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A national study of postoperative thyroid hormone supplementation rates after thyroid lobectomy

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ABSTRACT

Background: The American Thyroid Association updated guidelines in 2015 to allow lobectomy for low-risk thyroid cancers. The objectives of this study were (1) to determine thyroid hormone supplementation rates after lobectomy and (2) to evaluate the effect of the American Thyroid Association guideline change on lobectomy and hormone supplementation rates among thyroid cancer patients.
Methods: The Merative MarketScan Databases was used to identify adult (≥age 18) patients who underwent thyroidectomy for benign nodules or thyroid cancer. The association between indication for surgery and postoperative thyroid hormone supplementation was examined using χ^2 analyses and multivariable logistic regression models. Among patients with thyroid cancer, lobectomy and hormone supplementation rates were compared in the periods before (2008–2015) and after the guideline change (2016–2019).
Results: Of the 81,926 patients identified, 33,756 (41.2%) underwent thyroid lobectomy, 45,104 (55.1%) underwent total thyroidectomy, and 3,066 (3.7%) underwent completion thyroidectomy. Patients who underwent lobectomy for malignancy were significantly more likely to require hormone supplementation (59.3% vs 39.4% [$P < .001$], adjusted odds ratio 2.34 [95% confidence interval 2.20–2.48]) compared to those with benign disease. Compared to the 2008 to 2015 period, the proportion of patients who underwent lobectomy for thyroid cancer was higher in the 2016 to 2019 period (34.3% vs 30.3%, $P < .001$), with fewer patients requiring completion thyroidectomy (25.6% vs 29.8%, $P < .001$) and thyroid hormone supplementation (56.9% vs 60.1%, $P = .04$).
Conclusion: The postoperative thyroid hormone supplementation rate was significantly higher in patients who had thyroid cancers compared to benign diseases. After the American Thyroid Association guidelines changed, lobectomy rates increased significantly without a concomitant increase in the completion of thyroidectomy.

Introduction

Thyroid nodules are very common, occurring in up to 68% of individuals in the general population.[1,2] Most thyroid nodules are benign and asymptomatic, but some may require surgical management due to compressive or cosmetic symptoms, hyperthyroidism, and/or the risk of malignancy. Thyroid lobectomy is often favored under these circumstances due to the potential for preserving thyroid function postoperatively. Unfortunately, some patients do not produce enough thyroid hormone to maintain normal thyroid function and require postoperative hormone supplementation. The incidence of clinical hypothyroidism after lobectomy for benign disease in the literature ranges from 9% to 49%, depending on the definition of hypothyroidism and the duration of follow-up.[3,4] Furthermore, there is a trend toward preserving thyroid function for a known malignancy as well. In 2015, the American Thyroid Association (ATA) released updated guidelines to consider thyroid lobectomy an acceptable operation for small, low-risk, well-differentiated thyroid cancers and to allow for more lenient targets for postoperative thyroid-stimulating hormone (TSH) suppression (TSH 0.5–2 mU/L).[1]

Appropriate patient preoperative counseling on the extent of surgery and postoperative management for benign, indeterminate,

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suspicious, or malignant indications for thyroid surgery should include an estimate of the need for postoperative thyroid hormone supplementation. Published rates of thyroid hormone supplementation after lobectomy are historically derived from single-institution studies of patients who underwent lobectomy for benign thyroid diseases.[3,4] More recent studies after the 2015 ATA guideline change include patients with thyroid cancers, which are still primarily single-institution studies.[5–8] The objectives of this study were (1) to determine the contemporary rate of postoperative thyroid hormone supplementation after lobectomy in a national patient cohort for both benign and malignant indications and (2) to evaluate the effect of the 2015 ATA guidelines on lobectomy and hormone supplementation rates among thyroid cancer patients.

