Food and Chemical Toxicology 146 (2020) 111778

Contents lists available at ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

Dietary habits and thyroid cancer risk: A hospital-based case–control study in Sicily (South Italy)

Maria Fiore *, Antonio Cristaldi, Valeria Okatyeva, Salvatore Lo Bianco, Gea Oliveri Conti, Pietro Zuccarello, Chiara Copat, Rosario Caltabiano, Matteo Cannizzaro, Margherita Ferrante

Department of Medical, Surgical and Advanced Technologies "G.F. Ingrassia", University of Catania, Via Santa Sofia, 87, 95123, Catania, Italy

ARTICLE INFO

Keywords:
Thyroid cancer
Food items
Diet
Risk factors

ABSTRACT

Several studies have investigated the role of diet as a risk and/or protective factor against thyroid cancer, both considering individual foods, groups of foods and dietary patterns, but the results are not consistent. The aim of the study was to investigate the relationship between dietary habits and thyroid cancer. Cases and controls were recruited at the University Hospital "G. Rodolico" of Catania. The dietary habits were defined through the "Lifestyle Assessment Questionnaire". The frequency of consumption of each food item was reported on a 4-level scale (never, one time a week, 2–3 times a week, every day of the week). We computed the odds ratios (ORs) of thyroid cancer and the corresponding 95% confidence intervals (CIs) according to the median of control group daily intake of each food group, using multiple logistic regression models adjusted for major confounding factors. Starchy foods (OR = 1.39, 95% CI 0.83–2.32), sweets (OR = 1.39, 95% CI 0.81–2.40) and products rich in salt and fat showed a positive association with thyroid cancer risk. Conversely, an inverse association with disease risk was found for vegetables (cruciferous OR = 0.30, 95% CI 0.10–0.92, non cruciferous OR = 0.57 (0.20–1.57) milk and dairy products (OR = 0.68, 95% CI 0.40–1.13) and seafood (OR = 0.68, 95% CI 0.34–1.22). An increased risk was observed for consumption of iodized salts (OR 2.06, 95% CI 1.21–3.51), tea (OR = 1.42, 95% CI 0.84–2.41) and coca-cola (OR = 3.08, 95% CI 1.53–6.20). Finally, our results confirm the protective effect of a daily water intake of 1–2 L, but unfortunately this quantity is usually consumed by about a quarter of the sample. Dietary habits appear to modify the risk of thyroid carcinoma. A diet with a limited consumption of starchy foods, products rich in salt, fat and sugar and a higher consumption of, cruciferous/non-cruciferous vegetables, milk and dairy products and seafood could be protective towards thyroid cancer. Moreover, the water intake should be increased and the actual need to consume iodized salt should be verified for each subject/area. These results warrant further investigations and, if confirmed, they might have important public health implications for the reduction of thyroid cancer through the improvement of dietary habits.

1. Introduction

According to GLOBOCAN 2018 (Global Cancer Statistics 2018) estimates of cancer incidence and mortality, produced by the International Agency for Research on Cancer (IARC), thyroid cancer is responsible for 567 000 cases worldwide. In particular, the global incidence rate calculated for women in 2018 was 10.2 per 100 000 three times higher than in men. Mortality rates are much lower with rates from 0.4 to 0.5 per 100 000 in men and women respectively, and an estimated 41 000 deaths (Bray et al., 2018).

The etiology of thyroid cancer is not well established. The only well confirmed risk factor for thyroid cancer is ionizing radiation (Ron et al., 2012), although there is evidence that other factors may play a role (Kitahara et al., 2018). History of benign thyroid nodules/adenoma or goiter, sex (women), a diet low in iodine (follicular thyroid cancer) and obesity are known to increase the risk of thyroid cancer (Choi et al., 2014; Dal Maso et al., 2009; Bray et al., 2018; Fiore et al., 2019a; Memon et al., 2002; Zhang et al., 2013; Franceschi et al., 1999; Peterson et al., 2012). On the contrary, unlike other cancers, cigarette smoking and alcohol consumption were associated with a decreased risk of thyroid cancer (Kitahara et al., 2012).

Several authors investigated the role of the dietary factors on thyroid cancer risk (Choi et al., 2014; Dal Maso et al., 2009; Franceschi et al., 1991). In particular, goitrogenic foods such as cruciferous vegetables

* Department "GF Ingrassia", University of Catania, Via Santa Sofia, 87, 95123, Catania, Italy.
E-mail address: mfiore@unict.it (M. Fiore).

https://doi.org/10.1016/j.fct.2020.111778
Received 28 May 2020; Received in revised form 14 September 2020; Accepted 21 September 2020
Available online 26 September 2020

(cabbage, broccoli, cauliflower, etc.), cassava (Higdon et al., 2007; Bosetti et al., 2002), other iodine-rich foods (Choi et al., 2014; Dal Maso et al., 2009), vegetables and fruits (Choi et al., 2014; Dal Maso L, 2009; Bosetti et al., 2002;
Jung et al., 2013;
Markaki et al., 2003), seem to have protective effects on thyroid cancer (Antognelli et al., 2019). Conversely, starchy food have been found associated positively with thyroid cancer (Markaki et al., 2003). Nevertheless the evidence on the relationship between some food items or nutrients and the risk of thyroid cancer is not yet conclusive. For example although different studies investigated the relationship between fish consumption and thyroid cancer, the results were inconsistent (Choi et al., 2014). Others studies examined the relationship between meat and dairy consumption and thyroid cancer, and the results were either positive or insignificant (Choi et al., 2014). In this study, we aimed to assess the relationship between dietary habits and thyroid cancer.

2. Material and methods

2.1. Study setting and data collection

Study population and methods have been reported previously (Fiore et al., 2019b). In brief, the study was conducted with subjects diagnosed with thyroid cancer between January 1st 2009 and July 31st 2018 at the Endocrine-Surgery operative unit of the University Hospital "Policlinico – Vittorio Emanuele" of Catania (Sicily, Italy). Of 118 cases initially notified, 12 patients refused to participate, leaving 106 subjects eligible for the study. The response rate from the cases was 89,8%.

Controls were enrolled at the laboratory of clinical analysis of the same university hospital. Eligible criteria for controls were not to have thyroid cancer or other ones, as well hormonal and gynecological diseases within two years prior to interview. The negative history of previous diseases was auto-refered and validation by medical records was unfeasible. Of 241 eligible controls, 24 refused to participate. Finally, 217 controls (response rate 90.0%) were included in the analysis.

The study was approved by the Ethics Committee of the University Hospital "Policlinico – Vittorio Emanuele" of Catania (agreement no. 553). Written informed consent was obtained from all participants.

Between January 2015 and July 2018, two trained investigators interviewed the cases and control participants using a structured questionnaire. The questionnaire included items on socio-demographic characteristics (age, residence, education level and occupation), anthropometric parameters, reproductive and hormonal history, smoking status, alcohol consumption, exposure to radiation or chemicals, personal and family medical history. The subject who answered "yes" to the question "smokes daily" (daily smoker = who smokes at least one cigarette a day) has been considered "smoker", and was considered "alcohol consumer" who reported to consume at least one glass a day of wine, beer, alcohol or spirits.

