Effectiveness of Food in Preventing Thyroid Cancer: Systematic Review

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Efetividade da Alimentação na Prevenção do Câncer de Tireoide: Revisão Sistemática

Eficacia de los Alimentos en la Prevención del Cáncer de Tiroides: Revisión Sistemática

Laura Faustino Gonçalves[1]; Cláudia Tiemi Mituuti[2]; Patrícia Haas[3]

ABSTRACT

Introduction: The thyroid gland undergoes metabolic changes that can cause benign or malignant diseases, one of which is thyroid cancer, which is increasing worldwide, and women are most prone to develop this disease. **Objective:** To present scientific evidences based on a systematic review of the literature (PRISMA) verifying the effectiveness of food in preventing thyroid cancer. **Method:** For the selection of studies, the combination based in the Medical Subject Heading Terms (MeSH) was used. The MEDLINE (PubMed), LILACS, SciELO, BIREME and Scopus databases were utilized. The search period for the articles ranged from January 2010 to March 2020, with no language or localization restrictions. **Results:** 32 articles with potential for inclusion were retrieved, and three articles responded to the guiding question that consisted in analyzing the effectiveness of food in preventing thyroid cancer. **Conclusion:** Studies have reported a possible association between food intake and the prevention of thyroid cancer. It is suggested that food rich in calcium may play a protective role against thyroid cancer, but excessive levels of iodine in the diet may also affect thyroid function negatively due to changes in hormone levels. The researches also demonstrate that women have significantly higher incidence of thyroid cancer than men.
Key words: Thyroid Neoplasms/prevention & control; Food/adverse effects; Diet, Healthy; Systematic Review.

RESUMO

Introdução: A glândula tireoide sofre alterações metabólicas que podem ocasionar doenças benignas ou malignas, sendo uma delas o câncer de tireoide, o qual está crescendo cada vez mais ao redor do mundo, sendo as mulheres mais propensas a desenvolver essa doença. **Objetivo:** Apresentar evidências científicas com base em revisão sistemática da literatura (PRISMA), verificando a efetividade da alimentação na prevenção do câncer de tireoide. **Método:** Para a seleção dos estudos, utilizou-se a combinação baseada no *Medical Subject Heading Terms* (MeSH). Foram utilizadas as bases de dados MEDLINE (PubMed), LILACS, SciELO, BIREME e *Scopus*. O período de busca dos artigos compreendeu entre janeiro de 2010 até março de 2020, sem restrição de idioma e localização. **Resultados:** Foram recuperados 32 artigos com potencial de inclusão, sendo que três responderam à pergunta norteadora que consistiu em analisar qual a efetividade da alimentação na prevenção do câncer de tireoide. **Conclusão:** Os estudos relataram uma possível associação entre a ingestão de alimentos e a prevenção do câncer de tireoide. Sugere-se que os alimentos ricos em cálcio possam fornecer um papel protetor contra esse tipo de câncer, porém níveis excessivos de iodo na dieta também podem, de forma negativa, afetar a sua função da tireoide em razão das alterações nos seus níveis de hormônio. As pesquisas demonstram também que as mulheres apresentam significativamente maior incidência de câncer de tireoide em relação aos homens.
Palavras-chave: Neoplasias da Glândula Tireoide/prevenção & controle; Alimentos/efeitos adversos; Dieta Saudável; Revisão Sistemática.

