



Nutrient-based dietary patterns and pancreatic cancer risk

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ABSTRACT

Purpose: Few data are available on the role of combinations of foods and/or nutrients on pancreatic cancer risk. To add further information on dietary patterns potentially associated to pancreatic cancer, we applied an exploratory principal component factor analysis on 28 major nutrients derived from an Italian case-control study.

Methods: Cases were 326 incident pancreatic cancer cases and controls 652 frequency-matched controls admitted to hospital for non-neoplastic diseases. Dietary information was collected through a validated and reproducible food frequency questionnaire. Multiple logistic regression models adjusted for socio-demographic variables and major recognized risk factors for pancreatic cancer were used to estimate the odds ratios (OR) of pancreatic cancer for each dietary pattern.

Results: We identified four dietary patterns—named “animal products,” “unsaturated fats,” “vitamins and fiber,” and “starch rich,” that explain 75% of the total variance in nutrient intake in this population. After allowing for all the four patterns, positive associations were found for the animal products and the starch rich patterns, the OR for the highest versus the lowest quartiles being 2.03 (95% confidence interval [CI], 1.29–3.19) and 1.69 (95% CI, 1.02–2.79), respectively; an inverse association emerged for the vitamins and fiber pattern (OR, 0.55; 95% CI, 0.35–0.86), whereas no association was observed for the unsaturated fats pattern (OR, 1.13; 95% CI, 0.71–1.78).

Conclusions: A diet characterized by a high consumption of meat and other animal products, as well as of (refined) cereals and sugars, is positively associated with pancreatic cancer risk, whereas a diet rich in fruit and vegetables is inversely associated.

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Introduction

Cancer of the pancreas is the fifth most common cause of cancer death in men and the fourth in women in Europe [1]. It has a very poor prognosis and it is among the few neoplasms for which mortality trends have not changed over the past 40 years in developed countries [2–4]. Although the etiology of pancreatic cancer remains largely unknown, recognized risk factors are tobacco smoking, heavy alcohol drinking, overweight/obesity, history of diabetes and chronic pancreatitis, and family history of the disease [5,6].

With reference to dietary habits, several epidemiologic studies have reported an excess pancreatic cancer risk for high consumption of (red) meat and starchy foods/sweets, and a decreased risk for high consumption of fruit, vegetables, and folate-rich foods [7–13], although the evidence remains inconsistent [8,14]. A limited number of studies have considered the role of combinations of foods and/or nutrients—identified through a priori scores or a posteriori—derived dietary patterns. In the U.S. prospective National Institutes of Health—AARP Diet and Health study, a nonsignificant 8% reduced risk of pancreatic cancer was found for high versus low no-alcohol Mediterranean dietary score, which became 27% comparing the most extreme categories of the dietary score [15]. A Canadian case-control study of 585 pancreatic cancer cases reported a 49% reduced risk for the fruit and vegetables pattern (characterized by high

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intake of fresh fruit and cruciferous vegetables) in men but not in women, and found no significant associations for the Western pattern (characterized by high intake of processed meat, sweets/desserts, refined grains, and potatoes) and the drinker pattern, characterized by elevated consumption of liquor, wine, and beer [16]. In a combined analysis of the Health Professionals Follow-up Study and the Nurses' Health Study, including a total of 366 pancreatic cancer cases, no overall associations were reported with either the prudent pattern (characterized by high consumption of vegetables, legumes, fruit, whole grains, fish, and poultry) and the Western diet (characterized by high consumption of red and processed meat, refined grains, French fries, high-fat dairy products, sweets, desserts, and high-sugar drinks) [17]. A pattern characterized by high flavonol intake from tea, fruit, cabbage, and wine was found to be inversely related to the risk of pancreatic cancer in smokers in the Multiethnic Cohort including 610 pancreatic cancers, but not in the European Prospective Investigation into Cancer and Nutrition cohort, which included 517 cases [18]. In the Iowa Women's Health Study, which included 256 postmenopausal women with pancreatic cancer, no significant associations were found with any of the four dietary patterns identified, namely, the Mediterranean, the high fiber, the high fruit, and the high sweet [19].

To add further information on dietary patterns potentially associated to pancreatic cancer, we applied an exploratory principal component factor analysis (PCFA) on selected major nutrients derived from an Italian case-control study.

Methods

Between 1991 and 2008, we conducted a multicenter, case-control study on pancreatic cancer in the province of Pordenone and in the greater Milan area, northern Italy [12]. Cases were 326 patients (174 men and 152 women; median age, 63 years) with incident, confirmed pancreatic cancer, admitted to major teaching and general hospitals. Controls were 652 patients (348 men, 304 women; median age, 62 years), frequency matched to cases by study center, gender, and age (with a control to case ratio of 2:1), admitted to the same hospitals as cases for a wide spectrum of acute conditions other than neoplastic or digestive tract diseases. They were hospitalized for traumas (31%), other orthopedic disorders (31%), acute surgical conditions (28%), and miscellaneous other illnesses (10%). More than 95% of cases and controls approached to be interviewed agreed to participate.

