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The influence of dietary patterns on the development of thyroid cancer

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Abstract

To elucidate the role of diet in the development of thyroid cancer, we conducted a case–control study of 113 persons with histologically-verified thyroid cancer and 138 controls, matched by age, gender and health unit. Socio-economic data, known risk factors and food consumption of more than 100 items were recorded by interviewer-administered prestructured questionnaire. Factor analysis was used to identify possible dietary patterns and logistic regression analysis was used to explore the effect of food items or dietary patterns on thyroid cancer. After adjustment for age, gender, body mass index (BMI), and total energy intake, significant positive associations were observed for pork consumption, while negative ones were observed for tomatoes, lemons and pasta. Dietary patterns of fruits, raw vegetables and mixed raw vegetables and fruits, led to a reduced risk (corresponding odds ratios (ORs) 0.68, 0.71, 0.73) for all thyroid cancers and similar figures were obtained for papillary thyroid cancers. A dietary pattern of fish and cooked vegetables led to an increased risk (OR 2.79) of follicular cancer.

Keywords: Nutrition; Food items; Dietary patterns; Factor analysis; Thyroid; Cancer

1. Introduction

Thyroid cancer is a rather rare neoplasm that occurs more often in females and has been increasing in incidence over recent decades [1]. The best-established risk factor for thyroid cancer is ionising radiation [2]. A history of goitre and benign thyroid nodules are potential risk factors [3]. An increased risk among women with a higher body mass index (BMI) was suggested in the past, but a pooled analysis of case–control thyroid cancer studies verified that this association exists for females only [4]. Weak associations of menstrual and reproductive factors with a thyroid cancer risk have recently been confirmed [5]. Furthermore, the role of exogenous hormone use (oral contraceptives, hormonal replacement therapy and other female hormones) is controversial [6]. Diet in general, as well as dietary iodine, have been implicated in the aetiology of thyroid cancer by several authors [7–16]. Food items, associated positively or negatively with thyroid cancer, include meat, shellfish, cheese, starchy food, fish, fruits and green vegetables [7,11,17]. All these studies have handled nutritional data either as isolated items or as groups of items. Several authors have argued [18–20] that none of the mechanisms assumed to act independently for each food item is sufficient to explain completely their protective or aetiological effect on malignancies, including that of the thyroid. Recent publications have directed interest towards the application of factor analysis (with the principal component method) on dietary data with the ultimate aim of exploring their combined, rather than their isolated, effect on various types of carcinomas [18–21]. However, to the authors' knowledge, no previous investigation regarding thyroid cancer has treated nutritional data as dietary patterns.

To evaluate the possible effect of nutrition, as reflected by dietary items and patterns, on thyroid cancer risk, we conducted an interview-based case–control epidemiological study in Athens, Greece.

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2. Patients and methods

Between June 1990 and June 1993, 113 Greek patients with histologically-confirmed cancer of the thyroid were admitted to the departments of endocrinology or endocrine surgery in two major hospitals in the Athens metropolitan area. 140 controls, serially matched with the cases by age (±5 years), gender and health unit, were selected from the same two hospitals. The controls were either healthy subjects or patients of other departments with a variety of diseases, almost equally distributed; persons with diseases related to thyroid cancer, other endocrine abnormalities or diet-related conditions were excluded. The two hospitals accept patients (including emergencies) from the Greater Athens metropolitan area, and most of central and southern Greece and the pool from which the controls were selected was presumed to be comparable with that of the thyroid cases. Because the two hospitals (one University and one private) accept patients of potentially different socio-economic backgrounds, we also matched patients and controls by the hospital used.