RESUMEN

Introducción: La glándula tiroides sufre cambios metabólicos que pueden causar enfermedades benignas o malignas, una de las cuales es el cáncer de tiroides. Lo cáncer de tiroides está creciendo cada vez más en todo el mundo, siendo las mujeres las más propensas a desarrollar esta enfermedad. **Objetivo:** Presentar evidencia científica basada en una revisión sistemática de la literatura (PRISMA) que verifique la efectividad de los alimentos en la prevención del cáncer de tiroides. **Método:** Para la selección de los estudios, se utilizó la combinación basada en los términos de encabezado de temas médicos (MeSH). Se utilizaron las bases de datos MEDLINE (PubMed), LILACS, SciELO, BIREME y *Scopus.* El período de búsqueda de los artículos varió desde enero de 2010 hasta marzo de 2020, sin restricciones de idioma y localización. **Resultados:** Se recuperaron 32 artículos con potencial de inclusión, y tres artículos respondieron a la pregunta guía que consistió en analizar la efectividad de los alimentos para prevenir lo cáncer de tiroides. **Conclusión:** Los estudios han reportado una posible asociación entre la ingesta de alimentos y la prevención de cáncer de tiroides. Se sugiere que los alimentos ricos en calcio pueden proporcionar un papel protector contra lo cáncer de tiroides, pero los niveles excesivos de yodo en la dieta también pueden afectar negativamente la función tiroidea debido a los cambios en los niveles hormonales. La investigación también muestra que las mujeres tienen una incidencia significativamente mayor de cáncer de tiroides en comparación con los hombres.
Palabras clave: Neoplasias de la Tiroides/prevención & control; Alimentos/efectos adversos; Dieta Saludable; Revisión Sistemática.

[1]Center of Sciences of Health of the Federal University of Santa Catarina (CCS/UFSC). Florianópolis (SC), Brazil. Orcid iD: https://orcid.org/0000-0002-0043-4349
[2]CCS/UFSC. Florianópolis (SC), Brazil. Orcid iD: http://orcid.org/0000-0002-8991-3812
[3]CCS/UFSC. Florianópolis (SC), Brazil. Orcid iD: https://orcid.org/0000-0001-9797-7755
Corresponding author: Patrícia Haas. CCS/UFSC. Rua Eng. Agronômico Andrei Cristian Ferreira, s/n.º - Trindade. Florianópolis (SC), Brazil. CEP 88040-900. Email: patricia.haas@ufsc.br

INTRODUCTION

Thyroid is an endocrine gland located at the base of the neck and secretes thyroid hormones. This gland undergoes metabolic changes that can cause benign or malignant diseases, one of them, cancer[1].

In 2018 there were 567 thousand new cases of thyroid cancer in the world equivalent to 3% of all the cancers, occupying the ninth world position. Nearly 141 thousand new cases of thyroid cancer and 35,575 deaths were registered in the world. In Brazil, there were 748 deaths by thyroid cancer, 239 in men and 509 in women. Women are more prone to develop changes as nodes because of the estrogen, a female hormone that stimulates the proliferation of thyroid cancer cells. Thyroid cancer corresponds to nearly 1% of all the malignant neoplasms, however, is the most frequent of the malignant endocrine tumors[2].

The diagnostic of thyroid cancer results from the clinical exam of the neck region associated to ultrasound. Later, a biopsy of a tissue sample is performed to classify the tumor as malignant or benign. Although the rate of thyroid cancer has increased relatively, little is known about the etiology of this disease. However, differences in the international thyroid cancer incidence rates suggest that lifestyle or environmental risk factors including diet can play a significant role in the appearance of thyroid cancer[3].

Cordeiro and Martini[4] report that dietarian factors are being significantly related with the appearance of thyroid cancer. Among the food factors, vegetables as green kale, broccoli, cauliflower and cassava appear to be related to the prevention of the development of thyroid cancer. Epidemiologic studies indicate that food habits can play a relevant role in the protection of this type of cancer. Iodine is the most common factor investigated because of its role in the production of thyroid hormones in the thyroid gland and its disorders. Epidemiologic studies demonstrate close relation between thyroid cancer, obesity, lifestyle and nutrition. As prevention measure for this type of disease, it is important the introduction of food containing antioxidant properties in the diet, being recommended the high intake of fruits and vegetables[5-8].

The present study has as main and steering objective to verify the scientific evidences about the efficacy of food for the prevention of thyroid cancer in order to respond to the following research question: Is food effective to prevent thyroid cancer?

