



## Featured Article

# Postoperative thyroid hormone supplementation rates following thyroid lobectomy

Madeleine Wilson <sup>a</sup>, Anery Patel <sup>b</sup>, Whitney Goldner <sup>b</sup>, John Baker <sup>c</sup>, Zafar Sayed <sup>d</sup>, Abbey L. Fingeret <sup>e,\*</sup>

<sup>a</sup> University of Nebraska Medical Center, USA

<sup>b</sup> Department of Medicine, Division of Diabetes, Endocrinology and Metabolism, University of Nebraska Medical Center, USA

<sup>c</sup> Department of Pathology and Microbiology, University of Nebraska Medical Center, USA

<sup>d</sup> Department of Otolaryngology, Division of Head and Neck Oncology, University of Nebraska Medical Center, USA

<sup>e</sup> Department of Surgery, Division of Surgical Oncology, University of Nebraska Medical Center, USA



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## ABSTRACT

**Background:** Thyroid lobectomy is performed for symptomatic benign nodules, indeterminate nodules, or low-risk well-differentiated thyroid cancer. We aimed to determine factors associated with need for thyroid hormone supplementation following thyroid lobectomy.

**Methods:** We performed a retrospective single-institution cohort study of patients undergoing thyroid lobectomy from January 2016 to December 2017. Thyroid hormone supplementation was assessed postoperatively based on guidelines for thyroid stimulating hormone (TSH) level goal for benign (0.5–4.5mIU/L) or malignant (<2mIU/L) final pathology. Univariate and multivariate logistic regression analysis was performed.

**Results:** One hundred patients were included and overall 47% required thyroid hormone supplementation after thyroid lobectomy: 73% of those with cancer, 38% with benign pathology ( $p = 0.002$ ). Patients requiring thyroid hormone supplementation were more likely to have thyroiditis 26% versus 3.8% of those who remained euthyroid ( $p = 0.002$ ); have a higher preoperative TSH: mean 1.88mIU/L (SD 1.17) versus 1.16mIU/L (SD 0.77) ( $p = 0.0002$ ), and have a smaller remnant thyroid lobe adjusted for body surface area 2.99ml/m<sup>2</sup> versus 3.72ml/m<sup>2</sup> ( $p = 0.003$ ).

**Conclusions:** After thyroid lobectomy, the need for thyroid hormone supplementation is associated with higher preoperative TSH level, thyroiditis, remnant thyroid volume, and malignancy on final pathology. The majority of patients with final pathology of carcinoma will require thyroid hormone supplementation to achieve TSH goal. For patients with benign pathology after thyroid lobectomy the majority will not require thyroid hormone supplementation to achieve TSH goal.

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## Introduction

Thyroid nodules are commonly detected by physical examination or incidentally discovered on imaging for other indications. The prevalence of thyroid nodules is estimated to be up to 68% in adult patients.<sup>1</sup> Though thyroid carcinoma is less common with a malignancy rate of 5–15% of all thyroid nodules.<sup>2</sup> Thyroid lobectomy is often indicated for treatment of benign symptomatic nodules, indeterminate nodules, or low risk well-differentiated

carcinoma less than 4 cm.<sup>2,3</sup> Historically, the rates of thyroid hormone supplementation after thyroid lobectomy were determined from patients with benign pathology, as those with malignant results were recommended for completion thyroidectomy based on previous guidelines.

Prior to 2015, thyroid cancers were most commonly treated with total thyroidectomy per society guidelines from the American Thyroid Association (ATA).<sup>4</sup> In January of 2016, the ATA published new guidelines allowing thyroid lobectomy as an acceptable operation for well differentiated thyroid cancers under 4 cm without high-risk features such as extrathyroidal extension, nodal metastasis, family history of thyroid cancer, or personal history of external beam radiation.<sup>4</sup> This paradigm shift in the management

\* Corresponding author 986880 Nebraska Medical Center, Omaha, NE, 68198-6880, USA.

