Original Article

Prevalence of Hashimoto's thyroiditis in papillary thyroid cancer and its association with aggressive characteristics

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Background: Hashimoto's thyroiditis (HT) has been associated with papillary thyroid cancer (PTC), yet whether the clinicopathological features of PTC are affected by HT remains unknown. The purpose of this study was to investigate the association of HT with clinicopathological features of PTC.

Methods: We conducted a multicenter cross-sectional study to retrospectively evaluate the association of HT with clinicopathological features of PTC in the central provinces of China. The association between HT with clinicopathological features of PTC (including pathological HT and clinical HT) was evaluated by logistic regression analysis.

Results: A total of 15,305 patients with PTC were enrolled to this study, with a median age of 42 years at diagnosis, including 11,465 women (74.9%) and 3,840 men (25.1%). The overall prevalence of HT in PTC patients was 22.9% (3,505/15,305). Compared with PTC patients without HT, pathological HT was a potential protective factor for several aggressive characteristics of PTC, including $BRAF^{V600E}$ mutation (P<0.001), extrathyroidal extension (P=0.04), larger primary tumor size (P<0.001), advanced primary tumor stage (P<0.001), and the number of metastatic lymph nodes >5 (P=0.006), whereas this effect was not observed in clinical HT except for the $BRAF^{V600E}$ mutation and bilateral tumors (P<0.001 for both). Notably, both pathological (P<0.001) and clinical HT (P=0.04) are potential risk factors for multifocal tumors.

Conclusions: PTC patients often have concomitant HT. Some potential links between the 2 entities are present. Pathological HT is a potential protective factor for some aggressive characteristics of PTC, whereas this effect does not present in clinical HT, which has guiding significance for clinical treatment decision-making.

Keywords: Aggressive; papillary thyroid cancer (PTC); prevalence; Hashimoto's thyroiditis (HT)

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Introduction

Background

Thyroid cancer is a common endocrine malignancy, and papillary thyroid cancer (PTC) is the primary pathological subtype, accounting for more than 90% (1,2). Despite PTC being considered generally indolent, a proportion of PTC exhibits more aggressive features which can lead to a poor prognosis for patients (3-5). Therefore, proper preoperative evaluation of clinicopathological features is crucial for making decisions regarding treatment measures and surgical scope for PTC, thereby improving patient prognosis.

Hashimoto's thyroiditis (HT) is the most common autoimmune disease, which is characterized by diffuse lymphocytic infiltrate of intrathyroidal and inflammatory response, primarily identified through histology and serology testing for thyroid autoantibodies (6,7). In recent years, the relationship between HT and thyroid cancer has attracted increasing attention, as PTC patients are often concomitant with HT (8,9). However, whether the clinicopathological features of PTC will be affected by HT, and if so, the clinical significance and relationship between the two, has remained controversial.

Rationale and knowledge gap

Originally, several studies suggested that HT was associated with PTC risk (10-13). In addition, some studies have also found an association between HT and clinicopathological features of PTC. Although most studies suggest that HT may be a protective factor against invasion and metastasis of PTC (14-16), there is also some contradictory research evidence against this association, and the conflicting results may be partially attributed to differences in diagnostic criteria for HT (17-19). Most cross-sectional studies diagnose HT based on histology and serum markers, but their diagnostic criteria may also include other types of autoimmune thyroid disease in the study, which might influence the results.

Objective

To investigate the association of HT with clinicopathological features of PTC, we conducted a multicenter study including 15,305 cases and aimed to determine the effect of HT on the aggressive characteristics of PTC. We present this article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-24-445/rc).

Highlight box

Key findings

- Papillary thyroid cancer (PTC) patients frequently present with concomitant Hashimoto's thyroiditis (HT), at a rate significantly higher than the average prevalence in the global population.
- Pathological HT was identified as a potential protective factor for some aggressive characteristics of PTC, whereas this effect was not present in clinical HT.

What is known and what is new?

- The relationship between HT and thyroid cancer has garnered increasing attention, as PTC patients often present concomitantly with HT.
- This study has identified that pathological HT could serve as a potential protective factor against some aggressive characteristics of PTC, whereas this effect was not observed in clinical HT.

