Thyroid Carcinoma and Focal Lymphocytic Thyroiditis Share Common Features in Ultrasonography: A Diagnostic Predictor Model for Discrimination

Sena Hwang

Department of Medicine

The Graduate School, Yonsei University

Thyroid Carcinoma and Focal Lymphocytic Thyroiditis Share Common Features in Ultrasonography: A Diagnostic Predictor Model for Discrimination

Directed by Professor Eun Jig Lee

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This certifies that the Master's Thesis of

Sena Hwang is approved.

Thesis Supervisor : Eun Jig Lee

Thesis Committee Member: Eun-Kyung Kim

Thesis Committee Member: Woo-Ick Yang

The Graduate School
Yonsei University

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ABSTRACT

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Department of Medicine

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Background:

Thyroid carcinoma is suspected when a nodule shows suspicious ultrasound (US) features. However, it is often difficult to discriminate focal lymphocytic thyroiditis (FLT) from thyroid carcinoma because of similar US findings. The objective was to discriminate FLT from thyroid carcinoma.

Methods:

One hundred thirty patients had undergone fine-needle aspiration biopsy (FNAB) and had shown thyroid nodules with suspicious US features. Papillary thyroid carcinoma (PTC) was confirmed by postoperative histology and FLT was confirmed through at least 2 FNAB. Clinical and biochemical findings, and

US features were evaluated.

Results:

One hundred patients (76.9%) had PTC and 30 patients (23.1%) had FLT. US showed that the absence of calcification or “diffuse thyroid disease” (DTD) pattern was more common in patients with FLT than with PTC (P<0.001). The median TSH level was higher in FLT than PTC patients (P=0.016). The prevalence of antithyroid peroxidase antibody (TPO-Ab) or antithyroglobulin antibody (Tg-Ab) was more frequent in FLT than in PTC patients (P<0.001). To discriminate FLT from PTC, I created a diagnostic predictor model using logistic regression which included TSH, TPO- or Tg-Ab positivity, calcification, and DTD pattern. The model’s predictor probability of FLT rather than PTC was 85.4%.

Conclusion:

In patients presenting a thyroid nodule with suspicious US features, FLT is more likely than PTC when the nodule lacks calcification or is accompanied by a DTD pattern, the TSH level is ≥ 2.5 μIU/dL, and the patient is the patient is TPO- or Tg-Ab positive.

Key words: Differential diagnosis, Papillary thyroid cancer, Focal lymphocytic thyroiditis

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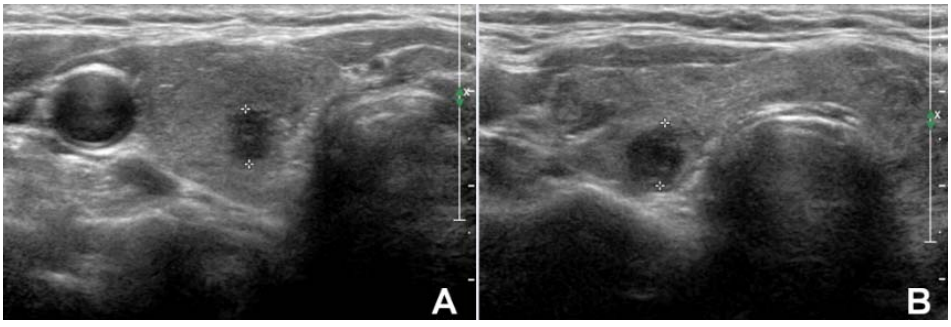
I. INTRODUCTION

Thyroid nodules are common worldwide, and the prevalence of palpable thyroid nodules is 4–7% of the adult population. With the advent of the use of ultrasound (US) in medical practice, an increasing number of nonpalpable thyroid nodules can be detected in 20–67% of the general population.[1,2] The majority of the nodules are benign: fewer than 5% are malignant.[3] Many studies have suggested a sonographic criteria that would allow the differentiation of benign from malignant lesions,[4-6] but thyroid US cannot at present clearly allow this distinction despite its wide acceptance and usefulness.[7]