Trained interviewers administered a structured questionnaire to both cases and controls during their hospital stay. The questionnaire included information on sociodemographic and anthropometric characteristics, selected lifestyle habits, physical activity, personal medical history, and family history of cancer. Usual diet during the 2 years before cancer diagnosis (for cases) or hospital admission (for controls) was assessed through a validated [20] and reproducible [21] food frequency questionnaire. Study participants were asked to indicate their average weekly frequency of consumption of 78 specific foods, food groups, and Italian recipes, as well as lifetime consumption of alcoholic beverages. Several questions were also included to assess seasoning fat intake patterns. Foods consumed less than once a week but at least once a month were coded as 0.5 per week. Total energy intake and intake of nutrients and fiber were computed using an Italian food composition database, integrated with other sources when needed [22,23].

Data analysis

We carried out an exploratory PCFA on the correlation matrix of 28 selected major macro- and micronutrients to derive a smaller set of

uncorrelated underlying factors, known as dietary patterns [24]. Analyses were performed on the overall group of cases and controls. The PCFA-derived dietary patterns were labeled quantitatively according to those nutrients that loaded 0.63 or higher on the respective factors [25]. To assess reliability and refine the identified patterns, we calculated standardized Cronbach's coefficient alpha for each factor and coefficient alpha when item deleted (i.e., calculated excluding each nutrient, one at a time) for each factor and for each nutrient loading 0.40 or greater. Spearman rank-correlation coefficients between the continuous factor scores derived from PCFA and the weekly number of portions of 29 selected food groups were calculated to improve interpretability of the identified dietary patterns.

For each dietary pattern, study subjects were grouped into four categories according to quartiles of factor scores among controls. Logistic regression models conditioned on age (5-year groups), sex, and center, and adjusted for year of interview (continuous), education (<7, 7–11, ≥12 years), and major recognized risk factors for pancreatic cancer: Body mass index (BMI; <25.0, 25.0–29.9, ≥30.0 kg/m²), tobacco smoking (never smoker, ex-smoker, current smoker <15 cigarettes/d, current smoker ≥15 cigarettes/d), alcohol drinking (0, 1–2, ≥3 drinks/d), and diabetes (yes/no) were used to estimate odds ratios (OR) of pancreatic cancer and the corresponding 95% confidence intervals (CI) for each quartile category of the dietary patterns, compared with the lowest one. Further allowance for other risk factors as family history did not meaningfully modified our risk estimates. Separate models including one dietary pattern at a time, and a composite model including all the patterns simultaneously, were fitted. Tests for trend were based on the difference of the likelihood ratio test between models with and without a linear term for the variable considered. All the analyses were performed using the SAS software, version 9.1 (SAS Institute, Inc., Cary, NC).

Results

The correlation matrix of the original nutrients was suitable for the factor analysis. Each nutrient showed at least 10 correlation coefficients greater than 0.30 in absolute value (data not shown), thus allowing to perform the analyses on the entire set of the selected nutrients. Results of Bartlett's test of sphericity ($P < .001$) allowed to reject the null hypothesis that the correlation matrix is an identity matrix (Appendix Table). The Kaiser–Meyer–Olkin statistic was 0.85, indicating that the sample size for the factor analysis was adequate. The individual measures of sampling adequacy were generally very high, with 26 nutrients having measures of at least 0.70, and the remaining nutrients (i.e., linoleic acid and monounsaturated fatty acids) showing an acceptable value of the statistic. Overall, the correlations among individual nutrients were strong enough to suggest that the correlation matrix was factorable.

Table 1 gives the factor loading matrix for the four retained dietary patterns, which together accounted for about 75% of the variance of the 28 original nutrients. The greater the loading of a given nutrient to a factor, the higher the contribution of that nutrient was on that factor. Thus, the first pattern, labeled “animal products,” had the greatest loadings on calcium, animal protein, phosphorus, riboflavin, saturated fatty acids, cholesterol, and zinc. The second pattern, named “unsaturated fats,” had the greatest loadings on linoleic acid, vitamin E, linolenic acid, and other polyunsaturated fatty acids. The third pattern, labeled “vitamins and fiber,” had the greatest loadings on vitamin C, total fiber, beta-carotene equivalents, soluble carbohydrates, total folate, and potassium. The fourth pattern, named “starch rich,” had the greatest loadings on starch, vegetable protein, and sodium. All the examined nutrients showed at least one loading greater than 0.30 on any factor, thus confirming a role of each nutrient in the original list.

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