All eligible (100%) cases and controls asked by their physician (or the physician of the person they were visiting, for the controls) agreed to participate in the study. This is largely due to the fact that, in Greece, the bond between consulting physician and patient is personal and strong. A prestructured questionnaire, covering a wide range of demographic and socio-economic factors, medical history, as well as a detailed food-frequency questionnaire (FFQ), which has been used repeatedly by one of the authors in several earlier projects [22,23], were used for the data collection. The questionnaire has been internally tested for reproducibility during which correlation coefficients above 0.40 were found for most nutrients (data not published). Trained interviewers completed the questionnaire during a face-to-face interview. The interviewers were blind with regard to the disease status and they were unaware of the specific hypothesis to be tested. The interviews took place in the Hospital immediately before or after surgery for cases (±2 days) and always before the patients knew the final histological diagnosis. For hospitalised controls, the interview also took place during hospitalisation and for visitors during their visit to the respective hospital.

Values of total energy intake were outliers for five subjects (4 controls and 1 case), all in the upper tail of the distribution (total energy intake over 4600 Kcal/day). We opted to exclude only the two extremes (both were controls) with values over 5700 Kcal/day, since for the remaining three their BMI could justify their total energy intake. Therefore, the analysis and results are based on 113 cases (27.4% males, 72.6% females) and 138 controls. The median energy intake for cases was 2265.2 with a range of 4117.7, whereas for controls the median was 2240.9 with a range of 4486.6. Of the 251 participants, 74 were males (with mean age±standard devation (S.D.) of 40±16 years) and 177 females (mean±S.D. 41±14 years); the mean ages±S.D. of cases and controls were 44.5±15.8 and 38.2±13.2 years, respectively. Data on the characteristics of cases and controls, including histological type for the cases, are presented in Table 1.

2.1. Dietary assessment

Initially, the FFQ comprised of approximately 130 food items, including traditional Greek dishes and desserts. During the process of data collection, the interviewers decided there was a need for some changes in the dietary questionnaire and a new questionnaire with minor revisions was devised. These changes were accounted for in the statistical analysis. The proportion of cases and controls answering each type of questionnaire was similar.

The final number of food items included in the analysis was reduced to 100 as a result of the elimination of food items that were reported as never or rarely consumed. Some food items were also combined into broader categories (e.g. frozen peas and fresh peas were formed into one new category: peas; margarine from olive oil and margarine from seed-oil were formed into one new category: margarine).

Participants were asked about their average lifetime consumption of each food item, prior to the diagnosis of thyroid cancer for the cases and on a matching date for the controls.

For each food item, the subject had to give their level of consumption (i.e. the number of servings per month, week or day depending on the item) and checkboxes

Table 1
Characteristics of the populations under study

	Cases (113) *N* (%)	Controls (138) *N* (%)
Histological type		
Papillary	81 (72)	
Follicular	10 (9)	
Medullary	10 (9)	
Anaplastic	3 (3)	
Mixed	9 (8)	
Gender		
Males	31 (27)	43 (31)
Females	82 (73)	95 (69)
Therapeutic radiation		
No	100 (88)	132 (96)
Yes	13 (12)	6 (4)
	Mean (S.D.)	Mean (S.D.)
Age (years)	44.5 (15.8)	38.2 (13.2)
Body mass index (kg/m^2)	25.4 (4.5)	24.3 (3.8)
Total energy (Kcal/day)	2308.3 (778.7)	2339.7 (794.3)

S.D., standard deviation; *N*, number.

were available for the responders who 'never consumed' or 'rarely consumed' an item. All frequencies reported were converted to a monthly consumption value. Thus, a response of '4 times a week' was converted to 16 servings per month (serv/m). 'Never consumed' was coded as zero and 'rarely consumed' was coded as 0.5 (serv/m).

Total energy intake (Kcal/month) was estimated by multiplying the servings per month of each food item by the corresponding energy of that item in a typical portion, and adding the values for all items together. Since seasonal items are considered to be consumed for approximately 3 months per year to adjust for over-representation during the energy intake calculations, the corresponding energy intake was divided by 4. The computations were based on the composition tables of Greek Foods and Recipes [24]. Admittedly, portion sizes may vary, but given our data (we asked "how often did you consume ..."), we feel that the estimate of energy intake is generally acceptable, as we had no indication of any systematic differences among our groups of subjects.

