

Prevalence of Hashimoto's thyroiditis in adults with papillary thyroid carcinoma and association with cancer recurrence and outcomes



Author: Siyuan Xu, Hui Huang, Jiaxin Qian, Yang Liu, Ying Huang, Xiaolei Wang, Shaoyan Liu, Zhengang Xu, Jie Liu

Organization: Department of Head and Neck Surgical Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100021, P.R. China

Importance

- Hashimoto's thyroiditis (HT) has been suggested to be associated with papillary thyroid cancer (PTC) development. However, its impact on PTC progression remains unclear.

Objective

- To examine the association between HT and PTC presentation and outcomes.

Table 1. Patient demographic, clinical and pathological characteristics according to the coexistence of HT.

	Coexistence of HT		P value
	Absent (n=7459) 44±12	Present (n=1751) 41±11	
Patient age, years median±SD			<0.001
Sex n (%)			<0.001
male	2196 (29)	142 (8)	
female	5263 (71)	1609 (92)	
Primary size, cm median±SD	1.1±1.2	1.0±0.7	<0.001
<2cm	5430(73)	1440(82)	
<4cm, ≥2cm	1588(21)	294(17)	
≥4cm	441(6)	17(1)	
Extrathyroidal extension n (%)			<0.001
absent	4231 (57)	1093(62)	
present	3228 (43)	658(38)	
Multifocality n (%)			0.07
absent	4769 (64)	1079 (62)	
present	2690 (36)	672(38)	
Bilateral lesions n (%)			0.41
absent	5655 (76)	1311 (75)	
present	1804 (24)	440 (25)	
Nodal status n (%)			<0.001
none	3713 (50)	874 (50)	
N1a	1851 (22)	492 (27)	
N1b	1831 (28)	352 (23)	
Number of nodes removed* median±SD	25±28	18±27	0.65
Number of metastasis* median±SD	5±9	4±8	<0.001
>3 cm node metastasis* n (%)			<0.001
absent	3590 (96)	875 (99)	
present	161 (4)	6 (1)	
Lymph nodes ratio* median±SD	0.30±0.28	0.24±0.22	<0.001
Extranodal extension* n (%)			<0.001
absent	2680 (71)	741 (84)	
present	1071 (29)	140 (16)	
Distant metastasis			<0.001
absent	7379 (98.9)	1749 (99.9)	
present	80 (1.1)	2 (0.1)	
Stage			<0.001
I	6560(87.9)	1620(93.6)	
II	653(8.8)	105(6)	
III	213(2.9)	25(1.4)	
IV	33(0.4)	1(0)	
Extent of surgery			0.03
lobectomy	4718(63)	1059(61)	
total thyroidectomy	2741(37)	692(39)	
RAI administration			0.33
absent	5785(77)	1339(76)	
present	1674(23)	412(24)	

*Including patients with lymph node metastasis (n=4526)

Design

- This retrospective cohort study included a review of patients with PTC treated from January 2001 to December 2014.
- Logistic and cox regression models were performed.

Setting

- Single institute study in a referral cancer center.

Participants

- Inclusion criteria:** Patients (18-75 years old) with pathological confirmed PTC.
- Exclusion criteria:** Evidence of poorly differentiated PTC or a second malignancy, previous history of thyroid surgery and insufficient follow-up data.

Table 2. Various aggressive characteristics at presentation of PTC and odds ratios for coexistent HT vs absent by logistic regression.

Aggressive characteristics	Unadjusted OR (95%CI)	P value	Adjusted OR* (95%CI)	P value
Primary size≥4cm	0.16 (0.10-0.33)	<0.001	0.20 (0.12-0.33)	<0.001
Extrathyroidal extension	0.79 (0.71-0.88)	<0.001	0.90 (0.81-1.01)	0.08
Gross extrathyroidal extension	0.36 (0.30-0.44)	<0.001	0.44 (0.36-0.54)	<0.001
Lymph node metastasis	1.00 (0.90-1.11)	0.98	NA	
Lateral neck metastasis**	0.74 (0.66-0.84)	<0.001	0.93 (0.82-1.07)	0.31
Extranodal extension**	0.52 (0.43-0.62)	<0.001	0.66 (0.55-0.80)	<0.001
Distant metastasis	0.11(0.03-0.43)	0.002	0.17 (0.04-0.71)	0.02

*HR adjusted with sex, age and primary size except primary size≥4cm, which were adjusted with sex and age.

** Including patients with lymph node metastasis (n=4526)

Exposures

- Coexistent HT** was defined according to postoperative paraffin sections.