An association between papillary thyroid carcinoma (PTC), and

lymphocytic thyroiditis is widely recognized, however the precise relationship between the two diseases remains debatable. Charateristic sonographic features of lymphocytic thyroiditis, also known as Hashimoto's thyroiditis, is diffuse heterogeneous hypoechogenicity. However, lymphocytic thyroiditis can present as a focal thyroid nodule that appears hypoechoic with ill-defined margins; an appearance that is indistinguishable from that of a malignant nodule (Figure 1).[8]

Figure 1. Examples of nodules with suspicion of malignancy on thyroid ultrasonographic findings. A, There was a 0.6-cm suspicious nodule (delineated by electronic calipers) on the right thyroid gland, and PTC was confirmed by thyroidectomy. B, There was a 0.7-cm suspicious nodule (delineated by electronic calipers) on the right thyroid gland, and FLT was confirmed by fine needle aspiration biopsy more than twice. The thyroid gland showed diffuse heterogeneous echogenicity, a characteristic finding when the DTD pattern is shown on US.



Fine-needle aspiration biopsy (FNAB) is considered to be the best diagnostic tool for differentiating between malignant and benign nodules. However, FNAB has limitations in the diagnosis of thyroid nodules, such as the potential for false-positive, false-negative, and inadequate diagnoses. The false-negative rate of FNAB ranges from 2.3% to 6.2%, and the false-positive rate of FNAB ranges from 0.5% to 11.6%. [9] A pathological diagnosis of lymphocytic thyroiditis on FNAB for suspicious thyroid nodules often leads the clinician to question whether thyroid nodules should be followed up with US or whether a repeat aspiration should be performed.

I sought to identify the clinical and biochemical findings in addition to sonographic features that could be used to differentiate focal lymphocytic thyroiditis (FLT) from PTC. A diagnostic predictor model to differentiate between FLT and PTC was created using logistic regression analysis.

II. MATERIALS AND METHODS

1. Patient

I retrospectively analyzed the clinicopathologic findings of 130 patients who had been found with “suspicious thyroid nodules” on US among the patients who had undergone FNAB of the thyroid between January 2006 and December 2009 at Severance Hospital, Seoul, Korea. The cytological diagnosis of 100 patients (76.9%) was PTC, and that of 30 patients (23.1%) was FLT. PTC was confirmed by postoperative histopathology, and FLT was at least two confirmed to be lymphocytic thyroiditis by cytopathology of two or more FNAB samples. The records of each patient were reviewed at the time of the initial examination, and I retrospectively reviewed the patients’ US, cytological, and pathological results as well as clinical and serologic findings. Only two patients who had FLT were treated, one with levothyroxine and the other with methimazole. Hashimoto’s thyroiditis was defined as a combination of elevated TSH, low FT4 and the positive of TPO- and/or Tg-Ab in serum.

2. Thyroid function test and thyroid autoantibodies

The serum free T4 (FT4) level was measured using an Amerlex-MAB* FT4 kit (Trinity Biotech PLC, Wicklow, Ireland), and serum TSH level was measured by immunoradiometric assay (TSH-CTK-3, Sorin Biomedica, Saluggia, Italy). The reference ranges are 0.73–1.95 ng/dL for FT4 and 0.3–4.0

μIU/mL for TSH. Serum antithyroid peroxidase antibody (TPO-Ab) and antithyroglobulin antibody (Tg-Ab) were detected by Radio Immuno Assay (BRAHMS AG, Berlin, Germany). In this assay, 60 IU/mL was used as the cutoff for differentiating between TPO-Ab- or Tg-Ab-negative and TPO-Ab- or Tg-Ab-positive samples.

3. Thyroid ultrasonography

US and US-guided FNAB were performed using an Acuson Sequoia 8–15-MHz linear probe (Siemens Medical Solutions, Montain View, CA), an HDI 5000 7–15-MHz linear probe (Philips Medical Systems, Bothell, WA), or an iU22 5–12-MHz linear probe (Philips Medical Systems). Key feature "suspicious for malignancy" on US included microcalcification, irregular or microlobulated margin, hypoechogenicity, and taller than wider in shape (i.e., greater anteroposterior dimension than transverse dimension. "Diffuse thyroid disease" (DTD) pattern was defined as diffuse heterogeneous hypoechogenicity on the sonography.[10]

4. Fine-needle aspiration and cytological diagnosis

US-guided FNAB was performed with a 23-gauge needle attached to a 20-mL disposable plastic syringe and an aspirator or a 23-gauge needle attached to a 2-mL disposable plastic syringe. Each lesion was aspirated at least twice. Materials obtained from the aspiration biopsy were expelled onto glass slides

and then placed immediately in 95% alcohol for Papanicolaou staining. The remainder of material was rinsed with saline and processed as a cell block. Six cytopathologists interpreted the cytology slides.

