Clinical Features of Early and Late Postoperative Hypothyroidism After Lobectomy

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Context: Lobectomy is preferred in thyroid cancer to decrease surgical complications and avoid lifelong thyroid-hormone replacement. However, postoperative hypothyroidism, requiring thyroid-hormone replacement, may occur.

Objective: We aimed to identify the incidence and risk factors of postoperative hypothyroidism to develop a surveillance strategy after lobectomy for papillary thyroid microcarcinoma (PTMC).

Methods: This historical cohort study involved 335 patients with PTMC treated by lobectomy. Postoperative thyroid functions were measured regularly, and patients were prescribed levothyroxine according to specific criteria. Patients not satisfying hormone-replacement criteria were closely followed up.

Results: Postoperative hypothyroidism occurred in 215 patients (64.2%) including 5 (1.5%) with overt hypothyroidism and 210 (62.7%) with subclinical hypothyroidism. Forty patients (11.9%) were required thyroid hormone replacement. One hundred nineteen patients (33.5%) experienced temporary hypothyroidism and spontaneously recovered to euthyroid state. High preoperative thyroid-stimulating hormone (TSH) was the most important factor predicting postoperative hypothyroidism and failure of recover from hypothyroidism (odds ratio [OR], 2.82 and 1.77; 95% confidence interval [CI], 2.07 to 3.95 and 1.22 to 2.63; $P < 0.001$ and 0.002, respectively). Of the 215 patients eventually developing postoperative hypothyroidism, 70 (32.6%) developed hypothyroidism after the first postoperative year. Postoperative 1-year TSH levels were able to differentiate patients developing late hypothyroidism or euthyroidism (OR, 2.29; 95% CI, 1.68 to 3.26; $P < 0.001$).

Conclusions: Preoperative and postoperative TSH levels might be predictive for patients who develop postlobectomy hypothyroidism and identify those requiring long-term surveillance for hypothyroidism. Additionally, mild postoperative hypothyroidism cases should be followed up without immediate levothyroxine replacement with the expectation of spontaneous recovery. **(*J Clin Endocrinol Metab* 102: 1317–1324, 2017)**

Lobectomy has been generally recommended as an optimal surgical approach for symptomatic unilateral goiter, toxic adenoma, cytologically indeterminate nodule, and low-risk differentiated thyroid cancer (DTC) (1, 2). With recent advances in early diagnosis of low-risk thyroid cancer, the role of lobectomy as the optimal treatment of thyroid cancer has been expanding (3, 4). Lobectomy provides the advantage of lower surgical complications such as recurrent laryngeal nerve palsy and postoperative hypoparathyroidism, and patients do not

ISSN Print 0021-972X ISSN Online 1945-7197
Printed in USA

Received 3 November 2016. Accepted 6 January 2017.
First Published Online 11 January 2017

Abbreviations: CI, confidence interval; DTC, differentiated thyroid cancer; fT4, free thyroxine; IQR, interquartile range; OR, odds ratio; PTMC, papillary thyroid microcarcinoma; RIA, radioimmunoassay; Tg, thyroglobulin; TgAb, antithyroglobulin antibody; TPOAb, thyroperoxidase autoantibody; TSH, thyroid-stimulating hormone.

require lifelong thyroid-hormone replacement after lobectomy, in contrast to total thyroidectomy (5).

Although patients are expected to maintain normal thyroid function after lobectomy (5, 6), some patients develop hypothyroidism that requires thyroid-hormone replacement. The reported incidence of postlobectomy hypothyroidism is variable, ranging from 0% to 43%. Critically, studies investigating risk factors for this postlobectomy complication are not in agreement because of varying follow-up durations, hypothyroidism definitions, thyroid-function assessment timings, and thyroid-hormone–supplementation criteria between the studies (1, 7–10). Most studies reported that postoperative hypothyroidism developed within the first postoperative year in 90% of patients; however, median follow-up periods in previous studies were relatively short, generally being <24 months (7, 8, 10–12), which may have underestimated the incidence of postoperative hypothyroidism.