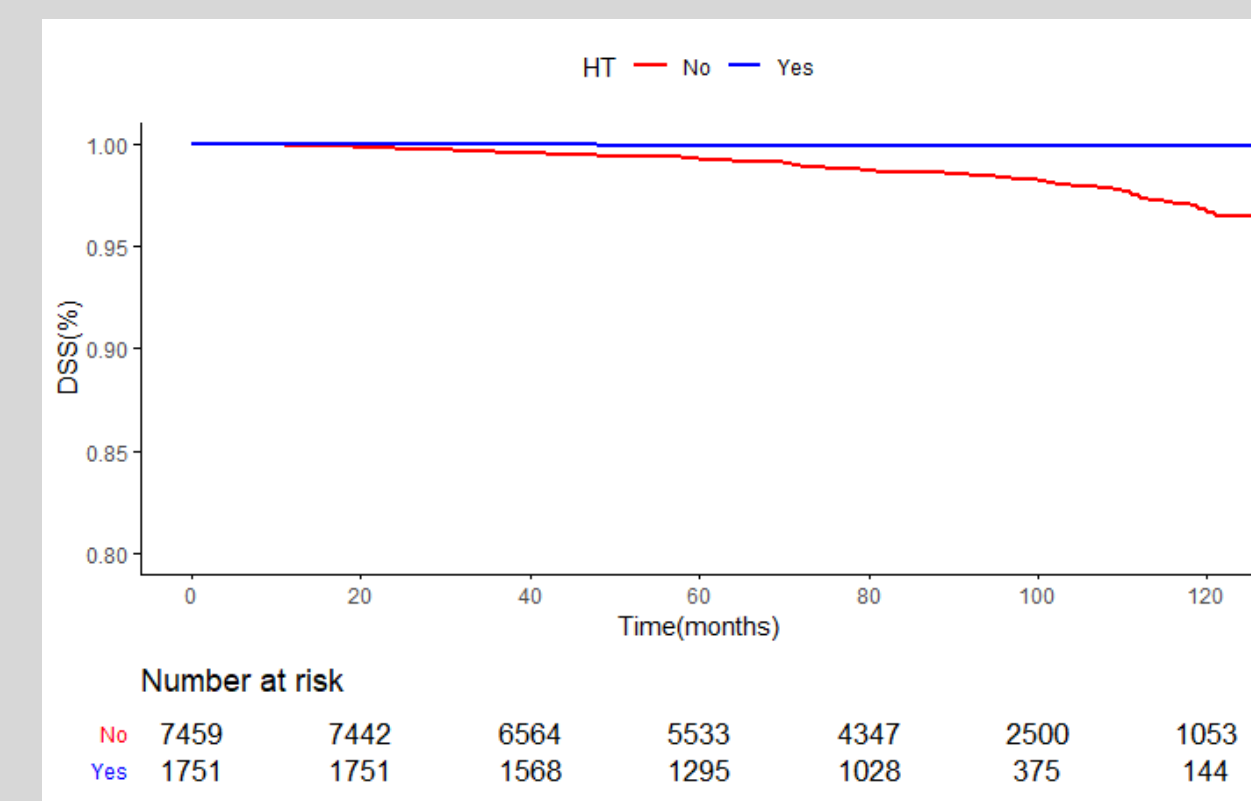


Fig.1 Unadjusted disease-specific survival of patients with and without HT (P<0.01).