2.2. Statistical methodology

The effect of the 100 food items (as serv/m) on the risk of thyroid cancer was examined using logistic regression analysis [25]; due to the rather large number of regressors, forward stepwise variable selection was applied, with probability of entry 0.05 and probability of removal 0.10. Age, gender, BMI (weight (kg)/height (m)^2), and total energy intake in Kcal per month (Kcal/m) [26] were included in the model as covariates, to control for confounding. To control for possible biases introduced by the revision of the questionnaire, we initially analysed key factors for each type of questionnaire. No significant discrepancies were observed. Nevertheless, we also controlled for the 'questionnaire identification index', a binary indicator that was created to identify the use of the initial or revised questionnaire. In the remainder of this paper, we refer to these covariates as 'risk factors'.

The next step was to perform factor analysis, using a principal component method of estimation. This is a multivariate analysis technique for exploring a set of correlated variables. It aims to (a) reduce the effect of intercorrelation by identifying new, meaningful and uncorrelated underlying variables (factor scores) and (b) reduce the number of variables to be included in the subsequent analysis [27]. By this latter attainment of the method, the possibility of statistically significant findings that occur by chance is reduced. This 'transformation' of the correlated variables into uncorrelated ones and the reduction of the explanatory variables to be used in further analysis are among the important advantages of the method. We used factor analysis in order to identify dietary patterns of the general population under study, and thereby subsequently could use these patterns to investigate the combined effect of dietary items on the risk of the disease, rather than treating them as isolated parameters.

Orthogonal VARIMAX rotation method was applied to achieve a simpler structure with a greater interpretability [28] and the correlation matrix rather than the covariance matrix was used (since the variables were not all of the same type and magnitude) [27].

In determining the number of factors to retain, it is common practice to consider all factors with eigenvalues greater than 1. However, according to Chatfield and Collins [27], this is a general 'rule of thumb' that has no theoretical justification. As suggested by the same authors, it may be better to look at the pattern of eigenvalues and see if there is a natural breakpoint. For this reason, and in order to limit the number of factors and identify more meaningful patterns, we focused on those factors for which eigenvalues were greater than 1.5 (similar selection criteria can be found in previous studies described in Refs. [18,19]). Factor scores were then calculated for each individual and for each component extracted. The next step was to identify and 'name' the patterns formed. The subjective 'labelling' is one of the drawbacks of the method. Logistic regression analysis was subsequently performed to reveal the effect of the dietary patterns on the risk of thyroid cancer. The derived factor scores, with simultaneous adjustment for the above-mentioned possible confounding risk factors, were included as explanatory variables, using as response the thyroid cancer status of the individuals. Since it has been previously suggested [7,29] that different histological types of the disease may be affected by different predictors or even by the same predictors with a different effect, we also used a separate logistic regression analysis for cases with the two main histological types of thyroid cancer: papillary and follicular.

In all of the above logistic regression models, adjustment was made for all possible risk factors: age, gender, BMI, questionnaire identification index and total energy intake [25]. Exposure to therapeutic radiation and smoking (as pack years) were also among the factors initially considered to be included in the models. However, when we did include them, their effect was found not to be significant, and the estimates were not substantially altered. Thus, results adjusting for these latter factors are not presented.

Other factors related to thyroid cancer such as parity and benign thyroid nodules were also not included in our logistic regression models since, as far as we know, they are not related to dietary patterns and therefore could not act as confounders.

All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) v.10. Odds ratios (ORs) and confidence intervals (CIs) at 95% are presented, for each unit—or a specified number of units—increase of the parameter under examination.