Data on food items and water consumption, food supplements, vitamin and caffeinated beverages use, relating to the year preceding the thyroid cancer diagnosis, were collected using the Lifestyle Assessment Questionnaire of the Italian Health Institute (Istituto Superiore di Sanità. Osservatorio Fumo, Alcol e Droga–OSSFAD. Available online: http://old.iss.it/binary/ofad/cont/questionario%20giovani%20in%20forma.1225957648.pdf (accessed on 20 February 2019).

2.2. Data analysis

Food items were categorized into major food groups and sub-groups, based on chemical composition criteria and hypothetical association with thyroid cancer,. as follows reported: Starchy foods (bread, pasta, rice, pizza, rusks, crackers/breadsticks, potatoes, cereal flakes and cereals); Sweets (biscuits, brioches, croissants, chocolate, others sweets); Products rich in salt and fat (packaged snacks, sandwiches, ready-made foods and sauces as mayonnaise and ketchup;, Cruciferous vegetables (cabbage, broccoli, cauliflower.), Non-cruciferous vegetables: (rocket, soy, spinach, lettuce and others vegetables), Legumes. and Fruit; Meat and meat products (red meats, eggs, cold cuts); Milk and diary products (milk, fresh and aged cheeses); Fish and seafood (fish, mollusks and crustaceans).

The frequency of consumption of each food item was reported on a 4-level scale (never = 1, one-time a week = 2, two–three times a week = 3, every day of the week = 4) (Table S2).

The values of the Likert scale assigned to each individual food item were added by group of foods (higher number corresponded to higher consumption), then we created two categories (higher and less consumption) using as cut off the median consumption of the controls. The "Products rich in salt and fat", "legumes" and "fruit" were analyzed individually using cut off 2 (≤ 2 = never + 1 time a week and >2 = 2–3 times a week + every day).

Type (tap water, bottled water) and quantity of drinking water consumed (1/2 L, 1 L, 2 or more liters) were investigated. Food supplements, iodized salt and vitamin were inquired both for use (yes/no) and for at least weakly consumption time (0–2 years, > 2 - ≥10 years). Caffeinated drinks consumption was reported on a 3-level scale (never, 1–3 cups/die, 4-≥6 cups/dies).

Univariate and multivariate unconditional logistic regression were performed to estimate odds ratios (ORs) and 95% confidence intervals (CIs) of thyroid cancer both for each food item (Table S2) and food groups consumption with "never" and "≤ median of control group" categories as a reference, respectively. We included age, BMI and educational attainment as possible confounders; moreover in the analysis in women only we included irregular period (yes/no) and number of pregnancy (continuous variables) as hormonal confounding factors. Others variables were not included in the final analysis because they did not meet criteria for confounding and hence did not substantially alter odd ratio estimates. We also carried out stratified analysis by sex and BMI as potential effect modifier. We did not perform a stratified analysis by thyroid cancer histology because of small sample size. Statistical analyses were performed using statistical software SPSS for Windows (Statistical Package for the Social Science, version 21.0; SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Baseline characteristics of study participants

A total of 106 patients (mean age at diagnosis 47 ± 14 years, females: 78.3%) and 217 controls (mean age 42 ± 17 years, females: 70.0%) were included in the study. Papillary carcinoma was the most frequent histological type (97 cases; 91.5%), followed by five (4.7%) cases with a follicular carcinoma and 4 (3.8%) cases with medullary type. Baseline characteristics of cases and controls are shown in Table S1. Most cases were diagnosed among women (83/106, 78.3%), with a slightly higher frequency in the age group ≥50 years (61/106, 57.5%).

No clear association emerged for smoking status (OR = 0.28, 95% CI 0.06–1.25). We observed a slightly positive association with alcohol habits (yes/no) (OR = 1.38, 95%CI 0.77–2.48). However, considering the alcohol daily consumption (glass/day) by wine (21% cases vs 12% controls), beer (10% cases vs 5% controls) and spirits (0% case vs 1.5% controls), we observed a decreased risk for wine (OR = 0.43, 95% CI 0.15–1.20) and an increased risk for beer (OR = 1.61 95% CI 0.18–15) though statistically unstable risks due to small sample size. The risk for the consumption of spirits was not calculated due to the zero consumption of the cases. Finally, about median daily alcohol consumption it must be highlighted how for neither cases nor for controls it was more than 1 glass/day.

3.2. Frequency of food items consumption by cases and controls and risk associated with food item consumptions

Table 1 shows the frequency of food items consumption within case and control groups. The cases had a daily consumption of bread (82.5% cases vs 63.0% controls) and rusks (31.8% cases vs 12.9% controls) higher than the controls. Almost 80% of cases consumed pizza 2–3 times a week. Cases, more than controls, had a daily consumption for most of Sweet group (biscuits, brioches/croissants, chocolate, packaged snacks, sandwiches, ready-made foods, sauces like mayonnaise and ketchup). Also the consumption of 2–3 times a week of sauces was more frequent in cases than in controls. Controls more than cases consumed daily most of the cruciferous vegetables (cabbage, broccoli, cauliflower), non-cruciferous vegetables (rocket, soy and spinach), legumes and fruit. Cauliflower was consumed 2–3 times a week more frequently from cases than controls (65.0% vs 54.4%, respectively). More than 90% of cases and controls did not consume soy. Cases consumed red meat, eggs and cold cuts 2–3 times a week more frequently than controls, conversely controls consumed 2–3 times week milk and cheeses more than the cases. Controls consumed 2–3 times a week most fish and seafood items (breeding fish, caught fish, freshwater fish, molluscs) more than cases.

The ORs and 95% CIs associated with each food item consumptions highlighted an increased risk for some foods (e.g. bread, pizza, chocolate, sweet, eggs and cold cuts) and a potential protective effect for legumes, fruit and vegetables as cabbage, broccoli rocket and lettuce; while for some food items we could not estimate the risk due to the small sample size (Supplementary Table S2).

3.3. Risk of thyroid cancer associated with food group consumptions

Table 2 shows the risk of thyroid cancer associated with food group consumption and the analysis in women only including irregular period (yes/no) and number of pregnancy (continuous variables) as hormonal confounding factors. Stratified analysis by sex and BMI is reported in Table S3. We have found a positive association with thyroid cancer risk for "Starchy foods" consumption above the median, particularly in men (OR = 1.39, 95% CI 0.83–2.32; Female OR = 1.13, 95% CI 0.62–2.08; Male OR = 3.21, 95% CI 1.04–9.91) and in subjects with higher BMI (BMI <24.9 OR = 1.21, 95% CI 0.69–2.13, BMI 24.9->30 OR = 1.98, 95% CI 0.57–6.89).

Moreover, the analysis only on women including hormonal confounding factors showed an increasing risk associated with a greater consumption of starchy foods (OR = 1.77, 95% CI 0.95–1.02) (Table 2 and S3).

