

Thyroid cancer and Hashimoto thyroiditis

Joanna Szczepanik

Faculty of Health Sciences, School of Socio-Economics in Sroda Wielkopolska, Poznan, Poland, kontakt@dietetyka.poznan.pl

ABSTRACT

Thyroid cancer is the most prevalent neoplasm that affects the endocrine system. Hashimoto's thyroiditis is the most common autoimmune thyroid disease and a major enemy of the thyroid gland. Some studies suggest a greater risk of thyroid cancer among patient with thyroid autoimmunity, while others, investigate its relationship with thyroid cancer etiology, progression and patient prognosis.

In this review, we have analyzed published data on the relation to the association between thyroid autoimmunity and thyroid cancer, addressing influence on thyroid cancer progression, diagnosis, and prognosis of the patients with thyroid autoimmunity (especially Hashimoto's thyroiditis) but not on pathogenesis.

MEDLINE database (PubMed) platform was used and keywords combination "thyroid cancer and Hashimoto thyroiditis" or "thyroid cancer and thyroid autoimmune disease".

Most studies show that thyroid autoimmunity is an independent risk factor for thyroid cancer.

Hashimoto's disease is associated with an increased risk of thyroid cancer, but patients with HT and PTC have a better prognosis

Keywords: thyroid cancer, Hashimoto thyroiditis, thyroid autoimmune disease

INTRODUCTION

In Hashimoto's disease, symptoms of subclinical hypothyroidism are observed in the initial stage, which, as the disease progresses and the thyroid is destroyed, turns into an overt hypothyroidism. Therefore, the symptoms of Hashimoto's disease are those of an underactive thyroid. In some patients, lymphocytic infiltrates, progressive fibrosis and, consequently, atrophy of the gland are observed. Although not in all patients, it is

clearly marked (Ai, 2003). It is also suggested that Hashimoto's disease predisposes to the occurrence of neoplasms within the thyroid gland, in particular primary lymphoma and papillary carcinoma (Łęcka, 2011). The aim of this study is to verify the current know-ledge about the impact of Hashimoto's disease on the development of thyroid neoplasms.

MATERIAL AND METHODS

LITERATURE SEARCH

Relevant studies were identified by searching PubMed (NCBI). The search included studies published from the January, 1, 2020 up to March, 5, 2022. Keywords used in this search

were "thyroid cancer and Hashimoto thyroiditis", "thyroid cancer and thyroid autoimmune disease". The searches were limited to studies in English.

INCLUSION AND EXCLUSION CRITERIA

The inclusion and exclusion criteria for studies are described in Table 1. The literature review only focused on articles linking the topic of Hashimoto's disease and thyroid cancer. Especially in the context of the risk of developing thyroid cancer in people with Hashimoto's

disease. Studies with comorbidities other than Hashimoto disease have not been allowed. Potentially studies eligible for further review were selected by screening their abstracts and title.

Table 1. Inclusion and Exclusion Criteria as Based on the PICOS Elements

PICOS	Inclusion Criteria	Exclusion Criteria
Participants	Adult patients with Hashimoto disease with or without thyroid cancer	Other thyroid diseases and comorbidities, animals, single samples
Interventions	All stages of the disease, substitution treatment	

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Comparators	Patients with Hashimoto disease Patient with Hashimoto disease and thyroid cancer Healthy subjects
Outcomes	The impact of Hashimoto's disease on the risk development of thyroid neoplasms
Study design	All types of research

PICOS = participants, interventions, comparators, outcomes, study design.

DATA EXTRACTION

Researcher reviewed all titles and abstracts individually, extracted related results and duplicate results were omitted. Table 2 summarizes the data extraction.

Table 2. Summary of the extraction criteria

Keywords	thyroid cancer and Hashimoto thyroiditis	thyroid cancer and thyroid autoimmune disease	Elimination criteria
Medical base – number of results			
Pubmed	1,741	3,716	more than 2 years old science article case study (single sample) books other than Hashimoto's disease comorbidities animal research
Qualified articles: 26			

RESULTS

4 articles from 2022, 8 from 2021 and 14 from 2020 were found. These are studies that referred to the impact of Hashimoto's disease on the risk development of thyroid neoplasms. Because

there are also articles in Pubmed on the assessment of possible common pathophysiological features of both disease entities.