What is the implication, and what should change now?

- Pathological HT may be a potential protective factor against invasion and metastasis of PTC, which has guiding significance for clinical treatment decision-making.

Methods

Study participants

A comprehensive retrospective analysis was conducted involving 28,986 cases from 3 medical centers, of which 13,681 cases were excluded for failing to meet the established criteria (see in *Figure 1*). Finally, 15,305 patients diagnosed with PTC were successfully enrolled in this study. The electronic medical records of patients at each center were consecutively retrospectively collected from different periods at the 3 centers, which overall spanned 2010–2023 (*Table 1*). All patients underwent thyroidectomy and cervical lymph nodes dissection was performed in patients with indications reported in our previous study (20).

Study design

This study was conducted at 3 medical centers in the central provinces of China, including Xiangya Hospital, Changsha First Hospital, and LiXian People's Hospital, and was approved by the Xiangya Hospital Ethics Committee (No. 202211733). As a result of the study being conducted retrospectively and the data retaining patient anonymity, the requirement for written informed consent was waived. The

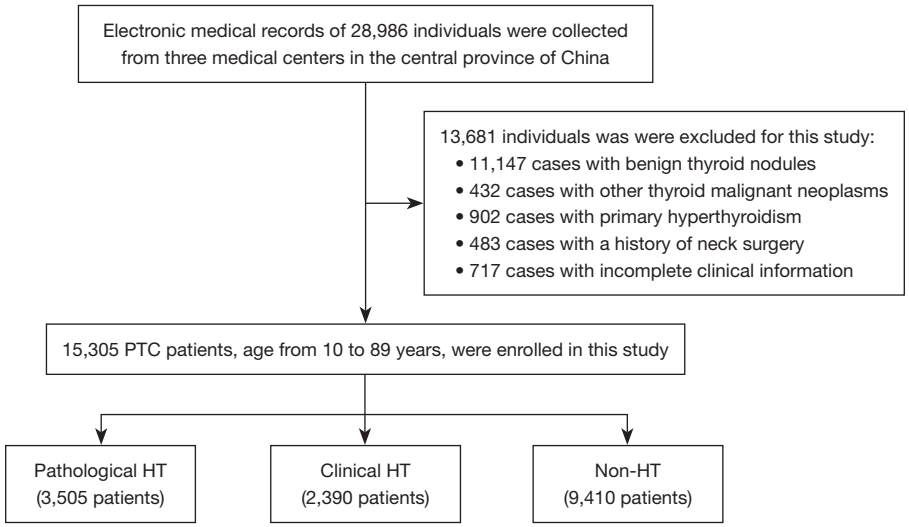

Figure 1 The process of selecting and excluding participants. HT, Hashimoto's thyroiditis; PTC, papillary thyroid cancer.

Table 1 Distribution of centers and patients participating in the study

Characteristic	Xiangya Hospital	Changsha First Hospital	Lixian People's Hospital
No. of patients	14,957 (97.7)	131 (0.9)	217 (1.4)
Sex			
Male	3,768 (98.1)	28 (0.7)	44 (1.1)
Female	11,189 (97.6)	103 (0.9)	173 (1.5)
Age at diagnosis, years			
Median [IQR]	42 [33–50]	45 [34–55]	50 [44–55]
<55	12,781 (98.1)	97 (0.7)	152 (1.2)
≥55	2,176 (95.6)	34 (1.5)	65 (2.9)
HT			
Present	3,415 (97.4)	64 (1.8)	26 (0.7)
Absent	11,542 (97.8)	67 (0.6)	191 (1.6)

Data are presented as N (%) unless otherwise specified. HT, Hashimoto's thyroiditis; IQR, interquartile range.

study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Additionally, in this study, none of the AI tools (e.g., ChatGPT, Bing) were applied in the manuscript writing, production of images nor graphical elements of the paper, nor in the collection and analysis of data.