Consumption of "Sweets" foods showed an increased risk, particularly in women (OR = 1.39, 95% CI 0.81–2.40; Female OR = 1.40, 95% CI 0.75–2.62; Male OR = 1.06, 95% CI 0.31–3.65) and in subjects with higher BMI. In the model including only women and adjusted also for hormonal confounding factors we observed an increased risk associated with "sweet" consumption (OR = 1.95, 95% CI 0.83–4.58) (Table 2 and S3).

Consumption of "Products rich in salt and fat" showed an increased risk for all items, particularly in men and in subjects with higher BMI and in the model including only women and adjusted also for hormonal confounding factors (Table 2 and S3).

Consumption of cruciferous and non-cruciferous foods showed a not clear risk (OR = 0.30, 95% CI 0.10–0.92; OR = 0.57, 95% CI 0.20–1.57); conversely non-cruciferous foods in sex stratified analysis showed an increased risk for men (Male OR = 1.46, 95% CI 0.21–10; Female OR = 0.55, 95% CI 0.13–2.29), though statistically unstable risks. A negative association was found with thyroid cancer risk for "Legumes" consumption (OR = 0.81, 95% CI 0.49–1.34) (Table 2 and S3).

"Fruit" consumption showed no risk (OR = 0.99, 95% CI 0.54–1.86), the sex and BMI stratified analysis showed a higher risk for men (OR = 5.89, 95% CI 0.70–49), and for higher BMI (OR = 8.63, 95% CI 0.94–79). The model including only women and adjusted also for hormonal confounding factors highlighted a protective effect associate with a higher consumption of fruit (OR = 0.65, 95% CI 0.28–1.51) (Table 2 and S3).

Consumption of "Meat and meat products" showed an increased risk (OR = 1.35, 95% CI 0.78–2.34); sex and BMI stratified analysis highlighted a slightly increased risk for women (Female OR = 1.44, 95% CI 0.75–2.78 Male OR = 1.31, 95% CI 0.40–4.29) and for higher BMI (OR = 1.53, 95% CI 0.42–5.49), though statistically unstable risks (Table 2 and S3).

Consumption of "Milk and diary products" showed a decreased risk (OR = 0.68, 95% CI 0.40–1.13); sex stratifies analysis highlighted no association only for men (Male OR = 1.02, 95% CI 0.37–2.84; Female OR = 0.52, 95% CI 0.28–0.95), though statistically unstable risks.

Finally, we have found a negative association with thyroid cancer risk for "Fish and seafood" consumption under the median (OR = 0.68, 95% CI 0.34–1.22). The analysis only on women including hormonal confounding factors showed a decreasing risk associated with a greater consumption of "Milk and dairy products" (OR = 0.37, 95% CI 0.18–0.79) and "Fish and seafood" (OR = 0.31, 95% CI 0.12–0.80) (Table 2 and S3).

3.4. Risk of thyroid cancer associated with consumption of water, food supplements, iodized food and vitamins use

Table 3 provides OR and 95% CI for developing thyroid cancer according to water consumption, food supplements, iodized salt and vitamine use. No substantial difference was detected between bottled vs tap water consumption (OR = 1.03, 95% CI 0.55–1.91). Conversely, an inverse association with the amount of water consumed was observed, with odd ratio 0.42 (95% CI 0.22–0.81) for consuming of at least 1 L and odd ratio 0.40 (95% CI 0.19–0.83) for consuming two or more liters compared with a consume of half liter, slightly higher in men (Male OR = 0.21, 95% CI 0.04–1.11; Female OR = 0.50, 95% CI 0.24–1.03). The latest ORs remained constant even for consuming two or more liters compared with half liter.

No clear association emerged both for food supplements (yes/no) (OR = 0.87, 95% CI 0.45–1.66) and the duration of their use between 2 and 10+ years (OR = 1.14, 95% CI 0.28–4.69); the stratified analysis by sex highlighted similar results for food supplements (yes/no) (Male OR = 0.59, 95% CI 0.11–3.35; Female OR = 0.78, 95% CI 0.37–1.65) and an increasing risk for the duration of their use between 2 and 10+ years (Female OR = 2.74, 95% CI 0.45–16; Male have no risk measure because of zero frequencies). A positive association with thyroid cancer risk was observed for consumption of iodized salt (yes/no) (OR 2.06, 95% CI 1.21–3.51), higher in women (Female OR = 2.24, 95% CI 1.19–4.20; Male OR = 1.16, 95% CI 0.38–3.58), no clear association emerged for the duration of their use between 2 and 10+ years (OR = 1.11, 95% CI 0.50–2.44), the stratified analysis by sex highlighted an increasing risk for the duration of their use between 2 and 10+ years (Male OR = 2.44, 95% CI 0.21–29; Female OR = 0.95, 95% CI 0.39–2.31), though statistically unstable risks.

No clear association emerged for both vitamin (yes/no) (OR = 0.91, 95% CI 0.43–1.93) and the duration of their use between 2 and 10+ years (OR = 0.28, 95% CI 0.05–1.75). The stratified analysis by sex highlighted similar results for vitamine (yes/no) (Male OR = 1.08, 95% CI 0.24–4.98; Female OR = 0.78, 95% CI 0.31–1.92) and a decreasing risk for the duration of their use between 2 and 10+ years (Female OR = 0.19, 95% CI 0.01–2.92; Male have no risk measure because of zero frequencies), though statistically unstable risks.

3.5. Risk of thyroid cancer associated with consumption of caffeinated beverage

Table 4 presents the ORs and 95% CIs for developing thyroid cancer according to daily intake for each caffeinated beverages (coffee, tea, coca-cola, Red bull). We observed a direct association for higher

Table 1
Frequency of food item consumptions according to case and control groups.