3. Results

Descriptive statistics of histological type, age, gender, BMI and total energy intake (in Kcal/day, for simplicity reasons) are presented in Table 1. Cases and controls did not differ with respect to the gender distribution (P value = 0.52), mean BMI (borderline P value of 0.050), or mean total energy intake (P value = 0.76). Conversely, exposure to therapeutic radiation was observed in a significantly higher number of cases (12%) than controls (4%) with an OR of 2.9 and 95% CI (1.05–7.79). For males, the corresponding OR (95% CI) was 6.22 (0.66–58.68), and for females 2.21 (0.71–6.91), without the hypothesis of homogeneity of the two ORs being rejected (P value = 0.4).

Despite the effort to match cases and controls with respect to age, the mean age (±S.D.) of the cases was 44.5 (±15.8) years old, and of controls 38.2 (±13.2), a statistically significant difference (P = 0.001). For this reason, in the multiple statistical analysis, age was among the factors controlled for.

The inclusion of all 100 dietary items in the logistic regression model indicated that pork was significantly positively associated with thyroid cancer (Table 2a). Specifically, increasing the consumption of pork by one serving per week (1 serv/w) leads to a relative risk of 1.63, retaining the other factors constant. However, a significant negative association with the risk of the disease was noted for raw tomatoes and lemons (OR for an increase of 1 serv/w 0.92 and 0.91, respectively), while the effect of pasta was of borderline significance (OR = 0.76).

In the attempt to further investigate these specific results, we explored the distribution (and corresponding

Table 2a
Results of the logistic regression analysis examining the association of thyroid cancer with all (100) food items[a]

Food items[b]	P value	OR (4 serv/m increase)[c]	95% CI[d]
Pork	0.01	1.63	1.13–2.35
Tomatoes, raw	0.02	0.92	0.85–0.99
Lemons	0.02	0.91	0.85–0.98
Pasta	0.05[e]	0.76	0.58–1.00

[a] Controlling for age (years), gender, body mass index (BMI) (kg/m^2), questionnaire identification index and total energy intake (Kcal/m).
[b] Only statistically significant associations are presented ($P \leqslant 0.05$).
[c] Odds ratio, after increase in consumption by one serving per week, i.e. four servings per month.
[d] Confidence interval.
[e] borderline significance.

Table 2b
Odds ratios and 95% CI of food items—in quartiles—found to be significantly associated with Thyroid cancer according to the logistic regression analysis

Food items	Quartiles				P trend
	1 (low)[a]	2	3	4 (high)	
	⩽0.5	0.6–15	15.1–28	>28	
Tomatoes, fresh					
Cases:controls	12:7	26:23	27:30	48:78	0.012
OR[b] (95% CI)	1	0.66 (0.22–1.96)	0.53 (0.18–1.53)	0.36 (0.13–0.97)	
OR_{adj}[c] (95% CI)	1	0.76 (0.22–2.55)	0.59 (0.18–1.96)	0.32 (0.1–1.01)	0.002
	⩽4	4.1–15	15.1–28	>28	
Lemons					
Cases:controls	24:24	28:35	22:13	39:66	0.173
OR[b] (95% CI)	1	0.80 (0.38–1.70)	1.69 (0.69–4.12)	0.59 (0.30–1.18)	
OR_{adj}[c] (95% CI)	1	0.91 (0.40–2.07)	1.59 (0.60–4.22)	0.53 (0.24–1.15)	0.001
	⩽0.5	0.6–4	4.1–8	>8	
Pasta					
Cases:controls	9:8	56:63	33:37	15:30	0.126
OR[b] (95% CI)	1	0.79 (0.29–2.19)	0.79 (0.27–2.29)	0.44 (0.14–1.38)	
OR_{adj}[c] (95% CI)	1	0.95 (0.28–3.21)	1.05 (0.30–3.69)	0.56 (0.14–2.18)	0.147
	⩽0.5	0.6–1	1.1–3	>3	
Pork					
Cases:controls	50:66	12:18	16:25	35:29	0.224
OR[b] (95% CI)	1	0.88 (0.38–1.99)	0.84 (0.41–1.75)	1.59 (0.86–2.94)	
OR_{adj}[c] (95% CI)	1	0.97 (0.41–2.33)	1.09 (0.48–2.47)	2.82 (1.36–5.86)	0.001