Table 3 summarized the most recent results (from 2020 and 2022 year) of the search for the association between the occurrence of Hashimoto's disease and thyroid cancer

Author /year	Population/ type of research	Type of cancer	Results/ Conclusions
2022			
[Klubo-Gwiedzinska]	Review article	All types	HT is associated with 1.6 times higher risk of PTC and 60 times higher risk of thyroid lymphoma than in general population
[Lau]	521 patients with papillary thyroid cancer, two groups, with or without Hashimoto thyroiditis	PTC	Only one-fifth of patients with PTC have coexisting HT. These patients tend to have less-aggressive tumor features such as extrathyroidal extension

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[Lynch]	266 adult patients with unilateral thyroid nodules demonstrating atypia	All types, malignancy	HT was not associated with malignancy on both univariate and multivariate analysis
[Wang]	444 patients diagnosed with PTC	PTC	The autoimmune response of HT seems to reduce the central lymph node metastasis of HT PTCs.
2021			
[Abbasgholizadeh]	Review article		It is significant role for HT in developing papillary TC, medullary thyroid cancer and lymphoma but not anaplastic thyroid cancer and follicular thyroid cancer
[Albano]	314 consecutive patients	All types	HT does not seem to have a prognostic role considering progression-free survival and overall survival
[Gan]	310 samples, including 42 PTC occurring with HT and 268 simple PTC samples	PTC	PTC concurrent with HT had a lower risk of recurrence versus non-HT groups
[Hamouri]	951 patients	PTC	A background of HT does not seem to reflect a more aggressive cancerous biologic behavior
[Liu]	756 patients with PTC coexistent with the HT than non-HT group	PTC	PTC combined with HT is more common in women, and TSH level in HT group is higher than that in patients with PTC alone.
[Machens]	852 (58.4%) patients with papillary thyroid cancer, 181 (12.4%) patients with follicular thyroid cancer, and 426 (29.2%) patients with sporadic medullary thyroid cancer	Papillary, follicular, and medullary thyroid cancer	HT may be associated with differentiated (papillary and follicular) thyroid cancer but not with medullary thyroid cancer
[Sakiz]	1409 patients with PTC, comprising 443 patients with pathology-proven PTC with CLT and 447 patients with PTC without CLT	PTC	The coexistence of PTC and CLT is very frequent. No positive effect of the CLT and PTC combination was detected on any clinicopathologic factor
[Xu]	9210 patients with papillary thyroid cancer, 19% had Hashimoto thyroiditis	PTC	Patients with coexistent HT had less aggressive characteristics at presentation and better outcomes of PTC than did patients without HT
2020			
[Dedivitis, 2020]	155 patients	PTC	There was no relationship between thyroiditis and multifocality in cases of PTC
[Dias Lopes, 2020]	Review article	All types	The presence of autoimmune thyroid disease is a factor that increases the risk of thyroid cancer
[Feldt-Rasmussen, 2020]	Review article	PTC	Recent evidence indicates that (auto)immunity and inflammation may be strong risk factors for papillary thyroid cancer development
[Hussein]	644 patient with cancer without HT, 26 patient with cancer and HT	PTC	These observations suggest interaction between iodine supply, autoimmunity, and carcinogenesis
[Mochamed]	80 patients, 80% were PTC without HT and 20% were PTC with HT.	PTC	HT represents a step in the process of autoimmune inflammatory disease ending by the evolution of PTC with better prognosis

[Lee]	2928 patients with PTC, two groups: with chronic lymphocytic thyroiditis and without	PTC	The CLT patients with PTC had better behavior features and prognoses than did those with PTC alone despite frequent multifocality and extrathyroidal extension
[Osorio]	1136 patients, 1047 (92.2%) women and 89 (7.8%) men	PTC	There is a greater probability of diagnosing PTC in surgical specimens with confirmatory histological data for chronic lymphocytic thyroiditis; in addition, in males under 40 years old this probability increases
[Paparodis & Karvounis]	3909 subjects	PTC	The incidence of PTC was significantly higher in chronic autoimmune thyroiditis compared with multinodular goiter
Paparodis & Bantouna]	1357 subjects	PTC	TSH concentrations might play a role in thyroid cancer development and severity in patients with thyroid nodular disease in the absence of chronic thyroid autoimmunity
[Rotond]	510 patients with chronic autoimmune thyroiditis	All types	The presence of chronic autoimmune thyroiditis appears to be associated with a negligible risk of developing clinically overt differentiated thyroid cancer
[Ryu]	850 patients with PTC	PTC	CLT is associated with less aggressive tumor characteristics and lymph node metastasis
[Schiffman]	2787 patients with thyroid cancer and 2787 individuals without cancer	All types	Any kind of benign thyroid alteration is associated with an elevated risk of thyroid cancer, such as HT too
[Słowińska-Klencka]	557 patients	-	The presence of the “multiple, discrete marked hypoechoic areas” variant significantly increased the odds of obtaining a cytological outcome which would be an indication for surgical treatment
[Sulaieva, 2020)	30 patients with PTC and 30 patients with PTC and HT	PTC	HT coexistence could facilitate the activation of antitumor immunity and the promotion of a cancer immune cycle

HT – Hashimoto thyroiditis, PCT – papillary thyroid cancer, CLT – chronic lymphocytic thyroiditis.