Food groups	Cases n (%)				Controls n (%)			
	Never	1 time a week	2-3 times a week	Every day of the week	Never	1 time a week	2-3 times a week	Every day of the week
Starchy foods								
Bread	1 (1.0)	6 (5.8)	16 (16.5)	80 (82.5)	11 (5.8)	21 (10.0)	59 (31.2)	119 (63.0)
pasta and/or rice	1 (1.1)	7 (6.9)	35 (36.8)	59 (62.1)	1 (0.5)	21 (10.0)	79 (42.0)	108 (57.4)
Pizza	8 (21.1)	65 (63.1)	30 (78.9)	0 (0)	22 (32.8)	137 (67.2)	42 (62.7)	3 (4.5)
Rusks	42 (49.4)	18 (17.5)	16 (18.8)	27 (31.8)	92 (62.6)	51 (25.8)	36 (24.5)	19 (12.9)
crackers/breadsticks	50 (64.1)	25 (24.3)	18 (23.1)	10 (12.8)	104 (63.8)	35 (17.7)	44 (27.0)	15 (9.2)
Potatoes	9 (17.0)	50 (48.5)	42 (79.2)	2 (3.8)	16 (14.5)	89 (44.7)	92 (83.6)	2 (1.8)
cereal flakes	74(80.4)	11 (10.7)	8 (8.7)	10 (10.9)	110 (65.1)	30 (15.1)	41 (24.3)	18 (10.7)
cereals	58 (72.5)	23 (22.3)	21 (26.3)	1 (1.3)	53 (42.4)	75 (37.5)	68 (54.4)	4 (3.2)
Sweets								
biscuits,	29 (39.7)	30 (29.1)	20 (27.4)	24 (32.9)	36 (22.5)	49 (23.4)	83 (51.9)	41 (25.6)
Brioches/croissants	53 (68.8)	24 (23.8)	9 (11.7)	15 (19.5)	63 (47.7)	70 (34.7)	48 (36.4)	21 (15.9)
chocolate	28 (48.3)	45 (43.7)	22 (37.9)	8 (13.8)	74 (53.6)	63 (31.3)	50 (36.2)	14 (10.1)
Others sweets	12 (24.0)	53 (51.5)	25 (50.0)	13 (26.0)	46 (34.8)	74 (35.9)	60 (45.5)	26 (19.7)
Products rich in salt and fat								
packaged snacks	71 (79.8)	14 (13.6)	9 (10.1)	9 (10.1)	119 (76.3)	44 (22.0)	23 (14.7)	14 (9.0)
sandwiches	58 (73.4)	24 (23.3)	16 (20.3)	5 (6.3)	97 (71.3)	64 (32.0)	34 (25.0)	5 (3.7)
ready-made foods	89 (95.7)	10 (9.7)	3 (3.2)	1 (1.1)	164 (95.9)	31 (15.3)	7 (4.1)	0 (0)
Sauces (mayonnaise, ketchup)	80 (90.9)	15 (14.6)	8 (9.1)	0 (0)	138 (92.6)	54 (26.6)	11 (7.4)	0 (0)
Cruciferous								
Cabbage	32 (43.8)	30 (29.1)	35 (47.9)	6 (8.2)	31 (24.8)	72 (36.5)	69 (55.2)	25 (20.0)
Broccoli	18 (28.6)	40 (38.8)	37 (58.7)	8 (12.7)	29 (24.0)	77 (38.9)	68 (56.2)	24 (19.8)
cauliflower	14 (23.3)	43 (41.7)	39 (65.0)	7 (11.7)	33 (26.4)	73 (36.9)	68 (54.4)	24 (19.2)
Non cruciferous								
Rocket	49 (69.0)	32 (31.1)	17 (23.9)	5 (7.0)	59 (47.6)	76 (38.0)	51 (41.1)	14 (11.3)
Soy	97 (98.0)	4 (3.9)	0 (0)	2 (2.0)	162 (91.0)	19 (9.6)	12 (6.7)	4 (2.2)
Spinach	20 (36.4)	48 (46.6)	34 (61.8)	1 (1.8)	38 (33.6)	87 (43.5)	67 (59.3)	8 (7.1)
Lettuce	9 (11.7)	25(24.5)	49 (63.6)	19 (24.7)	16 (10.6)	52 (25.6)	105 (69.5)	30 (19.9)
Others vegetables	4 (4.5)	14 (13.6)	44 (49.4)	41 (46.1)	12 (7.1)	37 (18.0)	106 (62.7)	51 (30.2)
Legumes	19 (31.1)	41 (40.2)	40 (65.6)	2 (3.3)	14 (11.9)	89 (43.0)	102 (86.4)	2 (1.7)
Fruit	7 (7.5)	10 (9.7)	16 (17.2)	70 (75.3)	15 (8.5)	28 (13.7)	52 (29.4)	110 (62.1)
Meat and meat products								
red meat	6 (10.0)	43 (41.7)	50 (83.3)	4 (6.7)	15 (13.5)	96 (46.4)	85 (76.6)	11 (9.9)
cold cuts	18 (28.6)	40 (38.8)	41 (65.1)	4 (6.3)	43 (35.5)	84 (41.0)	69 (57.0)	8 (6.6)
Eggs	10 (21.3)	55 (53.9)	36 (76.6)	1 (2.1)	24 (23.5)	105(50.7)	74 (72.5)	4 (3.9)
Milk and dairy products								
Milk	35 (37.2)	9 (8.7)	13 (13.8)	46 (48.9)	59 (31.6)	20 (9.7)	57 (30.5)	71 (38.0)
Fresh cheeses	13 (21.3)	42 (40.8)	40 (65.6)	8 (13.1)	26 (18.1)	57 (24.8)	101 (70.1)	17 (11.8)
Aged cheeses	32 (45.1)	31 (30.4)	30 (42.3)	9 (12.7)	33 (25.0)	64 (32.7)	83 (62.9)	16 (12.1)
Fish and seafood								
breeding fish	41 (64.1)	39 (37.9)	22 (34.4)	1 (1.6)	58 (58.6)	102(50.7)	41 (41.4)	0 (0)
caught fish	32 (49.2)	38 (36.9)	32 (49.2)	1 (1.5)	57 (51.8)	94 (46.1)	53 (48.2)	0 (0)
Freshwater fish	92 (97.9)	9 (8.7)	2 (2.1)	0 (0)	104 (76.5)	62 (31.3)	32 (23.5)	0 (0)
Mollusks	72 (94.7)	27 (26.2)	4 (5.3)	0 (0)	127 (90.1)	58 (29.1)	14 (9.9)	0 (0)

Table 2
Odds ratios (OR) and 95% confidence interval (CI) for developing thyroid cancer according to food group consumptions.