METHOD

A systematic review according to the recommendations of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[9] was conducted. The present systematic review was registered with the number 190685 – PROSPERO (Centre for Reviews and Dissemination). Two independent investigators searched for scientific articles in the electronic databases MEDLINE (PubMed) (https://www.ncbi.nlm.nih.gov/pubmed/), LILACS (http://lilacs.bvsalud.org/), SciELO (http://www. scielo.br/), BIREME (https://bvsalud.org/) and Scopus (https://www.scopus.com) in any language, period and country. The trial was structured and organized pursuant to PICOS, the acronym standing for **P**opulation-target, **I**ntervention, **C**ontrol, **O**utcomes, **S**tudy (Table 1). The acronym Control was not utilized for not being applicable to the trial objective.

Table 1. Description of the acronym PICOS

Acronym	Definition
P	Patients
I	Food
C	Not applicable
O	Thyroid cancer
S	Descriptive Study Cross-sectional study Observational study

The descriptors were selected from the dictionary Descriptors of Sciences of Health (DeCS) and Medical Subject Heading Terms (MeSH). For the search, the following descriptors and Boolean operators were proposed: (thyroid cancer) and (food) and (protective effect) AND (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials[mh] OR random allocation[mh] OR double-blind method[mh] OR singleblind method[mh] OR clinical trial[pt] OR clinical trials[mh] OR ("clinical trial"[tw]) OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw])) OR ("latin square"[tw]) OR placebos[mh] OR placebo*[tw] OR random*[tw] OR research design[mh:noexp] OR follow-up studies[mh] OR prospective studies[mh] OR cross-over studies[mh] OR control*[tw] OR prospectiv*[tw] OR volunteer*[tw]) NOT (animal[mh] NOT human[mh]).

The designs of the studies selected were descriptive, cross-sectional, cohort and case study only with humans. Articles in any language and country from January 2010 to March 2020 were searched. Table 2 presents the inclusion and exclusion criteria adopted in this trial. All the articles analyzed were in Portuguese, English, French and Spanish, the authors translated the articles.

Table 2. Summary of inclusion and exclusion criteria

Inclusion criteria	
Design	Case reports Studies of cases and control Controlled clinical trials Cohort studies Screening studies Observational studies
Country	All
Language	All
Exclusion criteria	
Design	Letters to the Editor Guidelines Reviews of the literature Systematic Reviews Meta-analyzes
Studies	Ambiguous texts, ill-drafted or inconsistent
Form of publication	Only abstract

Studies published as letter to the editor, guidelines, literature reviews, systematic reviews, meta-analysis and abstracts, which were inconsistent, unavailable or with insufficient data were excluded.

The extraction of the data to determine the eligibility of the studies was carried out through a card for systematic review created by the investigators in Excel to which the data extracted were added initially by one of the investigators and then, checked by another investigator. The data obtained of the eligible studies were migrated to an Excel spreadsheet in order to organize the results as described in Table 3.

RESULTS

Initially, 32 articles were identified, of which, eight abstracts were evaluated. Of these, two were excluded for failing to respond to the research question. Five articles were read fully and upon the application of the eligibility criteria, three studies[1,10,11] about food and prevention of thyroid cancer were object of the current analysis (Figure 1). The design of the studies analyzed were case-control and cross-sectional study. In the analysis they were categorized according to the theme investigated, food profile of subjects diagnosed with thyroid cancer, risky food for the development of thyroid cancer and foods that reduce the risk of developing thyroid cancer.

In the study of Cléro et al.[1], nearly 90% of the cases of thyroid cancer were in women, 80% with thyroid cancer and 60% of the case-control were overweight or obese (body mass index – BMI ≥25 kg/m^2), respectively. The objective was to compare the Western with the French Polynesian diet, and they did not find association between the Western food standard and the risk of thyroid cancer, but the traditional Polynesian standard indicated a considerable risk of developing this cancer.