We reviewed medical records and extracted some data including sex, age at diagnosis, $BRAF^{V600E}$ mutation, thyroid autoantibody level, primary tumor size, multifocality, bilateral tumors, extrathyroidal extension, and lymph node stage. Serum thyroid autoantibody was measured by electrochemiluminescence immunoassay before surgery. The results were considered positive when thyroid autoantibody levels exceeded normal values. In this study, we divided HT into 2 types: clinical HT and pathological HT. Clinical HT was defined as positive only for thyroid autoantibody (mainly thyroid peroxidase and thyroglobulin) but negative in pathological features. Pathological HT and PTC were diagnosed through histological examination of postoperative paraffin-embedded tissue specimens. The $BRAF^{V600E}$ mutation status was also determined using these specimens.

Statistical analysis

In univariable analysis, Mann-Whitney *U* test in non-parametric statistics was used to compare the differences between 2 independent samples groups of continuous variables with non-normal distribution, and Chi-squared test was used to compare the groups of categorical variables. Multivariable effect was estimated by logistic regression to compare the association of HT with clinicopathological features of PTC. All statistical analyses were used by the software including R version 4.2.4 for Windows (R Foundation for Statistical Computing, Vienna, Austria) and SPSS version 26.0 for Windows (IBM Corp., Armonk, NY, USA). All P values were 2-sided, and the value <0.05 was considered significant.

Results

Baseline characteristics of the participants

As summarized in *Table 2*, a total of 15,305 PTC patients were included in the study, including 11,465 women (74.9%) and 3,840 men (25.1%) (female:male ratio =3:1). Enrolled participants had a median age of 42 [interquartile range (IQR) 33–51] years at diagnosis, and 13,030 patients (85.1%) were younger than 55 years. A total of 3,505 cases of pathological HT were identified, with a significant predisposition observed in female patients diagnosed with PTC (P<0.001) (*Table 2*).

Prevalence of pathological HT in PTC

The overall detection rate of pathological HT in patients with PTC was 22.9% [95% confidence interval (CI): 22.2–23.6%]. This rate varied between 18.9% (95% CI: 16.4–21.4%) and 26.1% (95% CI: 24.2–28.1%), demonstrating consistency across different age groups. Furthermore, pathological HT was predominantly detected in females, with the prevalence in female PTC patients being twice that of their male counterparts, as illustrated in *Figure 2* and detailed in Table S1.

The detection rate of pathological HT in patients with PTC varies significantly based on the size of the primary tumor. Our findings indicate that pathological HT predominantly occurs in early-stage PTC patients with smaller primary tumors. Specifically, the detection rate of pathological HT was 24.1% (95% CI: 23.3–25.0%) in micro-PTC patients, whereas it dropped to 8.3% (95% CI: 5.3–11.4%) in advanced PTC patients with tumor size >40 mm (*Figure 3* and Table S2).

The variation in clinicopathological features of PTC associated with pathological HT

We focused on the comparison of clinicopathological features of PTC between the pathological HT and non-pathological HT groups. The findings indicated that PTC patients with pathological HT exhibited a lower prevalence of aggressive characteristics when compared to the non-pathological HT group. These characteristics included primary tumor size, $BRAF^{V600E}$ mutation status, bilateral tumor presence, extrathyroidal extension, primary tumor stage, lymph node stage, and the number of metastatic lymph nodes, with all comparisons yielding a significance level (*Table 2*). Additionally, a higher proportion of multifocality was noted in PTC patients with pathological HT compared to the non-pathological HT group, although this difference did not reach statistical significance (P=0.07).

Table 2 Demographic and clinicopathologic characteristics of PTC patients coexistence of HT

Characteristic	Total (n=15,305)	Pathologically HT present (n=3,505)	Pathologically HT absent (n=11,800)	P value
Sex				
Male	3,840 (25.1)	463 (13.2)	3,377 (28.6)	<0.001
Female	11,465 (74.9)	3,042 (86.8)	8,423 (71.4)	
Age at diagnosis, years				
Median [IQR]	42 [33–51]	40 [32–50]	42 [33–51]	<0.001
<55	13,030 (85.1)	3,032 (86.5)	9,998 (84.7)	0.009
≥55	2,275 (14.9)	473 (13.5)	1,802 (15.3)	