95% CI, corresponding 95% confidence interval.
[a] Reference category.
[b] OR, odds ratio, unadjusted; corresponding P trend = linear-by-linear association.
[c] OR_{adj}, odds ratio adjusted for age, gender, BMI (kg/m^2) and total energy intake (Kcal/month); corresponding P trend = based on servings/month.

ORs) of cases and controls across the levels of consumption (in approximate quartiles) of the food items found to be significant in the logistic regression analysis (Table 2b). For tomatoes and pork, there was a significant linear association (P for trend <0.01, negative for tomatoes, positive for pork). For lemons, although the P for trend was significant, we noticed that there was a strong protective effect, but not significant, for the highest consumption group compared with the very low consumption group in the first quartile. Similarly, for pasta, the high consumption group (more than twice a week) had a very low protective effect (OR = 0.53) as compared to other groups (Table 2b). This may be the reasons for the overall protective effect of pasta (Table 2a).

With the use of a factor analysis, we extracted 25 components (dietary factors or patterns), that met the criteria described in the statistical methodology. The first 25 factors explained 53.6% of the total variation. Table 3 depicts all appreciable (absolute value >0.30) factor loadings from the rotated pattern matrix of the four dietary patterns found to be significantly associated with the disease (see below for details).

The first dietary pattern (factor 1) was loaded heavily on fruits: peaches, cherries, melon, apricots, pears, apples, tangerines, watermelon, grapes, oranges, strawberries, lemons and, with a lower loading, figs. Mainly raw vegetables (cucumbers, fresh onions, peppers, tomatoes and lettuce) reflected the second dietary pattern (factor 2), with a modest involvement of figs. The third significant pattern (factor 17) was loaded heavily on cauliflower (a cruciferous vegetable) and pineapple (tropical fruit), with a modest involvement of leek (cooked), grapefruit (a citrus fruit) and dried fruits, that is, a mixture of specific vegetables and fruits. The fourth pattern (factor 4) was reflected by six types of cooked vegetables (okra, aubergines, green beans, courgettes, artichokes and peppers) and a relatively high involvement of fish.

General 'labels' for each pattern, based on the most heavily loaded food items, is provided in Table 3 and will be used to refer to a specific pattern in the remainder of this paper.

Logistic regression analysis with the 25 components revealed that the four above-mentioned patterns are significantly associated with the risk of thyroid cancer (Table 4).

Specifically, when the analysis involved a comparison of all thyroid cancer cases as opposed to controls, dietary patterns rich in fruit (pattern 1), raw vegetables (pattern 2) or the specific mixture of vegetables and fruits (pattern 3) led to reduced risks of 0.68, 0.71 and 0.73, respectively.

A separate analysis was performed for cases with the two main types of cancer included in our data-set, that is papillary (81 cases, 72%) and follicular (10 cases, 9%) carcinomas. The results from the examination of cases with papillary thyroid cancer were similar to those resulting from the examination of all cases, as expected due to the high proportion of papillary cases.

To be more specific, the dietary patterns of 'fruits' and 'raw vegetables' were significantly negatively associated with the papillary type of the disease with corresponding ORs of 0.68 and 0.67, respectively. The third pattern (cauliflower, pineapple, leek, grapefruit, dried fruits), although negatively associated with an OR of 0.74, was only of borderline significance ($P = 0.06$).

The risk of the follicular type of cancer was significant for the 4th pattern only, 'fish and cooked vegetables'. This dietary pattern was positively associated with the risk of follicular thyroid cancer, with an OR of 2.79.

All the ORs mentioned above and presented in Table 4 correspond to a 1-unit increase in each estimated factor score, after adjustment for age, gender, BMI, questionnaire identification index and total energy intake.