In the study of Cho et al.[10], the participants were asked about the frequency of intake and the portion size of specific food consumed in the previous year using the food frequency questionnaire validated (FFQ) with 106 food items. Categories of frequency (never or rarely, once a month, two or three times a month) and three portion sizes (small, medium and large) are evaluated in the FFQ. The intake of nutrients (for example, macronutrients, vitamins and minerals) was calculated, multiplying the frequency of intake of each unit of food by the content of nutrients of the specified portions. The intake of protein, fat, calcium and iron in the diet was calculated separately according to two sources (animal or vegetal). The result showed that the high intake of calcium is associated to reduced risk of thyroid cancer, but significant associations among the risk of this cancer and other nutrients were not encountered.

Through a base questionnaire, Haslam et al.[11] analyzed the demographic data, health status and intake of fish and concluded that the case-control (108 participants) reported higher medium intake of fish; in addition, the case-control were more prone to high intake of omega-3 in the long term in comparison with the cases of patients with thyroid cancer. The intake of omega-3 was associated to less odds of development of thyroid cancer. Furthermore, the intake of polychlorinated biphenyls (PCB), that is, synthetic chemical compounds were not significantly associated to the development of thyroid cancer.

DISCUSSION

Studies determined some relevant risk factors for thyroid cancer with exposure to different food patterns, lifestyles, nutrition or other environmental risk factors in several populations[12,13]. Some studies reported that food factors as processed and industrialized food can play a significant and broader role over the cause of thyroid cancer, possibly influencing the thyroid hormones and affecting its functioning[14,15].

The study of Cléro et al.[1] included 24 foods or groups of foods in the analyses as tubers, cereals, starchy food, cabbage, legumes, citrus fruits, banana, mango, papaya, guava, passion fruit, watermelon, apple, pear, apricots, cocoanut water, nuts, ocean fishes, lake fishes, clams, boiled pork meat, dairy products, eggs, Chinese food,

Table 3. Summary of the articles included

Author/ Year/ Country	Type of study	Participants	Age-range	Objective	Exam	Results	Conclusion
Cléro; Doyon; Chungue et al., 2012 French Polynesia	Case-control	229 participants with thyroid cancer diagnosed between 1979 and 2004 (case); 371 participants selected randomly (control)	56 and 62 years	Identify food patterns and investigate the association of food patterns or food items and risk of thyroid cancer in the traditional Polynesian and Western food	Questionnaire of the European Prospective Investigation in Cancer and Nutrition (EPIC) adapted	90% of the cases of thyroid cancer were in women 80% of the participants and 60% of the controls were overweight or obese (BMI $\geq$25 kg/m2) Western pattern was not associated to risk of thyroid cancer The intake of cassava was significantly associated to reduction of the risk of thyroid cancer	Traditional Polynesian food pattern led to a significant risk of development of thyroid cancer
Haslam; Robb; Bonner et al., 2016 EUA	Longitudinal cohort	27 participants with thyroid cancer and 108 participants selected randomly	Mean of 32 years	Examine the effects of intake of fishes of the Lake Ontario and estimated intake of PCB and omega-3 with the risk of development of thyroid cancer in a group of fishermen diagnosed with thyroid cancer between June 1 and December 31, 2008	Follow up questionnaire	The results did not indicate significant associations between fish intake and omega-3, estimated in the short term or estimated intake of PCB in the fishes of the Great Lakes and the development of thyroid cancer, but it was suggested that omega-3 of the Great Lakes fishes in the long term can prevent the development of thyroid cancer	Fish intake with possible contaminant PCB of the Great Lakes do not apparently increase the risk of thyroid cancer
Cho; Lee; Kim, 2016 Coreia	Case-control	113 women with thyroid cancer and 226 women participants selected	30 years or more	Investigate the role of nutrients in risk of thyroid cancer in Korean women between October 2007 and July 2014	Self-reported questionnaire and questionnaire of FFQ	It was found that the high intake of calcium was associated to reduced risk of thyroid cancer. Significant associations were observed among individuals older than 50 years, low BMI and low calory intake. However, other nutrients included in this study did not show significant associations with risk of thyroid cancer	Possible protective effect of calcium in the risk of development of thyroid cancer