Routine levothyroxine supplementation is commonly prescribed after lobectomy for patients with DTC, thereby hindering the evaluation of the actual incidence of postoperative hypothyroidism. However, recent evidence has questioned the efficacy of levothyroxine supplementation because of possible adverse effects of thyroid-stimulating hormone (TSH) suppression in patients with low-risk DTC, leading to its decreased utilization (13–15). Therefore, it is critical to have a better understanding of the incidence and causes of postoperative hypothyroidism and appropriate strategies for its surveillance in patients undergoing lobectomy for low-risk DTC.

We aimed to evaluate the incidence and risk factors for postoperative hypothyroidism in patients who underwent lobectomy for papillary thyroid microcarcinoma (PTMC). During the review of medical records of study subjects, we observed that there are 2 periods with peak frequency of postoperative hypothyroidism, which we defined as early and late hypothyroidism in this study. We also observed that some patients spontaneously recovered from postoperative hypothyroidism to euthyroidism. Thus, we also evaluated potential factors contributing to the development of early and late postoperative hypothyroidism and spontaneous recovery from postoperative hypothyroidism. This study was conducted to develop strategies for surveillance of postoperative hypothyroidism.

Methods

Patients

This historical cohort study included patients with PTMC who underwent lobectomy by 2 endocrine surgeons (S.J.H and T.Y.S) and were followed up without levothyroxine treatment at Asan Medical Center in Seoul between 2008 and 2011. Patients who received thyroid hormone replacement therapy at immediate postoperative periods (n = 19), underwent completion surgery (n = 4), and those with abnormal preoperative thyroid function (n = 26) were excluded from study. Patients without insufficient follow-up data were also excluded (n = 13). Finally, a total of 335 patients were eligible for this study. Postoperative serum free thyroxine (fT4) and TSH were measured within the first 2 to 3 months after lobectomy. Patients with euthyroid state were monitored every 6 to 12 months thereafter. Once hypothyroidism was diagnosed, all patients were regularly followed up with assessment of thyroid function every 3 to 6 months. Patients with overt hypothyroidism or those with serum TSH levels of >10 mIU/L were treated with levothyroxine. In addition, patients with mild subclinical hypothyroidism (>4.5 mIU/L) and subjective symptoms and signs of hypothyroidism also received levothyroxine replacement. This study was approved by the Institutional Review Board of Asan Medical Center.

Laboratory measurements

As previously described (16), serum TSH levels were measured using the TSH-CTK-3a radioimmunoassay (RIA; DiaSorin SpA, Saluggia, Italy) with a functional sensitivity of 0.07 mIU/L. Serum fT4 levels were determined using the fT4 RIA (Immunotech, Prague, Czech Republic). The reference ranges of TSH and fT4 were 0.4 to 4.5 mIU/L and 0.80 to 1.90 ng/dL, respectively. Serum thyroglobulin (Tg) levels were measured using the Tg-pluS RIA (BRAHMS AG, Henningsdorf, Germany) with a functional sensitivity of 0.2 ug/L, a coefficient of variation of 20%, and an analytical sensitivity of 0.08 ug/L. Antithyroglobulin antibody (TgAb) levels were measured using the anti-Tg RIA (BRAHMS AG) with a functional sensitivity of 20 IU/mL (17). Serum thyroperoxidase autoantibodies (anti-TPOAbs) were measured using a BRAHMS TPOAb RIA (Thermo Scientific, Limburg, Germany) with a functional sensitivity of 30 U/mL (16).

Definitions of postoperative hypothyroidism

Patients were divided into postoperative euthyroid and hypothyroid groups according to postoperative thyroid-function tests. Patients who remained euthyroid until the end of the follow-up period were classified into the postoperative euthyroid group. Euthyroidism was defined as normal serum TSH and fT4 levels within reference ranges. The postoperative hypothyroidism group included both subclinical and overt hypothyroidism cases. Subclinical hypothyroidism was defined as TSH elevation to >4.5 mIU/L with normal serum fT4 levels (18). Overt hypothyroidism was defined as low serum fT4 with elevated serum TSH (19). Patients with postoperative hypothyroidism were also categorized into 2 groups according to the time of emergence of postoperative hypothyroidism: Early hypothyroidism was defined as the development of hypothyroidism in ≤12 months after lobectomy, whereas this interval was >12 months in patients with late hypothyroidism. Some patients with subclinical hypothyroidism were found to spontaneously recover to euthyroidism without thyroid-hormone replacement. Therefore, patients with postoperative hypothyroidism who did not receive levothyroxine replacement were also categorized into recovered and unrecovered groups,

according to restore thyroid function. Figure 1 shows the study flowchart that includes the classification of patients according to the thyroid-function status.

