Published in final edited form as:

Ann Surg. 2013 August ; 258(2): 354–358. doi:10.1097/SLA.0b013e31826c8915.

The Relationship between Extent of Thyroid Cancer Surgery and Use of Radioactive Iodine

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Abstract

Objective—To determine the relationships between surgeon recommendations for extent of resection and radioactive iodine use in low-risk thyroid cancer.

Background—There has been an increase in thyroid cancer treatment intensity; the relationship between extent of resection and medical treatment with radioactive iodine remains unknown.

Methods—We randomly surveyed thyroid surgeons affiliated with 368 hospitals with Commission on Cancer accredited cancer programs. Survey responses were linked to the National Cancer Database. The relationship between extent of resection and the proportion of AJCC Stage I well-differentiated thyroid cancer patients treated with radioactive iodine after total thyroidectomy was assessed with multivariable weighted regression controlling for hospital and surgeon characteristics.

Results—The survey response rate was 70% (560/804). Surgeons who recommend total thyroidectomy over lobectomy for subcentimeter unifocal thyroid cancer were significantly more likely to recommend prophylactic central lymph node dissection for thyroid cancer regardless of tumor size ($P<0.001$). They were also more likely to favor radioactive iodine in patients with intrathyroidal unifocal cancer ≤ 1 cm ($P=0.001$), 1.1 – 2 cm ($P=0.004$), as well as intrathyroidal multifocal cancer ≤ 1 cm ($P=0.004$). In multivariable analysis, high hospital case volume, fewer surgeon years of experience, general surgery specialty, and preference for more extensive resection were independently associated with greater hospital-level use of radioactive iodine for Stage I disease.

Conclusion—In addition to surgeon experience and specialty, surgeons' tendency to perform more extensive thyroid resection is associated with greater use of radioactive iodine for Stage I thyroid cancer.

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Conflicts of Interest:

The authors have no conflicts of interests to disclose.

Introduction

The incidence of low-risk well-differentiated thyroid cancer is climbing with an estimated 56,460 new cases of thyroid cancer in 2012.(1–3) Treatment for thyroid cancer consists of resection, often followed by a therapeutic dose radioactive iodine. Total thyroidectomy is associated with improved survival in patients with tumor size ≥ 1 cm, but the benefit of total thyroidectomy compared to lobectomy in tumors less than 1 cm is unclear.(4, 5) Similarly, radioactive iodine after total thyroidectomy improves outcome in iodine-avid advanced stage disease, but the benefit in low-risk disease has not been demonstrated. (6, 7) The most recent clinical guidelines support thyroid lobectomy for tumors under 1 cm in size and recommend no radioactive iodine for intrathyroidal tumors ≥ 1 cm assuming there are no additional high risk features.(8)

Despite absence of clear benefit of aggressive treatment of low-risk disease,(9) in the United States there has been an intensification of treatment, with increasing rates of total thyroidectomy and greater use of radioactive iodine for low-risk thyroid cancer.(10, 11) The explanation for the rise in thyroid cancer treatment intensity remains unknown. Although we know there is wide variation in thyroid cancer management, with factors other than disease severity influencing radioactive iodine use,(11) the relationship between extent of resection and subsequent medical treatment with radioactive iodine remains unclear. It is not known if a treatment cascade exists, whereby select patients undergo more extensive resection followed by more aggressive medical management, or if more extensive resection decreases the likelihood of residual disease and thus reduces the perceived need for adjuvant therapy with radioactive iodine.

To understand the relationship between extent of surgery and radioactive iodine use in low-risk disease, we used surgeon surveys linked to the National Cancer Database. We hypothesized that in hospitals reporting a higher proportion of low-risk patients treated with radioactive iodine, surgeons would be more likely to perform extensive thyroid surgery and also favor greater use of radioactive iodine for low-risk disease.

Methods

Data Source and Study Population

Between 2004–2008 1,282 Commission on Cancer-accredited (CoC) cancer programs reported treating thyroid cancer patients to the National Cancer Data Base (NCDB), a joint project of the American College of Surgeons and the American Cancer Society. We selected the 1,159 hospitals that reported to the American College of Surgeons' CoC for four of the five specified years. We eliminated the 235 hospitals that treated less than seven thyroid cancer patients a year. We then randomly sampled the remaining hospitals across quartiles of case volume and radioactive iodine use. Exemption was granted for this study by the University of Michigan Institutional Review Board.