5. Statistical analysis

All statistical analysis was performed using PASW v. 18.0 for Windows (SPSS Inc., Chicago, IL, USA). Results of the two groups were compared using the χ2-test for categorical variables and Student's t test for paired data for continuous variables. P-value for FT4 and TSH was determined with use of the Mann-Whitney U-test. The significance of the clinical, biochemical, and sonographic variables was determined by univariate analysis. A *P*-value <0.05 was considered significant. Odds ratios (ORs) for FLT and the predicted probabilities for discriminating FLT from PTC were calculated using logistic regression analysis.

III. RESULTS

1. Clinical characteristics

Table 1 shows the clinical characteristics of the two groups. One hundred patients (76.9%) had PTC, and 30 patients (23.1%) had FLT. Females were dominant in both groups. Age, sex, and nodule size did not differ significantly between the two groups. Clinically diagnosed Hashimoto's thyroiditis was more frequent in FLT than in PTC patients ($P < 0.001$); the incidence was 30/100 (30%) in PTC patients and 22/30(73.3%) in FLT patients.

Table 1. Clinical characteristics of the two groups

	Total	PTC	FLT	*P*-value
Number of the patients (%)	130 (100%)	100 (76.9%)	30 (23.1%)	
Age (years)	51.2 ± 11.5	50.9 ± 11.8	52.4 ± 10.6	0.536
Sex (M:F)	10 : 120	8 : 92	2 : 28	0.812
Nodule size (cm)	0.89 ± 0.56	0.92 ± 0.55	0.78 ± 0.61	0.219
Hashimoto's thyroiditis*(%)	53 (40.8%)	30 (30%)	22 (73.3%)	**< 0.001**

Data are mean ± SD or number of patients.

Significant differences are shown in bold.

PTC, papillary thyroid cancer; FLT, focal lymphocytic thyroiditis

FT4, free T4; TSH, thyroid stimulating hormone

Tg-Ab, antithyroglobulin antibody; TPO-Ab, antithyroid peroxidase antibody

2. Sonographic characteristics

Each nodule was described by its sonographic features including the shape, margin, echogenicity, calcification, and cystic degeneration (Table 2). A lesion without calcification was observed in a lower percentage of PTC patients (59 patients, 59%) than FLT patients (26 patients, 86.7%) (P = 0.001). The DTD pattern on US was shown by fewer PTC patients (11 patients, 11%) than FLT patients (21 patients, 70.0%) (P < 0.001). The other sonographic features did not differ between the two groups.

Table 2. Ultrasound findings of suspicious nodules according to cytological diagnoses

		PTC	FLT	*P*-value
Shape	Ovoid to round	94	29	1.000
	Round	6	1	
	Taller than wide	53	15	0.836
	Wider than tall	47	15	
Margin	Well-defined	1	0	1.000
	Ill-defined	99	30	
Echo	Hypoechoic	95	28	0.659
	Isoechoic	2	1	
	Hyperechoic	1	1	
	Mixed echoic	2	0	
Calcification	No calcification	59	26	**0.005**[a]
	Microcalcification	22	2	
	Macrocalcification	18	2	
	Rim calcification	1	0	
Cystic degeneration	Present	2	0	1.000
	Absent	98	30	
DTD pattern	Present	11	21	**< 0.001**
	Absent	89	9	
Total		100	30	

Data are number of patients.

Significant findings are shown in bold.

