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RISK FACTORS THAT PREDICT LEVOTHYROXINE MEDICATION AFTER THYROID LOBECTOMY

H.S. Song[1], C.J. Kim[1], S. Lee[1,*], J.S. Bae[1], C.K. Jung[2], J. Jang[3]

Catholic University of Korea College of Medicine - [1]Department of Surgery, [2]Department of Hospital Pathology, [3]Department of Radiology, Seoul, Republic of Korea

Abstract

Context and Objective. The risk of needing lifelong thyroid hormone supplementation is an important factor affecting treatment decisions for both patients and clinicians ahead thyroid lobectomy. The purposes of this study were to assess the predictive factors of levothyroxine medication after thyroid lobectomy.

Methods. We retrospectively reviewed 252 patients who had undergone lobectomy for benign thyroid nodules between April 2009 and April 2017. We conducted two independent analyses: patients who started taking levothyroxine after surgery were compared with those who did not, and patients who did not need levothyroxine at last follow-up were compared with those who required continued treatment. We investigated the correlations of patient clinicopathological characteristics and levothyroxine medication after lobectomy.

Results. Ninety-eight patients started levothyroxine after surgery. Of these, 34 patients successfully ceased medication and 64 patients continued treatment as of their last follow-up. In multivariate analysis, older age and preoperative TSH ≥2.0mIU/L were associated with levothyroxine initiation after surgery. In terms of continuity of levothyroxine, both older age and TSH ≥ 3.0mIU/L showed a significant correlation with continuous medication. We created a risk-scoring system to predict likelihood of starting and maintaining levothyroxine using the two significant factors in each comparison. A risk score of 3 or more indicated an increased risk of starting levothyroxine (specificity = 81.8%; sensitivity = 48.0%). A risk score of 3 or more indicated increased risk of continuous medication, (specificity = 94.2%; sensitivity = 35.9%).

Conclusions. Greater age and higher preoperative TSH levels correlated with initiation and continuity of levothyroxine medication after lobectomy.

Keywords: levothyroxine, lobectomy, thyroid, risk factor.

INTRODUCTION

Thyroid nodules are common clinical problems that occur in 20-76% of individuals (1, 2). Thyroid gland lobectomy is a surgical treatment option for indeterminate thyroid nodules as well as low-risk, well-differentiated, thyroid cancer (1). Although after lobectomy, the contralateral lobe remains, the incidence of hypothyroidism after lobectomy ranges from 9% to 49%, depending on the duration of follow-up evaluation and the definition of hypothyroidism (3-5). Some patients require lifelong levothyroxine supplementation because they fail to produce enough thyroid hormone to maintain normal thyroid function. (6-9). If taken over long periods with inappropriate dosage, levothyroxine medication can cause various adverse effects, including cardiovascular events such as atrial fibrillation and left heart disease, osteoporosis or osteopenia caused by calcium loss, and mood disorders (10, 11). Lifetime thyroid hormone dependency affects not only the patient's quality of life, but it also causes socioeconomic impacts. These factors have a significant impact on treatment decisions and policies for both patients and clinicians (12-15). The purpose of this study was to evaluate possible preoperative factors that could predict the need for postoperative levothyroxine supplementation after thyroid lobectomy.

METHODS AND MATERIALS

A retrospective analysis was conducted on patients who had undergone lobectomy due to an indeterminate thyroid nodule between April 2009 and April 2017 at Seoul St. Mary's Hospital. 336 consecutive patients who were ultimately diagnosed with benign thyroid disease after surgery were enrolled in this study. Among these, seven patients were excluded because they had been taking levothyroxine

*Correspondence to: Sohee Lee MD, Catholic University of Korea College of Medicine, Department of Surgery, 1021, Tongil-ro, Eunpyeong-gu, Seoul, 06591, Republic of Korea, E-mail: leesohee@catholic.ac.kr

or anti-thyroid medication for thyroid dysfunction prior to their surgery. Forty-eight patients were excluded because the medical records lacked preoperative thyroid ultrasonography and/or test results for thyroid auto-antibodies. Additionally, 29 patients were excluded due to an insufficient follow-up period after surgery. In total, 252 patients were included. This study was approved by the institutional review board of the Catholic University of Korea, St. Mary's Hospital, Seoul, South Korea (KC16RISI0531).