Table 2 (*continued*)

Table 2 (*continued*)

Characteristic	Total (n=15,305)	Pathologically HT present (n=3,505)	Pathologically HT absent (n=11,800)	P value
Primary tumor size, mm				
Median [IQR]	9.0 [6.3–14.0]	9.0 [6.3–13.0]	9.0 [6.3–15.0]	<0.001
≤10	8,912 (58.2)	2,152 (61.4)	6,760 (57.3)	<0.001
11–20	4,335 (28.3)	1,003 (28.6)	3,332 (28.2)	
21–40	1,734 (11.3)	323 (9.2)	1,411 (12.0)	
>40	324 (2.1)	27 (0.8)	297 (2.5)	
BRAF^{V600E} mutation status*				
Positive	10,149 (85.6)	1,999 (75.7)	8,150 (88.4)	<0.001
Negative	1,713 (14.4)	642 (24.3)	1,071 (11.6)	
TSH, median [IQR], uIU/mL	1.91 [1.26–2.84]	2.23 [1.41–3.38]	1.84 [1.24–2.69]	<0.001
TPOAb, median [IQR], IU/mL	15.9 [8.84–36.26]	80.32 [17.13–284.42]	13.62 [8.01–23.21]	<0.001
TgAb, median [IQR], IU/mL	19.31 [13.00–101.40]	226.10 [55.83–512.49]	16.44 [11.77–25.71]	<0.001
Multifocality	2,173 (14.2)	531 (15.1)	1,642 (13.9)	0.07
Bilateral tumor	2,969 (19.4)	590 (16.8)	2,379 (20.2)	<0.001
Extrathyroidal extension				
Absent	13,436 (87.8)	3,230 (92.2)	10,206 (86.5)	<0.001
Intrathyroidal[a]	11,920 (88.7)	2,927 (90.6)	8,993 (88.1)	<0.001
Capsular[b]	1,516 (11.3)	303 (9.4)	1,213 (11.9)	
Present	1,869 (12.2)	275 (7.8)	1,594 (13.5)	
Mild[c]	1,377 (73.7)	227 (82.5)	1,150 (72.1)	<0.001
Moderate[d]	470 (25.1)	48 (17.5)	422 (26.5)	
Severe[e]	22 (1.2)	NA	22 (1.4)	
Primary tumor stage				
pT1	12,148 (79.4)	2,970 (84.7)	9,178 (77.8)	<0.001
pT2	1,115 (7.3)	243 (6.9)	872 (7.4)	
pT3	1,550 (10.1)	244 (7.0)	1,306 (11.1)	
pT4	492 (3.2)	48 (1.4)	444 (3.8)	
Lymph nodes stage[#]				
pN0	7,153 (50.0)	1,604 (52.9)	5,549 (49.3)	0.001
pN1a	5,515 (38.6)	1,085 (35.8)	4,430 (39.3)	
pN1b	1,628 (11.4)	343 (11.3)	1,285 (11.4)	
No. of metastatic LNs[#]				
≤5	12,051 (84.3)	2,543 (83.9)	9,508 (84.4)	0.47
>5	2,245 (15.7)	489 (16.1)	1,756 (15.6)	

Data are presented as N (%) unless otherwise stated. [a], located within the gland and not involving the capsule; [b], involved capsule of lobe but not beyond; [c], direct extension to pericapsular tissues, strap muscles; [d], invasion of larynx, trachea, esophagus, recurrent laryngeal nerve, or subcutaneous soft tissue; [e], invasion of prevertebral fascia, encase the carotid artery or mediastinal blood vessels. *, including patients with *BRAF*^{V600E} (n=11,862); #, including patients with lymph node stage (n=14,296). HT, Hashimoto's thyroiditis; IQR, interquartile range; LNs, lymph nodes; NA, not applicable; PTC, papillary thyroid cancer; TgAb, anti-thyroglobulin antibodies; TPOAb, anti-thyroid peroxidase antibodies; TSH, thyroid stimulating hormone.