We contacted the hospital registrar at the 589 hospitals and searched hospital websites to identify the surgeons who performed the majority of the thyroid cancer procedures at each hospital. We identified 850 surgeons affiliated with the 589 hospitals. The Dillman survey method(12) was used to encourage survey response. This method consists of (1) an initial mailing of an introductory letter, the survey instrument, a postage-paid return envelope, and a gift, (2) a postcard reminder, (3) a second survey with postage-paid return envelope to all non-responders. Data from the survey were de-identified, scanned and confirmed.

Measures

The survey instrument was created and reviewed by a multidisciplinary group of providers, which included both health services researchers with expertise in survey design and specialists from the fields of endocrinology, surgery, and nuclear medicine. The instrument contained both survey questions and clinical vignettes. The instrument was piloted in a multidisciplinary cohort of surgeons attending the Frederick A. Collier Surgical Society Meeting in Ann Arbor, Michigan. After piloting, additional revisions were made to the survey instrument prior to survey administration.

There were two survey items from the same clinical vignette on total thyroidectomy versus lobectomy for subcentimeter intrathyroidal unifocal disease. Those surgeons who recommended total thyroidectomy for both items were classified as favoring “more extensive” resection and those who recommended lobectomy for either were classified as favoring “less extensive” resection. The results of the analysis did not change when we classified surgeons as preferring extensive resection if the surgeon selected total thyroidectomy for either survey item.

The de-identified surgeon responses were linked to the NCDB. Details on hospital case volume and hospital use of radioactive iodine for AJCC Stage I well-differentiated thyroid cancer patients were obtained from the NCDB. Since radioactive iodine is not recommended after thyroid lobectomy, we evaluated radioactive iodine use only in those patients undergoing total thyroidectomy, thus eliminating the likelihood that lower radioactive iodine use in select hospitals was directly related to more frequent use of thyroid lobectomy. The dependent variable was the proportion of Stage I thyroid cancer patients treated with radioactive iodine at each hospital, obtained from the NCDB. Since hospital case volume is known to correlate with radioactive iodine use,(11) this independent variable also was obtained from the NCDB. As described by Haymart et al. (10) hospitals were divided into quintiles based on thyroid cancer case volume. As previously mentioned in Data Source and Study Population, for this study there was exclusion of hospitals seeing less than seven cases a year, resulting in the following four case volume categories: low (7–11 thyroid cancer cases/year), low-moderate (12–19 thyroid cancer cases/year), moderate (20–34 thyroid cancer cases/year), and high (≥ 35 thyroid cancer cases/year). All other independent variables, including practice setting, number of years in practice, specialty, and recommendation for total thyroidectomy versus lobectomy for subcentimeter unifocal intrathyroidal thyroid cancer, were obtained from the survey data. Since surgeons could select more than one practice setting, an algorithm previously described by Alderman et al. was used.(13) If academic tertiary care center was selected (including when community and private practice were selected) then the practice setting was classified as academic. Similarly, when community based academic affiliate was selected (including when private practice was selected) then the practice setting was classified community. If only private practice was selected, then the practice setting was classified as private practice.

Statistical Analyses

The majority of hospitals had only one surgeon surveyed; but when more than one surgeon responded from the same hospital, the surveys were weighted by reported surgeon case volume. Surgeon case volume was categorized as 1, 5, 25, 50, or 100 based on the lower limit of the selected thyroid cancer case volume range per year (for the 0–4 interval, the assigned value was 1). The analysis was then repeated with the surgeon case volume categorized 1–5. The findings did not differ when case volume was categorized as 1, 5, 25, 50, or 100 versus 1–5.

Univariate analysis was used to compare surgeons who preferred total thyroidectomy to lobectomy. The surgeons who favored more extensive resection were compared across the following four domains: thyroid procedure volume, surgeon training/continuing education, recommendations for prophylactic central lymph node dissection, and preference for radioactive iodine.