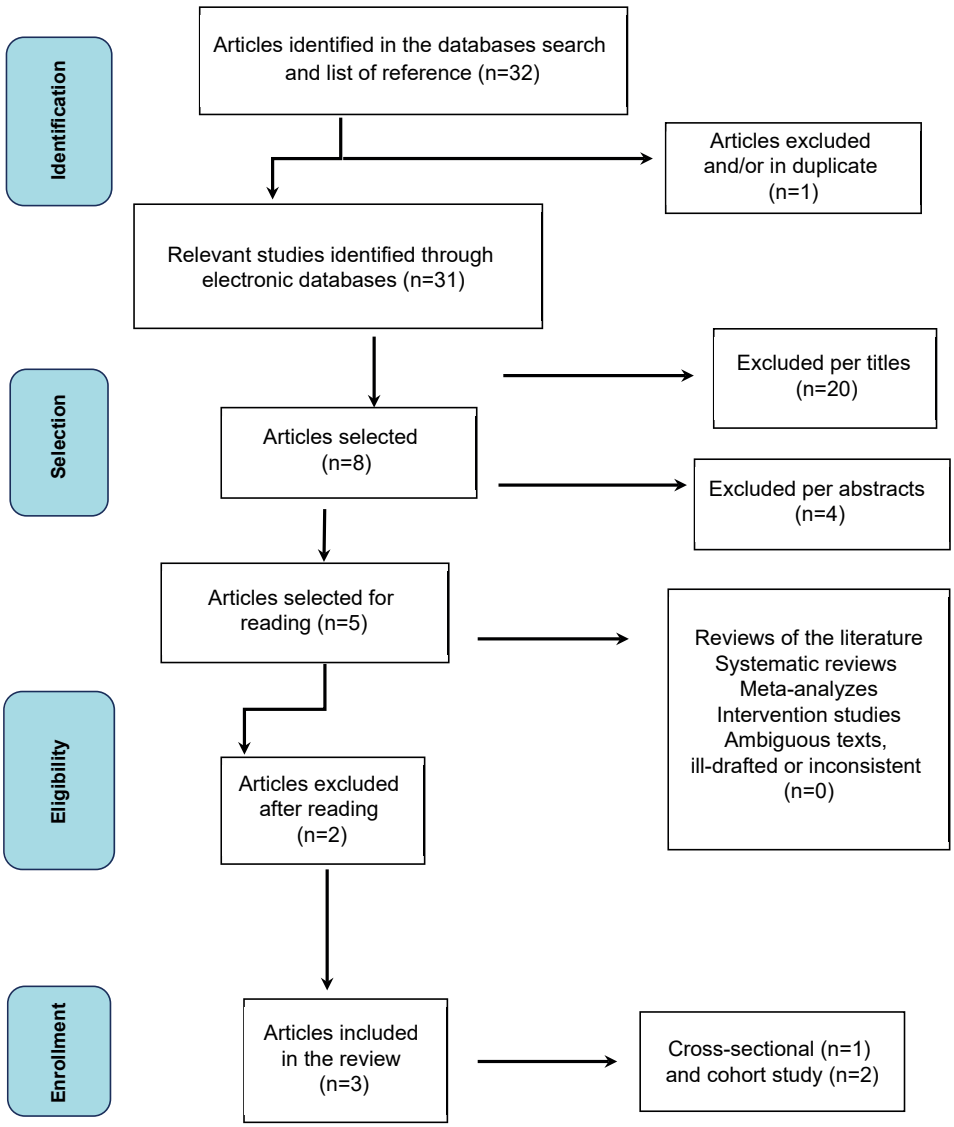

Figure 1. Flowchart of search and analysis of articles

cakes, tea, coffee, sweet beverages and alcohol beverages. The authors used food content tables to convert food in nutrients. For each individual, the mean daily intake of energy in the diet was calculated too. Two diet patterns were established, the first, Western, containing red meat, boiled pork meat, eggs, Chinese food, cereals (pasta, rice and bread), starchy food as potatoes and legumes, cabbage and other vegetables, cakes, sweet beverages, alcoholic beverages and coffee.