Food groups	Categories below (≤) and above (>) the median	Case n (%)	Control n (%)	OR[a]	OR[b]	(95% CI)	OR[c]	(95% CI)
Starchy foods (Bread, pasta, pizza, rice, rusks, crackers, breadsticks, potatoes, cereal flakes, cereals)	≤16	44 (43.1)	98 (50.8)	[d]	[d]		[d]	
	>16	58 (56.9)	95 (49.2)	1.36	1.39	(0.83–2.32)	1.77	(0.95–1.02)
Sweets (Biscuits, brioches, croissants, chocolate, others sweets)	≤9	68 (64.2)	131 (60.4)	[d]	[d]		[d]	
	>9	38 (35.8)	86 (39.6)	0.85	1.39	(0.81–2.40)	1.95	(0.83–4.58)
Products rich in salt and fat[e]								
Packaged snacks	≤2	88 (83.0)	180 (82.9)	[d]	[d]		[d]	
	>2	18 (17.0)	37 (17.1)	0.99	1.42	(0.72–2.82)	2.60	(0.91–7.43)
Sandwiches	≤2	85 (80.2)	178 (82.0)	[d]	[d]		[d]	
	>2	21 (19.8)	39 (18.0)	1.13	1.77	(0.91–3.46)	2.73	(0.95–7.81)
Ready-made foods	≤2	102 (96.2)	210 (96.8)	[d]	[d]		[d]	
	>2	4 (3.8)	7 (3.2)	1.18	1.79	(0.44–7.20)	1.37	(0.11–17)
Sauces (mayonnaise, ketchup)	≤2	98 (92.5)	206 (94.9)	[d]	[d]		[d]	
	>2	8 (7.5)	11 (5.1)	1.53	2.57	(0.92–7.23)	2.92	(0.45–19)
Cruciferous vegetables (Cabbage, broccoli, cauliflower)	≤9	43 (87.8)	88 (78.6)	[d]	[d]		[d]	
	>9	6 (12.2)	24 (21.4)	0.51	0.30	(0.10–0.92)	0.46	(0.08–2.69)
Non cruciferous vegetables (rocket, soy, spinach, lettuce, others vegetables)	≤13	28 (77.8)	41 (66.1)	[d]	[d]		[d]	
	>13	8 (22.2)	21 (33.9)	0.56	0.57	(0.20–1.57)	0.52	(0.08–3.53)
Legumes[e]	≤2	104 (98.1)	215 (99.1)	[d]	[d]		[d]	
	>2	2 (1.9)	2 (0.9)	0.71	0.81	(0.49–1.34)	0.78	(0.37–1.65)
Fruit[e]	≤2	20 (18.9)	55 (25.3)	[d]	[d]		[d]	
	>2	86 (81.1)	162 (74.7)	1.46	0.99	(0.54–1.86)	0.65	(0.28–1.51)
Meat and meat products (Red meat, cold cuts, eggs)	≤7	66 (64.7)	133 (66.2)	[d]	[d]		[d]	
	>7	36 (35.3)	68 (33.8)	1.07	1.35	(0.78–2.34)	1.58	(0.69–3.62)
Milk and diary products (milk, fresh cheeses and aged cheeses)	≤7	61 (57.5)	111 (51.2)	[d]	[d]		[d]	
	>7	45 (42.5)	106 (48.8)	0.77	0.68	(0.40–1.13)	0.37	(0.18–0.79)
Fish and seafood (Breeding fish, caught fish, freshwater fish, mollusks and crustaceans)	≤7	78 (75.7)	128 (66.7)	[d]	[d]		[d]	
	>7	25 (24.3)	64 (33.3)	0.64	0.68	(0.34–1.22)	0.31	(0.12–0.80)

[a] Crude model.
[b] Model adjusted by age, BMI and educational attainment.
[c] Model with women only adjusted by age, BMI, educational attainment and hormonal confounding factors (irregular period and number of pregnancy).
[d] Reference category.
[e] Cut off ≤2 (Never + once time a week) vs > 2 (2–3 times a week + everyday).

consumers of the following caffeinated beverages: tea (OR = 1.42, 95% CI 0.84–2.41), coca-cola (OR = 3.08, 95% CI 1.53–6.20 medium consumption vs never and OR = 2.42, 95% CI 0.20–28 highest consumption vs never), and Red bull (OR = 2.57, 95% CI 0.56–12); the latest two had instable associations (e.g. highest consumption of coca-cola vs never), probably because of the small sample size. Finally, we found an unclear association for coffee (OR = 0.65, 95% CI 0.32–1.31 and OR = 0.97, 95% CI 0.34–2.77 for a consumption of 1–3 cups/day vs never and 4-≥6 cups/day vs never).

4. Discussion

This study highlighted an increased risk of thyroid cancer associated with the consumption of some food items (starchy foods/refined cereal, products rich in salt and fat, and sweets), caffeinated drinks and iodized salt. On the contrary a decreased risk was associated to higher consumption of fish, cruciferous vegetables and not, legumes, milk and diary products and fruit.

The consumption of refined cereal and higher sugar foods has been associated with the risk of thyroid cancer because of their high glycemic index (Sieri et al., 2015, 2017). The main mechanism for these associations is thought to be due to chronic hyperinsulinemia. Insulin is itself a mitogen and increases the bioactivity of insulin-like growth factor, which can promote cancer by inhibiting apoptosis and stimulating cell proliferation (Sieri et al., 2017; Wu et al., 2018; Turati et al., 2019; Antognelli et al., 2019). Moreover, it was demonstrated that leptin, a factor involved in glucose metabolism and directly associated with obesity, insulin levels and female sex, may plays an important role in papillary thyroid cancer pathogenesis (Hedayati et al., 2011). Accordingly, our results highlighted that a high intake of high sugar foods could increase thyroid cancer risk especially in women.

In agreement with previous findings, our results highlighted a

Table 3
Odds ratios (OR) and 95% confidence intervals (CI) for developing thyroid cancer according to water consumption, food supplements, iodized salt and vitamin use.

	Case n(%)	Control n(%)	OR[a]	OR[b]	(95% CI)
You normally drink					
Tap water	23 (21.9)	40 (18.7)	[c]	[c]	
Bottled water	82 (78.1)	174 (81.3)	0.82	1.03	(0.55–1.91)
How many liters?					
Half liter	29 (27.6)	37 (17.3)	[c]	[c]	
One liter	48 (45.7)	114 (53.3)	0.54	0.42	(0.22–0.81)
Two or more liters	28 (26.7)	63 (29.4)	0.57	0.40	(0.19–0.83)
Do you use food supplements?					
No	18 (17.1)	42 (19.5)	[c]	[c]	
Yes	87 (82.9)	173 (80.5)	0.85	0.87	(0.45–1.66)
How many years have you used food supplement at least weekly for?					
0–2 years	13 (72.2)	31 (73.8)	[c]	[c]	
>2–10+ years	5 (27.8)	11 (26.2)	1.08	1.14	(0.28–4.69)
Do you consume iodized salt?					
No	58 (55.2)	96 (46.6)	[c]	[c]	
Yes	47 (44.8)	110 (53.4)	1.47	2.06	(1.21–3.51)
How many years have you used iodized food weekly for?					
0–2 years	15 (25.4)	29 (30.2)	[c]	[c]	
>2–10+ years	44 (74.6)	67 (69.8)	1.27	1.11	(0.51–2.44)
Do you use vitamine?					
No	14 (13.6)	27 (13.0)	[c]	[c]	
Yes	89 (86.4)	181 (87.0)	1.06	0.91	(0.43–1.93)
How many years have you used vitamin at least weekly for?					
0–2 years	11 (78.6)	16 (59.3)	[c]	[c]	
>2–10+ years	3 (21.4)	11 (40.7)	0.40	0.28	(0.05–1.75)

NA: not applicable, because one of category had 0 frequencies.
[a] Crude model.
[b] Model adjusted by age, BMI and educational attainment.
[c] Reference category.

Table 4
Odds ratios (OR) and 95% confidence interval (CI) for developing thyroid cancer according to caffeinated beverages.