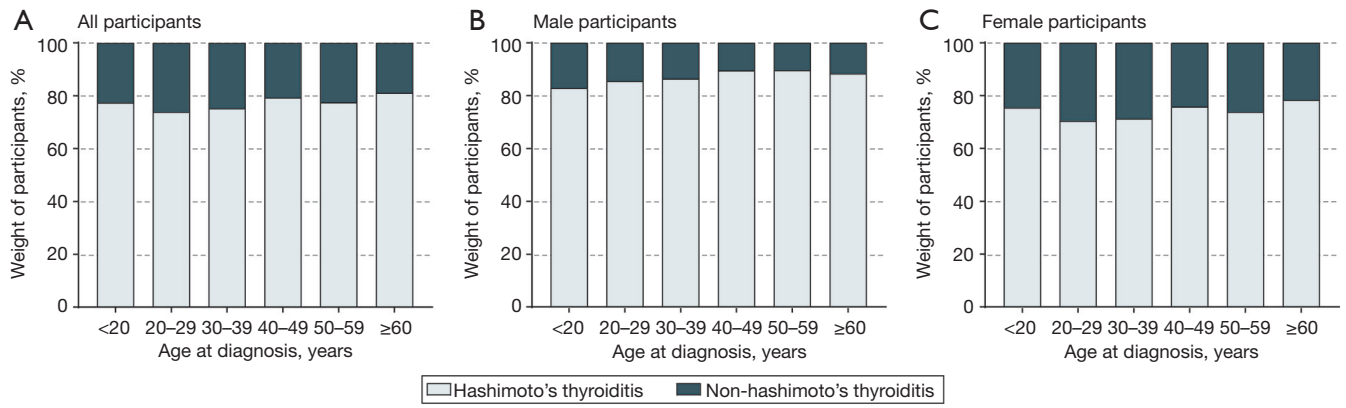

Figure 2 Prevalence of Hashimoto's thyroiditis in patients with papillary thyroid cancer by age at diagnosis.

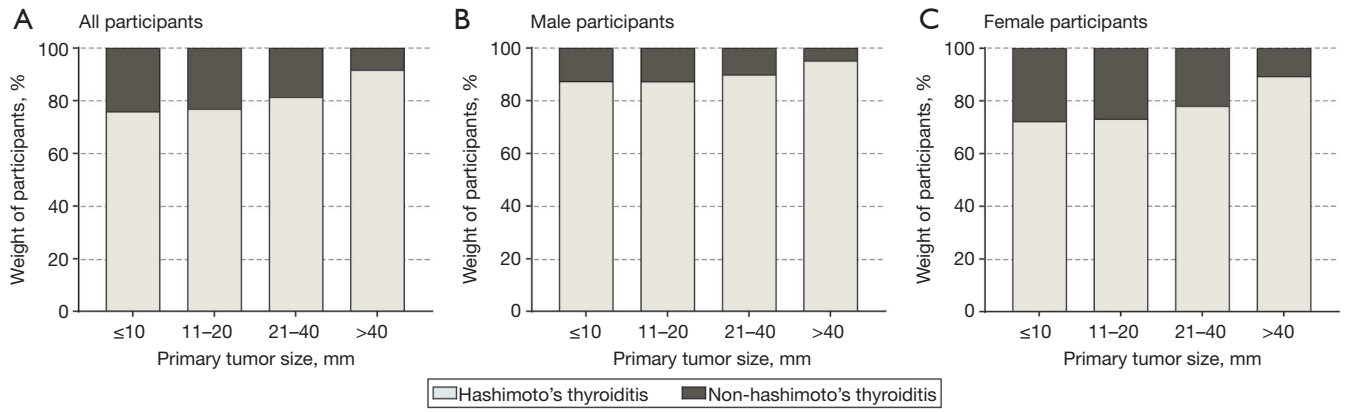

Figure 3 Prevalence of Hashimoto's thyroiditis in patients with papillary thyroid cancer by primary tumor size.