The second pattern presented by Cléro et al.[1] was called traditional Polynesian with high intake of fish (lakes and oceans), clams, banana and citrus fruits, mango, papayas, guava, cocoanut water, breadfruit, tubers (cassava, sweet potato) and dairy. The result is that the Western diet failed to associate significantly with the risk of thyroid cancer and to the Polynesian food pattern, but a significant reduction of thyroid cancer was noticed with the intake of cassava, but not with cabbage, for instance.

According to the literature, the main forms of avoiding cancer is eating healthy food, do physical activity and have adequate body weight. The intake of vegetable-based food as fruits, legumes, greens, whole grains, beans and other legumes and avoid ultra-processed food and sugary beverages can prevent new cases of cancer[16]. Baenal[17] study mentions that vegetable-based food as fruits, greens, legumes and whole grains containing great quantity of bioactive phytochemicals tend to reduce the risk of chronic diseases. The increase of fish intake is associated to lower mortality and cardiovascular morbidity further to positive effects in the metabolism of lipoproteins, coagulation and function of platelets, endothelial function and arterial stiffness[18].

The Przybylik-Mazurek et al.[19] case-control with the application of questionnaire included information about food patterns. In this study, 284 patients with thyroid cancer (case group) with 30 men with mean age of 58 years and 254 women with mean age of 52 years and 345 patients without thyroid cancer as control were randomly enrolled (58 men with mean age of 60 years and 287 women with mean age of 53 years) and evaluated. The participants selected randomly were paired per age and gender with the group who had thyroid cancer. The main nutritional products, that is, starchy food, meat, dairy, vegetables, fruits and beverages were reviewed. The result showed that the intake of vegetables, fruits, ocean fishes and cheese was significantly lower in patients with thyroid cancer than for the participants without diagnosis of thyroid cancer. The authors concluded that the food patterns appear to modify the risk of development of thyroid cancer. A diet rich in vegetables and fruits and ocean fish and low-fat meat may be reported as an important protective factor.

Schwingshackl and Hoffmann[20] quote that the Mediterranean diet consists of antioxidant and anti-inflammatory food. This diet is related, according to studies, to the prevention of cellular ageing and several chronic diseases. It comprises fresh fruits, oil seeds, legumes and cereals. The literature indicates that the incidence of general cancer is lower in countries of the Mediterranean Sea and report that the adherence to a Mediterranean feeding pattern may be correlated with reduced risk of several types of cancer, in addition to reduction of mortality by cancer[21].

Cho et al.[10] categorized the participants in two groups according to the levels of calcium intake and investigated whether the general characteristics of the participants were compatible with these levels. The general characteristics of the participants were not significantly different in the groups of high and low calcium intake. To examine the effects of other risk factors in the association of calcium intake and thyroid cancer, the investigators analyzed the subgroups per age, BMI, tobacco use and level of total calory intake. Significant associations were observed in individuals older than 50 years with low calory intake. However, these associations were not observed in the analysis of the subgroup with different source of calcium (plant or animal).

Liang et al.[12], in a case-control study analyzed the association between the food standard and risk of thyroid cancer in 2010 and 2011. The study included 390 cases of thyroid cancer and 436 individuals without thyroid cancer. The participants responded to diet history questionnaires (DHQ), where three food frequency standards were noticed according to the participants main food intake: diet with prevalence of starchy and sugary products; fruits and legumes diet; and diet with prevalence of protein and fat. The findings show that the diet with predominance of fruits and vegetables was significantly associated to reduced risk of thyroid cancer. When compared to younger women, it was noticed a greater protective effect in women ≥50 years in relation to the risk of developing thyroid cancer. Diet rich in starchy food was effective to protect against thyroid cancer, however, diets with predominance of sugared food were proven as not effective in protecting against thyroid cancer.