	Case	Control	OR[a]	OR[b]	(95% CI)
Coffee					
Never	18 (17.3)	43 (19.8)	[c]	[c]	
1-3 cup/day	74 (71.2)	160 (73.7)	1.11	0.65	(0.32–1.31)
4 - ≥6 cups/day	12 (11.5)	14 (6.5)	2.05	0.97	(0.34–2.77)
Tea					
Never	63 (61.2)	144 (67.0)	[c]	[c]	
1-3 cup/day	40(38.8)	71 (33.0)	1.29	1.42	(0.84–2.41)
Coca-Cola					
Never	78 (75.7)	182 (84.7)	[c]	[c]	
1-3 glass/day	24 (23.3)	31 (14.4)	1.81	3.08	(1.53–6.20)
4 - ≥6 glass/day	1 (1.0)	2 (0.9)	1.17	2.42	(0.20–28)
Red bull energy drink					
Never	100 (97.1)	209 (97.2)	[c]	[c]	
1-3 glass/day	3 (2.9)	6 (2.8)	1.05	2.57	(0.56–12)

[a] Crude model.
[b] Model adjusted by age, BMI and educational attainment.
[c] Reference category.

possible protective role of cruciferous vegetables (cabbage, broccoli, cauliflower, rocket, soy, spinach and lettuce) consumption. Cruciferous vegetables may affect the risk of thyroid cancer via multiple pathways: by a goitrogenous effect due to thyocyanates production (Gaitan et al., 1988; Verhoeven et al., 1997; Zhang et al., 2012), by an anticarcinogenic effect (Beecher et al., 1994), and also a weak estrogenic/antiestrogenic effect (Liu et al., 1994) and by their interaction with other dietary components, above all iodine intake (Higdon et al., 2007).

We have analyzed the relationship between thyroid cancer risk and the consumption of **legumes and fruit** revealing a protective effect. Fruit and vegetable intake are considered as probably protective against overall cancer risk, but results in previous studies are not consistent for thyroid cancer (Jung et al., 2013; Zamora-Ros et al., 2018). Legumes represent an important source of folate, phytochemicals, sterols and various substances with presumed antioxidant properties and anticancer properties such as glutathione, tocopherols and phenolic compounds (Kouris-Blazos et al., 2016; Antognelli et al., 2019).

According to some previous studies we found an unstable negative association of thyroid cancer risk with fish consumption (Choi et al., 2014; Del Maso et al., 2009). However, other authors reported increased risk with seafood (Memon et al., 2002; Peterson et al., 2012) while, other authors reported no risk (Mack et al., 2002; Zamora-Ros et al., 2017) or no relationship with fish consumption (Dal Maso et al., 2009). Unfortunately, the comparison of studies is difficult due to the geographical variability of iodine exposure levels; in particular high consumption is protective in areas with severe iodine deficiency, deleterious in areas where iodine is readily available, and has no effect in areas where iodine intake is adequate (Bosetti et al., 2001). Iodine deficiency may lead to reduced thyroid hormone (T3 and T4) production and consequent hypersecretion of thyroid stimulating hormone (TSH). This induces hypertrophy and hyperplasia of thyroid follicular cells and promotes the onset of cancer (Knobel et al., 2007). The lack of influence of iodine from fish is not surprising because there are currently few mildly iodine-deficient areas in Europe and iodized salt is widely available (Andersson et al., 2012). Moreover, our results highlighted a greater risk of thyroid cancer associated with the use of iodized salt, and an unstable positive association with, fresh cheeses and aged cheeses (van der Reijden OL et al., 2017). The association between iodine exposure levels and the histology of thyroid cancer is well known: in particular, iodine deficiency is associated with an increased risk of follicular thyroid cancer, whereas chronically high iodine intake may increase the risk of papillary thyroid cancer (Vuong et al., 2016; Dijkstra et al., 2007; Zimmermann et al., 2015). In our cases group the most frequent histological type was the papillary type (91.5%) and our study area is not at severe iodine deficiency (Moleti et al., 2016; Vermiglio et al., 1989), therefore considering that high iodine consumption is protective in areas with severe iodine deficiency, deleterious in areas where iodine is readily available, and has no effect in areas where iodine intake is adequate, future studies should investigate the iodine exposure level in order to verify for example whether the consumption of iodized salt is still necessary indiscriminately for all or for some subjects such as pregnant women. Our results showed a protective effect associated with a daily water consumption of 1–2 L. However, we observed that about in a quarter of the cases the water daily intake was equal to one third of the quantity deemed necessary to satisfy the daily needs of the human organism (1.5–2.0 L/day) (EFBW Guidelines). Water consumption as a vital component of the human is under-researched in dietary studies. Sui et al. (2016), found water consumption below recommendations, particularly for the elderly population, and an association of higher intakes of total water with positive dietary features.

The role of excessive sugar intake on health and disease is currently an active area of scientific and policy debate; WHO recommends reducing the free sugar intake to less than 10% of total energy intake for children and adults (WHO, 2015). The review of Azaïs-Braesco et al. (2017), found that a large proportion of the European population, especially, but not only children, appears to exceed the 10% threshold recommended by WHO.

We found an increasing risk for tea, coca-cola and Red bull consumption, conversely an unclear effect was observed for coffee consumption (Papetti et al., 2014). The greater risk associated with the consumption of coca cola and Red bull might be associated with the high sugar content. Moreover, other chemicals than sugar might be associated with the increased risk of caffeinated beverages, for example Taurine whose effects are not yet fully known, especially those affecting the adolescents (Perdan Curran et al., 2017).

A recent large prospective study and a meta-analysis suggest that coffee consumption has no effect on the thyroid cancer risk, though the latest fails to give final conclusions because of potential biases and confounding variables (Zamora-Ros et al., 2019; Mi Ah Han et al., 2017). The hypothesized mechanism for coffee and cancer risk relationship lays in the observation that caffeine increases intracellular cyclic adenosine monophosphate (AMP), which has an inhibitory effect on cell (tumor) growth (Mack et al., 2003). It is important to emphasize that in adults, coffee is the most important source of caffeine and sugar, accounting for 40–94% of daily caffeine intake (Verster et al., 2018; Demura et al., 2013). So, coffee and tea consumption should also be of concern because of their contribute to sugar intake; the greatest contribution to total sugar intakes was observed in Southern European centers (up to ~ 20%) (Landais et al., 2018).

Limitations of this study must be noted. The first limitation is the small sample size. Second, recall bias cannot be excluded, as in most case-control studies. Third, the type and quantity of vitamine and supplements were not investigated. Fourth, the questionnaire referred to cured meats and meat without distinguishing between red meat and white meat. Fifth, about the representativeness of the controls of the general population we cannot rule out that such a difference may exist. Sixth, the information about medical history are self-reported so we cannot exclude information bias Our study has some strength. The diagnosis of thyroid cancer was validated through extensive histopathology review, and responce rate close to 90% among eligible cases and controls. Further, the repeatability of the food items consumption assessment was been guaranteed by the use of a validated questionnaire.

Finally, our findings must be carefully evaluated due to the limited precision of the risk estimates; in addition it is necessary to carry out studies with a larger sample and for a longer time.

5. Conclusions

Dietary habits appear to modify the risk of thyroid carcinoma. A diet with a limited consumption of starchy foods, products rich in salt, fat and sugar and a higher consumption of, cruciferous/non-cruciferous vegetables, milk and dairy products and seafood could be protective towards thyroid cancer. Moreover, the water intake should be increased and the actual need to consume iodized salt should be verified for each subject/area. These results warrant further investigations and, if confirmed, they might have important public health implications for the reduction of thyroid cancer through the improvement of dietary habits.