Multivariable weighted regression controlling for hospital case volume, practice setting, surgeon years of experience, and surgeon specialty was then used to analyze the relationship between extent of resection and the proportion of Stage I well-differentiated thyroid cancer patients treated with radioactive iodine after total thyroidectomy. Surgeon profiles that were clinically interesting were defined using combinations of covariates (e.g., surgeons favoring more extensive surgery, <10 years of experience, and general surgery specialty; surgeons favoring less extensive surgery, >10 years of experience, and endocrine surgery specialty, etc.). Based on the regression model, for these surgeon profiles we predicted their hospital's use of radioactive iodine for Stage I thyroid cancer.

All statistical tests were performed using SAS 9.2 (SAS Institute Inc., Cary, North Carolina). Two sided tests were used with $P < 0.05$ considered statistically significant.

Results

Forty-six of the 850 surveyed surgeons were found to be ineligible because they were deceased, ill, retired, not currently treating thyroid cancer patients, or we had an incorrect mailing address. Of the 804 response eligible surgeons, 560 (70%) completed the survey. The 560 surgeons represent 368 of the sampled hospitals (62%). Of the 368 hospitals, 56% had one surgeon surveyed and 93% had two or fewer surveyed surgeons.

Table 1 shows the respondent characteristics. The mean surgeon age was 51 years and the surgeons had an average of 19 years in practice. The majority of surgeons were white males (83% and 90% respectively) with 39% general surgeons, 9% endocrine surgeons, 44% otolaryngologists, and 8% in another surgical specialty.

Of the 560 surgeons, 340 (61%) favored total thyroidectomy for subcentimeter unifocal intrathyroidal thyroid cancer and 218 (39%) favored lobectomy. Between the surgeons favoring more versus less extensive resection, there was no statistical difference in reported thyroid procedure case volume. In addition, there was no statistically significant difference in training/continuing education including type of facility for residency training, likelihood of training with a thyroid surgeon, professional membership, number of national meetings attended per year, or likelihood of reading the American Thyroid Association (ATA) or National Comprehensive Cancer Network (NCCN) clinical guidelines.

There was a statistically significant difference in the likelihood of recommending prophylactic central lymph node dissection and radioactive iodine. Of those who recommended more extensive resection, 27% recommended prophylactic central lymph node dissection regardless of tumor size, whereas only 6% of those who recommended less extensive surgery recommended prophylactic central lymph node dissection ($P < 0.001$). Similarly, 44% versus 30% of those who recommended more versus less extensive resection recommended prophylactic central lymph node dissection specifically in patients with tumor size > 1 cm ($P = 0.002$) (Figure 1). For intrathyroidal unifocal thyroid cancer > 1 cm, although there was a spectrum of five possible answers: "almost none," "about 1/3," "about 1/2," "about 2/3," "almost all," most surgeons indicated that almost none of the patients should receive radioactive iodine but the proportion choosing "almost none" was less for those who favored more versus less extensive resection (70% versus 82%, $P = 0.001$).

As shown in Figure 2a, there was a bimodal distribution with regard to preference for radioactive iodine for intrathyroidal multifocal thyroid cancer ≤ 1 cm. Of those who favored more extensive resection, 40% indicated that almost all patients with multifocal intrathyroidal sub-centimeter disease should receive radioactive iodine treatment whereas 27% of the surgeons who favored less extensive resection, indicated almost all should receive radioactive iodine treatment. Of those who favored more extensive resection 26% indicated almost none should receive radioactive iodine and in contrast, 35% of those who favored less extensive surgery indicated almost none should receive radioactive iodine ($P=0.004$). As shown in Figure 2b, for the vignette describing a 30 year old woman with a 1.9 cm papillary thyroid cancer without extrathyroidal extension, capsular invasion, vascular invasion, known lymph node involvement or positive margins, 40% of those who favored more extensive resection strongly favored radioactive iodine treatment, and 30% were moderately in favor of radioactive iodine treatment. Those who favored less extensive resection were less likely to favor radioactive iodine treatment—as 23% strongly favored, and 39% moderately favored, radioactive iodine treatment ($P=0.006$). In contrast, there was no significant difference between surgeons who prefer more versus less extensive resection with regard to preference for radioactive iodine in patients with microscopic extrathyroidal extension ($P=0.149$), gross extrathyroidal extension ($P=0.096$), or distant metastases ($P=0.157$).

