the larger set of data including Italy and Switzerland (41), wherein red and processed meat, eggs, fish, and sugars were directly related, and fruit and vegetables were inversely related to laryngeal cancer risk.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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