DISCUSSION

In recent years, the occurrence of thyroid cancer among adolescents has been steadily rising. Papillary thyroid carcinoma (PTC) accounts for at least 70% of thyroid malignancies (Vita, 2018). There are some known risk factors for developing thyroid cancer including exposure to ionizing radiation, gender, family history, obesity, substance abuse and exposure to flame retardants (Han, 2018; Hoffmann, 2017; Schmid, 2015). It has been shown that changes in the thyroid gland itself also contribute to the development of thyroid cancer (Brito, 2014; Staniforth, 2016; Yun, 2019; Schiffman, 2020). Thyroid cancer can coexist with Hashimoto’s thyroiditis (HT), adenoma, and nodular goiter. Some study shows a 20-27.9% coexistence between PTC and CLT (Mohamed, 2020; Kim, 2018). The variation in the incidence between studies; may be attributed to the differences in pathological interpretation of HT.

HT, also named Hashimoto’s disease or chronic lymphocytic thyroiditis, is the most common autoimmune disease, characterized by high serum thyroid autoantibody titers. Thyroid peroxidase antibody (TPOAb) and thyroglobulin antibody (TgAb) are important clinical markers for the diagnosis of HT, and were positive in 75% and 90% of HT cases, respectively (Wen, 2019). HT results in the formation of a goiter and the development of hypothyroidism. HT occurs most frequently in middle-aged women (Lee, 2020).

Also the coexistence of thyroid cancer and HT has been increasing in recent years, and an increase in the risk of developing papillary cancer has been reported for HT patients (Lau, 2022, Zeng, 2018). Abbasgholizadeh et al. reported that HT is factor for developing papillary thyroid cancer, medullary thyroid cancer and lymphoma but not anaplastic thyroid cancer and

follicular thyroid cancer (Abbasgholizadeh, 2021). Klubo-Gwieżdźńska suggest, that HT is associated with 1.6 times higher risk of PTC and 60 times higher risk of thyroid lymphoma than in general population (Klubi-Gwieżdźńska, 2022). Three different mechanisms have been proposed to clarify the association between chronic lymphocytic thyroiditis and risk of development PTC: (i) TSH stimulation, (ii) chemokines and other molecules produced by the lymphocytic infiltrate, (iii) expression of certain proto-oncogenes (Vita, 2018).

Our recent literature review suggests that Hashimoto's disease is associated with an increased risk of thyroid cancer, what previous findings published also (Zeng, 2018; Schmid, 2015). However, in parallel there are studies showing that, there are no positive effect of the CLT and PTC combination was detected on any clinicopathologic factor (Sakiz, 2021).

Thyroid cancer prognosis and survival rate of about 97% when detected early, but the patients who develop lymph node metastasis tend to

have disease recurrence, decreasing the survival rate (Dias Lopes, 2020). Some authors argue that HT patients with PTC did better behavioral characteristics and prognosis than those only with PTC despite frequent multifocals and extrathyroidal extension (Lee, 2020). Some of researches suggest that CLT is associated with less aggressive tumor characteristics and lymph node metastasis (Ryu, 2020). HT appears to have some potential protective effect against thyroid cancer, reducing the risk of malignancy (Lynch, 2022). Moreover, a less aggressive form of malignancy in PTC patients in the top of HT has been reported, though but this conclusion was associated with controversies in an endemic area of iodine deficiency goiter (Hussein, 2020). HT appears also to reduce the central lymph node metastasis, what is more significant in male sex with HT PTCs (Wang, 2022). Some potential positive effect of HT on PTC may be related to gender, tumor size and the size of thyroid peroxidase antibody level and more research is required to confirm (Wen, 2019).

COCNLUSIONS

In summary, HT is a risk factor for the occurrence of thyroid neoplasms, but comorbidity

will play a protective role in the progression of cancer prognosis.

LIMITATIONS

Researchers focus only on English literature. The literature review concerned only the PubMed platform.

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