In multivariable analysis (Table 2) evaluating hospital characteristics, surgeon characteristics, and resection recommendations (total thyroidectomy versus lobectomy for subcentimeter unifocal disease), high hospital case volume ($P<0.001$), less surgeon years in practice ($P=0.033$), general surgery specialty ($P=0.036$), and recommendation for more extensive resection ($P=0.010$) were associated with a significantly higher proportion of patients at the hospital receiving radioactive iodine for stage I thyroid cancer.

Figure 3 shows that the greatest hospital-level use of radioactive iodine for Stage I thyroid cancer (52%) was associated with a hospital with a general surgeon who has less than 10 years of experience and recommends more extensive resection. In contrast, the lowest hospital-level radioactive iodine use for Stage I thyroid cancer (39%) was associated with a hospital with an endocrine surgeon who has over 10 years of experience and recommends less extensive resection ($P<0.001$).

Discussion

The results of this study improve our understanding of the relationship between surgeon characteristics and hospital-level radioactive iodine use. Surgeons who recommend total thyroidectomy over lobectomy for subcentimeter unifocal thyroid cancer were more likely to favor prophylactic central lymph node dissection and use of radioactive iodine for patients with low-risk disease. High hospital case volume, fewer surgeon years of experience, general surgery specialty, and preference for more extensive resection each were independently associated with greater hospital-level use of radioactive iodine for stage I disease.

Previous work has found that health care providers can differ in treatment intensity, with some providers consistently recommending more intensive therapy than their peers. (14) The difference we demonstrate in surgeon practice intensity is similar to what has been identified in other settings. (14–16) Surgeons who recommend total thyroidectomy over lobectomy for subcentimeter unifocal papillary thyroid cancer are more likely to recommend prophylactic central lymph node dissection and to favor use of radioactive iodine for low-risk disease. These surgeon treatment recommendation preferences appear to influence

hospital treatment patterns, or are at least associated with broader provider preferences at those facilities.

Even though the most recent clinical guidelines support use of lobectomy for unifocal tumors under 1 cm in size and recommend against radioactive iodine for intrathyroidal tumors ≥ 1 cm regardless of whether they are unifocal or multifocal,(8) 61% of surveyed surgeons favored total thyroidectomy for subcentimeter intrathyroidal thyroid cancer and a substantial proportion favor radioactive iodine for intrathyroidal multifocal tumors ≥ 1 cm. We believe that this discrepancy from the expected is because despite guideline recommendations, the optimal extent of resection and appropriate use of radioactive iodine in low-risk thyroid cancer remains a controversial topic.(17–27) In the setting of this controversy, studies have demonstrated increasing treatment intensity, including more extensive thyroid cancer resections and greater use of radioactive iodine.(10, 11, 28) It has previously been shown that more extensive resection can identify more disease, increase a patient's stage, and thus lead to more radioactive iodine use.(29, 30) However, in this study, we controlled for upstaging by only evaluating radioactive iodine use for Stage I disease. Stage I thyroid cancer is a heterogeneous population, but, by allowing surgeons to address the same vignettes and survey questions there is in essence a case-mix adjustment. Surgeons could “treat” the same patients. Inconsistent with the theory that increased radioactive iodine use is solely related to more extensive resection detecting more disease, we found that surgeons who recommended more extensive resection were not necessarily more likely to favor radioactive iodine in high-risk disease. They were more likely to favor radioactive iodine use in the patients with small intrathyroidal tumors.

As described above, our data suggest that surgeon treatment style influences downstream medical management. Although not assessed in this study, the relationship we identified between greater hospital-level use of radioactive iodine and both general surgeon specialty and less surgeon years of experience may be related to lack of surgeon confidence in adequacy of surgical resection leading to greater use of adjuvant treatment with radioactive iodine by either the surgeon or the surgeons' colleagues. It is plausible that surgeons with less experience managing thyroid cancer patients would have less first hand familiarity with disease prognosis, less confidence in the role of their surgery as primary management, and less knowledge on the indications for radioactive iodine.

Since thyroid cancer is often managed in a multidisciplinary setting, decisions on radioactive iodine administration may involve surgeons, endocrinologists, and nuclear medicine physicians. The results of this study imply that either the surgeons' views are influential in the radioactive iodine decision-making process or represent the views of colleagues co-managing thyroid cancer patients.