E-mail address: [abbey.fingeret@unmc.edu](mailto:abbey.fingeret@unmc.edu) (A.L. Fingeret).

of differentiated thyroid carcinoma was spurred by lack of evidence of survival benefit following total thyroidectomy for lower risk tumors.<sup>5–8</sup> Moreover, the pervasive use of radioactive iodine ablation for thyroid cancers over 1 cm had been revised to selective use for intermediate and high-risk pathology.<sup>4,9</sup> The extent of surgery for thyroid malignancy - lobectomy or total thyroidectomy - should be selected to optimize patient disease-free and overall survival and quality of life while limiting overtreatment and treatment related complications. Thyroid lobectomy, in contrast to total thyroidectomy, avoids the risk of hypoparathyroidism and potential for bilateral recurrent laryngeal nerve injury and is associated with a lower risk of postoperative neck hematoma.<sup>10</sup>

Following thyroid lobectomy for malignancy, the ATA guidelines specify the recommended level of thyroid stimulating hormone (TSH) be less than 2 mIU/L.<sup>4</sup> Because previous guidelines did not recommend thyroid lobectomy for patients with a known diagnosis of cancer, a thyroid lobectomy was typically only performed for an indeterminate biopsy result or a symptomatic unilateral nodule. If final pathology for indeterminate nodule showed a cancer, previously that patient would have been recommended to have a completion thyroidectomy. Because of this practice, historically most thyroid cancer patients required thyroid hormone replacement for postsurgical hypothyroidism. Avoidance of lifelong need for medication is appealing to many patients with thyroid disease including thyroid cancer.

For those patients with benign pathology after thyroid lobectomy, the reported rates of thyroid hormone supplementation are 8–50%.<sup>10–24</sup> For cancer patients with a TSH goal of <2 mIU/L the rate of thyroid hormone supplementation is higher. One recent study found that 73% of all included patients and 78% of patients with well-differentiated thyroid carcinoma had a TSH >2 mIU/L after thyroid lobectomy.<sup>25</sup> This study did not assess remnant thyroid volume for association with need for thyroid hormone or long term follow up after one year post thyroid lobectomy.

Numerous patient factors may influence the need for thyroid hormone supplementation following thyroid lobectomy. Remnant thyroid lobe volume adjusted for body surface area, preoperative TSH level, heterogeneous sonographic echotexture of the thyroid gland, anti-thyroid peroxidase antibodies, and lymphocytic thyroiditis have all been associated with postsurgical hypothyroidism.<sup>11–16,18,19,21–23,26</sup> Understanding the contemporary rate of thyroid hormone supplementation after thyroid lobectomy for benign or malignant pathology while considering patient factors will aid in preoperative counseling on extent of surgery. We sought to determine the rate of thyroid hormone supplementation after thyroid lobectomy both immediately postoperatively and in long term follow up for patients with benign and malignant pathology. We hypothesize there are preoperative factors that predict the need for thyroid hormone supplementation including preoperative cytology, preoperative TSH, remnant thyroid lobe volume, malignancy and presence of thyroiditis.

## Materials and methods

A retrospective cohort review was performed for adult patients undergoing thyroid lobectomy at a single institution by two high volume thyroid surgeons from January of 2016 through December of 2017. Our institution adopted the use of thyroid lobectomy for well differentiated thyroid carcinoma without high risk features by the cohort start date of January of 2016. Exclusion criteria included: age less than 18 years, prior thyroid surgery, preoperative hypothyroidism or thyroid hormone supplementation, Graves' disease, and lack of TSH measurements for 12 months following surgery. This study was approved by the Institutional Review Board.

Clinicopathologic variables were collected including sex, age, size of greatest dimension of the thyroid nodule, nodule cytology, preoperative thyroid sonographic characteristics, thyroid lobe and thyroid remnant sonographic size and volume adjusted for body surface area (BSA), TSH, anti-thyroid peroxidase antibodies, histopathology of thyroid nodule and thyroid parenchyma, completion thyroidectomy, and thyroid hormone supplementation status. The remnant thyroid lobe volume was measured by ultrasound during the preoperative evaluation. Remnant volume was adjusted for BSA also obtained during the preoperative evaluation. To estimate the volume of the lobe, we used the following formula: volume (mL) = width (cm) x depth (cm) x length (cm) x  $\pi/6$ . BSA was estimated using the Mosteller formula: BSA (m<sup>2</sup>) = (height (cm) x weight (kg)/3600). The remnant volume to BSA ratio in ml/m<sup>2</sup> was compared between the groups. Preoperative TSH was also assessed as a categorical variable in association with need for thyroid hormone supplementation with groups of <1.0, 1.0–1.9, 2–2.9, 3–3.9, or >4 mIU/L.