Table 3
Factor loadings of the four factors significantly associated with thyroid cancer

Pattern 1: Fruits		Pattern 2: Raw vegetables		Pattern 3: Mixed vegetables and fruits		Pattern 4: Fish and cooked vegetables	
Peaches	0.791	Cucumbers	0.807	Cauliflower	0.659	Okra	0.709
Cherries	0.771	Fresh onions, raw	0.800	Pineapple	0.555	Aubergines	0.705
Melon	0.754	Peppers, raw	0.777	Leeks	0.371	Green beans	0.686
Apricots	0.748	Tomatoes, raw	0.736	Grapefruit	0.341	Courgettes	0.490
Pears	0.706	Lettuce, raw	0.491	Dried fruits	0.301	Fish	0.462
Apples	0.678	Figs	0.379			Artichokes	0.413
Tangerine	0.672					Peppers, cooked	0.401
Water melon	0.671						
Grapes	0.666						
Oranges	0.662						
Strawberries	0.607						
Lemons	0.541						
Figs	0.370						

Table 4
Results of logistic regression analysis examining the 25 dietary patterns meeting the preset criteria in the statistical methodology[a]

Dietary patterns[b]	1. Fruits		2. Raw vegetables		3. Mixed vegetables and fruits		4. Fish and cooked vegetables	
Associations	OR	*P* value	OR	*P* value	OR	*P* value	OR	*P* value
All Th. Ca cases versus controls	0.68	0.01	0.71	0.02	0.73	0.04		NS
Papillary Th. Ca versus controls	0.68	0.02	0.67	0.02	0.74	0.06[3]		NS
Follicular Th. Ca versus controls		NS		NS		NS	2.79	0.02

NS, non-significant; Th. Ca. thyroid cancer.
[a] Controlling for age, gender, BMI (kg/m^2), questionnaire identification index and total energy intake (Kcal/m).
[b] Only statistically significant associations are presented.
[c] Borderline significance.

4. Discussion

In this study, emphasis is given in the influence of dietary patterns and not isolated food items on the development of thyroid cancer. The effect of diet has previously been investigated either with the use of extensive FFQs [9] or with questionnaires that record the frequency of consumption of a limited number of specific food items or groups [7,11,12,17] that are suspected to be related to the disease, such as seafood, particularly shellfish, and cruciferous vegetables. Seafood has long been suspected due to its high content of iodine [8,9,30,31] and cruciferous vegetables due to their goitrogenic nature [9,17]. In addition, a series of studies based on Italian populations have been published, each one examining the effect of particular food groups on various malignancies, including that of the thyroid [13–16].

In this study, a FFQ with more than 100 food items was used. This was more extensive than those used by other researchers, with the exception of a study in Hawaii [9], which included more than 150 food items. Cases and controls were matched for age, gender and Hospital (the latter to partially control for socio-economic status). All three factors could potentially be related to dietary preferences, therefore controlling for them was necessary to avoid any confounding effects. However, we do not believe that this adjustment led to a reduction in dietary variability.

When considering the simultaneous effect of food items on the disease, tomatoes, lemons and pasta were found to be negatively associated (with ORs of 0.92, 0.91 and 0.76, respectively, for an increased consumption of 1 serv/w). Two previous Italian-based studies [11,12] have also found a negative association with consumption of fresh fruits, particularly with regard to citrus fruits, and green vegetables, and they found a positive association with consumption of starchy foods and refined cereals. However, with regard to tomato consumption, they observed a non-significant but slightly above unity, OR. Negri and colleagues [13] reported in 1991 that all vegetables that they examined were protective, while in the Norwegian study of Galanti and colleagues in 1997, there was a significant positive association with citrus fruit consumption alone [32].