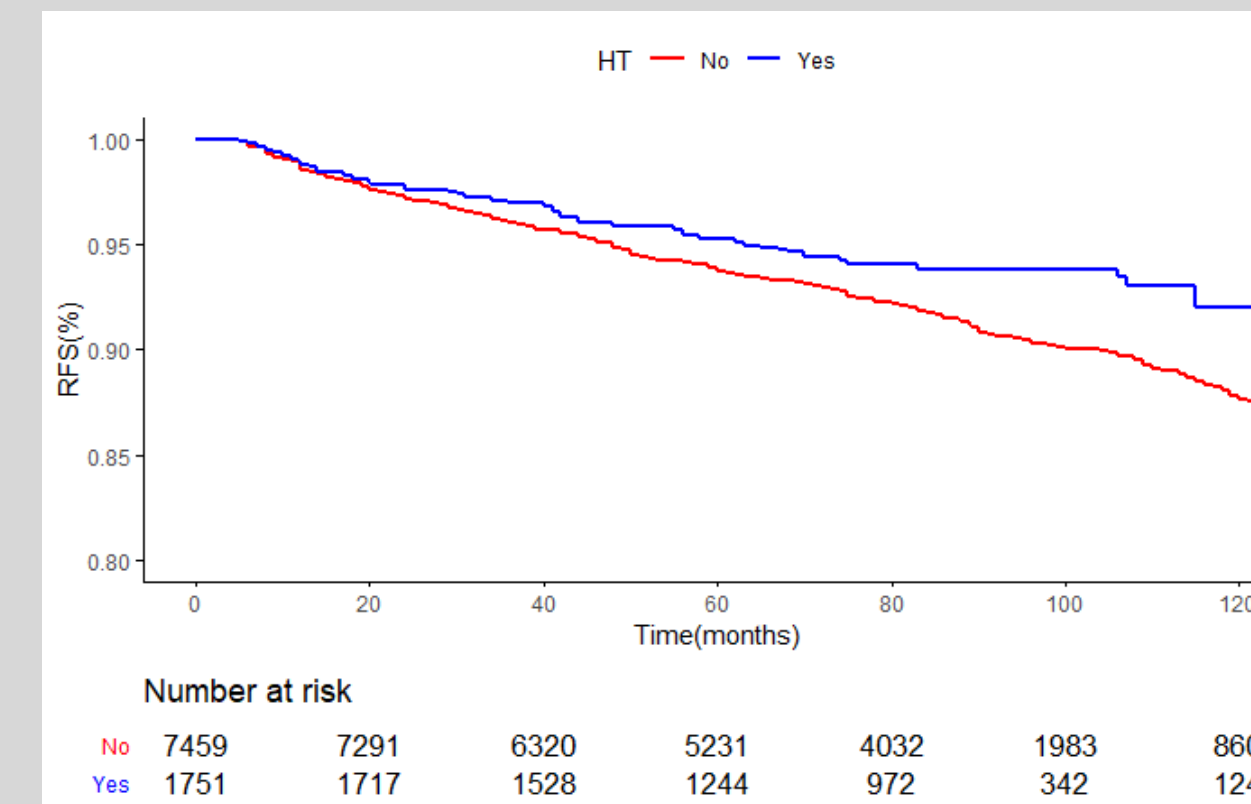


Fig.2 Unadjusted recurrence-free survival of patients with and without HT (P=0.001).

Main outcomes

- The primary outcome was the association of HT with PTC-related mortality. Secondary outcomes included the association of HT with aggressive characteristics and structural recurrence of PTC.

Results

- A total of 9210 patients with PTC (median [SD] age; 43.0 [12.0] years; 6872 [75%] women) were analyzed (Table 1). After a median follow-up of 85 months, 131 PTC-related deaths were identified in the whole cohort while 2 of which had HT.
- HT was present in 1751 (19%) patients, which correlated negatively with frequencies of primary size≥4cm, gross extrathyroidal extension (ETE), extranodal extension and distant metastasis (logistic regression; adjusted OR [95%CI]; 0.20 [0.12-0.33], 0.44 [0.36-0.54], 0.66 [0.55-0.80], 0.17 [0.04-0.71], all P<0.05) (Table 2).
- Patients with HT had significantly superior outcomes compared to patients without HT in terms of unadjusted 10-year disease-specific survival (99.9% vs 96.6%, log rank P<0.01) (Fig.1) and recurrence-free survival (92.0% vs 87.6%, log rank P<0.01) rates (Fig.2). After adjusting for sex, age, primary size, ETE, lymph node metastasis (LNM), distant metastasis, extent of surgery and radioactive iodine ablation, HT was associated with decreased PTC-related mortality (HR [95%CI], 0.19[0.05-0.76], P=0.02) (Fig.3).