Our institutional protocol is to measure TSH at 6 weeks, 6 months, 12 months, and then annually following thyroid lobectomy. Patients were considered to be on thyroid hormone supplementation if any form of synthetic or natural T3 or T4 therapy was initiated during follow-up. Patients who underwent completion thyroidectomy were categorized as requiring thyroid hormone supplementation based on an intent to treat methodology. TSH goal for patients with well differentiated thyroid carcinoma were defined by ATA guidelines as less than 2 mIU/L and TSH goal for patients with benign pathology were defined by our institutional normal lab values of TSH 0.5–4.5 mIU/L. Patients whose TSH exceeded these goals were given thyroid hormone supplementation.

Univariate statistical analysis was performed with Fisher's exact and Kruskal-Wallis testing for categorical variables and Wilcoxon rank sum for continuous variables with a significance of  $p < 0.05$ . A logistic regression analysis was performed to determine factors associated with need for thyroid hormone supplementation. Statistical analysis was performed with STATA version 15 (College Station, TX).

## Results

One hundred and thirty-nine patients underwent thyroid lobectomy during the study period, of these, 100 met inclusion criteria. Twenty patients were excluded due to lack of TSH values for 12 months postoperatively, three patients were excluded for a diagnosis of Graves disease, and 16 patients were excluded for prior thyroid surgery. The included patients were mostly female (74%), and white (84%). The overall characteristics of the included patients are detailed in [Table 1](#). Preoperative cytology results are shown in [Table 2](#). For patients who proceeded to surgery without a biopsy, five had solitary symptomatic low sonographic risk appearing thyroid nodules where biopsy would not have changed management and six had solitary toxic thyroid nodules. Overall, 26% of patients had well differentiated thyroid carcinoma on final pathology: 19 with papillary thyroid carcinoma, four with follicular variant of papillary thyroid carcinoma, and three with follicular thyroid carcinoma ([Table 3](#)). Four patients had initial benign thyroid nodule cytology but were found to have incidental thyroid microcarcinoma on final pathology. Two patients with malignant final pathology underwent completion thyroidectomy based on intermediate or high-risk tumor features. Two patients had post-operative complications: one had temporary recurrent laryngeal neuropraxia that resolved at six-week follow up, one had severe allergic dermatitis to the operative skin preparation that required oral steroids. No patients required a reoperation for recurrence during the study period. Mean follow up was 16 months (standard

**Table 1**  
Clinical and pathologic factors of patients undergoing thyroid lobectomy.

n	100
Age, years, mean (SD)	50.5 (16.2)
Female sex, n (%)	74
Caucasian Race, n (%)	84
Ultrasound heterogeneity, n (%)	29
Preoperative cytology	
No biopsy, n (%)	11
Nondiagnostic biopsy, n (%)	7
Benign, n (%)	33
Indeterminate, n (%)	34
Suspicious or Malignant, n (%)	15
Thyroiditis on pathology, n (%)	14
Final pathology benign, n (%)	74
Preoperative TSH mIU/L, mean (SD)	1.50 (1.04)
Preoperative TPO IU/mL, mean (SD)	4.9 (7.1)
Specimen size, grams, mean (SD)	20.7 (20.5)
Remnant volume:body surface area, ml/m <sup>2</sup> mean (SD)	3.37 (2.22)
Follow up, months, mean (SD)	16.0 (8.5)

Key: Indeterminate cytology includes AUS: atypia of undetermined significance, FLUS: follicular lesion of undetermined significance, FN: follicular neoplasm, SFN: suspicious for follicular neoplasm, HCN: Hurthle cell neoplasm; TSH: thyroid stimulating hormone; TPO: anti-thyroid peroxidase antibody.

**Table 2**  
Preoperative cytologic diagnosis for patients undergoing thyroid lobectomy.

Preoperative cytology, n (%)	Final pathology	
	Benign	Malignant
All, 100	74	26
No biopsy, 11	9 (82%)	2 (18%)
Nondiagnostic, 7	5 (71%)	2 (29%)
Benign, 33	29 (88%)	4 (12%)
AUS or FLUS, 13	12 (93%)	1 (8%)
FN, SFN, or HCN, 21	19 (90%)	2 (10%)
Suspicious for malignancy, 7	0	7 (100%)
Malignant, 8	0	8 (100%)

Key: AUS: atypia of undetermined significance, FLUS: follicular lesion of undetermined significance, FN: follicular neoplasm, SFN: suspicious for follicular neoplasm, HCN: Hurthle cell neoplasm.

deviation 8.5 months) with a median of 15 months.