Association of pathological HT with aggressive characteristics of PTC

We performed an analysis to assess the risk associated with pathological HT in relation to the aggressive characteristics of PTC utilizing logistic regression methods. The findings revealed a significant association between pathological HT and aggressive characteristics of PTC. Specifically, pathological HT demonstrated a negative correlation with several aggressive features of PTC, including the *BRAF*^{V600E} mutation, bilateral tumors, extrathyroidal extension, larger primary tumor size, and advanced primary tumor stage (P<0.001 for all). This correlation persisted even after adjusting for various confounding factors. Moreover, we also found that pathological HT was negatively correlated with the number of metastatic lymph nodes >5 (P=0.03) (*Table 3*).

Interestingly, when we categorized HT into pathological HT and clinical HT, we found that pathological HT appeared to serve as a protective factor against several aggressive characteristics of PTC, including the *BRAF*^{V600E} mutation (P<0.001), extrathyroidal extension (P=0.04), larger primary tumor size (P<0.001), advanced primary tumor stage (P<0.001), and the number of metastatic lymph nodes >5 (P=0.006), whereas this association was not present in clinical HT, except for the *BRAF*^{V600E} mutation, and bilateral tumors (P<0.001, both). Notably, both pathological (P<0.001) and clinical HT (P=0.04) are potential risk factors for multifocal tumors, as indicated in multivariate analysis (*Table 4*).

Discussion

Thyroid cancer is frequently concomitant with autoimmune thyroiditis, sparking significant interest in their interrelation. Previous research regarding the relationship between HT and PTC has yielded mixed results. Studies

Table 3 The OR of HT associated risk for aggressive characteristics of PTC by logistic regression

Characteristic	Unadjusted		Adjusted 1*		Adjusted 2*	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
BRAF^{V600E} mutation*	0.409 (0.367–0.456)	<0.001	0.422 (0.377–0.473)	<0.001[a]	0.500 (0.440–0.568)	<0.001[a]
Multifocality	1.105 (0.993–1.228)	0.07	1.346 (1.195–1.515)	<0.001[b]	1.219 (1.066–1.393)	0.004[b]
Bilateral tumor	0.802 (0.726–0.885)	<0.001	0.895 (0.800–1.002)	0.054[b]	0.706 (0.621–0.804)	<0.001[b]
Extrathyroidal extension						
Absent	Reference		Reference		Reference	
Intrathyroidal	Reference		Reference		Reference	
Capsular invasion	0.767 (0.672–0.876)	<0.001	0.985 (0.850–1.140)	0.84[b]	1.097 (0.931–1.294)	0.27[b]
Present	0.545 (0.477–0.623)	<0.001	0.759 (0.646–0.891)	0.001[b]	0.818 (0.683–0.979)	0.03[b]
Mild	0.624 (0.538–0.723)	<0.001	0.821 (0.690–0.976)	0.03[b]	0.910 (0.749–1.105)	0.34[b]
Moderate	0.359 (0.266–0.486)	<0.001	0.562 (0.398–0.792)	0.001[b]	0.538 (0.366–0.790)	0.002[b]
Severe	0.001 (0.000–0.001)	<0.001	0.001 (0.000–0.001)	<0.001[b]	0.001 (0.000–0.001)	<0.001[b]
Primary tumor size, mm						
≤10	Reference		Reference		Reference	
11–20	0.946 (0.868–1.030)	0.20	1.063 (0.961–1.175)	0.23[c]	0.911 (0.813–1.370)	0.11[c]
21–40	0.719 (0.631–0.819)	<0.001	0.901 (0.769–1.055)	0.20[c]	0.738 (0.617–0.882)	0.001[c]
>40	0.286 (0.192–0.425)	<0.001	0.422 (0.261–0.682)	<0.001[c]	0.308 (0.181–0.524)	<0.001[c]
Primary tumor stage						
pT1	Reference		Reference		Reference	
pT2	0.861 (0.743–0.999)	0.048	1.090 (0.856–1.388)	0.49[c]	1.155 (0.968–1.379)	0.11[c]
pT3	0.577 (0.501–0.666)	<0.001	0.747 (0.611–0.913)	0.004[c]	0.739 (0.617–0.886)	0.001[c]
pT4	0.334 (0.247–0.451)	<0.001	0.503 (0.350–0.721)	<0.001[c]	0.423 (0.292–0.612)	<0.001[c]
Lymph nodes stage#						
pN0	Reference		Reference		Reference	
pN1a	0.847 (0.777–0.924)	<0.001	0.937 (0.846–1.037)	0.21[d]	1.068 (0.952–1.197)	0.26[d]
pN1b	0.923 (0.810–1.053)	0.24	1.100 (0.931–1.298)	0.26[d]	1.081 (0.897–1.304)	0.41[d]
No. of metastatic LNs#						
≤5	Reference		Reference		Reference	
>5	0.960 (0.861–1.071)	0.47	0.801 (0.700–0.916)	0.001[d]	0.841 (0.722–0.979)	0.03[d]