[a] Comparison between the absence and presence of calcification

PTC, papillary thyroid cancer; FLT, focal lymphocytic thyroiditis

DTD pattern, “diffuse thyroid disease” pattern on US

3. Biochemical markers

The results of the thyroid function test and the distribution of thyroid autoantibodies grouped according to different cytological diagnoses are summarized in Table 3. The median TSH level (interquartile range) was 1.63 (1.09–2.24) μIU/dL for PTC patients and 3.23 (1.38–5.94) μIU/dL for FLT patients (P = 0.016). A higher percentage of FLT patients were positive for thyroid autoantibodies (P < 0.001). Sixteen PTC patients (16%) were Tg-Ab positive and 21 FLT patients (70.0%) were Tg-Ab positive. The values for TPO-Ab positivity were 21 in the PTC group (21%) and 19 in the FLT group (63.3%).

Table 3. Biochemical markers in the two groups

	PTC	FLT	*P*-value
FT4 (μg/dL)	1.18 (1.07–1.36)	1.05 (0.83–1.29)	**0.037**[a]
TSH (μIU/mL)	1.63 (1.09–2.24)	3.23[b] (1.38–5.94)	**0.016**[a]
Tg-Ab positive (>60 IU/mL)	16/100 (16%)	21/30 (70.0%)	**<0.001**
TPO-Ab positive (>60 IU/mL)	21/100 (21%)	19/30 (63.3%)	**0.001**

Data are median (interquartile range) or number of patients (percentage).

Significant differences are shown in bold.

[a]P-values were determined with use of the Mann-Whitney U test.

[b]Two patients were treated, one with levothyroxine and the other with methimazole.

PTC, papillary thyroid cancer; FLT, focal lymphocytic thyroiditis

FT4, free T4; TSH, thyroid stimulating hormone

Tg-Ab, antithyroglobulin antibody; TPO-Ab, antithyroid peroxidase antibody

4. Diagnostic predictor model

Univariate analysis showed a significant correlation between FLT and TSH level (OR = 1.35, *P* = 0.010, 95% confidence interval [CI] = 1.07–1.70), calcification (OR = 0.19, *P* = 0.004, 95% CI = 0.06–0.58), Hashimoto's thyroiditis (OR = 6.42, *P* < 0.001, 95% CI = 2.57–16.02), Tg-Ab-positive status (OR = 12.25, *P* < 0.001, 95% CI = 4.75–31.56), TPO-Ab-positive status (OR = 6.50, < 0.001, 95% CI = 2.68–15.74), and DTD pattern (OR = 18.88, *P* < 0.001, 95% CI = 6.94–51.37). Binary grouping for a TSH level ≥ 2.5 and < 2.5 μIU/dL also correlated with FLT (OR = 5.23, *P* < 0.001, 95% CI = 2.19–12.52).

I used four significant variables identified in the univariate analysis for subsequent logistic regression: TSH level ≥ 2.5 μIU/dL, TPO- or Tg-Ab-positive status, calcification, and DTD pattern on the US (Table 4). Patients with the following results were more likely to have FLT: the absence of calcification, TSH level ≥ 2.5 μIU/dL, TPO- or Tg-Ab-positive status, and DTD pattern on the US; 50% of FLT patients had all four variables. A DTD pattern on the US was found in 21 FLT patients and was the most significant variable, with a sensitivity of 89.0%, specificity of 70.0%, positive predictive value of 65.6%, and negative predictive value of 90.8%.

Table 4. Predicted probabilities of FLT rather than PTC using combinations of significant variables derived from univariate analysis

Characteristics	PTC (n = 100)	FLT (n = 30)	Odds ratio (95% CI)	*P*-value
TSH ≥ 2.5 μIU/mL	1.18 (1.07–1.36)	1.05 (0.83–1.29)	2.96 (0.94–9.33)	*0.064*
TPO- or Tg-Ab positive	30 (30%)	23 (76.7%)	1.95 (0.55–6.93)	*0.304*
Absence of calcification	55 (55%)	26 (86.7%)	6.65 (1.66–26.66)	**0.007**
DTD pattern	11 (11%)	21 (70.0%)	10.51 (3.03–36.46)	**<0.001**

Data are median (interquartile range) or number of patients (percentage).

Significant differences are shown in bold.