Overall, 47% required thyroid hormone supplementation (Table 4). The rate of thyroid hormone supplementation after thyroid lobectomy for patients with benign preoperative cytology was 39%, for indeterminate preoperative cytology was 44% and for suspicious or malignant preoperative cytology was 67% ( $p = 0.21$ ). For those with benign final pathology the rate of thyroid hormone supplementation was 38% compared to 73% for those with malignancy on final pathology ( $p = 0.002$ ). A TSH above goal was detected at 6 weeks postoperatively for 37 patients (79%), at 6 months postoperatively for 8 patients (17%), and at greater than 1 year postoperatively for 2 patients (4%). When stratifying for preoperative TSH by category, the likelihood of requiring thyroid hormone supplementation following thyroid lobectomy increased with increasing value (Table 5).

**Table 3**  
Histology results following thyroid lobectomy.

	All	Euthyroid	Thyroid Hormone Supplementation	p value
n	100	53	47	
Benign, n (%)	74	46 (62%)	28 (38%)	0.002
Malignant, n (%)	26	7 (27%)	19 (73%)	0.002
Papillary Thyroid Carcinoma, n (%)	19	5 (26%)	14 (74%)	
Follicular Variant of Papillary Thyroid Carcinoma, n (%)	4	2 (50%)	2 (50%)	
Follicular Thyroid Carcinoma, n (%)	3	0 (0%)	3 (100%)	

There were no differences in age, sex, race, or preoperative sonographic echotexture of the thyroid gland, thyroid nodule size, or preoperative level of anti-thyroid peroxidase antibodies between those who did and did not require thyroid hormone supplementation. Length of follow up did not differ between the groups, with 16.1 months for the euthyroid group and 15.8 months for patients who required thyroid hormone supplementation ( $p = 0.73$ ). All patients who were initiated on thyroid hormone supplementation remained on thyroid hormone for the duration of the study. The remnant volume to body surface area ratio was higher in those that did not require thyroid hormone with 3.72 ml/m<sup>2</sup> compared with 2.99 ml/m<sup>2</sup> in patients who did require thyroid hormone supplementation ( $p = 0.003$ ). Thyroiditis on final pathology was associated with need for thyroid hormone supplementation, with 14% of patients with thyroiditis remaining euthyroid and 86% of patients with thyroiditis requiring thyroid hormone supplementation ( $p = 0.002$ ). Patients who required thyroid hormone supplementation had a higher preoperative TSH with a mean of 1.88mIU/L compared with 1.16mIU/L for those who remained euthyroid following thyroid lobectomy (Table 4). In a multivariate logistic regression, each of these factors remained significantly associated with the need for thyroid hormone supplementation. Based on this multivariate logistic regression, thyroiditis, preoperative TSH, remnant thyroid lobe volume to body surface area ratio, and malignant final pathology were all independently associated with the need for thyroid hormone supplementation (Table 6).

## Discussion

Appropriate preoperative counseling and informed consent for patients offered thyroid lobectomy for benign, indeterminate, suspicious or malignant indications should include an estimate of the need for thyroid hormone supplementation postoperatively. In this study, 47% of patients required thyroid hormone supplementation after thyroid lobectomy. While this rate is concordant with previous published reports, when stratifying by final pathologic diagnosis the proportion requiring thyroid hormone increases significantly.<sup>10</sup> In our study, for those with benign final pathology the rate of thyroid hormone supplementation was 38% compared to 73% for those with malignancy on final pathology. This finding is concordant with the study by Cox et al., who also found that 73% of patients had a TSH >2 mIU/L within one year of thyroid lobectomy and thus would require thyroid hormone supplementation to be compliant with ATA guidelines for TSH goal for patients with well differentiated thyroid carcinoma.<sup>4,25</sup>

Patients and providers may ascribe potential for avoidance of daily lifelong thyroid hormone replacement as the main advantage of thyroid lobectomy over total thyroidectomy for differentiated thyroid carcinoma without high-risk features. While this may be possible in a minority of patients, we found that 73% of our study population would require thyroid hormone supplementation to be compliant with ATA guidelines. Despite this outcome, it is possible that patients with a remnant thyroid lobe may have superior quality of life compared to athyroid patients even if they require thyroid hormone supplementation. Up to 36% of patients following

**Table 4**  
Clinical and pathologic factors associated with the need for postoperative thyroid hormone supplementation after thyroid lobectomy.

