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Clinico-pathological Features and Survival Time of Papillary Thyroid Carcinoma in Patients With and Without Hashimoto's Thyroiditis: A Cross-sectional Study

Mansour Moghimi[1], Fateme Sadat Shamsadini Ezabadi[2*], Seyed Mohammadreza Mortazavi Zadeh[3], Saead Hossein Khalilzade[4]

Abstract

Objectives: Researchers have reported different results regarding the association between Hashimoto's disease and papillary thyroid carcinoma (PTC). Some believe that the coexistence of these diseases can lead to fewer tumor invasion and recurrence rates. This study evaluated the clinico-pathological features and survival time of PTC in patients with and without Hashimoto's thyroiditis.

Materials and Methods: In this cross-sectional study, medical records of 251 participants who underwent total or subtotal thyroidectomy due to PTC from 2012 to 2019 were reviewed. The clinico-pathological features of participants, such as age, gender, tumor stage, tumor size, lymph node involvement, metastasis, capsular invasion, single or multi-focal tumor status, and survival time were recorded from their medical records and pathology report and compared in two groups with and without Hashimoto's thyroiditis.

Results: From 251 participants, 92 (36.6%) had Hashimoto's thyroiditis, whereas 159 (63.4%) did not show any signs of this disease. Fifteen participants in the Hashimoto group and 46 in the non-Hashimoto group had a recurrence. Although there were no significant differences between the two groups in the term of recurrence rate ($P = 0.08$), the mean survival time was significantly difference between the two groups (69.03 and 58.78, respectively; $P = 0.038$)

Conclusions: Results of the study revealed that Hashimoto's thyroiditis could increase the survival time of patients with PTC.

Keywords: Cancer, Papillary thyroid carcinoma, Hashimoto's thyroiditis, Recurrence.

Introduction

Hashimoto's disease (chronic lymphocytic thyroiditis or autoimmune thyroiditis) is one of the most common inflammatory thyroid disorders, with an incidence of approximately 0.3 to 1.5 per 1000 people (1). This chronic thyroid problem is a type of autoimmune disease involving various cells and antibodies involved in the immune response (2). It is the most common cause of early hypothyroidism and non-endemic goiter, with a 10 to 15 times incidence rate in women than in men (3). The association between Hashimoto's thyroiditis (HT) and papillary thyroid carcinoma (PTC), the most common malignant thyroid neoplasm, was first described in 1955 by Dailey and colleagues (4). Since then, conflicting results have been reported on the association between HT and thyroid malignancies. Some scholars have shown that PTC is associated with HT, and their coexistence is accompanied by more minor invasive symptoms, including the smaller size of the tumor and lower stage of the disease (1,5, 6). It is also associated with a reduced rate of tumor recurrence in patients (1,3,5). Zhu et al reported that the presence of HT in patients with PTC reduces the risk of central lymph node metastases, which may indicate a potential protective effect (7). Another study in the United States found that HT increased the risk of differentiated thyroid cancer only in people with euthyroidism and people who had only part of their thyroid gland functioning. But it does not increase in people with hypothyroidism. Therefore, they concluded that high anti-TPO titers have a protective effect against differentiated thyroid cancer in patients with HT (8). Accordingly, based on the previous studies and the inconsistencies among the results, we aimed to investigate the clinico-pathological features and survival time of PTC in patients with and without HT.

Materials and Methods

Setting and Participants

In this cross-sectional study, the medical records of 251 participants with PTC underwent total or sub-total thyroidectomy referring to Shahid Sadoughi Hospital,

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[1]Department of Pathology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. [2]Faculty of Medicine, Islamic Azad University of Yazd, Yazd, Iran. [3]Department of Hematology-Oncology, Islamic Azad University of Yazd, Yazd, Iran. [4]Yazd Diabetes Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
***Corresponding Author:** Fatemesadat Shamsadini Ezabadi, Tel: +989135202184, Email: fateme.1992.sh@gmail.com

Key Messages

- Hashimoto's thyroiditis can increase the survival time of patients with papillary thyroid carcinoma.

Yazd, Iran, from 2012 to 2019 were studied in two groups: with HT and without HT, according to their pathology reports.