Serum thyroid stimulating hormone (TSH) was measured using an immunoradiometric assay kit (TSH IRMA KIT, Immunotech, Czech Republic). Serum-free thyroxine (fT4; FT4 RIA KIT, Immunotech, Czech Republic), anti-thyroglobulin (Tg) antibody (ANTI-TGn RIA kit, BRAHMS AG, Germany), and anti–thyroid peroxidase (TPO) antibody (ANTI-TPOn RIA kit, BRAHMS AG, Germany) were measured using a radioimmunoassay kit. Analytical sensitivity of TSH, fT4, anti-Tg antibody, and anti-TPO antibody were 0.04 mIU/L, 0.003 ng/mL, 5.5 U/mL, and 5.5 U/mL, respectively. Reference ranges for TSH, fT4, anti-Tg antibody, and anti-TPO antibody were 0.17~4.05 mIU/L, 0.85~1.86 ng/mL, 0.0~70.0 IU/mL, and 0.0~80.0 IU/mL, respectively.

Patients with low fT4 and elevated serum TSH measured at postoperative follow-up were diagnosed with overt hypothyroidism, and thyroid hormone supplementation was initiated. Patients with normal fT4 and elevated TSH were diagnosed with subclinical hypothyroidism, and those with subjective symptoms of hypothyroidism were prescribed thyroid hormones. Tapering of levothyroxine was attempted for patients with normal thyroid function. This process involved decreasing the dose of levothyroxine by 0.025 mg/day at each regular visit of 3 to 6 months. Successful discontinuation of levothyroxine medication was defined as maintenance of euthyroid status for 3 to 6 months after cessation of levothyroxine.

Patients were stratified into 4 groups: patients who were not prescribed levothyroxine after surgery (Group A), patients who were prescribed postoperative levothyroxine at least once (Group B), patients who were not taking levothyroxine medication at last follow-up (Group C), and patients who failed to discontinued medication and kept levothyroxine at last follow-up (Group D). Group C consisted of Group A members and Group B members who had successfully stopped taking levothyroxine. The definition of a sufficient follow-up period differs depending on the group. Patients who did not start medication after surgery were enrolled if they had completed a follow-up period of at least 3 months. For patients on continued levothyroxine, patients with at least 18 months of follow-up were enrolled to determine a spontaneous recovery of thyroid function. For patients who had stopped the medication, follow-up periods of less than 3 months after discontinuation of levothyroxine were excluded in this study.

The serum-free thyroxine (fT4) and thyroid stimulating hormone (TSH) levels were checked pre-operatively and postoperatively at 1 week, 1-3 months, 6 months, and annually and/or biannually thereafter. The serum anti-thyroglobulin antibody (anti-Tg Ab) and/or anti-thyroid peroxidase antibody (anti-TPO Ab) were checked pre-operatively. Laboratory thyroiditis was defined as anti-Tg Ab >70 mIU/mL and/or anti-TPO Ab >80 mIU/mL. The presence of radiological thyroiditis was based on the preoperative ultrasound (US) report and images. US images that included a definitively diffuse enlarged thyroid gland, heterogeneous hypo-echogenicity, and increased vascularity indicated definite radiological thyroiditis (15). US images with mild-to-moderate coarse, heterogeneous parenchyma with slightly increased vascularity indicated intermediate radiological thyroiditis. The presence of histological thyroiditis was determined according to the final histological report, including Hashimoto's thyroiditis or chronic lymphocytic thyroiditis.