	All	Euthyroid	Thyroid Hormone Supplementation	Univariate analysis p-value
n	100	53	47	
Age, years, mean (SD)	50.5 (16.2)	49.7 (15.5)	51.4 (17.0)	0.59
Female sex, n (%)	74	40 (75%)	34 (72%)	0.82
Caucasian Race, n (%)	84	42 (79%)	42 (89%)	0.07
Ultrasound heterogeneity, n (%)	29	14 (44%)	15 (44%)	0.58
Preoperative cytology				0.21
No biopsy, n (%)	11	6 (55%)	5 (45%)	
Nondiagnostic biopsy, n (%)	7	3 (43%)	4 (36%)	
Benign, n (%)	33	20 (61%)	13 (39%)	
Indeterminate, n (%)	34	19 (56%)	15 (44%)	
Suspicious or Malignant, n (%)	15	5 (33%)	10 (67%)	
Thyroiditis on pathology, n (%)	14	2 (14%)	12 (86%)	0.002
Final pathology benign, n (%)	74	46 (62%)	28 (38%)	0.002
Preoperative TSH mIU/L, mean (SD)	1.50 (1.04)	1.16 (SD 0.77)	1.88 (SD 1.17)	0.0002
Preoperative TPO IU/mL, mean (SD)	4.9 (7.1)	3.83 (6.7)	6.1 (8.2)	0.65
Specimen size, grams, mean (SD)	20.7 (20.5)	22.1 (22.0)	19.0 (18.9)	0.76
Remnant volume:body surface area, ml/m <sup>2</sup> , mean (SD)	3.37 (2.22)	3.72 (2.1)	2.99 (2.3)	0.003
Follow up, months, mean (SD)	16.0 (8.5)	16.1 (9.2)	15.8 (7.8)	0.73

Key: Indeterminate cytology includes AUS: atypia of undetermined significance, FLUS: follicular lesion of undetermined significance, FN: follicular neoplasm, SFN: suspicious for follicular neoplasm, HCN: Hurthle cell neoplasm; TSH: thyroid stimulating hormone; TPO: anti-thyroid peroxidase antibody.

**Table 5**  
Preoperative thyroid stimulating hormone category association with thyroid hormone supplementation after thyroid lobectomy by final pathology.

Preoperative TSH level, mIU/L	<1.0	1.0–1.9	2.0–2.9	3.0–3.9	>4
All patients, n	33	38	16	1	5
All patients requiring thyroid hormone supplementation, n (%)	8 (24)	20 (53)	11 (69)	1 (100)	4 (80)
Benign pathology, n (%)	25 (76)	29 (76)	10 (63)	0 (0)	5 (100)
Benign pathology requiring thyroid hormone, n (%)	4 (16)	12 (41)	6 (60)	0 (0)	4 (80)
Malignant pathology, n (%)	8 (24)	9 (24)	6 (37)	1 (100)	0 (0)
Malignant pathology requiring thyroid hormone, n (%)	4 (50)	8 (89)	5 (83)	1 (100)	0 (0)

total thyroidectomy experience chronic fatigue, or asthenia, despite biochemical euthyroidism on replacement, compared with only 2% following thyroid lobectomy.<sup>27,28</sup> This potential for chronic fatigue contributing to decrement in quality of life must be balanced with the potential need for completion thyroidectomy leading to increased stress or anxiety and implications of a second operation. In our series, only 2 patients required completion thyroidectomy based on intermediate or high-risk final pathology. In contrast, a recent study found that up to 60% of patients considered for thyroid lobectomy would be predicted to need completion thyroidectomy.<sup>29</sup> This predicted rate of completion thyroidectomy may differ widely from our actual institutional rate of completion thyroidectomy because we have a robust preoperative multidisciplinary team to determine whether a patient is appropriate for a lobectomy. Based on this consensus recommendation and patient preference we perform either lobectomy or total thyroidectomy. Our rates of completion thyroidectomy may be less than predicted at other institutions because of our patient selection process.

Counseling for extent of surgery for thyroid disease should be patient centered and utilize all available risk factors. In this study, the presence of thyroiditis, higher preoperative TSH, or small remnant thyroid lobe were associated with the need for thyroid hormone supplementation. For patients with benign preoperative

indications for thyroidectomy, if thyroiditis or small remnant lobe is present counseling should include a higher likelihood of postoperative thyroid hormone supplementation. For patients with suspicious or malignant preoperative cytology counseling should include that a majority of patients will require thyroid hormone but there are fewer surgical complications and quality of life may be improved compared with total thyroidectomy. However, detection of recurrence may be delayed despite no difference in overall survival. Patients should be appropriately counseled that completion thyroidectomy may be recommended based on intermediate or high-risk pathology.

