

## Editorial

# Nutritional Protective and Risk Factors of Thyroid Cancer: Still Controversial

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Thyroid Cancer (TC) is the most common endocrine cancer and accounts for roughly 1% of human cancers [1]. Main types of thyroid cancer consist of papillary, follicular, and anaplastic thyroid cancers, which stem from thyroid follicular cells, and medullary thyroid cancer, which arises from thyroid C cells [2]. Thus, when compared with other human cancers, a scenario of a thyroid cancer tsunami should seem unlikely. Seemingly, fast growing rate of thyroid cancer is higher than that of any other type of cancer. It is crucial to look for biological reasons and/or specific environmental carcinogens. A burst incidence of thyroid carcinoma must be preceded by a drastic increase in the incidence of its risk factors. The most important risk factors for thyroid cancer are iodine deficiency and radiation exposure [3].

A large number of studies have examined protective and/or risk factors for thyroid cancer in order to describe the growing rates of TC all over the world. Nevertheless, there are inconsistent and unsatisfactory data on nutritional factors related to the risk. This survey will outline some of the outstanding factors.

## Iodine

First and foremost, thyroid cancer incidence is relatively high in regions where the population's daily iodine intake is inadequate. The consumption of goitrogenic food, such as cruciferous vegetables, presented a positive association with TC risk [4]. While, a 2012 systematic review exhibits that there is no consistent association of thyroid cancer risk with iodine intake through fortification or fish consumption, nor with diets high in cruciferous vegetables. Only, a small number of studies suggest a steady protective effect of diets high in non-cruciferous vegetables [5]. One paper revealed that the presence of iodine excess contributes to the changes in TSH so that it may raise TC risk, particularly in women [6]. Another study indicated that fish and shellfish consumption may decrease the risk of TC in iodine deficiency areas [7].

Second, thyroid iodide uptake through the sodium-Iodide Symporter (NIS) is not only an essential step for thyroid hormone

synthesis, but also important for the diagnosis and treatment of thyroid diseases. Nonetheless, part of patients with thyroid cancer is refractory to radioiodine therapy, owing to decreased ability to uptake iodide, which considerably reduces the chances of survival. Hence, compounds able to improve thyroid iodide uptake are of great interest. It has been shown that some flavonoids are able to elevate iodide uptake and NIS expression *in vitro* [8]. Contrarily, a systematic review asserts that worldwide changes over time in iodine intake may not be a major cause to increase thyroid carcinoma incidence rates, and diet does not appear to be a factor that could explain the high TC prevalence observed globally [5]. And among dietary factors, fish (the major natural source of iodine in human diet) is not constantly related to TC risk [9].

Last but not least, the American Thyroid Association and ThyCa Medical Advisors recommend a low-iodine diet (less than 50 micrograms per day) in order to prepare patients before receiving radioactive iodine (radioiodine) for papillary or follicular thyroid cancer. This diet reduces the consumption of regular iodine so that when the radioactive iodine is given for treatment, any remaining thyroid cells, including cancerous, will be "hungry" for iodine. These cells will then more readily absorb radioiodine, which will eventually destroy them. Therefore, avoiding foods and ingredients are high in iodine such as iodized salt, sea salt, seafood and sea products (including agar-agar and carrageenan), dairy products (egg yolks or foods with whole eggs), bakery products with iodine/iodate dough conditioners, most chocolates (due to milk content), soybeans and soybean products (however, soy oil is allowed) and iodine-containing vitamins and food supplements, is a matter of great concern [10].

## Other dietary factors

Dietary patterns appear to modify the risk of TC. A diet rich in vegetables and fruit, as well as saltwater fish and low-fat meat, could be a significant protective factor, quite the contrary to starchy foods, especially white bread [11]. High intakes of animal and/or processed food products are associated with the risk of TC. Excess calorie intake is more frequent in patients with TC. Higher protein and carbohydrate consumption are associated with an augmented risk of TC as well [12]. Additionally, high consumption of chicken, pork, and poultry showed a positive association with the risk, but dairy products showed no significant association. While considered to be a risk factor for other types of cancers, alcohol intake showed a protective role against thyroid cancer [4]. Another study emerged no effect on TC risk of alcohol, coffee, or other food-groups/nutrients [9]. Interestingly, traditional Asian diets (tea and soy products) are associated with a 70 percent lower risk for thyroid cancer in women [13].

## Fruits and vegetables

High intake of cruciferous vegetables displays a weak inverse association with TC. Among other food groups, vegetables other than

cruciferous are the only food group showing a favorable effect on TC, with an approximate 20% reduction in risk for subjects with the highest consumption [9]. Also, large amounts of fruit consumption appear to reduce thyroid cancer risk by nearly 10 to 30 percent [13]. Based on a case-control study in South Korea, high consumption of raw vegetables, persimmons and tangerines may decrease TC risk and help prevent early-stage thyroid cancer [14].

### Omega-3 fatty acids

Foods that are rich in omega-3 fatty acids such as walnuts, flaxseed, and cold-water oily fish, are critical to thyroid function because they help form the structures of every cellular membrane in our bodies, increase energy levels of the cells and improve the efficiency of hormones at the receptor sites. Sufficient levels of essential fatty acids, especially EPA and DHA, might make the thyroid hormone receptors work more efficient. Evidence suggests fish oil may increase thyroid hormone uptake. A 2010 study, rats received diets containing fish oil, found that thyroid hormone receptors and enzyme levels involved in thyroid hormone uptake were higher [15]. In a variety of cancer types, different anticancer chemotherapeutic agents have been shown to be more therapeutically effective when fish oil is added to the diet [16,17]. Furthermore, in a population-based case-control study, a significant inverse relation between the sum of arachidonic acid and DHA serum concentrations and thyroid cancer risk was revealed [18].

### Micronutrients

Experimental studies state that flavonoids, found in nuts, grains, fruits and vegetables, may influence thyroid carcinogenesis. Some flavonoids are able to enhance thyroid iodide uptake and Sodium-Iodide Symporter (NIS) expression, besides having anti-proliferative effect on thyroid cancer cell lines [8]. Selenium is an essential trace element that is influential for thyroid hormone metabolism and has antioxidant properties which protect the thyroid gland from oxidative stress. In addition, individuals with higher intake of beta-carotene have half the risk for TC compared with persons who consume the lowest [13]. By contrast, a large prospective cohort of men and women does not propose strong evidence for an association between dietary intake of Se or other micronutrients and thyroid cancer risk [19]. Moreover, other works demonstrate that regular use of multivitamins and dietary nitrate and nitrite also have a positive association with follicular and papillary thyroid cancer risk [4,20].

Considering that thyroid cancer is the most common endocrine cancer and taking into account the above findings, this report would like to conclude that, generally, one of the most protective factors against thyroid cancer is to manage a healthy diet, which can be attained by controlling the use of high-calorie and/or sugary foods and drinks. Other crucial dietary actions include switching to plant-based diets, increasing consumption of omega-3 fatty acids, reducing intakes of red meat, and avoiding processed, refined, salty and high-in-iodine foods. Dietary supplements are not recommended for the prevention of thyroid cancer. The mentioned controversies are probably due to different ethnicity, lifestyles, eating habits, dietary patterns and other environmental factors. Thus, much more clinical trials on dietary factors and thyroid cancer seem to be essential. Also, more prospective cohort studies with large samples are needed to clarify the interaction between particular diets and types of thyroid cancer. And further research on the relationship between

different types of food and TC could be taken into consideration. Lastly, analyses of the mechanism(s) for how micronutrients influence thyroid hormones and function are required.

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