PTC, papillary thyroid cancer; FLT, focal lymphocytic thyroiditis; DTD, diffuse thyroid disease

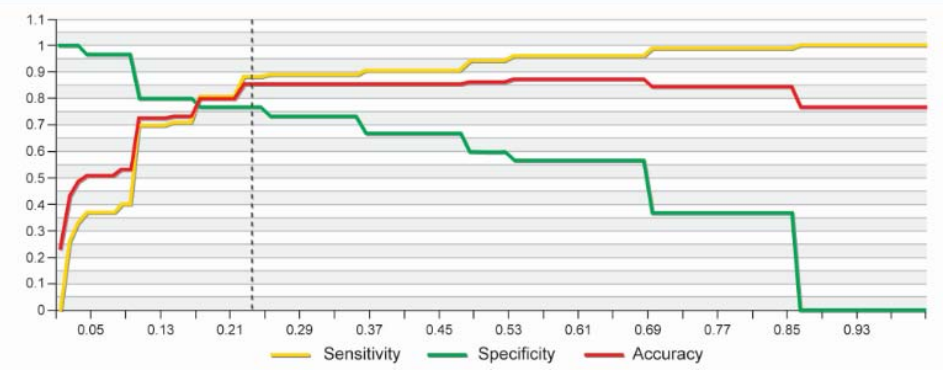
FT4, free T4; TSH, thyroid-stimulating hormone

Tg-Ab, antithyroglobulin antibody; TPO-Ab, antithyroid peroxidase antibody

DTD pattern, “diffuse thyroid disease” pattern

The model’s prediction of FLT from PTC, as represented by the accuracy of the curve of sensitivity and specificity, is presented in Figure 2. The accuracy curve represents the predicted probability of FLT. The predicted probability of this model was 85.4%, with 88.0% sensitivity and 76.7% specificity. The predicted probability of FLT increased to 86.9% when the threshold level of posterior probability was changed.

Figure 2. Overall accuracy of the diagnostic predictor model with sensitivity and specificity according to multiple thresholds of posterior probability. The y-axis indicates percentage, and the x-axis the threshold level of posterior probability between 0 and 1. We selected 0.23 (dotted line) as the threshold, which yielded 85.4% accuracy, 88.0% sensitivity, and 76.7% specificity.



IV. DISCUSSION

Many studies have attempted to investigate a useful indicator of thyroid malignancy based on US findings. Suspicious features of a thyroid nodule on US include irregular or microlobulated margins, hypoechogenicity, a taller-than-wide shape, microcalcification, and solidity.[4,11-14] However, a micronodule of lymphocytic thyroiditis can increase in size as the disease progresses, resulting in a large hypoechoic mass on US.[15] Langer et al. showed that FLT can present hyperechoic nodules with ill-defined margins on the US.[8] In contrast, Takashima et al. reported that focal nodules, confirmed to be thyroiditis, showed ill-defined hypoechoic nodules on the US, and thus focal thyroiditis is difficult to differentiate from PTC or lymphoma.[16] These so-called pseudotumors constituted 36% of the nodules of focal thyroiditis detected on the US.[8] However, specific sonographic features of focal thyroiditis are not well established. In this study, the most common suspicious indicators for FLT were ill-defined margins (100%), hypoechogenicity (93.3%) and a taller-than-wide shape (50.0%). Calcification was noted in four patients (13.3%); two of these patients had macrocalcification and the other two had microcalcification, which is a greater concern for malignancy. Calcification has been noted in focal thyroiditis.[17] Partial cystic changes in focal thyroiditis were noted in other studies,[8] but they were not observed in our study. Lymphocytic thyroiditis shows diffuse heterogeneous hypoechogenicity on the US, which appeared as a DTD pattern in our study. This feature is not specific to lymphocytic thyroiditis

and may be observed in multinodular goiters, Graves' disease, and subacute thyroiditis.[5,18,19] Although nonspecific, a DTD pattern in patients with suspicious features on the US correlated significantly with FLT, but not with PTC in our study (OR = 18.88, $P < 0.001$, 95% CI = 6.94–51.37).