Methods

Data source

The Merative MarketScan Commercial Claims and Encounters Database and the Medicare Supplemental and Coordination of Benefits Database (2008–2020) were used to identify adult (≥18 years old) patients who underwent thyroid resection for benign nodules or thyroid cancer. The MarketScan Database encompasses the largest convenience sample of patients with employer-provided health insurance, capturing health insurance claims on clinical services and expenditures in inpatient and outpatient settings and outpatient prescription drug spending. The databases include health data from approximately 350 payers covering more than 40 million insured patients annually, including active employees and early retirees with employer-sponsored Medicare fee-for-service plans. Because this study used preexisting, deidentified data, the Columbia University Institutional Review Board deemed it to be nonhuman subject research.

Patient selection

Thyroidectomy procedures were identified using Current Procedural Terminology (CPT) codes and included thyroid lobectomy (CPT 60220), total thyroidectomy (CPT 60240), and completion thyroidectomy (CPT 60260). The first encounter was considered the index procedure in patients with multiple encounters for the same procedure. Patients with claims for total thyroidectomy or completion thyroidectomy on the same day or within 7 days after the initial lobectomy claim were classified as total thyroidectomy, whereas those with lobectomy followed by completion thyroidectomy or total thyroidectomy more than 7 days apart were categorized as an initial lobectomy followed by a completion thyroidectomy. Only patients with continuous medical and pharmaceutical coverage from 3 months before and 18 months after the date of the index surgery were included.

Patient demographics

Patient demographic information included age, year of surgery, sex, indication for surgery, region (northwest, north-central, south, west, and unknown), and Metropolitan Statistical Area (MSA, non-MSA, unknown). Indications for surgery were determined with *International Classification of Diseases* (ICD) codes occurred on the same day or within 3 months before surgery and included thyroid nodules (ICD-9 241.0, 241.1, 241.9, 242.20, 242.21, 242.30, 242.31, ICD-10 E04.1, E04.2, E04.9, E05.10, E05.11, E05.20, E05.21) or thyroid cancer (ICD-9 193, ICD-10 C73). Patients with both diagnoses of thyroid nodule and thyroid cancer were classified as thyroid cancer. Patients with diagnoses other than thyroid nodules or thyroid cancer were excluded.

Thyroid hormone supplementation

Thyroid hormone supplementation was defined as a prescription filled for levothyroxine in the 18 months after surgery. Levothyroxine prescription was defined using National Drug Codes. In patients with at least 1 prescription for levothyroxine, temporary supplementation was defined as no levothyroxine prescription for at least 4 weeks before the 18-month follow-up endpoint. Patients with a levothyroxine prescription after 17 months were classified as requiring long-term hormone supplementation.

Statistical analysis

Patient demographics, stratified by benign nodule and thyroid cancer, were compared across types of surgery using χ^2 analysis. For patients who underwent thyroid lobectomy, the proportion of patients who required thyroid hormone supplementation after surgery for benign nodules and thyroid cancer were compared using χ^2 analyses. Multivariable logistic regression models were then used to assess the association between the indication for surgery and the need for postoperative thyroid hormone supplementation. The model included indication for surgery, age, sex, year of surgery, MSA, and region. Patients with a levothyroxine prescription in the 3 months before surgery were excluded. Among those patients who required postoperative thyroid hormone supplementation, the proportion of patients who required long-term supplementation (ie, hormone supplementation beyond the end of the 18-month follow-up period) was also compared to patients who required short-term supplementation.

To examine the lobectomy trends over time, the proportion of patients who underwent initial lobectomy was plotted over time, stratified by indication for surgery. Among patients with a thyroid cancer diagnosis, the effect of the ATA guideline change was assessed using χ^2 analyses to compare the proportions in the period before the guideline change (2008–2015) to after the guideline change (2016–2019). To evaluate the change in lobectomy rates, the proportion of patients who underwent lobectomy was compared, and, for this analysis, patients who underwent completion lobectomy after an initial lobectomy were included in the lobectomy group for intent-to-treat analysis of the trend. Among this group of patients who underwent initial lobectomy, the proportion of patients requiring subsequent completion lobectomy was also evaluated using χ^2 analyses. To evaluate the change in hormone supplementation rates, the proportion of patients requiring levothyroxine supplementation 18 months after only lobectomy was compared. Finally, multivariable logistic regression models were constructed to adjust for indications for surgery, age, sex, year of surgery, MSA, and region. All tests of statistical significance were 2-sided with $\alpha = .05$. All statistical analyses were performed in SAS Studio 3.71 (SAS Institute, Cary, NC).