Variables

The clinico-pathological features of participants, such as age, gender, tumor stage, tumor size, lymph node involvement, metastasis, capsular invasion, single or multi-focal tumor status, and survival time, were compared in two groups. All incomplete records which could not be completed by follow-up or telephone contact were excluded. The "survival time" was defined as the interval between the end of treatment and recurrence time (month) if recurrence occurred and the telephone contact time if there is no recurrence. The tumor stage was recorded according to the AJCC staging system (Table 1).

Statistical Analysis

Statistical analyses were done using Statistical Package for the Social Sciences (SPSS) version 22 (SPSS Inc, Chicago, Illinois, USA) by the student's *t* test and chi-square test. Log rank test was also used to compare the survival time and its relationship with the variables. *P* value < 0.05 was considered significant.

Results

Overall, the data of 251 participants were included in this study in two groups: HT (n = 92) and non-HT (n = 159). The mean ± SD of age in the two groups was 42.43 ± 13.97 years. Most of the participants were women

Table 1. Thyroid Cancer Staging System (The AJCC/TNM Staging System) (9)

AJCC Stage	Age at Diagnosis	Stage Grouping	Differentiated Thyroid Cancer Stage Description
I	Younger than 55 years	Any T Any N M0	The cancer is any size (Any T) and might or might not have spread to nearby lymph nodes (Any N). It has not spread to distant sites (M0).
			OR
	55 years or older	T1 N0 or NX M0	The cancer is no larger than 2 cm [0.8 inches] across and confined to the thyroid (T1). It has not spread to nearby lymph nodes (N0) or distant sites (M0).
			OR
	55 years or older	T2 N0 or NX M0	The cancer is larger than 2 cm [0.8 inches] across but no larger than 4 cm and confined to the thyroid (T2). It has not spread to nearby lymph nodes (N0) or distant sites (M0).
II	Younger than 55 years	Any T Any N M1	Cancer can be any size (any T). It might or might not have spread to nearby lymph nodes (Any N). It has spread to other body parts, such as distant lymph nodes, internal organs, bones, etc. (M1).
			OR
	55 years or older	T1 N1 M0	The cancer is no larger than 2 cm [0.8 inches] across and confined to the thyroid (T1). It has spread to nearby lymph nodes (N1). It has not spread to distant sites (M0).
			OR
	55 years or older	T2 N1 M0	The cancer is larger than 2 cm [0.8 inches] across but no larger than 4 cm and confined to the thyroid (T2). It has spread to nearby lymph nodes (N1). It has not spread to distant sites (M0).
			OR
	55 years or older	T3a or T3b Any N M0	The cancer is larger than 4 cm but confined to the thyroid (T3a), or it has grown into the strap muscles around the thyroid (T3b). It might or might not have spread to nearby lymph nodes (Any N). It has not spread to distant sites (M0).
III	55 years or older	T4a Any N M0	The cancer is any size and has grown extensively beyond the thyroid gland into nearby tissues of the neck, such as the larynx (voice box), trachea (windpipe), esophagus (tube connecting the throat to the stomach), or the nerve to the larynx (T4a). It might or might not have spread to nearby lymph nodes (Any N). It has not spread to distant sites (M0).
IVA	55 years or older	T4b Any N M0	The cancer is any size and has grown extensively beyond the thyroid gland back toward the spine or into nearby large blood vessels (T4b). It might or might not have spread to nearby lymph nodes (Any N). It has not spread to distant sites (M0).
IVB	55 years or older	Any T Any N M1	The cancer is any size (Any T) and might or might not have spread to nearby lymph nodes (Any N). It has spread to other body parts, such as distant lymph nodes, internal organs, bones, etc. (M1).

T: The extent (size) of the tumor; N: The spread to nearby lymph nodes, M: The spread (metastasis) to distant sites; FNA: Fine Needle Aspiration; CNS: Central Nervous System; TSH: Thyroid Stimulating Hormone; TPOAB: Thyroid Peroxidase Antibodies; LN: Lymph Node; PTC: Papillary Thyroid Carcinoma.