Preoperative and postoperative characteristics of patients

We reviewed preoperative clinical characteristics of patients, including age, sex, preoperative TSH, and presence of thyroid autoantibodies. Positive TgAb was defined as a serum TgAb value of ≥60 IU/Ml, and positive TPOAb was defined as serum TPOAb ≥60 IU/Ml, as previously described (17). Postoperative clinical characteristics included lymphocytic thyroiditis by assessment of pathological specimen, location of lobectomy (right or left), serum TSH level at 1-year follow-up visit (postoperative 1-year TSH), and maximal serum TSH level at any time after lobectomy (postoperative maximal TSH).

Statistical analysis

R® version 3.0 and the R libraries survival, car, Hmisc, Cairo, mlogit, and pROC were used to analyze data (R Foundation for Statistical Computing, www.R-project.org). Continuous variables were described as means with standard deviation or medians with interquartile range (IQR), and they were examined using Student's *t* test. Categorical variables were presented as frequencies with percentages and analyzed by χ^2 test. We performed receiver operating characteristic curve analysis and determined the ability of optimal cutoff values for preoperative TSH in predicting postoperative hypothyroidism, postoperative 1-year TSH in predicting late hypothyroidism compared with euthyroidism, and postoperative maximal TSH levels in predicting recovery to euthyroidism. Logistic regression model was used to identify predictive variables of age, sex, preoperative TSH, presence of thyroid autoantibodies, site of lobectomy, presence of lymphocytic thyroiditis, postoperative 1-year TSH and maximal TSH level for development of postoperative hypothyroidism and recovery. Logistic regression results were presented as 95% confidence intervals (CIs) and *P* values. All *P* values were 2-sided, with values of <0.05 considered statistically significant.

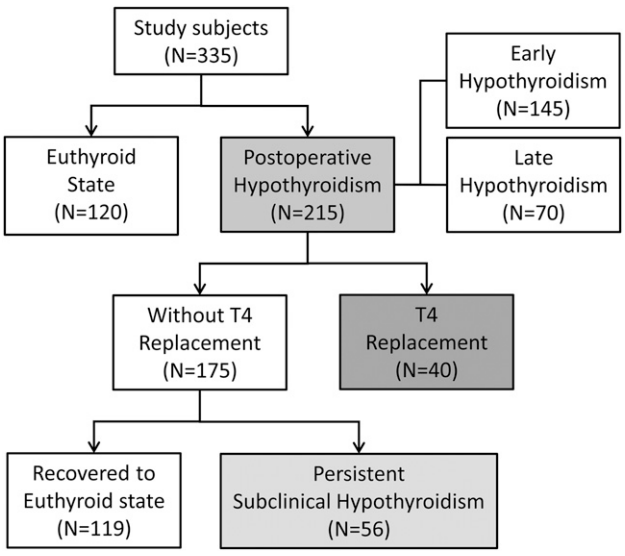

Figure 1. Study design.

Results

Clinicopathological characteristics of patients with postoperative hypothyroidism after lobectomy

Preoperative baseline characteristics of 335 PTMC patients who underwent lobectomy are presented in Table 1. Mean age was 47.9 ± 10.5 years, and the majority of patients (79.4%) were female. Geometric mean of preoperative TSH levels was 2.00 ± 0.96 mIU/L. After lobectomy, 215 of 335 (64.2%) patients experienced postoperative hypothyroidism, including 5 (1.5%) and 210 (62.7%) patients with overt and subclinical hypothyroidism, respectively (Fig. 1). Additionally, 40 of 335 (11.9%) patients required postoperative levothyroxine replacement. Median follow-up duration was 56.2 (IQR, 46.87 to 59.96) months and only 3 (0.8%) patients were diagnosed with recurrence of PTMC during follow-up.

In univariate analysis, there was no significant difference in the mean age between the euthyroid and hypothyroid groups (Table 2; $P = 0.30$). Female sex, high preoperative serum TSH level (>1.7 mIU/L), TgAb positivity, and right lobectomy were associated with development of postoperative hypothyroidism development ($P = 0.01$, $P < 0.001$, $P = 0.03$, $P = 0.02$, respectively). There was no significant difference in TPOAb positivity between the 2 groups ($P = 0.24$). However, only high preoperative serum TSH level (>1.7 mIU/L) was independently associated with the development of postoperative hypothyroidism in multivariate analysis [odds ratio (OR), 2.82; 95% CI, 2.07 to 3.95; $P < 0.001$].