Correlations of patient clinicopathological characteristics and postoperative thyroid function were investigated and analyzed to determine the risk factors that predict the need for levothyroxine medication after lobectomy. Two independent analyses were conducted. First, patients who started taking levothyroxine after surgery (Group B) were compared with those who did not (Group A). Second, patients who did not need levothyroxine at the last follow-up (Group C) were compared with those who should continue medication (Group D). The categorical, qualitative data are expressed as frequencies and percentages, and the two groups were compared using the $\chi 2$ test. The comparative analysis of continuous, quantitative data was performed using independent t-test and expressed as the means ± standard deviation. The serum TSH level was not normally distributed, and the comparative analysis between the two groups was performed using the Wilcoxon rank sum test; the data are expressed as median values with quantile ranges. Univariate and multivariate analyses of associated factors were performed by logistic regression analysis and Cox regression models were used in multivariate analyses to identify independent factors for levothyroxine

supplementation. Receiver operating characteristic analysis (ROC) of curves and area under curves (AUC) were used to determine the cutoff values to predict the start and cessation of levothyroxine usage after lobectomy. A P value of less than 0.05 was considered statistically significant. Statistical analyses were performed using Statistical Analysis System (SAS) software.

RESULT

In the full patient cohort, the mean follow-up period was 38.3 ± 26.2 months (range: 3-104 months). Among the included 252 cases, 98 patients (38.9%) had started levothyroxine supplementation after lobectomy (Group B). We compared the clinicopathological factors of patients who never took levothyroxine (Group A) with those who started medication (Group B; Table 1). Mean age was significantly older in Group B than Group A (51.1 years *vs*. 45.5 years, p = 0.001). Body mass index and gender ratio were not significantly different between the two groups. Of the available preoperative laboratory results, only median serum TSH level was significantly higher in Group B than in Group A (1.51 mIU/L *vs*. 2.27 mIU/L; p< 0.001). Serum-free T4 and autoimmune antibody, including anti-Tg and anti-TPO, were not significantly different between Groups A and B. The presence of laboratory thyroiditis did not differ between the two groups. Among the radiological findings, intermediate to definite radiological thyroiditis was more frequent in Group B than in Group A (31.6% *vs*. 20.1%, p = 0.039). Coexistence of histological thyroiditis did not differ between the two groups. The amount of resected thyroid was not different between the two groups. Combined resections, which included isthmus or the contralateral thyroid nodule did not differ between the two groups.

Of the 98 patients who started levothyroxine after surgery, 34 patients successfully ceased levothyroxine medication, while 64 patients were still taking levothyroxine medication at their last follow-up. We compared the clinicopathological factors between 188 patients (74.6%) who had no levothyroxine at last follow-up (Group C) and 64 patients (25.4%) who failed to stop medication as of last follow-up (Group D; Table 2).

Table 1. Comparison of clinicopathological characteristics between patients who were not prescribed levothyroxine after surgery (Group A) *versus* patients who were prescribed postoperative levothyroxine at least once (Group B)

	Group A N=154	Group B N=98	P value
Age (yrs, mean, range)	45.5±13.7	51.1±11.8	0.001
Body mass index (kg/m^2)	24.1±4.0	24.1±3.6	0.986
Gender (F:M)	29:125(1:4.3)	18:80(1:4.4)	0.927
Preoperative Laboratory results			
Free T4 (ng/dL)	1.33±0.20	1.29±0.20	0.090
TSH (mIU/L) (median, IQR)	1.66(1.00-2.22)	2.39(1.58-3.93)	<0.001
Anti-Tg ab (U/mL) †			0.476
Normal	140(94.0%)	87(91.6%)	
positive	6(6.0%)	8(8.4%)	
Anti TPO ab (U/mL) ‡			0.083
normal	128(93.4%)	70(86.4%)	
positive	9(6.6%)	11(13.6%)	
Laboratory thyroiditis§			0.270
None	139(90.3%)	84(85.7%)	
Yes	15(9.7%)	14(14.3%)	
Radiologic thyroiditis			0.039
None	123(79.9%)	67(68.4%)	
Intermediate to definite	31(20.1%)	31(31.6%)	
Combined resection			0.322
None	130(84.4%)	89(90.8%)	
Isthmus	20(13.0%)	7(7.1%)	
Contralateral nodule	4(2.6%)	2(2.0%)	
Histologic thyroiditis			0.366
None	128(83.1%)	77(78.6%)	
Yes	26(16.9%)	21(21.4%)	
Resected Specimen size (mg)	20.7±17.4	21.4±19.3	0.763