Table 2. Demographic Characteristics of the Study Participants (n = 251)

Variables	
Gender, No. (%)	
Male	34 (13.5)
Female	217 (86.5)
Hashimoto's disease, No. (%)	92 (36.6)
Lymph node involvement, No. (%)	87 (34.7)
Capsular involvement, No. (%)	93 (37.1)
Tumor status, No. (%)	
Single Focal	201 (80.1)
Multifocal	50 (19.9)
Metastasis	87 (34.7)
Tumor stage, No. (%)	
I	153 (61)
II	76 (30.3)
III	7 (2.7)
IV	15 (6)
Tumor recurrence, No. (%)	61 (24.3)
Age (y), Mean ± SD	42.43 ± 13.97
Tumor size (mm), Mean ± SD	15.94 ± 10.9
Survival time (y), Mean ± SD	62.77 ± 2.51

(86.5%), and 36.6% of them suffered from HT (Table 2). Results revealed no significant differences in terms of age, tumor size, gender, lymph node involvement, capsular involvement, single- or multi-focal thyroid tumor status, metastasis, and tumor stage in the two groups. Fifteen participants in the HT group and 46 in the non-HT group had a tumor recurrence, and their difference was not significant ($P=0.088$). However, the mean survival time was higher in the HT group than in the non-HT group ($P=0.038$) (Table 3).

Then, the participants in each group were divided into two subgroups according to age, 12-39 years and 40-76 years old. The mean survival time in both age groups was higher in the HT group than the other ($P=0.037$). The mean survival time in men with HT was impossible to calculate due to the absence of recurrence. But in men without HT was 62.63 months. In women, the survival time proved to be higher in the HT group than in the non-HT group. In other words, in women, HT increases the survival time. In tumor stage, I, the mean survival time in the HT and the non-HT groups were 67.37 and 72.08 months, respectively. Concerning other stages, the HT group's survival time was longer than the non-HT group ($P = 0.110$) (Table 4).

Discussion

In this study, 251 medical records of participants with PTC were reviewed to evaluate their clinico-pathological features and compare their survival time based on the coexistence of HT.

According to our results, 36.56% of participants had HT, and the difference in terms of age was not significant. However, the results of a study by Zhang et al in 2014 showed that patients with PTC and HT were younger than those without HT (10).

The results of the present study identified no significant difference between gender and HT. However, in the Eslami and Monsefi's study, the frequency of women in the HT group was significantly higher than men (11). However, despite the higher number of women in the HT group in the present study, there was no statistically significant difference between the two groups.

Further, we did not find a significant difference between the two groups in terms of tumor size and tumor metastasis. In the study of Campos et al, the mean tumor size in patients with and without HT amounted to 12.7 and 20.5 mm, respectively, thus proving to be statistically significant (12). Molnár and colleagues also reported lymph node metastasis in patients with HT being significantly lower than in the non-HT group (13). However, no statistically significant difference was detected between the two groups in the present study.

Of our 92 participants with HT, 86 (93.5%) were in

Table 3. Comparison of the Clinico-Pathological Features in Two Study Groups

Variables		Hashimoto's Group (n=92)	Non-Hashimoto's Group (n=159)	*P* Value
Age (y), mean ± SD		42.43±13.1	42.42±14.48	0.997[a]
Tumor size (mm), mean ± SD		15.36±10.81	16.27±10.97	0.529[a]
Number of recurrences, mean ± SD		15 (16.30)	46 (28.93)	0.088[a]
Survival time (month), mean ± SD		69.03±3.06	58.78±3.19	0.038[a]
Gender, No. (%)	Male	8 (8.7)	26 (16.4)	0.088[b]
	Female	84 (91.3)	133 (83.6)	
Lymph node involvement, No. (%)		29 (31.5)	58 (36.5)	0.427[b]
Capsular involvement, No. (%)		38 (41.3)	55 (34.6)	0.289[b]
Tumor status, No. (%)	Single focal	75 (81.5)	126 (79.2)	0.663[b]
	Multifocal	17 (18.5)	33 (20.8)	
Metastasis, No. (%)		27 (29.3)	60 (37.7)	0.178[b]
Tumor Stage, No. (%)	I	60 (65.2)	93 (58.5)	0.469[b]
	II	26 (28.2)	50 (31.5)	
	III	3 (3.3)	4 (2.5)	
	IV	3 (3.3)	12 (7.5)	

[a] Student's *t* test; [b] Chi-square test.