Results

Patient characteristics

A total of 81,926 patients underwent thyroidectomy from 2008 to 2019, of which 33,756 (41.2%) underwent thyroid lobectomy, 45,104 (55.1%) underwent total thyroidectomy, and 3,066 (3.7%) underwent lobectomy followed by completion thyroidectomy (Table I).

Table I
Patient demographics

	Benign nodule				Thyroid cancer			
	Lobectomy *N* = 27,452 (51.3%)	Completion thyroidectomy *N* = 510 (1%)	Total thyroidectomy *N* = 25,510 (47.7%)	*P* value	Lobectomy *N* = 6,304 (22.2%)	Completion thyroidectomy *N* = 2,556 (9%)	Total thyroidectomy *N* = 19,594 (68.9%)	*P* value
Age				< .001				< .001
18–30	1,733 (57.2%)	38 (1.3%)	1,260 (41.6%)		401 (19.3%)	227 (10.9%)	1,447 (69.7%)	
31–40	4,408 (53.6%)	110 (1.3%)	3,701 (45%)		1,046 (21.5%)	510 (10.5%)	3,318 (68.1%)	
41–50	6,944 (50.7%)	154 (1.1%)	6,610 (48.2%)		1,579 (21.5%)	673 (9.2%)	5,101 (69.4%)	
51–60	8,752 (50.1%)	150 (0.9%)	8,563 (49%)		1953 (22.3%)	783 (8.9%)	6,032 (68.8%)	
61–70	3,905 (49.8%)	41 (0.5%)	3,890 (49.6%)		905 (23.8%)	269 (7.1%)	2,622 (69.1%)	
70+	1,710 (53.2%)	17 (0.5%)	1,486 (46.2%)		420 (26.4%)	94 (5.9%)	1,074 (67.6%)	
Sex				< .001				< .001
Male	5,198 (59.4%)	96 (1.1%)	3,452 (39.5%)		1,527 (23.5%)	687 (10.6%)	4,271 (65.9%)	
Female	22,254 (49.8%)	414 (0.9%)	22,058 (49.3%)		4,777 (21.7%)	1,869 (8.5%)	15,323 (69.7%)	
Year of Surgery				< .001				< .001
2008	2,367 (54.9%)	55 (1.3%)	1,890 (43.8%)		492 (23%)	171 (8%)	1,475 (69%)	
2009	3,278 (53.1%)	60 (1%)	2,834 (45.9%)		685 (23.7%)	287 (9.9%)	1,923 (66.4%)	
2010	3,336 (51.9%)	66 (1%)	3,028 (47.1%)		701 (21.2%)	313 (9.5%)	2,286 (69.3%)	
2011	3,379 (51.6%)	61 (0.9%)	3,107 (47.5%)		693 (20.8%)	267 (8%)	2,366 (71.1%)	
2012	2,805 (49.5%)	53 (0.9%)	2,814 (49.6%)		637 (21.1%)	274 (9.1%)	2,115 (69.9%)	
2013	2,381 (47%)	58 (1.1%)	2,626 (51.8%)		538 (19.5%)	251 (9.1%)	1,964 (71.3%)	
2014	2,200 (49.4%)	37 (0.8%)	2,219 (49.8%)		500 (19.6%)	244 (9.6%)	1,803 (70.8%)	
2015	2,097 (50.1%)	36 (0.9%)	2,049 (49%)		520 (21.3%)	219 (9%)	1,706 (69.8%)	
2016	1,826 (50.9%)	31 (0.9%)	1,729 (48.2%)		486 (24.2%)	161 (8%)	1,364 (67.8%)	
2017	1,711 (53.9%)	23 (0.7%)	1,442 (45.4%)		423 (24%)	171 (9.7%)	1,167 (66.3%)	
2018	1,440 (53.4%)	23 (0.9%)	1,236 (45.8%)		395 (25.6%)	142 (9.2%)	1,008 (65.2%)	
2019	632 (53.8%)	7 (0.6%)	536 (45.6%)		234 (33.1%)	56 (7.9%)	417 (59%)	
Region				< .001				< .001
Northeast	4,339 (53.9%)	88 (1.1%)	3,622 (45%)		1,558 (23.7%)	610 (9.3%)	4,399 (67%)	
North Central	6,628 (54.1%)	99 (0.8%)	5,528 (45.1%)		1,530 (23.1%)	615 (9.3%)	4,478 (67.6%)	
South	12,138 (47.4%)	239 (0.9%)	13,252 (51.7%)		2,208 (20.8%)	914 (8.6%)	7,485 (70.6%)	
West	4,071 (57.9%)	77 (1.1%)	2,882 (41%)		953 (21.7%)	394 (9%)	3,052 (69.4%)	
Unknown	276 (54.2%)	7 (1.4%)	226 (44.4%)		55 (21.3%)	23 (8.9%)	180 (69.8%)	
MSA				.084				<.001
Non-MSA	4,395 (52.1%)	73 (0.9%)	3,964 (47%)		884 (23.3%)	362 (9.5%)	2,553 (67.2%)	
MSA	22,223 (51.1%)	425 (1%)	20,846 (47.9%)		5,203 (21.8%)	2,121 (8.9%)	16,539 (69.3%)	
Unknown	834 (53.9%)	12 (0.8%)	700 (45.3%)		217 (27.4%)	73 (9.2%)	502 (63.4%)	