† A total 149 patients and 95 patients underwent anti-Tg ab analysis preoperatively in each group. ‡ A total 137 patients and 81 patients underwent anti-TPO ab analysis preoperatively in each group. § Laboratory thyroiditis was defined as elevated at least one of anti-thyroid ab.

Table 2. Comparison of clinicopathological characteristics between patients who were not taking levothyroxine medication at last follow-up (Group C) *versus* patients who failed to discontinued medication (Group D)

	Group C N=188	Group D N=64	P value
Age (yrs, mean, range)	46.0±13.3	52.7±12.0	<0.001
Body mass index (kg/m^2)	24.2±3.9	23.9±3.6	0.632
Gender (F:M)	35:153(1:4.4)	12:52(1:4.3)	0.981
Preoperative Laboratory results			
Free T4 (ng/dL)	1.32±0.20	1.30±0.20	0.297
TSH (μIU/mL) (median, IQR)	1.66 (1.00-2.22)	2.39 (1.58-3.93)	<0.001
Anti-Tg ab (U/mL) †			0.694
normal	170(93.4%)	57(91.9%)	
positive	12(6.6%)	5(8.1%)	
Anti TPO ab (U/mL) ‡			0.098
normal	152(92.7%)	46(85.2%)	
positive	12(7.3%)	8(14.8%)	
Laboratory thyroiditis§			0.232
None	169(89.9%)	54(84.4%)	
Yes	19(10.1%)	10(15.6%)	
Radiologic thyroiditis			0.274
None	145(77.1%)	45(70.3%)	
Intermediate to definite	43(22.9%)	19(29.7%)	
Combined resection			0.591
None	161(85.6%)	58(90.6%)	
Isthmus	22(11.2%)	5(7.8%)	
Contralateral nodule	5(2.7%)	1(1.6%)	
Histologic thyroiditis			0.981
None	153(81.4%)	52(81.3%)	
Yes	35(18.6%)	12(18.8%)	
Resected Specimen size (mg)	21.0±17.7	20.8±19.3	0.943

† A total 182 patients and 62 patients underwent anti-Tg ab analysis preoperatively in each group. ‡ A total 164 patients and 54 patients underwent anti-TPO ab analysis preoperatively in each group. § Laboratory thyroiditis was defined as elevated at least one of anti-thyroid ab.

The mean age of Group D was significantly greater than of Group C (52.7 years *vs*. 46.0 years, p<0.001). Among the preoperative laboratory findings, only serum TSH was different between the two groups: Group D had a significantly higher median serum TSH than Group C (2.39 mIU/L *vs*. 1.66 mIU/L; p < 0.001). Laboratory, radiological and histological thyroiditis results did not show any differences between the two groups. Body mass index, gender ratio, combined resection, and the amount of resected thyroid were not different between Groups C and D.