This study has several limitations, including the retrospective nature and single institution cohort. Our academic medical center is a tertiary care facility in the Midwest and thus our patient population is more homogeneous with 84% white patients which may limit generalizability of these findings to the general population. This study included a heterogeneous cohort of preoperative indications for thyroid lobectomy inclusive of nondiagnostic, benign, indeterminate, and suspicious or malignant cytology. Due to the heterogeneity of the group some subsets of the cohort were low volume which may have been underpowered to detect significant differences within the subset. Our patient population may also differ from the general population due to our underlying malignancy rates and

**Table 6**  
Clinical and pathologic factors independently associated with the need for postoperative thyroid hormone supplementation after thyroid lobectomy on multivariate logistic regression analysis.

	All	Euthyroid	Thyroid Hormone Supplementation	Multivariate Logistic Regression Analysis p-value
n	100	53	47	
Thyroiditis on pathology, n (%)	14	2 (14%)	12 (86%)	0.038
Final pathology benign, n (%)	74	46 (62%)	28 (38%)	0.001
Preoperative TSH mIU/L, mean (SD)	1.50 (1.04)	1.16 (SD 0.77)	1.88 (SD 1.17)	0.011
Remnant volume:body surface area, ml/m <sup>2</sup> , mean (SD)	3.37 (2.22)	3.72 (2.1)	2.99 (2.3)	0.017

institutional practices. Our malignancy rate for nondiagnostic cytology was 29% which is higher than the Bethesda criteria expected rate of 1–5%.<sup>2</sup> At our institution we utilize onsite cytology for adequacy so our overall nondiagnostic rates are very low. Patients have at least two attempts at biopsy before they are offered lobectomy for definitive diagnosis of a thyroid nodule with nondiagnostic cytology and therefore may have higher rates of malignancy in this group than the overall population rates of malignancy in all thyroid nodules. Additionally, our malignancy rate for patients with a thyroid nodule and benign cytology was 12%, this reflects both a thyroid cancer in the index biopsied nodule as well as a finding of a benign thyroid nodule with an incidental thyroid carcinoma in the specimen. These results are consistent with published rates of incidental thyroid carcinoma of 3–16%.<sup>30,31</sup> Because these patients had malignancy on final pathology despite it not being in the index nodule, they still require a TSH goal of <2 mIU/L.

Though rates of thyroid hormone supplementation after thyroid lobectomy are most dependent upon final pathology, preoperative counseling must depend on available information prior to surgery so we felt this was the ideal cohort for inclusion. Additionally, the two patients who underwent completion thyroidectomy were included in the analysis as patients requiring thyroid hormone supplementation after thyroid lobectomy. This was designated a priori as our overall goal was to provide data for clinicians to accurately counsel patients on their potential need for thyroid hormone supplementation following thyroid lobectomy at the initial preoperative evaluation. Since these patients who ultimately went on to have completion thyroidectomy will require lifelong thyroid hormone, our study group felt that it would be most appropriate to include them in this group based on our original intent to treat them with thyroid lobectomy only.

## Conclusions

In conclusion, the rate of thyroid hormone supplementation after thyroid lobectomy for benign preoperative cytology was 39%, for indeterminate preoperative cytology 44% and for suspicious or malignant preoperative cytology 67%. To be compliant with the 2015 ATA guidelines for differentiated thyroid carcinoma, 73% of patients with final pathology of thyroid carcinoma after thyroid lobectomy required postoperative thyroid hormone supplementation to maintain a TSH less than 2 mIU/L. Additional factors independently associated with thyroid hormone supplementation after thyroid lobectomy include thyroiditis, higher preoperative TSH, and smaller thyroid lobe remnant. It is important to counsel patients appropriately regarding the likelihood of thyroid hormone supplementation after thyroid lobectomy for benign, indeterminate, or malignant preoperative diagnosis. While avoidance of thyroid hormone supplementation may not be possible for most patients with differentiated thyroid carcinoma, further study is needed to assess the impact on quality of life for those treated with thyroid lobectomy or total thyroidectomy.

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