Table 4. Comparison of Survival Times in Two Study Groups in Terms of the Age, Gender, and Tumor Stage

Variables		Hashimoto's Group (n=92)	Non-Hashimoto's Group (n=159)	*P* value[a]
Age (y)	12-39	67.39±4.40	56.97±4.63	0.037
	40-76	62.28±3.68	54.33±3.47	
Gender	Male	-	62.62±6.99	0.028
	Female	67.75±3.33	58.07±6.99	
Tumor stage	I	67.37±2.23	78.02±3.09	0.110
	II	51.80±7.48	40.93±5.47	
	III	-	40.75±6.28	
	IV	34.00±13.06	14.67±4.83	

Data are expressed as mean ± SD. [a] Student's *t* test.

stages I and II. In addition, HT had a preventive effect on PTC progression. Similar results were reported by Liu et al. They showed that in patients with higher stages of PTC, the association of HT with this carcinoma is less evident, i.e., HT is more associated with low-risk PTC and lower tumor stages (14).

This study showed that the thyroid tumor was multifocal in 18.5% of participants with HT and 20.8% of participants who were not suspected of having HT, which this difference is not significant. However, Zhu et al reported that the presence of HT in the patients affected with PTC is associated with a multifocal increase and greater invasion of the thyroid capsule (7).

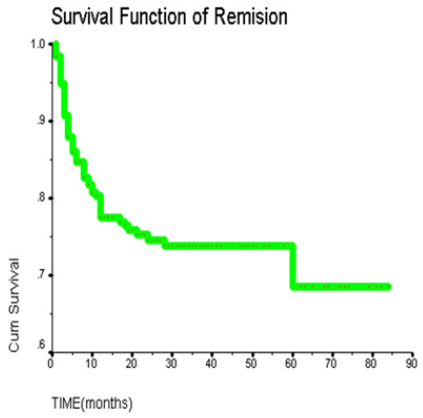

Figure 1. Survival Time in All Study Participants.

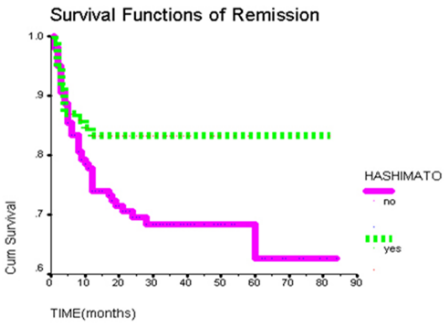

Figure 2. Survival Time in Two Study Groups (Hashimoto's and Non-Hashimoto).

Additionally, the two groups were not significantly different in thyroid capsular involvement in our study. Still, Zhu et al showed a higher incidence of capsular involvement in patients with HT (7). In this study, the survival time in the HT and non-HT groups amounted to 69.03 and 58.78 months, respectively (p = 0.038), meaning survival time grew higher in the HT group. In other words, HT hinders the recurrence of cancer. Further, in our study, the survival time in men with HT was not possible to be calculated due to the absence of recurrence, but the mean maintenance of relapse in men without HT turned out to be 62.6 months. The maintenance of relapse in the women of the HT group was longer than that of non-HT one. In other words, in women, HT prolongs the maintenance of relapse. In other words, Hashimoto's disease delayed the recurrence of papillary thyroid cancer in women. In this study, the relapse duration in the HT group was 69.03 months, and in the non-HT group was 58.78 months ($P = 0.038$). Anand et al showed that the management of papillary thyroid cancer with and without HT was no different. However, the papillary thyroid cancer with HT had less recurrence and better survival considering the age and tumor stage (15).

Limitations of the Study

One of the limitations of this study was the failure to record some data in the participants' files, including the type of recurrence, type, and extent of metastasis, as well as complete information on the type of treatment and thyroid surgery performed for each participant.

Conclusions

Based on the findings of this study, it can be concluded that the simultaneous presence of HT delays the recurrence of PTC. It is recommended that similar studies be performed in different populations with more sample sizes and longer follow-up times to achieve more reliable results.

Authors' Contribution

MM and SMMZ designed and conducted the study. FShE and SHKh conducted the research, monitored, evaluated, and analyzed the results. All authors reviewed the article and approved the final manuscript and took responsibility for the integrity of the data.

Conflict of Interests

Authors have no conflict of interest.