MSA, Metropolitan Statistical Area.

Indication for surgery

Of the 33,756 patients who underwent thyroid lobectomy, 27,452 (81.3%) did so for benign disease and 6,304 (18.7%) for malignancy. Of the 45,104 patients who underwent total thyroidectomy, 25,510 (56.6%) had benign disease, and 19,594 (43.4%) had malignancy. Finally, of the 3,066 (3.7%) who underwent lobectomy followed by completion thyroidectomy, 510 (16.6%) had benign disease, and 2,556 (83.4%) had malignancy (Table I).

Thyroid hormone supplementation

Of the 33,756 patients who underwent thyroid lobectomy, 29,708 patients were not taking levothyroxine before surgery. Of these, 12,797 (43.1%) patients filled at least 1 prescription for levothyroxine in the 18 months after surgery (Table II). Compared to patients who had benign indications for surgery, patients with malignant indications were significantly more likely to require hormone supplementation (59.3% vs 39.4% [$P < .001$], adjusted odds ratio [aOR] 2.34 [95% CI 2.20–2.48]). At the end of the 18-month follow-up period, 10,661 (83.3%) patients remained on levothyroxine supplementation. Patients with thyroid cancer were also less likely to wean off supplementation compared to patients with benign thyroid nodules (13.3% vs 17.9% [$P < .001$], aOR 0.73 [95% CI 0.65–0.82]).

Lobectomy trends over time

The proportion of patients who underwent lobectomy over the study period was plotted against time, stratified by indication for surgery (Figure). Compared to the period before the guideline change (2008–2015), there were no visually obvious changes in the proportion of lobectomy or completion thyroidectomy in the period after the guideline change (2016–2019) among patients who underwent surgery for benign thyroid nodules. However, among patients who underwent surgery for thyroid cancer, there was an

Table II
Thyroid hormone supplementation after lobectomy

	Benign nodule (*N* = 24,208)	Thyroid cancer (*N* = 5,500)	*P* value	aOR (95% CI)
Hormone supplementation	9,537 (39.4%)	3,260 (59.3%)	< .001	2.34 (2.20–2.48)
Temporary supplementation	1,703 (17.9%)	433 (13.3%)	< .001	0.73 (0.65–0.82)
Long-term supplementation	7,834 (82.1%)	2,827 (86.7%)		Referent

aOR, adjusted odds ratio.