Nevertheless, the results of Haslam et al.[11] showed there were no significant associations between fish intake and the development of thyroid cancer. The ingestion of chemical compounds as PCB, found in fishes, was not significantly associated with the development of thyroid cancer. They also reported the possibility that the concentrations of PCB in the fishes do not change the hormone concentrations of the thyroid and, therefore, would not increase the incidence of cancer. The authors report there was no risk of developing thyroid cancer among the fishermen who are more exposed to the compound PCB of the fishes in comparison with those who have allegedly less exposure to PCB. Nonetheless, the prolonged ingestion of omega-3 apparently protects against the development of thyroid cancer.

Zamora-Ros et al.[15], in their cohort study with 748 patients with thyroid cancer (666 women and 601 papillary), aged between 35 and 70 years old attempted to relate the intake of fishes and the development of thyroid cancer. The data about the intake of lean fish, fat fish, fish products and clams were collected with validated questionnaires. The study showed that the intake of fishes and clams was not associated to differentiated risk of thyroid cancer. Zamora-Ros et al.[15] carried out a cohort study to examine the association of fruits, vegetables and fruit juices with the risk of developing thyroid cancer. The participants were enrolled between 1991 and 2000 and the intake of fruits and legumes and fruit juices was assessed through validated questionnaires. The authors did not find significant association among the intake of fruits and vegetables and the risk of developing thyroid cancer, however, it was encountered a positive tendency of protection with the intake of fruit juice.

In counterpart, Jung et al.[13] using a 121-items questionnaire evaluated the association between the intake of raw fruits and vegetables and thyroid cancer in a case-control study and observed 111 cases of thyroid cancer where the intake of food and nutrients was estimated. The authors reported the result that the high intake of raw vegetables, persimmon and tangerines can reduce the risk of thyroid cancer and help to prevent this cancer in initial stage.

Cho et al.[10] investigated the high intake of calcium that appears to be associated to reduced risk of thyroid cancer. Significant associations of the development of thyroid cancer were noticed in individuals older than 50 years, low BMI and low caloric intake. Nevertheless, other nutrients included in this study did not show significant associations with thyroid cancer risk. Therefore, the authors reported a possible protective effect of calcium against the risk of developing thyroid cancer.

The objective of the study of Bandurska-Stankiewicz et al.[14] was to investigate the role of nutritional habits and errors in the incidence of thyroid cancer with 297 patients with thyroid cancer and 589 healthy patients, of which, 46% (total) claimed frequent intake of milk and dairy products. Patients with thyroid cancer usually ate cruciferous greens (rich in antioxidant, vitamins, fibers and minerals), significantly more frequent than healthy individuals while eggs intake in the two groups of patients was similar. The low intake of fish and median use of salt in the food were paired for both groups. The study showed that the risk of thyroid cancer increased in patients who ate cruciferous greens in the province of Olsztyn, Poland. Their regular intake was associated to 1.5 bigger risk of incidence of thyroid cancer.

CONCLUSION

The data found from this systematic review demonstrated that the high intake of calcium appears to be associated with reduced risk of thyroid cancer. In addition, the authors corroborate that the prolonged intake of omega-3 appears to protect against the development of thyroid cancer. The analyzes demonstrate too that women have significantly more odds of developing thyroid cancer than men. The scientific production about this theme is still scarce and the progress of the investigation is essential, considering different populations with diverse food patterns and lifestyles, in addition of exposure to dissimilar environmental factors.

CONTRIBUTIONS

Laura Faustino Gonçalves and Cláudia Tiemi Mituuti contributed for the conception and/or design of the study, collection, analysis and interpretation of the data. Patrícia Haas contributed for the conception and/or design of the study, collection, analysis and interpretation of the data, wording and critical review. All the authors approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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