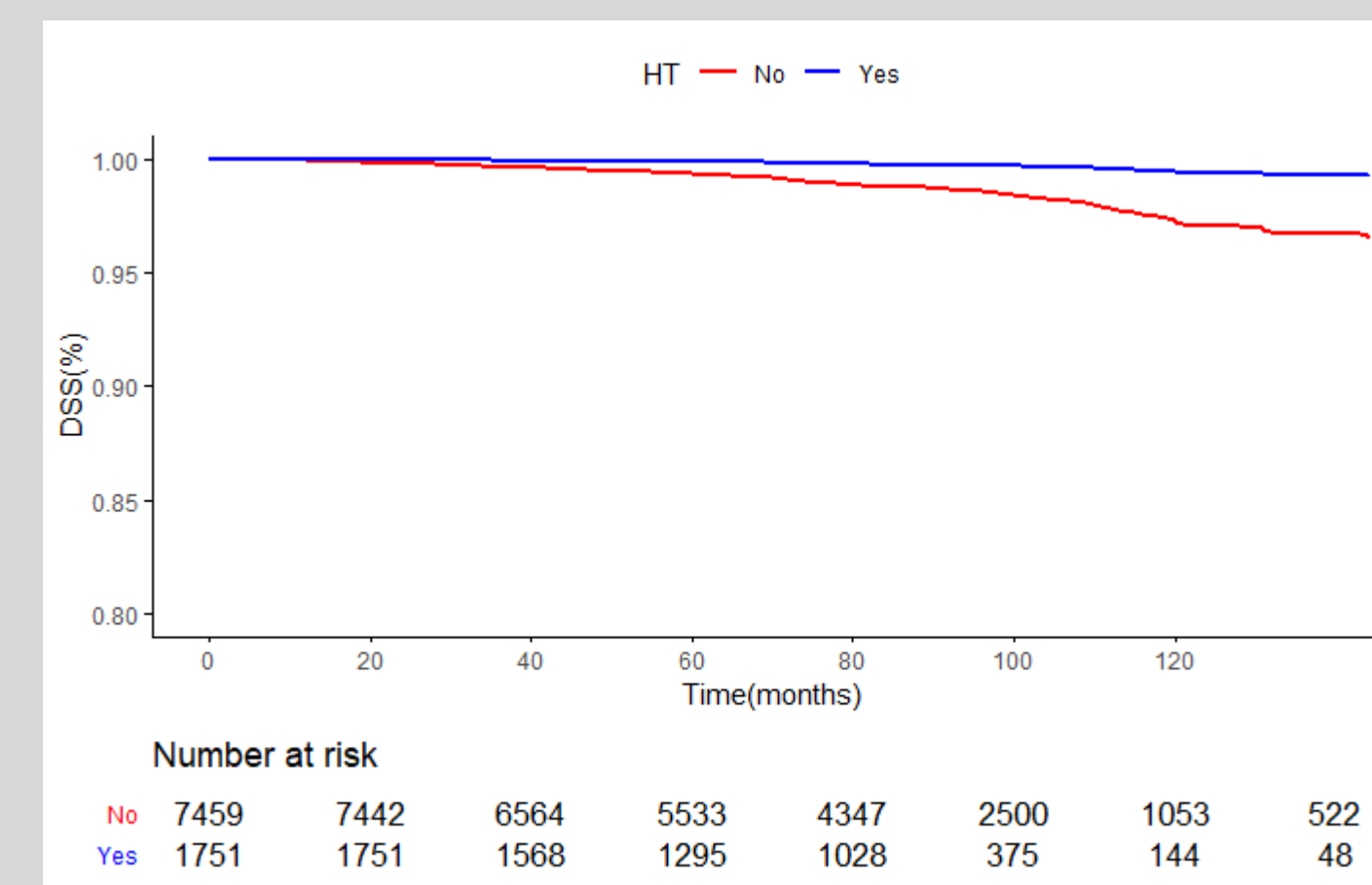


Fig.3 Disease-specific survival of patients with and without HT after adjusting for sex, age, primary size, ETE, LNM, distant metastasis, extent of surgery and RAI ablation (P=0.02).

- Stratified analysis shown HT was associated with less structural recurrence in patients with ETE or after total thyroidectomy (HR[95%CI], 0.52[0.38-0.71], 0.50[0.35-0.69], respectively, both p<0.001, p for interaction<0.01) (Table 3).

Table 3. Stratified analysis of unadjusted hazard ratios of structural recurrence for coexistent HT vs. absent by Cox proportional hazard models.

Stratification	HR (95% CI)	P value	P value for interaction
Age			0.29
<45	0.76 (0.58-0.98)	0.04	
≥45	0.59 (0.41-0.84)	<0.01	
Sex			0.07
female	0.88 (0.70-1.11)	0.27	
male	0.47 (0.23-0.94)	0.03	
Primary size			0.06
<2cm	0.95 (0.73-1.25)	0.72	
≥2cm	0.61 (0.43-0.86)	<0.01	
Extrathyroidal extension			<0.01
absent	1.08 (0.81-1.44)	0.61	
present	0.52 (0.38-0.71)	<0.001	
LNM			0.82
absent	0.73 (0.48-1.12)	0.15	
present	0.68 (0.53-0.87)	<0.01	
Extent			<0.01
lobectomy	0.88 (0.67-1.15)	0.35	
total thyroidectomy	0.50 (0.35-0.69)	<0.001	
RAI			0.55
absent	0.74 (0.59-0.93)	0.01	
present	0.59 (0.35-0.99)	<0.046	

Conclusions

Coexistent HT was associated with less aggressive characteristics at presentation and better outcomes of PTC.

Contact information

[name] Jie Liu
[organization] National Clinical Research Center for Cancer, Chinese Academy of Medical Sciences and Peking Union Medical College
[address] No.17 Panjiayuan Nanli, Chaoyang District, Beijing 10021, China
[email] liuj@cicams.ac.cn
[phone] +86-13910217810