Development of early and late hypothyroidism

We evaluated the timing of initial hypothyroidism after lobectomy in the hypothyroid group [Fig. 2(A)]. Median time interval to develop initial hypothyroidism was 3.98 months (IQR, 3.25 to 21.9). One hundred forty-five (67.4%) patients developed hypothyroidism within postoperative 12 months (early hypothyroidism), whereas the remaining 70 (32.6%) patients developed hypothyroidism after postoperative 12 months (late hypothyroidism). Preoperative TSH levels and the number of TPOAb-positive patients were significantly higher among patients with early hypothyroidism than those with late hypothyroidism ($P = 0.001$, $P = 0.03$, respectively; Supplemental Table 1).

Clinical characteristics associated with late hypothyroidism in patients remaining euthyroid at 1 year after lobectomy

One year after lobectomy, there were 190 (56.7%) patients who did not experience hypothyroidism and remained in euthyroid (Fig. 1). We compared the clinical features of patients in the euthyroid group (n = 120) with those who developed late hypothyroidism (n = 70) to determine clinical

Table 1. Baseline Clinical Characteristics of Patients With Euthyroidism State and Postoperative Hypothyroidism After Lobectomy

	Total Patients (N = 335)	Euthyroidism (n = 120)	Hypothyoidism (n = 215)	*P* Value
Age (y)				
Mean ± SD	47.9 ± 10.5	46.8 ± 10.1	48.5 ± 10.8	
≤45	141 (42.1%)	55 (45.8%)	86 (40.0%)	0.36
>45	194 (57.9%)	65 (54.2%)	129 (60.0%)	
Sex				
Male	72 (21.5%)	35 (29.2%)	37 (17.2%)	0.01
Female	266 (79.4%)	85 (70.8%)	178 (82.8%)	
Preoperative TSH (mIU/L)				
Mean[a] ± SD	2.00 ± 0.96	1.49 ± 0.68	2.28 ± 0.99	
≤1.7[b]	141 (42.1%)	81 (84.2%)	60 (27.9%)	<0.001
>1.7[b]	194 (57.9%)	39 (15.8%)	155 (72.1%)	
TgAb positivity[c]	50 (14.9%)	11 (9.2%)	39 (18.1%)	0.04
TPOAb positivity[c]	40 (11.9%)	11 (9.2%)	29 (13.5%)	0.32
Site of lobectomy				
Left	163 (48.7%)	69 (57.5%)	94 (43.7%)	0.02
Right	172 (51.3%)	51 (42.5%)	121(56.3%)	
Presence of lymphocytic thyroiditis	270 (80.6%)	102 (85.0%)	168 (78.1%)	0.17
	65 (19.4%)	18 (15.0%)	47 (21.9%)	

Abbreviations: SD, standard deviation; TgAb, antithyroglobulin antibodies; positive TgAb ≥ 60 IU/mL; positive TPOAb ≥ 60 IU/mL.

[a] Geometric mean.

[b] $P < 0.05$, The optimum cut- off point for preoperative TSH was 1.7 mIU/L using by receiver operating characteristic curve analysis (area under the curve = 0.75).

[c] Refers to values ≥60IU/mL.

features associated with late hypothyroidism. In univariate analysis, high postoperative 1-year TSH level (>3.1 mIU/L) was significantly associated with the development of late hypothyroidism ($P < 0.001$; Supplemental Tables 3 and 4), which remained significant in multivariate analysis after adjustment for age and sex (OR, 2.29; 95% CI, 1.68 to 3.26; $P < 0.001$; Supplemental Table 4).

