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HIGHER TSH CAN BE USED AS AN ADDITIONAL RISK FACTOR IN PREDICTION OF MALIGNANCY IN EUTHYROID THYROID NODULES EVALUATED BY CYTOLOGY BASED ON BETHESDA SYSTEM

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Introduction

➢Recently, it has been suggested that thyrotropin (TSH) concentration can be used as a marker for prediction of thyroid malignancy. However, the association between the cytology results and TSH levels is not clear. In this study, we aimed to investigate the relationship between TSH levels and Bethesda categories and determine the role of TSH levels in prediction of malignancy in patients with different Bethesda categories.

Methods

➢ The data of 1433 euthyroid patients with 3206 thyroid nodules who underwent thyroidectomy were screened retrospectively. The preoperative cytology results, thyroid function tests, thyroid autoantibodies, and presence of histopathological Hashimoto's thyroiditis (HT) were recorded.

Results

➢ Of the 1433 patients, 585 (40.8%) had malignant and 848 (59.2%) had benign histopathology. Malignant group had smaller nodule size, elevated TSH levels, a higher rate of presence of HT compared to benign group ($p<0.001$, all). Cytology results of 3206 nodules were as follows; 832 nondiagnostic (ND), 1666 benign, 392 atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS), 68 follicular neoplasm/suspicious for follicular neoplasm (FN/SFN), 133 suspicious for malignancy (SM), and 115 malignant.

➢ ND cytology group had lower TSH levels compared to AUS/FLUS, SM, and malignant cytology groups ($p<0.001$, for all), while TSH levels were similar between the FN/SFN and ND cytology groups ($p=0.086$). Benign cytology group had significantly lower TSH levels compared to ND, AUS/FLUS, FN/SFN, SM, and malignant cytology groups ($p=0.009$ for ND, $p=0.012$ for FN/SFN, $p<0.001$ for other cytology groups). AUS/FLUS cytology group had significantly higher TSH levels than ND and benign cytology groups ($p<0.001$, all), while it had significantly lower TSH levels than SM and malignant cytology groups ($p=0.012$ and $p<0.001$). Additionaly, AUS/FLUS cytology group had similar TSH levels with FN/SFN group ($p=0.686$). FN/SFN cytology group had significantly lower TSH levels compared to SM and malignant cytology groups ($p=0.048$ and $p=0.009$, respectively). Both SM and malignant cytology groups had higher TSH levels than other 4 Bethesda categories ($p<0.05$, all) (Table 1). As Bethesda category proceeded towards cytologies with higher estimated risk of malignancy, TSH levels tended to increase gradually.

➢ Patients with malignant final histopathology in ND and AUS/FLUS cytology groups had significantly higher TSH levels compared to patients with benign final histopathology ($p<0.05$, all) (Table 2).

Table 1. Comparison of thyroid function tests, presence of HT, anti-TPOAb, and anti-TgAb positivity of six different Bethesda category groups

	ND (n=832)	Benign (n=1666)	AUS/FLUS (n=392)	FN/SFN (n=68)	SM (n=133)	Malignant (n=115)	*p* value
TSH (μIU/mL)	1.10 (0.40 – 4.04)	1.07 (0.40 – 4.04)	1.31 (0.40 – 4.04)	1.30 (0.40 – 3.89)	1.56 (0.40 – 4.04)	1.62 (0.40 – 4.04)	<0.001
fT3 (pg/mL)	3.23 (1.90 – 4.77)	3.26 (1.57 – 4.77)	3.20 (1.90 – 4.73)	3.25 (2.05 – 4.49)	3.15 (1.97 – 4.35)	3.10 (2.10 – 4.16)	<0.001
fT4 (ng/dL)	1.15 (0.85 – 1.78)	1.15 (0.85 – 1.78)	1.16 (0.85 – 1.70)	1.15 (0.85 – 1.68)	1.20 (0.85– 1.78)	1.20 (0.81 – 1.68)	0.092
Anti-TPOAb positivity*, no (%)	99 (18.9)	171 (17.6)	60 (21.4)	6 (12.8)	23 (21.5)	17 (19.5)	0.706
Anti-TgAb positivity**, no (%)	98 (19.1)	161 (16.8)	67 (24.5)	14 (28.0)	24 (22.9)	20 (23.3)	0.128
Presence of HT,*** no (%)	218 (26.4)	431 (26.1)	132 (33.7)	17 (25.0)	45 (34.1)	33 (28.7)	0.088