Pork was found to be positively associated with the disease (an OR of 1.63 for a 1-serv/w increase). This finding is in agreement with the results of Tavani and colleagues in 2000 [16]. Among other methods that have been reported in the literature for combining the consumption of food items [33], recent publications have drawn attention towards the use of factor analysis [18–21]. The application of factor analysis on our data-set pinpointed four dietary patterns that were associated with the disease. Three patterns, namely fruits (including citrus fruits), salad (raw) vegetables and a combination of specific vegetables and fruits, were found to be negatively associated with the risk of thyroid cancer for all histological types.

As mentioned above, the protective effect of fresh fruits has been reported previously. At this point, it is worth noting that three main ‘families’ are marked out from the first pattern. These are the rose family (peaches, cherries, pears, apples, strawberries), the citrus family (tangerine, oranges, lemons) and the gourd family (melons and watermelons). Grapes, which we also found to be related in a protective manner univariately with the cancer risk, were also included in this pattern.

The ‘raw vegetables’ pattern included the ingredients of the traditional Greek salad (cucumbers, peppers, tomatoes), consumed widely in Greece during the summer months, as well as lettuce and fresh onions, which are also widely consumed in Greece as raw salad, especially during the winter months. Figs, widely cultivated in the Mediterranean region, are also included in this pattern.

The third pattern includes cauliflower, a cruciferous vegetable, which in the literature has been associated with a reduced risk of the disease as a goitrogen-containing vegetable [7,9,12], especially for females, and with the papillary histological type of thyroid cancer [17]. Grapefruit is a citrus fruit, while pineapple and dried fruits (all three included in the specific pattern) are rich in manganese. In general, the five items that were heavily weighted in the third pattern are not widely consumed fruits and vegetables in our study population. The mechanisms by which this dietary pattern acts protectively against the disease remain unclear. We suspect that a combination of goitrogen, citric acid (or possibly vitamin C) and manganese is acting protectively.

When we focused on the follicular thyroid cancer cases, a dietary pattern loaded heavily on fish and cooked vegetables was positively associated with the risk of the disease. An increased risk of follicular cancer (OR = 3.8), but not of papillary cancer, was also described in the case–control study of Ron and colleagues [7]. Conflicting evidence exists with regard to the effect of fish or shellfish in the development of thyroid cancer [7,9,11,17,32,34]. A recent pooled analysis of 13 case–control studies [35] concluded that fish and shellfish consumption have no association with the risk of developing thyroid cancer. In most of these studies, however, the follicular and papillary types of thyroid cancer were examined together. It is possible that if fish consumption plays a different role according to the histological type (e.g. protective or no effect for papillary and causative for follicular cancer), the end result will greatly depend upon the proportion of each type in the total number of thyroid cancer cases. This inability to consider follicular and papillary thyroid carcinoma separately is a further obstacle to the elucidation of the role of diet and other risk factors on the development of thyroid carcinoma [10]. Another explanation for the conflicting evidence is the possible correlation of fish with other food items that might prevent the true effect from being revealed, as might be the case in a recent study in Kuwait [34]. Indeed, in our study, when fish consumption was examined as an isolated item, its effect, although not significant, was found to be negative with regard to the development of both follicular and papillary carcinomas. However, the formation of a pattern that includes fish and cooked vegetables—a rather familiar dietary habit of the Greek population—was clearly associated with an increased risk of follicular thyroid cancer only. Nevertheless, to verify these findings with regard to follicular thyroid cancers, a larger number of cases is needed. As the human diet is a synthesis of food items, it is possible that the combined rather than the individual effect of various mechanisms is the key to any risk associations.

To conclude, this study has shown that the dietary patterns, rich in raw vegetables and fresh fruit, found in Greek population are significantly protective for thyroid cancer, while fish and cooked vegetables constitute a possible causal dietary pattern for follicular thyroid cancers. Our results prompt us to investigate further the possible combined effect of several nutrients in order to elucidate the mechanisms that associate diet with thyroid cancer risk.

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