Clinicopathological characteristics associated with spontaneous recovery from postoperative subclinical hypothyroidism

Among 210 patients with subclinical hypothyroidism during follow-up, 175 (83.3%) patients were regularly followed up without levothyroxine replacement (Fig. 1). Of these, 119 (68.0%) patients spontaneously recovered to euthyroidism. Median time interval from development of subclinical hypothyroidism to recovery was 12.2 months, and 83 of 175 (47.4%) patients recovered within 2 years after hypothyroidism diagnosis [Fig. 2(B)]. Analysis of clinical features associated with spontaneous thyroid-function recovery in patients with subclinical hypothyroidism who were followed up without levothyroxine replacement (Table 3) revealed that high preoperative serum TSH level (>1.7 mIU/L) and high postoperative maximal serum TSH level (>7.1 mIU/L) during follow-up were associated with sustained hypothyroidism in univariate analysis ($P = 0.01$ and < 0.001, respectively). Only high preoperative serum TSH level

Table 2. Univariate and Multivariate Analysis for Clinical Factors Associated With the Development of Postoperative Hypothyroidism

	Univariate			Multivariate		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Age (y) > 45	1.27	0.81–1.27	0.30			NA
Female	1.98	1.17–3.36	0.01			NA
Preoperative TSH (mIU/L) > 1.7	5.36	3.32–8.78	<0.001	2.82	2.07–3.95	<0.001
TgAb positivity[a]	2.19	1.11–4.67	0.03			NA
TPOAb positivity[a]	1.54	0.76–3.34	0.24			
Site of lobectomy (right)	1.72	1.10–2.72	0.02			NA
Presence of lymphocytic thyroiditis	1.59	0.88–2.94	0.13			

Abbreviation: NA, not applicable.

[a] Refers to values ≥60 IU/mL.

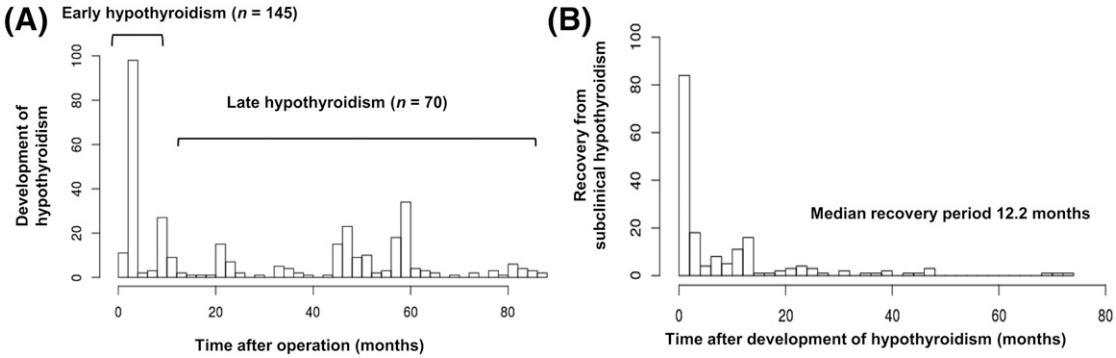

Figure 2. The time course of (A) development of postoperative hypothyroidism and (B) recovery from subclinical hypothyroidismin patients who underwent lobectomy.

during follow-up was significantly associated with sustained hypothyroidism in multivariate analysis (OR, 1.77; 95% CI, 1.22 to 2.63; P = 0.002; Supplemental Table 5).

We also evaluated differences in thyroid-function recovery according to the time to development of postoperative hypothyroidism. Among 175 patients who were followed up without immediate levothyroxine replacement, 108 (61.7%) and 67 (38.3%) patients had early and late hypothyroidism, respectively. Frequency of recovery to euthyroidism was significantly higher in the late-hypothyroidism group (P = 0.02), whereas mean recovery duration was shorter in the early-hypothyroidism group ($P < 0.001$, Table 4).

Discussion

This study demonstrated that the prevalence of postoperative hypothyroidism, including subclinical hypothyroidism, reached 64% in patients undergoing lobectomy. However, without immediate levothyroxine replacement, approximately 68% (119/175) patients spontaneously recovered to euthyroidism. Higher preoperative serum TSH level (>1.7 mIU/L) was an independent risk factor for

Table 3. Clinical Characteristics of Patients With Recovered to Euthyroidism and Remained Persistent Hypothyroidism