CRediT authorship contribution statement

Maria Fiore: Conceptualization, Methodology, Formal analysis, Writing - original draft, preparation, Writing - review & editing. **Antonio Cristaldi:** Visualization. **Valeria Okatyeva:** Data curation. **Salvatore Lo Bianco:** Visualization. **Gea Oliveri Conti:** Visualization. **Pietro Zuccarello:** Visualization. **Chiara Copat:** Writing - review & editing. **Rosario Caltabiano:** Visualization. **Matteo Cannizzaro:** Supervision, Data curation. **Margherita Ferrante:** Project administration, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors thank the Department “GF Ingrassia” of University of Catania for financial support.

Project funded by intradepartmental research plan 2016/2018 of Department of Medical, Surgical and Advanced Technologies, University of Catania (number 5C722012104, 2018).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.fct.2020.111778.

References

Andersson, M., Karumbunathan, V., Zimmermann, M.B., 2012. Global iodine status in 2011 and trends over the past decade. J. Nutr. 142 (4), 744–750. https://doi.org/10.3945/jn.111.149393.

Antognelli, C., Moretti, S., Frosini, R., Puxeddu, E., Sidoni, A., Talesa, V.N., 2019. Methylglyoxal acts as a tumor-promoting factor in anaplastic thyroid cancer. Cells 8 (6), 547. https://doi.org/10.3390/cells8060547.

Azaïs-Braesco, V., Sluik, D., Maillot, M., Kok, F., Moreno, L.A., 2017. A review of total & added sugar intakes and dietary sources in Europe. Nutr. J. 16 (1), 6. https://doi.org/10.1186/s12937-016-0225-2.

Beecher, C.W., 1994. Cancer preventive properties of varieties of Brassica oleracea: a review. Am. J. Clin. Nutr. 59 (5 Suppl. l), 1166S–1170S. https://doi.org/10.1093/ajcn/59.5.1166S.

Bosetti, C., Negri, E., Kolonel, L., Ron, E., Franceschi, S., Preston-Martin, S., et al., 2002. A pooled analysis of caseecontrol studies of thyroid cancer. VII. Cruciferous and other vegetables (International). Cancer Causes Control 13 (8), 765e75.

Bosetti, C., Kolonel, L., Negri, E., et al., 2001. A pooled analysis of case-control studies of thyroid cancer. VI. Fish and shellfish consumption. Canc. Causes Contr. CCC 12 (4), 375–382. https://doi.org/10.1023/a:1011267123398.

Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R.L., Torre, L.A., Jemal, A., 2018. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA A Cancer J. Clin. 68 (6), 394–424. https://doi.org/10.3322/caac.21492.

Choi, W.J., Kim, J., 2014. Dietary factors and the risk of thyroid cancer: a review. Clin. Nutr. Res. 3 (2), 75. https://doi.org/10.7762/cnr.2014.3.2.75.

Dal Maso, L., Bosetti, C., La Vecchia, C., Franceschi, S., 2009. Risk factors for thyroid cancer: an epidemiological review focused on nutritional factors. Cancer Causes Control 20 (1), 75–86. https://doi.org/10.1007/s10552-008-9219-5.

Demura, S., Aoki, H., Mizusawa, T., Soukura, K., Noda, M., Sato, T., 2013. Gender differences in coffee consumption and its effects in young people. Food Nutr. Sci. 4 (7), 748–757. https://doi.org/10.4236/fns.2013.47096.

Dijkstra, B., Prichard, R.S., Lee, A., et al., 2007. Changing patterns of thyroid carcinoma. Ir. J. Med. Sci. 176 (2), 87–90. https://doi.org/10.1007/s11845-007-0041-y.

Fiore, M., Oliveri Conti, G., Caltabiano, R., et al., 2019a. Role of emerging environmental risk factors in thyroid cancer: a brief review. Int. J. Environ. Res. Publ. Health 16 (7). https://doi.org/10.3390/ijerph16071185.

Fiore, M., Cristaldi, A., Okatyeva, V., et al., 2019b. Physical activity and thyroid cancer risk: a case-control study in Catania (south Italy). Int. J. Environ. Res. Publ. Health 16 (8), 1428. https://doi.org/10.3390/ijerph16081428.

Franceschi, S., Levi, F., Negri, E., Fassina, A., La Vecchia, C., 1991. Diet and thyroid cancer: a pooled analysis of four European case-control studies. Int. J. Canc. 48 (3), 395–398. https://doi.org/10.1002/ijc.2910480315.

Gaitan, E., 1988. Goitrogens. Baillieres. Clin. Endocrinol. Metabol. 2 (3), 683–702. https://doi.org/10.1016/s0950-351x(88)80060-0.

Hedayati, M., Yaghmaei, P., Pooyamanesh, Z., Zarif Yeganeh, M., Leptin, Hoghooghi Rad L., 2011. A correlated peptide to papillary thyroid carcinoma? J. Thyroid Res. 2011 https://doi.org/10.4061/2011/832163.

Higdon, J.V., Delage, B., Williams, D.E., Dashwood, R.H., 2007. Cruciferous vegetables and human cancer risk: epidemiologic evidence and mechanistic basis. Pharmacol. Res. Off. J. Ital. Pharmacol. Soc. 55 (3), 224–236. https://doi.org/10.1016/j.phrs.2007.01.009.

Jung, S.K., Kim, K., Tae, K., Kong, G., Kim, M.K., 2013. The effect of raw vegetable and fruit intake on thyroid cancer risk among women: a case–control study in South Korea. Br. J. Nutr. 109 (1), 118–128. https://doi.org/10.1017/S0007114512000591.

Kitahara, C.M., Linet, M.S., Beane Freeman, L.E., Check, D.P., Church, T.R., Park, Y., et al., 2012. Cigarette smoking, alcohol intake, and thyroid cancer risk: a pooled analysis of five prospective studies in the United States. Cancer Causes Control 23, 1615–1624.

Kitahara, C.M., Schneider, A.B., Brenner, A.V., 2018. Thyroid cancer. In: Thun, M.J., Linet, M.S., Cerhan, J.R., Haiman, C.A., Schottenfeld, D. (Eds.), Cancer Epidemiology and Prevention, fourth ed. Oxford University Press, New York, pp. 839–860.

Knobel, M., Medeiros-Neto, G., 2007. Relevance of iodine intake as a reputed predisposing factor for thyroid cancer. Arq. Bras. Endocrinol. Metabol. 51 (5), 701–712. https://doi.org/10.1590/s0004-27302007000500007.

Kouris-Blazos, A., Belski, R., 2016. Health benefits of legumes and pulses with a focus on Australian sweet lupins. Asia Pac. J. Clin. Nutr. 25 (1), 1–17. https://doi.org/10.6133/apjcn.2016.25.1.23.