When diagnosing focal thyroid nodules, FNAB is an essential tool in helping to decide whether a nodule requires surgery. Repeat aspiration can be performed to reduce the false-negative rate of FNAB. Repeat aspiration is important to avoid missing a cancer in thyroid nodules with initial benign cytological results.[20] In particular, most patients with suspicious features of thyroid nodules on thyroid US underwent repeated aspiration biopsy, although the cytopathology of the first FNAB indicated lymphocytic thyroiditis. One study showed nondiagnostic aspirates were initially 17.7%, and after repeated FNAB, 6.2%.[21] Therefore, I evaluated the additional risk factors associated with the US features and used these factors to create a diagnostic predictor model. A diagnostic predictor model would theoretically help both patients and physicians by providing a basis for making better decisions about the treatment plan.

Among the biochemical markers, the TSH level at presentation was proposed as a predictor of malignancy in patients with thyroid nodules; the prevalence of malignancy increases with TSH concentration, even within the normal range of TSH.[21] TSH has a trophic effect on thyroid cancer growth, which is most likely mediated by TSH receptors on tumor cells. TSH

suppression is an independent predictor of relapse-free survival from differentiated thyroid cancer.[22-24] With focal thyroiditis, 30% of patients with a high level of TSH have a clinical history of hypothyroidism.[8] Therefore, it may be difficult to differentiate FLT from PTC on the basis of the TSH level alone. However, even though TSH level correlated significantly with FLT, it did not correlate with PTC in this study (OR = 1.35, *P* = 0.010, 95% confidence interval [CI] = 1.07–1.70). The binary groupings according to TSH level ≥ 2.5 and < 2.5 μIU/dL increased the OR to 5.23. Previous studies have found the presence of Tg-Ab and TPO-Ab not to be useful in distinguishing benign from malignant lesions.[25] In this study, thyroid autoantibodies were significant predictors for distinguishing FLT from PTC. Previous studies have suggested that TPO-Ab can induce antibody-dependent cell-mediated cytotoxicity and that TPO-Ab titers correlate with the severity of lymphocytic infiltration.[26,27] However, the function of Tg-Ab remains uncertain.[28,29]

I was able to create a diagnostic predictor model for discriminating FLT from PTC using logistic regression analysis that included four factors: a TSH level ≥ 2.5 μIU/dL, TPO- or Tg-Ab-positive status, calcification, and a DTD pattern on the US. Overall, an informed prediction can be made using software that interprets the probabilities or confidence values with a fixed threshold value of 0.5. For searching proper sensitivity and specificity, we can set multiple threshold levels of posterior probability between 0 and 1. At a threshold of 0.23, the predictor accuracy for FLT from PTC was 85.4%, with 88.0% sensitivity

and 76.7% specificity.

I acknowledge the following limitations to this study. First, selection bias was inevitable. This study could not include a large proportion of nodules with FLT because we selected patients whose disease was confirmed at least twice by fine needle aspiration biopsy. Second, this study took samples from a small and concentrated population. Third, I did not analyze intanodular vascularity, which has been associated with a higher risk of malignancy.[30]

Ⅴ. CONCLUSION

In conclusion, a thyroid nodule with suspicious US features can be predicted FLT more likely than PTC when US features exhibit a DTD pattern without calcification, the TSH level is ≥ 2.5 μIU/mL, and the TPO- or Tg-Ab was positive.

REFERENCES

1. Mazzaferri EL. Management of a solitary thyroid nodule. N Engl J Med 1993;328:553-9.
2. Ross DS. Nonpalpable thyroid nodules--managing an epidemic. J Clin Endocrinol Metab 2002;87:1938-40.
3. Rago T, Vitti P. Role of thyroid ultrasound in the diagnostic evaluation of thyroid nodules. Best Pract Res Clin Endocrinol Metab 2008;22:913-28.
4. Kim EK, Park CS, Chung WY, Oh KK, Kim DI, Lee JT, et al. New sonographic criteria for recommending fine-needle aspiration biopsy of nonpalpable solid nodules of the thyroid. AJR Am J Roentgenol 2002;178:687-91.
5. Peccin S, de Castsro JA, Furlanetto TW, Furtado AP, Brasil BA, Czepielewski MA. Ultrasonography: is it useful in the diagnosis of cancer in thyroid nodules? J Endocrinol Invest 2002;25:39-43.
6. Kwak JY, Kim EK, Kim MJ, Hong SW, Choi SH, Son EJ, et al. The role of ultrasound in thyroid nodules with a cytology reading of "suspicious for papillary thyroid carcinoma". Thyroid 2008;18:517-22.
7. Hegedus L. Thyroid ultrasonography as a screening tool for thyroid disease. Thyroid 2004;14:879-80.
8. Langer JE, Khan A, Nisenbaum HL, Baloch ZW, Horii SC, Coleman BG, et al. Sonographic appearance of focal thyroiditis. AJR Am J Roentgenol 2001;176:751-4.