	Recovered Euthyroidism (N = 119)	Persistent Hypothyroidism (N = 56)	*P* Value
Age (y)			
Mean ± SD	48.03 ± 10.14	50.50 ± 10.63	
≤45	46 (38.7%)	18 (32.1%)	0.50
>45	73 (61.3%)	38 (67.9%)	
Sex			
Male	17 (14.0%)	12 (21.4%)	0.33
Female	102 (86.0%)	44 (78.6%)	
Preoperative TSH (mIU/L)			
Mean[a] ± SD	2.13 ± 0.92	2.38 ± 0.93	
≤1.7	41 (34.5%)	9 (16.1%)	0.01
>1.7	78 (65.5%)	47 (83.9%)	
TgAb positivity[b]	26 (21.8%)	6 (10.7%)	0.11
TPOAb positivity[b]	14 (11.7%)	6 (10.7%)	0.99
Site of lobectomy			
Left	65 (54.6%)	32 (57.1%)	0.88
Right	54 (45.4%)	24 (42.9%)	
Presence of lymphocytic thyroiditis	27 (22.7%)	10 (17.9%)	0.59
Postoperative maximal TSH (mIU/L)			
Mean[a] ± SD	7.34 ± 7.38	7.90 ± 2.71	
≤7.1[c]	82 (68.9%)	19 (33.9%)	<0.001
>7.1	37 (31.1%)	37 (66.1%)	

Abbreviation: SD, standard deviation.

[a] Geometric mean.

[b] Refers to values ≥60 IU/mL.

[c] $P < 0.05$, The optimum cut-off point for postoperative maximal TSH was 7.1 mIU/L (area under the curve = 0.65) using by receiver operating characteristic curve analysis.

Table 4. Early Hypothyroidism and Late Hypothyroidism in Patients Recovered to Euthyroidism

	Early Hypothyroidism (N = 108)	Late Hypothyroidism (N = 67)	*P* Value
Recovered euthyroidism	66 (61.1%)	53 (79.1%)	0.02
Persistent hypothyroidism	42 (38.9%)	14 (20.9%)	
Recovery duration (mean ± SD)	16.6 ± 17.61	31.35 ± 21.96	<0.001

Abbreviation: SD, standard deviation.

postoperative hypothyroidism and persistent hypothyroidism without recovery. Approximately 67% (145/215) patients were diagnosed with early hypothyroidism, whereas the remaining patients experienced postoperative hypothyroidism >1 year after lobectomy. In patients who remained euthyroid at 1 year after lobectomy, the postoperative 1-year serum TSH level (>3.1 mIU/L) was an independent factor for predicting late hypothyroidism during follow-up. Patients with late hypothyroidism needed more time to recover to euthyroidism, but they were more likely to return to normal than those who developed early hypothyroidism.

A meta-analysis showed that up to 90% patients diagnosed with hypothyroidism after lobectomy were reported to experience hypothyroidism within 1 year after surgery (1). This is in contrast to the findings of our study where only about 67% of patients developed hypothyroidism within 1 year after surgery. This finding might be partially explained by the relatively longer follow-up period in the current study, which allowed for the identification of a substantial number of patients who developed late hypothyroidism beyond the first year after lobectomy. At 1 year after lobectomy, about 57% patients remained euthyroid without levothyroxine replacement, and about 37% of these patients developed late hypothyroidism. Our study is thus the first to demonstrate that late postoperative hypothyroidism developed in a substantial number of patients 1 year after lobectomy. We also found that the postoperative 1-year serum TSH level might be an important clinical risk factor for postoperative late hypothyroidism. Specifically, patients with high postoperative 1-year TSH levels (>3.1 mIU/L) might require more frequent follow-up for thyroid-function evaluation, even if they might be euthyroid at 1 year after lobectomy.

Some studies suggested that postoperative hypothyroidism is not a true hypothyroid state but a transient one resulting from compensation of TSH elevation (1, 8). However, thyroid-hormone replacement was initiated as soon as hypothyroidism was diagnosed in most studies. Therefore, an opportunity to spontaneously recover thyroid function might be missed (8, 20). In the current study, patients with asymptomatic mild postoperative hypothyroidism were followed up without immediate thyroid-hormone replacement. Indeed, approximately 68% of these patients spontaneously recovered to euthyroidism within 24 months, especially those with preoperative serum TSH levels of <1.7 mIU/L. These findings indicated that serum TSH elevation might be a transient compensatory phenomenon in early postoperative period that could be followed up closely without immediate treatment until 24 months after development of hypothyroidism.