[a], odds ratio adjusted for age, sex, TSH, and primary tumor size; [b], odds ratio adjusted for age, sex, TSH, *BRAF*^{V600E}, and primary tumor size; [c], odds ratio adjusted for age, sex, TSH, and *BRAF*^{V600E}; [d], odds ratio adjusted for age, sex, TSH, *BRAF*^{V600E}, multifocality, bilateral tumor, extrathyroidal extension, and primary tumor size. *, including patients with *BRAF*^{V600E} (n=11,862); #, including patients with lymph node stage (n=14,296). Adjusted OR 2 adjusted for TPOAb and TgAb level based on Adjusted OR 1. CI, confidence interval; HT, Hashimoto's thyroiditis; LNs, lymph nodes; OR, odds ratio; PTC, papillary thyroid cancer; TgAb, anti-thyroglobulin antibodies; TPOAb, anti-thyroid peroxidase antibodies; TSH, thyroid stimulating hormone.

are increasingly indicating a negative impact of HT on the invasion and metastasis of PTC (14,21). Nevertheless, discrepancies remain, particularly concerning the association between HT and the aggressiveness of PTC, with some studies reporting a correlation but others not. These conflicting findings may be partially due to variations in the diagnostic criteria used for HT (22,23).

To this end, we conducted a multicenter cross-sectional

Table 4 The OR of clinically HT and pathologically HT associated risk for aggressive characteristics of PTC by logistic regression

Characteristic	HT (clinically, n=2,390)		HT (pathologically, n=3,505)	
	Adjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
BRAF^{V600E} mutation*	0.685 (0.585–0.802)	<0.001[a]	0.431 (0.374–0.497)	<0.001[a]
Multifocality	1.176 (1.011–1.369)	0.04[a]	1.298 (1.122–1.501)	<0.001[b]
Bilateral tumor	1.774 (1.560–2.018)	<0.001[a]	0.913 (0.795–1.050)	0.20[b]
Extrathyroidal extension				
Absent	Reference		Reference	
Intrathyroidal	Reference		Reference	
Capsular invasion	1.047 (0.875–1.251)	0.62[b]	0.875 (0.723–1.058)	0.17[b]
Present	0.983 (0.815–1.186)	0.86[b]	0.812 (0.668–0.987)	0.04[b]
Mild	0.987 (0.803–1.214)	0.90[b]	0.906 (0.734–1.118)	0.36[b]
Moderate	0.958 (0.676–1.358)	0.81[b]	0.527 (0.346–0.803)	0.003[b]
Severe	0.245 (0.007–9.133)	0.45[b]	0.001 (0.000–0.001)	<0.001[b]
Primary tumor size, mm				
≤10	Reference		Reference	
11–20	1.070 (0.942–1.215)	0.30[c]	0.935 (0.826–1.059)	0.29[c]
21–40	1.015 (0.835–1.233)	0.88[c]	0.741 (0.609–0.903)	0.003[c]
> 40	1.185 (0.765–1.835)	0.45[c]	0.337 (0.189–0.603)	<0.001[c]
Primary tumor stage				
pT1	Reference		Reference	
pT2	0.876 (0.687–1.118)	0.29[c]	0.864 (0.687–1.087)	0.21[c]
pT3	0.988 (0.818–1.194)	0.90[c]	0.736 (0.605–0.896)	0.002[c]
pT4	0.976 (0.702–1.358)	0.89[c]	0.419 (0.279–0.627)	<0.001[c]
Lymph nodes stage#				
pN0	Reference		Reference	
pN1a	1.018 (0.896–1.157)	0.79[d]	1.075 (0.950–1.216)	0.25[d]
pN1b	1.189 (0.968–1.460)	0.10[d]	1.162 (0.947–1.425)	0.15[d]
No. of metastatic LNs#				
≤5	Reference		Reference	
>5	0.923 (0.770–1.108)	0.39[d]	0.791 (0.670–0.933)	0.006[d]