Ethical Issues

The research proposal was reviewed and approved by the Ethics Committee of Islamic Azad University of Isfahan (Khorasgan Branch), Isfahan, Iran (Code: IR.IAU.KHUISF.REC.1397.215). All the study participants or their legal guardians were asked for written / verbal informed consent for using their data in this study. In addition, they were well ensured about the confidentiality of the extracted information.

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References

1. Girardi FM, Barra MB, Zettler CG. Papillary thyroid carcinoma: does the association with Hashimoto's thyroiditis affect the clinicopathological characteristics of the disease? Braz J Otorhinolaryngol. 2015;81(3):283-287. doi:10.1016/j.bjorl.2014.04.006
2. Fernández-Vañes L, Llorente JL, García-Cabo P, et al. Management of differentiated thyroid carcinomas. Acta Otorrinolaringol Esp (English Edition). 2019;70(4):200-206. doi:10.1016/j.otorri.2018.03.002
3. Singh B, Shaha AR, Trivedi H, et al. Coexistent hashimoto's thyroiditis with papillary thyroid carcinoma: impact on presentation, management, and outcome. Surgery. 1999;126(6):1070-1077. doi:10.1067/msy.2099.101431
4. Dailey ME, Lindsay S, Skahen R. Relation of thyroid neoplasms to Hashimoto disease of the thyroid gland. AMA Arch Surg. 1955;70(2):291-297. doi:10.1001/archsurg.1955.01270080137023
5. Kim SS, Lee BJ, Lee JC, et al. Coexistence of Hashimoto's thyroiditis with papillary thyroid carcinoma: the influence of lymph node metastasis. Head Neck. 2011;33(9):1272-1277. doi:10.1002/hed.21594.
6. Mazokopakis EE, Tzortzinis AA, Dalieraki-Ott EI, et al. Coexistence of Hashimoto's thyroiditis with papillary thyroid carcinoma. A retrospective study. Hormones (Athens). 2010;9(4):312-317. doi:10.14310/horm.2002.1282.
7. Zhu F, Shen YB, Li FQ, et al. The effects of Hashimoto thyroiditis on lymph node metastases in unifocal and multifocal papillary thyroid carcinoma: a retrospective Chinese Cohort Study. Medicine (Baltimore). 2016;95(6):e2674.1-8. doi:10.1097/MD.0000000000002674.
8. Paparodis R, Imam S, Todorova-Koteva K, et al. Hashimoto's thyroiditis pathology and risk for thyroid cancer. Thyroid. 2014;24(7):1107-1114. doi:10.1089/thy.2013.0588.
9. Byrd DR, Carducci MA, Compton CC, et al. AJCC Cancer Staging Manual. New York, NY: Springer; 2010.
10. Zhang Y, Dai J, Wu T, et al. The study of the coexistence of Hashimoto's thyroiditis with papillary thyroid carcinoma. J Cancer Res Clin Oncol. 2014;140(6):1021-1026. doi:10.1007/s00432-014-1629-z.
11. Eslami M, Monsefi N. Prevalence of Hashimato thyroiditis in patients with papillary thyroid cancer in Kerman, 2015-2017 [dissertation]. Kerman, Iran: School of Medicine, Kerman University of Medical Sciences; 2017.
12. Campos LAAF, Picado SM, Guimarães AV, et al. Thyroid papillary carcinoma associated to hashimoto's thyroiditis. Braz J Otorhinolaryngol. 2012;78(6):77-80 doi:10.5935/1808-8694.20120037
13. Molnár S, Győry F, Nagy E, et al. Clinico-pathological features of papillary thyroid cancer coexistent with Hashimoto's thyroiditis. Orvosi Hetilap. 2017;158(5):178-182. doi:10.1556/650.2017.30647
14. Liu X, Zhu L, Cui D, et al. Coexistence of histologically confirmed Hashimoto's thyroiditis with different stages of papillary thyroid carcinoma in a consecutive Chinese cohort. Int J Endocrinol. 2014;2014:769294. doi:10.1155/2014/769294
15. Anand A, Singh KR, Kushwaha JK, et al. Papillary thyroid cancer and Hashimoto's thyroiditis: an association less understood. Indian J Surg Oncol. 2014;5(3):199-204. doi:10.1007/s13193-014-0325-4