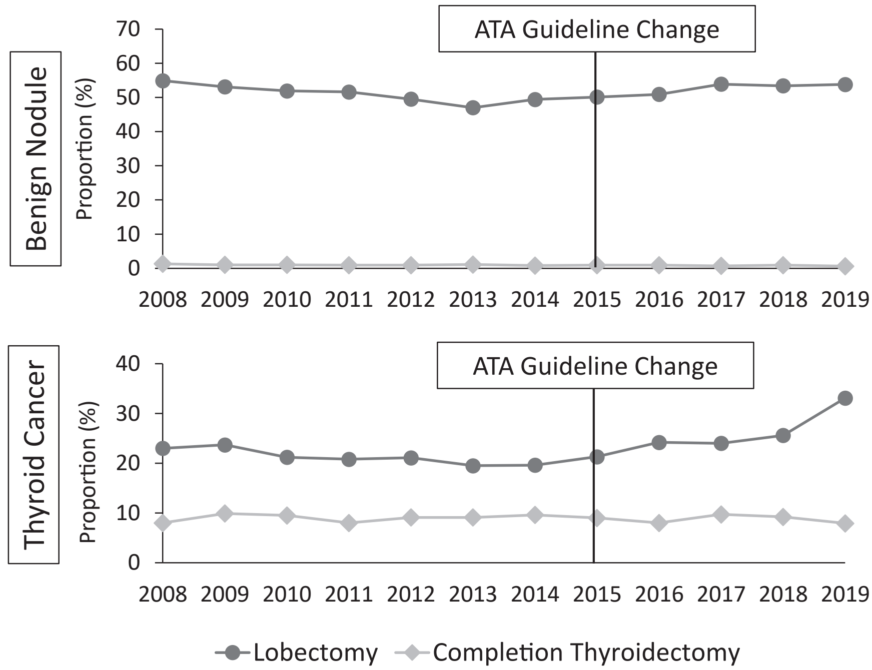

Figure. Lobectomy trends over time for benign nodule and thyroid cancer.

increase in the proportion of lobectomy performed and a slight decrease in the proportion of completion thyroidectomy performed after 2015.

To study this trend in thyroid cancer patients statistically, the proportions of lobectomy, completion thyroidectomy, and hormone supplementation were compared between the 2 periods. Compared to the 2008 to 2015 period, the proportion of patients who underwent lobectomy for thyroid cancer was higher in the 2016–2019 period (34.3% vs 30.3% [P < .001], aOR 1.19 [95% CI 1.12–1.27]). Among patients who underwent lobectomy, fewer patients required a completion thyroidectomy (25.6% vs 29.8% [P < .001], aOR 0.79 [95% CI 0.70–0.88]) and fewer patients who required thyroid hormone supplementation (56.9% vs 60.1% [P = .04], aOR 0.88 [95% CI 0.77–0.997]) in the 2016–2019 period compared to the 2008–2015 period (Table III).

Discussion

Understanding contemporary rates of thyroid hormone supplementation after lobectomy is important for appropriate preoperative patient counseling regarding the extent of surgery and postoperative management of benign, indeterminate, suspicious, or malignant diseases of the thyroid. The present study found that 43.1% of patients required thyroid hormone supplementation after lobectomy, concordant with prior studies. Further, this study demonstrated that the need for hormone supplementation was significantly higher for patients with thyroid cancer (59.3%) compared to benign nodules (39.4%). Similarly, Wilson et al showed that 73% of patients with malignancy on final pathology required thyroid hormone supplementation compared with 38% of patients with benign pathologies.[5]

Although almost 60% of patients with thyroid cancers required hormone supplementation in this study, this figure may underestimate the proportion of patients who should be on hormone supplementation in accordance with ATA guidelines on postoperative TSH suppression. TSH levels were not available in the MarketScan Database, but prior reports have found that rates of postoperative TSH levels >2 mU/L ranged from 73% to 90% after lobectomy.[6–8] Schumm et al demonstrated that 84% of patients with low-risk thyroid cancer treated with lobectomy had TSH values >2 mU/L, but only 63% of patients were started on levothyroxine postoperatively.[6] As the potential for avoidance of thyroid hormone supplementation is purportedly the main advantage of lobectomy over total thyroidectomy for small, low-risk thyroid cancers, it would be important to counsel patients appropriately that the likelihood of thyroid medication avoidance may not be as high as previously thought.