[a], odds ratio adjusted for age, sex, TSH, primary tumor size, TPOAb and TgAb level; [b], odds ratio adjusted for age, sex, TSH, *BRAF*^{V600E}, primary tumor size, TPOAb and TgAb level; [c], odds ratio adjusted for age, sex, TSH, *BRAF*^{V600E}, TPOAb and TgAb level; [d], odds ratio adjusted for age, sex, TSH, *BRAF*^{V600E}, multifocality, bilateral tumor, extrathyroidal extension, primary tumor size, TPOAb and TgAb level. *, including patients with *BRAF*^{V600E} (n=11,862); #, including patients with lymph node stage (n=14,296). CI, confidence interval; HT, Hashimoto's thyroiditis; LNs, lymph nodes; OR, odds ratio; PTC, papillary thyroid cancer; TgAb, anti-thyroglobulin antibodies; TPOAb, anti-thyroid peroxidase antibodies; TSH, thyroid stimulating hormone.

study in the central region of China to assess the association between pathological HT and PTC. Our findings revealed an overall prevalence of pathological HT at 22.9% among PTC patients, which is significantly higher than the average prevalence reported in the global population in previous studies (24-26). Furthermore, the detection rate of pathological HT within the PTC population remained consistent across all age groups, which contradicts earlier

reports suggesting that HT predominantly occurs in young and middle-aged women, with the prevalence increasing with age (25,27). The co-occurrence of HT and PTC implies a potential link between these 2 conditions. Additionally, pathological HT predominantly occurred in early-stage PTC patients with smaller primary tumors in this study, with a gradual decline in the proportion of pathological HT as tumor size increased. These findings may imply that pre-existing HT is associated with early-stage PTC risk (11,12).

Subsequently, we objectively assessed the association between the pathological HT and clinicopathological characteristics of PTC. Our findings indicate that PTC patients with pathological HT exhibit a reduced incidence of the *BRAF*^{V600E} mutation, bilateral tumors, and extrathyroidal extension. Additionally, these patients tend to present with smaller primary tumor sizes, earlier stages of primary tumors and lymph nodes, as well as a lower number of metastatic lymph nodes. These observations align with those of with previous studies (14,16,28). Importantly, our results indicate that the protective effect of HT on PTC is primarily associated with pathological HT, as this correlation was not observed in cases of clinical HT. The findings offer a prospective resolution to previous uncertainties regarding the association between HT and PTC, while also reinforcing the beneficial influence of pathological HT on the clinicopathological characteristics of PTC (16,29,30).

The study presents several limitations that warrant consideration. Firstly, the researchers lacked access to prognostic information for the participants, hindering their ability to assess the impact of HT on the overall prognosis of patients with PTC. Additionally, the absence of prospective study data restricts the investigation into the relationship between HT and PTC. Finally, despite being a multi-center study, the majority of the data were sourced from a single center, which may affect the generalizability of the findings. Consequently, it is imperative that future research endeavors strive to incorporate a larger number of cases from diverse centers.

Conclusions

PTC patients often have concomitant HT, and some potential links between the 2 entities are present. Pathological HT is a potential protective factor for some aggressive characteristics of PTC, whereas this effect does not present in clinical HT.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-24-445/rc

Data Sharing Statement: Available at https://gs.amegroups.com/article/view/10.21037/gs-24-445/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-24-445/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Xiangya Hospital Ethics Committee (No. 202211733). As a result of the study being conducted retrospectively and the data retaining patient anonymity, the requirement for written informed consent was waived.

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