In the univariate Cox regression analysis, greater age, preoperative TSH higher than 2.0 mIU/L, and coexistence of radiological thyroiditis were factors that correlated to increased risk of starting levothyroxine after lobectomy (Table 3). However, in multivariate analysis, only increased age and higher TSH were associated with levothyroxine initiation. Patients between the ages of 40 and 55 years had higher risk of starting the drug than those under 40 years of age (odds ratio (OR) = 2.25, 95% CI 1.110-4.558, p = 0.024). Moreover, patients aged 55 years and older had a higher risk of starting the drug than those between 40 and 55 years of age (OR = 3.104, 95% CI 1.533-6.286, p = 0.002). Patients with preoperative TSH ≥ 2.0 mIU/L were associated levothyroxine initiation (OR = 3.944, 95% CI 2.266-6.865, p < 0.001). In terms of continuous levothyroxine medication at last follow-up, both older age and TSH ≥ 3.0 mIU/L showed a significant correlation. In multivariate analysis, patients between the ages of 40 and 55 years had higher risk of remaining on medication than those under 40 years of age (OR = 2.860, 95% CI 1.213-6.743, p = 0.016). Patients 55 years and older also showed higher risk of taking medication continuously than those between 40 and 55 years of age (OR = 3.627, 95% CI 1.566-8.398, p = 0.002). Patients with preoperative TSH levels ≥ 3.0 mIU/L were associated with higher risk of levothyroxine maintenance (OR = 5.808, 95% CI 2.833-11.908, p<0.001).

We created a risk-scoring system to predict likelihood of starting levothyroxine after lobectomy. This score is the sum of the two significant factors. The risk scores of age and preoperative TSH were weighted according to odd ratio (age: score 0= <40 years, score 1= ≥ 40 and <55 years, score 2= ≥ 55

Table 3. Univariate and Multivariate Cox regression analysis

No medication (Group A) *versus* Start Levothyroxine medication (Group B)				
Univariate variables		OR	CI (95%)	P value
Age	<40			0.002
	40≤ <55	2.415	1.239-4.704	0.010
	≥55	3.263	1.672-6.368	0.001
Preoperative TSH(mIU/L)	<2.0			
	≥2.0	4.076	2.381-6.978	<0.001
Radiologic thyroiditis	No			
	Intermediate to definite	1.836	1.028-3.279	0.040
Multivariate variables		OR	CI (95%)	P value
Age (yrs)	<40			0.006
	40≤ <55	2.25	1.110-4.558	0.024
	≥55	3.104	1.533-6.285	0.002
Preoperative TSH(mIU/L)	<2.0			
	≥2.0	3.944	2.266-6.865	<0.001
Radiologic thyroiditis	No			
	Intermediate to definite	1.679	0.894-3.156	0.107
No medication at last follow-up (Group C) *versus* Levothyroxine medication at last follow-up (Group D)				
Univariate Variables		OR	CI (95%)	P value
Age (yrs)	<40			0.002
	40≤ <55	2.552	1.129-5.768	0.024
	≥55	4.153	1.872-9.211	<0.001
Preoperative TSH(mIU/L)	<3.0			
	≥3.0	6.086	3.058-12.113	<0.001
Multivariate variables		OR	CI (95%)	P value
Age (yrs)	<40			0.009
	40≤ <55	2.860	1.213-6.743	0.016
	≥55	3.627	1.566-8.398	0.003
Preoperative TSH(mIU/L)	<3.0			
	≥3.0	5.808	2.833-11.908	<0.001

OR; Odd ratio, CI; Confidence interval.

Table 4. Risk-scoring system to predict discontinuation of levothyroxine medication after lobectomy

Predict continuation of levothyroxine medication after lobectomy				
Variables				Risk score
Age (yrs)		<40		0
		40≤ <55		1
		≥55		2
Preoperative TSH(mIU/L)		<3.0		0
		≥3.0		2
Sum of Risk Scores	No medication (N)	Levothyroxine start (N)		Prevalence (%)
0	63	7		10.0
1	58	18		23.7
2	56	16		22.2
3	6	5		45.5
4	5	18		78.3
Cutoff of Risk score	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
1	0.891 (0.788-0.955)	0.335 (0.268-0.407)	0.313 (0.247-0.386)	0.900 (0.805-0.959)
2	0.609 (0.479-0.729)	0.644 (0.571-0.712)	0.368 (0.276-0.467)	0.829 (0.758-0.886)
3	0.359 (0.243-0.489)	0.942 (0.898-0.970)	0.677 (0.495-0.826)	0.812 (0.754-0.862)
4	0.281 (0.176-0.408)	0.973 (0.939-0.991)	0.783 (0.563-0.925)	0.779 (0.741-0.849)