In the current study, patients with early hypothyroidism had higher preoperative TSH levels and TPOAb positivity and were less likely to spontaneously recover than those with late hypothyroidism, suggesting that lower preoperative thyroid reserves might lead to early postoperative hypothyroidism. Nevertheless, patients with early postoperative hypothyroidism recovered to euthyroidism faster than those with late hypothyroidism; transient compensation of TSH elevation in the early-hypothyroidism group might contribute to this result.

Levothyroxine is typically prescribed for TSH suppression after lobectomy for thyroid cancer to prevent its recurrence (15, 21) according to previous data showing that thyroid-hormone supplementation decreased recurrence and cancer-related deaths by 25% and 50%, respectively (22). Other studies insisted that TSH suppression could prevent DTC progression (23–25). However, the efficiency of TSH suppression in low-risk DTC patients undergoing lobectomy is insufficient. In our cohort, only 3 patients (0.8%) had recurrent PTMC during follow-up, including 2 patients with newly developed central lymph node metastasis and 1 patient with recurrence in the operative bed. There was no cancer-related mortality. The incidence of recurrence in our study was similar to previous studies employing TSH suppression with routine levothyroxine replacement (26). Although the follow-up period was not sufficient to assess whether TSH suppression therapy with routine levothyroxine replacement was efficient in preventing recurrence, our study suggested that mild TSH elevation after lobectomy might be relatively safe for low-risk DTC patients. Prospective randomized trials or larger cohort studies with long-term follow-up are needed to confirm the role of TSH suppression in low-risk DTC patients treated by lobectomy.

Previous studies suggested that preoperative serum TSH level was an important risk factor for hypothyroidism after lobectomy (5, 11, 27). Higher prelobectomy serum TSH levels might reflect decreased functional reserves in the thyroid gland and might be a critical factor

for postoperative hypothyroidism (28). In the current study, we also confirmed previous studies that reported the cutoff value of preoperative serum TSH level as 1.7 mIU/L by receiver operating characteristic curve analysis. The cutoff values in previous studies ranged between 1.4 and 2.5 mIU/L (10, 11, 14, 29). Intriguingly, right-side lobectomy associated with postoperative hypothyroidism in the current study might be related to the residual thyroid volume, given that right thyroid lobe is usually bigger than left lobe (30); however, this conclusion is limited as the volume of the resected lobe was not measured.

This study has several limitations. This retrospective cohort study has a potential selection bias. Although patients were followed up according to institutional protocols, the schedule of thyroid-function measurements might have differed between patients. Additionally, only patients who underwent lobectomy for PTMC were included in this study, and it remains unclear whether our findings are applicable to patients undergoing lobectomy for other reasons. Furthermore, we did not evaluate iodine intake of the study cohort, which could affect serum TSH level as the cohort was from an iodine-sufficient population. We did not quantitatively evaluate lymphocytic-infiltration grade in thyroid tissue, which was suggested as a potential predictor of hypothyroidism in previous studies (12, 31). However, this was a unique study evaluating postlobectomy hypothyroidism with a relatively long-term follow-up to assess recovery of thyroid function in mild subclinical hypothyroidism without levothyroxine replacement.

The current study demonstrated that 64% patients experienced postlobectomy hypothyroidism, whereas late hypothyroidism developed at >1 year after surgery in one-third of them. Preoperative serum TSH level was an independent predictor of postoperative hypothyroidism, whereas postoperative 1-year TSH level was an important predictor of late hypothyroidism in patients who remained euthyroid at 1 year after surgery. Mild subclinical hypothyroidism recovered to euthyroidism in two-thirds of the patients without immediate levothyroxine replacement. These findings highlight the significance of evaluating hypothyroidism risk by preoperative and postoperative serum TSH values to determine the follow-up interval for thyroid-function tests in patients undergoing lobectomy. Mild postoperative subclinical hypothyroidism might be followed up without immediate levothyroxine replacement with the expectancy of recovery.

Acknowledgments

The Journal acknowledges that the author retains the right to provide an electronic copy of the final peer-reviewed manuscript to Korean Pubmed Central upon acceptance for publication, and to make it publicly available as soon as possible but no later than 12 months after publication.

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This study was supported by a grant of the Korean Health Technology R&D Project, Ministry of Health and Welfare, Republic of Korea (HC15C3372).

Disclosure Summary: The authors have nothing to disclose.

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