* Anti-TPOAb measurements were present in 2014 nodules. ** Anti-TgAb measurements were present in 1987 nodules. *** HT was evaluated in 3184 nodules.
ND: Nondiagnostic, AUS/FLUS: atypia of undetermined significance/follicular lesion of undetermined significance, ,FN/SFN: follicular neoplasm/suspicious for follicular neoplasm, SM: Suspicious for malignancy, TSH: thyrotropin, fT4: free thyroxine, fT3: free triiodothyronine, Anti-TPOAb: anti-thyroid peroxidase antibodies, Anti-TgAb: anti-thyroglobulin antibodies, HT: Hashimoto's thyroiditis

Table 2. Evaluation of thyroid function tests of different cytology groups based on histopathology results

Cytology	Pathology	TSH	*p* value	fT3	*p* value	fT4	*p* value	Anti-TPOAb no (%)	*p* value	Anti-TgAb no (%)	*p* value	HT no (%)	*p* value
ND (n=832)	B	1.10 (0.40 – 4.04)	**0.002**	3.22 (1.90 – 4.77)	0.771	1.15 (0.85 – 1.78)	**0.023**	92 (19.5)	0.289	92 (20.0)	0.130	200 (26.1)	0.460
	M	1.46 (0.40 – 4.04)		3.30 (2.14 – 4.59)		1.22 (0.85 – 1.66)		7 (13.5)		6 (11.3)		18 (30.5)	
Benign (n=1666)	B	1.06 (0.40 – 4.04)	**0.005**	3.26 (1.57 – 4.77)	0.738	1.15 (0.85 – 1.78)	0.580	154 (16.9)	**0.016**	153 (17.0)	0.491	409 (25.9)	0.337
	M	1.40 (0.40 – 4.04)		3.30 (2.37 – 4.23)		1.16 (0.85 – 1.61)		17 (29.3)		8 (13.6)		22 (31.0)	
AUS/FLUS (n=392)	B	1.22 (0.40 – 4.04)	**0.034**	3.20 (1.90 – 4.73)	0.952	1.15 (0.85 – 1.70)	0.758	42 (20.9)	0.767	45 (23.0)	0.362	104 (34.0)	0.804
	M	1.50 (0.40 – 4.04)		3.26 (1.90 – 4.71)		1.17 (0.85 – 1.66)		18 (22.5)		22 (28.2)		28 (32.6)	
FN/SFN (n=68)	B	1.10 (0.40 – 3.89)	0.145	3.15 (2.05 – 4.25)	**0.028**	1.16 (0.85 – 1.68)	0.577	4 (15.4)	0.549	6 (21.4)	0.243	9 (20.0)	0.183
	M	1.50 (0.60 – 3.30)		3.40 (2.52 – 4.49)		1.10 (0.85 – 1.46)		2 (9.5)		8 (36.4)		8 (34.8)	
SM (n=133)	B	1.39 (0.59 – 4.00)	0.922	3.09 (2.43 – 4.20)	0.588	1.20 (0.85 – 1.78)	0.562	6 (40.0)	0.060	6 (42.9)	0.056	11 (40.7)	0.414
	M	1.65 (0.40 – 4.04)		3.20 (1.97 – 4.35)		1.20 (0.87 – 1.62)		17 (18.5)		18 (19.8)		34 (32.4)	

ND: Nondiagnostic, AUS/FLUS: atypia of undetermined significance/follicular lesion of undetermined significance, ,FN/SFN: follicular neoplasm/suspicious for follicular neoplasm, SM: suspicious for malignancy, B: benign, M: malignant, TSH: thyrotropin, fT4: free thyroxine, fT3: free triiodothyronine, Anti-TPOAb: anti-thyroid peroxidase antibody, Anti-TgAb: anti-thyroglobulin antibody, HT: Hashimoto's thyroiditis

Conclusion

➢ In addition to cytology, TSH levels can be used as a supplementary marker in prediction of malignancy in certain Bethesda categories.