Table 5. Risk-scoring system to predict discontinuation of levothyroxine medication after lobectomy

Predict continuation of levothyroxine medication after lobectomy				
Variables				Risk score
Age (yrs)	<40			0
	40≤ <55			1
	≥55			2
Preoperative TSH(mIU/L)	<3.0			0
	≥3.0			2
Sum of Risk Scores	No medication (N)	Levothyroxine start (N)		Prevalence (%)
0	63	7		10.0
1	58	18		23.7
2	56	16		22.2
3	6	5		45.5
4	5	18		78.3
Cutoff of Risk score	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
1	0.891 (0.788-0.955)	0.335 (0.268-0.407)	0.313 (0.247-0.386)	0.900 (0.805-0.959)
2	0.609 (0.479-0.729)	0.644 (0.571-0.712)	0.368 (0.276-0.467)	0.829 (0.758-0.886)
3	0.359 (0.243-0.489)	0.942 (0.898-0.970)	0.677 (0.495-0.826)	0.812 (0.754-0.862)
4	0.281 (0.176-0.408)	0.973 (0.939-0.991)	0.783 (0.563-0.925)	0.779 (0.741-0.849)

years; preoperative TSH level: score 0= <2.0 mIU/L and score 2= ≥ 2.0 mIU/L) (Table 4). When the sum of risk score was 3 or more, the incidence of patients starting levothyroxine medication after surgery was 62.7% (sensitivity = 81.8% and specificity = 48.0%). Finally, we created a risk-scoring system to predict whether patients needed levothyroxine at their last follow-up (Table 5) using the same two significant factors. The risk score for age in this scoring system was as described above. The risk score of preoperative TSH level was weighted as follows: a score of "0" was given for < 3.0mIU/L and a score of "2" was given for ≥ 3.0mIU/L). In cases with a risk score of 3 or more, the incidence of patients who needed levothyroxine at last follow-up was 67.6% (sensitivity = 35.9% and specificity = 94.2%).

DISCUSSION

Hypothyroidism is a relatively common sequela after thyroid lobectomy, but its clinical significance has been underestimated (4, 14, 16). The quality of life for patients can be greatly affected by lifelong medication and regular visits to the hospital for monitoring, especially in young patients (17). Therefore, it is important to predict the risk of developing hypothyroidism and to find associated risk factors for levothyroxine medication after surgery. In this study, we analysed the predictive factors of both those who will start levothyroxine and who will continue levothyroxine supplementation due to unrecovered hypothyroidism. These results can inform patients in preoperative counselling and can help the patient and the physician decide on a treatment plan (12-15).

In our study, the incidences of levothyroxine initiation and continuous medication due to unrecovered hypothyroidism were 38.9% and 25.4%, respectively. These results are in accordance with previously reported studies of hypothyroidism and levothyroxine supplementation (3-5). Most transient postoperative hypothyroidism occurs within one year after surgery, especially within the first 6 months (9, 14, 16, 18-23). Tomoda *et al.* reported that serum TSH peaked postoperatively at 1-2 months and gradually decreased after 6 months (16). Many studies reported that most patients spontaneously recovered thyroid function within 2 years after postoperative hypothyroidism diagnosis (7, 9). In our study, 34 (34.7%) patients of 98 hypothyroidism patients successfully ceased levothyroxine medication during their follow-up period.