The second aim of the present study was to examine the effect of the 2015 ATA guideline change on lobectomy rates for patients with thyroid cancers. As expected, there was a significant increase in lobectomy rates from 30.3% in the period before 2015 to 34.3% in the period after 2015. Furthermore, the rates of completion thyroidectomy also decreased after the guideline change, likely representing the patients who underwent initial lobectomy for indeterminate or suspicious nodules with final pathology consistent with thyroid malignancies who would have required completion thyroidectomies according to prior guidelines. These findings are consistent with a National Surgical Quality

Table III
Lobectomy and hormone supplementation in thyroid cancer patients before and after 2015 ATA guideline change

	Before (2008–2015)	After (2016–2019)	P value	aOR (95% CI)
Lobectomy	6,792/22,430 (30.3%)	2,068/6,024 (34.3%)	< .001	1.19 (1.12–1.27)
Completion thyroidectomy	2,026/6,792 (29.8%)	530/2,068 (25.6%)	< .001	0.79 (0.70–0.88)
Hormone supplementation	2,490/4,146 (60.1%)	770/1,354 (56.9%)	.04	0.88 (0.77–0.997)

aOR, adjusted odds ratio.

Improvement Program (2015–2017) study, which also found an increase in lobectomy rates for patients with cancer from 17.3% to 22.0% ($P < .001$) without a corresponding increase in the completion thyroidectomy rate ($P = .213$).[9] Similar trends are observed in recent studies using cancer registries, including 2 recent studies using the National Cancer Database (2015–2019) and Surveillance, Epidemiology, and End Results (2015–2018) registries. Interestingly, both studies found a higher baseline rate of lobectomy as well as smaller increases in lobectomy rates for small tumors—Gordon et al (Surveillance, Epidemiology, and End Results) found that lobectomy rates increased from 22.8% to 29.2% in tumors <1 cm, 6.8% to 18.9% for tumors 1 to <2 cm, and 6.6% to 16.0% in tumors 2 to <4 cm, and Pasqual et al (National Cancer Database) found that lobectomy rates increased from 23% to 30% for tumors <1 cm, from 9% to 20% for tumors 1 to <2 cm, and from 11% to 18% for tumors 2 to <4 cm.[10,11] Although our data lacked granular information regarding tumor size, the higher baseline and smaller increase in lobectomy rates are likely representative of the patient population in the MarketScan Database, which consists of privately insured patients who are more likely diagnosed early with smaller cancers.

Interestingly, the rates of thyroid hormone supplementation also decreased in the period after the ATA guideline change from 60.1% to 56.9%. This may represent the more lenient TSH suppression recommendations in the 2015 guidelines. Before 2015, the ATA guidelines recommended total thyroidectomy and postoperative TSH suppression to undetectable levels for even low-risk thyroid cancers. Although lobectomy was not recommended for low-risk thyroid cancers, it is possible that patients and physicians who opted for lobectomy targeted an undetectable TSH postoperatively to reduce the risk of recurrence.

Study limitations

This study has several limitations. First, the study was retrospective in nature; thus, the results are correlative, and causality cannot be determined. Second, although some sociodemographic factors were available in MarketScan, the data set lacked granular details such as race/ethnicity, TSH levels, and other known factors affecting the need for postoperative hormone supplementation. The study's results were also limited by the accuracy of CPT and ICD codes and the potential for coding errors. Finally, MarketScan consists of voluntary participation in employer-provided health insurance and may not be generalizable to other populations, such as uninsured patients. Nevertheless, this study is the first study evaluating the postoperative need for hormone supplementation after lobectomy for both benign and malignant indications in a large cohort of commercially insured patients across the United States, unlike prior studies that relied primarily on single-institution data.

In conclusion, in a national study of patients who underwent lobectomy, the postoperative thyroid hormone supplementation rate was 43.1% across the entire cohort but significantly higher in patients who had thyroid cancers compared to benign disease. After the ATA guideline change in 2015 that de-escalated management for small, low-risk thyroid cancers, the proportion of patients undergoing lobectomy compared to total thyroidectomy increased significantly without a concomitant increase in completion thyroidectomy.

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Conflict of interest/Disclosure

The authors have no conflicts of interests or disclosures to report.

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