9. Kwak JY, Koo H, Youk JH, Kim MJ, Moon HJ, Son EJ, et al. Value of US correlation of a thyroid nodule with initially benign cytologic results. Radiology 2010;254:292-300.

10. Shin DY, Kim EK, Lee EJ. Role of ultrasonography in outcome prediction in subclinical hypothyroid patients treated with levothyroxine. Endocr J 2010;57:15-22.

11. Papini E, Guglielmi R, Bianchini A, Crescenzi A, Taccogna S, Nardi F, et al. Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and color-Doppler features. J Clin Endocrinol Metab 2002;87:1941-6.

12. Frates MC, Benson CB, Doubilet PM, Cibas ES, Marqusee E. Can color Doppler sonography aid in the prediction of malignancy of thyroid nodules? J Ultrasound Med 2003;22:127-31; quiz 32-4.

13. Kang HW, No JH, Chung JH, Min YK, Lee MS, Lee MK, et al. Prevalence, clinical and ultrasonographic characteristics of thyroid incidentalomas. Thyroid 2004;14:29-33.

14. Cappelli C, Castellano M, Pirola I, Cumetti D, Agosti B, Gandossi E, et al. The predictive value of ultrasound findings in the management of thyroid nodules. QJM 2007;100:29-35.

15. Yeh HC, Futterweit W, Gilbert P. Micronodulation: ultrasonographic sign of Hashimoto thyroiditis. J Ultrasound Med 1996;15:813-9.

16. Takashima S, Matsuzuka F, Nagareda T, Tomiyama N, Kozuka T.

Thyroid nodules associated with Hashimoto thyroiditis: assessment with US. Radiology 1992;185:125-30.

17. Takashima S, Fukuda H, Nomura N, Kishimoto H, Kim T, Kobayashi T. Thyroid nodules: re-evaluation with ultrasound. J Clin Ultrasound 1995;23:179-84.

18. Marcocci C, Vitti P, Cetani F, Catalano F, Concetti R, Pinchera A. Thyroid ultrasonography helps to identify patients with diffuse lymphocytic thyroiditis who are prone to develop hypothyroidism. J Clin Endocrinol Metab 1991;72:209-13.

19. Hayashi N, Tamaki N, Konishi J, Yonekura Y, Senda M, Kasagi K, et al. Sonography of Hashimoto's thyroiditis. J Clin Ultrasound 1986;14:123-6.

20. Menendez Torre E, Pineda Arribas J, Martinez de Esteban JP, Lopez Carballo MT, de Miguel C, Salvador P. Value of repeated fine needle aspiration cytology in patients with nodular goiter. Acta Cytol 2007;51:850-2.

21. Boelaert K, Horacek J, Holder RL, Watkinson JC, Sheppard MC, Franklyn JA. Serum thyrotropin concentration as a novel predictor of malignancy in thyroid nodules investigated by fine-needle aspiration. J Clin Endocrinol Metab 2006;91:4295-301.

22. Pujol P, Daures JP, Nsakala N, Baldet L, Bringer J, Jaffiol C. Degree of thyrotropin suppression as a prognostic determinant in differentiated

thyroid cancer. J Clin Endocrinol Metab 1996;81:4318-23.

23. Carayon P, Thomas-Morvan C, Castanas E, Tubiana M. Human thyroid cancer: membrane thyrotropin binding and adenylate cyclase activity. J Clin Endocrinol Metab 1980;51:915-20.

24. Ichikawa Y, Saito E, Abe Y, Homma M, Muraki T. Presence of TSH receptor in thyroid neoplasms. J Clin Endocrinol Metab 1976;42:395-8.