Previous studies on the risk factors of postoperative hypothyroidism have shown that associated factors are age, preoperative TSH level, presence of thyroid auto-antibodies and autoimmune thyroiditis (3, 5, 8-10, 16, 18, 20, 21, 23-28). Older age correlates to higher risk of postoperative hypothyroidism requiring levothyroxine (14, 16, 22). Ahn *et al.* reported that age ≥ 46 years was an independent risk factor for the development of unrecovered subclinical hypothyroidism after hemothyroidectomy (9). Tomoda *et al.* showed that patients older than 55 years had a higher incidence of hypothyroidism (16). In this study, we stratified patient age into three groups. As age increased, so did the frequency of initiation of levothyroxine administration and the persistence of postoperative hormone use.

High preoperative serum TSH was the most important factor to predict the development of

postoperative hypothyroidism (7, 23, 29). Furthermore, Park *et al.* reported that high preoperative TSH was the important factor for continuous thyroid hormone replacement without recovery (7). Cutoff values of preoperative TSH range between 1.4 to 2.5 mIU/L in various studies (7, 16, 18, 21, 23, 28). Here, the cutoff value of preoperative TSH for predicting onset of levothyroxine after surgery was 2.0 mIU/L and the cut-off value predicting continuous drug use was 3.0 mIU/L.

Some researchers have described a unique risk-scoring system to predict hypothyroidism after hemithyroidectomy (3, 16, 24, 30-33). Most of these scoring systems have only one variable, or they are often applicable after surgery, making them difficult to use in preoperative predictions (3, 24, 30-33). We created a simple preoperative risk-scoring system to predict levothyroxine need using two significant preoperative values: age and preoperative TSH level. The risk score for the TSH group was weighted because the odd ratio of TSH group was higher than that of age group. The advantage of this scoring system is that the specificity for predicting the onset of medication and the continuous use of medication is high at 81.8% and 94.2%, respectively. Thus, it can be easily used to communicate with patients and make treatment decisions as it provides the probability of taking the drug after surgery with higher specificity. In addition, it can predict whether the medication will be temporary or permanent for patients.

Coexistence of thyroiditis is associated with increased incidence of postoperative hypothyroidism (3, 14, 20, 23, 32). Because histological thyroiditis is confirmed postoperatively, it is difficult to apply this factor for preoperative prediction of levothyroxine medication need. Therefore, we checked both serum anti-thyroid auto-antibodies and US findings pre-operatively. The presence of serum thyroid auto-antibodies is known as a predictor of hypothyroidism after lobectomy (5, 20, 23, 25-27). Specifically, elevated serum anti-TPO antibody shows a stronger correlation with postoperative hypothyroidism than anti-Tg antibody (14, 21, 26). Morris *et al.* reported that preoperative US-identified thyroiditis, when combined with higher TSH, was a strong predictor of levothyroxine medication after surgery (15). In this study, none of the tested types of thyroiditis, including laboratory, radiological, and histological thyroiditis, showed a statistically significant relationship with postoperative levothyroxine medication, a result consistent with some other reports (9, 21, 26). The reasons for this discrepancy may be related to the small number of coexisting thyroiditis cases, differences in grade of histological thyroiditis, and incomplete thyroid auto-antibody data in this study.

This study had several limitations. First, it had a retrospective design using a small number of patients at a single institution. Second, there were some missing data, including for thyroid auto-antibodies. Third, because the area of study was benign thyroid disease, the follow-up period was relatively short at our tertiary medical institutions, especially in postoperative euthyroid patients. This fact could indicate a selection bias. Therefore, a multi-center, prospective large cohort study with structured protocols should be conducted for external validation of the risk scoring system.

In conclusion, greater age and higher preoperative TSH levels correlated with initiation and continuity of levothyroxine after lobectomy. These results could help in advising patients pre-operatively about the risk of needing thyroid hormone replacement. It may also help the patients and the physicians decide their treatment plan.

Conflict of interest

The authors declare that they have no conflict of interest.

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