Landais, E., Moskal, A., Mullee, A., et al., 2018. Coffee and tea consumption and the contribution of their added ingredients to total energy and nutrient intakes in 10 European countries: benchmark data from the late 1990s. Nutrients 10 (6), 725. https://doi.org/10.3390/nu10060725.

Liu, H., Wormke, M., Safe, S.H., Bjeldanes, L.F., 1994. Indolo(3,2-b)carbazole: a dietary-derived factor that exhibits both antiestrogenic and estrogenic activity. J. Natl. Cancer Inst. 86 (23), 1758–1765. https://doi.org/10.1093/jnci/86.23.1758.

Mack, W.J., Preston-Martin, S., Bernstein, L., Qian, D., 2002. Lifestyle and other risk factors for thyroid cancer in Los Angeles County females. Ann. Epidemiol. 12 (6), 395–401. https://doi.org/10.1016/s1047-2797(01)00281-2.

Mack, W.J., Preston-Martin, S., Dal Maso, L., et al., 2003. A pooled analysis of case-control studies of thyroid cancer: cigarette smoking and consumption of alcohol, coffee, and tea. Canc. Causes Contr. CCC 14 (8), 773–785. https://doi.org/10.1023/a:1026349702909.

Markaki, I., Linos, D., Linos, A., 1990. The influence of dietary patterns on the development of thyroid cancer. Eur. J. Canc. Oxf. Engl. 39 (13), 1912–1919. https://doi.org/10.1016/s0959-8049(03)00432-5, 2003.

Memon, A., Varghese, A., Suresh, A., 2002. Benign thyroid disease and dietary factors in thyroid cancer: a case–control study in Kuwait. Br. J. Canc. 86 (11), 1745–1750. https://doi.org/10.1038/sj.bjc.6600303.

Moleti, M., Sturniolo, G., Trimarchi, F., Vermiglio, F., 2016. The changing phenotype of iodine deficiency disorders: a review of thirthy-five years of research in north-eastern Sicily. Ann. Ist. Super Sanita 52 (4), 550–557.

Papetti, A., Mascherpa, D., Gazzani, G., 2014. Free α-dicarbonyl compounds in coffee, barley coffee and soy sauce and effects of in vitro digestion. Food Chem. 164, 259–265. https://doi.org/10.1016/j.foodchem.2014.05.022.

Perdan Curran, C., Marczinski, C.A., 2017. Taurine, caffeine, and energy drinks: reviewing the risks to the adolescent brain. Birth Defects Res. 109 (20), 1640–1648. https://doi.org/10.1002/bdr2.1177.

Peterson, E., De, P., Nuttall, R., 2012. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PloS One 7 (1). https://doi.org/10.1371/journal.pone.0029177.

Ron, E., Lubin, J.H., Shore, R.E., et al., 2012. Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies. Radiat. Res. 178 (2) https://doi.org/10.1667/RRAV05.1.

Sieri, S., Krogh, V., 2017. Dietary glycemic index, glycemic load and cancer: an overview of the literature. Nutr. Metabol. Cardiovasc. Dis. 27 (1), 18–31. https://doi.org/10.1016/j.numecd.2016.09.014.

Sui, Z., Zheng, M., Zhang, M., Rangan, A., 2016. Water and beverage consumption: analysis of the Australian 2011–2012 national nutrition and physical activity survey. Nutrients 8 (11). https://doi.org/10.3390/nu8110678.

Turati, F., Galeone, C., Augustin, L.S.A., La Vecchia, C., 2019. Glycemic index, glycemic load and cancer risk: an updated meta-analysis. Nutrients 11 (10). https://doi.org/10.3390/nu11102342.

van der Reijden, O.L., Zimmermann, M.B., Galetti, V., 2017. Iodine in dairy milk: sources, concentrations and importance to human health. Best Pract. Res. Clin. Endocrinol. Metabol. 31 (4), 385–395. https://doi.org/10.1016/j.beem.2017.10.004.

Verhoeven, D.T., Verhagen, H., Goldbohm, R.A., van den Brandt, P.A., van Poppel, G., 1997. A review of mechanisms underlying anticarcinogenicity by brassica vegetables - ScienceDirect. https://www.sciencedirect.com/science/article/pii/S0009279796037453?via%3Dihub. (Accessed 15 May 2020).

Vermiglio, F., Finocchiaro, M.D., Lo Presti, V.P., et al., 1989. Partial beneficial effects of the so colled "silent iodine orophylaxis" on iodine deficiency disorders (IDD) in northeastern Sicily endemia. J. Endocrinol. Invest. 12 (2), 123–126.

Verster, J.C., Koenig, J., 2018. Caffeine intake and its sources: a review of national representative studies. Crit. Rev. Food Sci. Nutr. 58 (8), 1250–1259. https://doi.org/10.1080/10408398.2016.1247252.

Vuong, H.G., Kondo, T., Oishi, N., et al., 2016. Genetic alterations of differentiated thyroid carcinoma in iodine-rich and iodine-deficient countries. Canc. Med. 5 (8), 1883–1889. https://doi.org/10.1002/cam4.781.

WHO. Physical status: the use and interpretation of anthropometry. WHO. https://www.who.int/childgrowth/publications/physical_status/en/. (Accessed 20 February 2019).

Wu, C., Liu, J., Liu, S., et al., 2018. Assessment of the health risks and odor concentration of volatile compounds from a municipal solid waste landfill in China. Chemosphere 202, 1–8. https://doi.org/10.1016/j.chemosphere.2018.03.068.

Zamora-Ros, R., Béraud, V., Franceschi, S., et al., 2018. Consumption of fruits, vegetables and fruit juices and differentiated thyroid carcinoma risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) study: fruits, vegetables, and fruit juices and thyroid cancer in EPIC. Int. J. Canc. 142 (3), 449–459. https://doi.org/10.1002/ijc.30880.

Zamora-Ros, R., Castañeda, J., Rinaldi, S., et al., 2017. Consumption of fish is not associated with risk of differentiated thyroid carcinoma in the European prospective investigation into cancer and nutrition (EPIC) study. J. Nutr. 147 (7), 1366–1373. https://doi.org/10.3945/jn.117.247874.

Zhang, L.R., Sawka, A.M., Adams, L., Hatfield, N., Hung, R.J., 2013. Vitamin and mineral supplements and thyroid cancer: a systematic review. Eur. J. Canc. Prev. Off. J. Eur. Canc. Prev. Organ. ECP 22 (2), 158–168. https://doi.org/10.1097/CEJ.0b013e32835849b0.

Zhang, Y., 2012. The molecular basis that unifies the metabolism, cellular uptake and chemopreventive activities of dietary isothiocyanates. Carcinogenesis 33 (1), 2–9. https://doi.org/10.1093/carcin/bgr255.

Zimmermann, M.B., Galetti, V., 2015. Iodine intake as a risk factor for thyroid cancer: a comprehensive review of animal and human studies. Thyroid Res. 8 (1), 8. https://doi.org/10.1186/s13044-015-0020-8.