25. DeGroot LJ, Hoye K, Refetoff S, Van Herle AJ, Asteris GT, Rochman H. Serum albumin and antibodies in the diagnosis of thyroid cancer. J Clin Endocrinol Metab 1977;45:1220-3.

26. Yoshida H, Amino N, Yagawa K, Uemura K, Satoh M, Miyai K, et al. Association of serum antithyroid antibodies with lymphocytic infiltration of the thyroid gland: studies of seventy autopsied cases. J Clin Endocrinol Metab 1978;46:859-62.

27. Kasagi K, Kousaka T, Higuchi K, Iida Y, Misaki T, Alam MS, et al. Clinical significance of measurements of antithyroid antibodies in the diagnosis of Hashimoto's thyroiditis: comparison with histological findings. Thyroid 1996;6:445-50.

28. Lindberg B, Svensson J, Ericsson UB, Nilsson P, Svenonius E, Ivarsson SA. Comparison of some different methods for analysis of thyroid autoantibodies: importance of thyroglobulin autoantibodies. Thyroid 2001;11:265-9.

29. Sinclair D. Clinical and laboratory aspects of thyroid autoantibodies.

Ann Clin Biochem 2006;43:173-83.

30. Bastin S, Bolland MJ, Croxson MS. Role of ultrasound in the assessment of nodular thyroid disease. J Med Imaging Radiat Oncol 2009;53:177-87.

ABSTRACT (IN KOREAN)

비슷한 초음파 소견의 갑상선암과 림프구성 갑상선염의 구별에 대한 예측 모델

<지도교수 이은직>

연세대학교 대학원 의학과

황세나

배경:

암을 시사하는 초음파 소견을 보이면 갑상선암을 의심할 수 있다. 그러나 이러한 초음파 소견은 림프구성 갑상선염에서도 보일 수 있어 갑상선암과 구별이 어렵다. 따라서 이번 연구의 목적은 비슷한 초음파 소견을 보이는 갑상선암과 림프구성 갑상선염을 구별하는 데에 있다.

방법:

2006년 1월부터 2009년 12월까지 세브란스 병원에서 암이 의심되는 초음파 소견을 보이는 환자 중 미세침흡인세포검사를 시행한 130명을 대상으로 하였다. 유두상 갑상선암은 수술 후 조직학적 병리소견으로 진단받은 환자를 대상으로 하였으며 림프구성 갑상선염은 2번 이상의 미세침흡인세포검사에서 진단받은 환자를 대상으로 하였다. 이들의 임상적 특징, 생화학적 검사, 갑상선 초음파 검사를 검토하였다.

결과:

총 100명 (76.9%)의 유두상 갑상선암 환자와 30명 (23.1%)의 림프구성 갑상선염 환자를 대상으로 하였다. 갑상선 초음파에서 석회화가 없거나 미만성 갑상선 질환의 특징은 유두상 갑상선암 환자군보다 림프구성 갑상선염 환자군에서 의미있게 더 흔하게 발견되었다 (P<0.001). 평균 갑상선 자극 호르몬 수치는 유두상 갑상선암 환자군보다 림프구성 갑상선염 환자군에서 더 높았다 (P<0.001). 림프구성 갑상선염을 유두상 갑상선암와 구별하기 위하여 갑상선 자극 호르몬, 갑상선 자가항체인 Antithyroid peroxidase antibody (TPO-Ab)와 Antithyroglobulin antibody (Tg-Ab), 석회화 유무, 미만성 갑상선 질환 유무를 포함하여 로지스틱 회귀분석을 통한 진단적 예측 모델을 만들었다. 유두상 갑상선암에 대한 림프구성 갑상선염을 구별하는데 있어서 이 모델의 예측력은 85.4%이다.

결론:

갑상선 초음파 검사에서 암이 의심되는 소견을 보이는 갑상선 결절을 가지고 있는 환자에서 미만성 갑상선 질환 소견을 보이면서 석회화가 없거나 갑상선 자극 호르몬이 2.5μIU 이상, 또는 갑상선 자가항체인 TPO-Ab 또는 Tg-Ab가 있다면 갑상선암 보다는 림프구성 갑상선염일 가능성을 더 시사하겠다.

핵심되는 말 : 감별진단, 유두상 갑상선암, 림프구성 갑상선염