Strengths of this study include a novel research question, a large sample size of surgeons and hospitals, and a high response rate among surgeons.

This study also has limitations. First, similar to other survey studies, there is a risk for non-response bias. Second, even though clinical vignettes and survey questions are commonly used to assess provider practice patterns in the setting of other malignancies,(13, 14, 16, 31, 32) we cannot be certain provider report is consistent with provider treatment behavior. Third, since we are unable to control for patient selection to hospitals, it is possible the relationship between hospital case volume and radioactive iodine use may reflect patient selection to specific hospitals. Finally, we cannot be certain the surveyed surgeons treated all patients at the affiliated hospital. In an attempt to address this potential limitation, we requested the hospital registrars provide us with the names of the highest volume thyroid surgeons. In addition, if more than one surgeon was surveyed from the same hospital, we

weighted the answers according to surgeon reported case volume as described in the Methods section above.

Despite these limitations, this study links granular survey data to a large national cancer registry. Through this method we were able to obtain details on the role of surgeon characteristics in hospital-level treatment patterns. Patients treated at hospitals with surgeons who have a tendency to perform more extensive thyroid surgery are more likely to receive radioactive iodine even in cases where the benefit of radioactive iodine has not been demonstrated. This study illustrates the interwoven relationship between the surgical and medical management of thyroid cancer and emphasizes the role of providers in treatment decisions. The results of this study may lead to future studies on thyroid cancer management and improve guideline dissemination. Ultimately, the goal is to streamline thyroid cancer care with treatment tailored to disease severity.

Acknowledgments

Source of Funding:

This study was funded by 1K07CA154595-01 to Dr. Haymart from the National Institutes of Health, the University of Michigan Comprehensive Cancer Center Idea Award, the Cancer Surveillance and Outcomes Research Team (CanSORT) Pilot of Feasibility Fund, and the Elizabeth Caroline Crosby Fund.

The authors would like to thank Brittany Gay, Barbara Salem, and Ashley Gay for their work in data collection and processing. Cornell University Survey Research Institute scanned the surveys for data file. This study was funded by 1K07CA154595-01 to Dr. Haymart from the National Institutes of Health, the University of Michigan Comprehensive Cancer Center Idea Award, the Cancer Surveillance and Outcomes Research Team (CanSORT) Pilot of Feasibility Fund, and the Elizabeth Caroline Crosby Fund.

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Recommendations for prophylactic central lymph node dissection

Figure 1.

Surgeons who recommend more extensive resection (total thyroidectomy instead of lobectomy for sub-centimeter unifocal papillary thyroid cancer) are more likely to recommend prophylactic central lymph node dissection regardless of tumor size ($P < 0.001$) and when tumor size is > 1 cm ($P = 0.002$).

Proportion of patients with intrathyroidal multifocal ≤ 1 cm thyroid cancer that RAI is favored

How strongly RAI is favored in 1.9 cm papillary thyroid cancer without lymph nodes

Figure 2.

Figure 2a. Surgeons who recommend more extensive resection are significantly more likely to favor radioactive iodine in “almost all” patients with intrathyroidal multifocal thyroid cancer ≤ 1 cm ($P=0.004$).

Figure 2b. Surgeons who recommend more extensive resection are significantly more likely to be “strongly for” radioactive iodine treatment in a 30 year old woman who undergoes total thyroidectomy for a 1.9 cm papillary thyroid cancer ($P=0.006$). In the clinical vignette, she does not have extrathyroidal extension, capsular invasion, vascular invasion, known lymph node involvement or positive margins.

Figure 3.

This bar graph demonstrates the impact of different combinations of surgeon characteristics (i.e. years of experience + preference for extent of surgery + specialty) on hospital-level radioactive iodine use ($P < 0.001$).

Table 1

Respondent Characteristics (N=560 surgeons)

	No. (%)
Mean age $\pm$ SD	51 $\pm$ 9
Mean years in practice $\pm$ SD	19 $\pm$ 10
Sex	
Male	499 (90%)
Female	58 (10%)
Race	
White	453 (83%)
Black	9 (2%)
Am. Indian/Alaska Native	1 (0%)
Asian	67 (12%)
Other	18 (3%)
Ethnicity	
Hispanic	19 (3%)
Specialization	
General Surgery	216 (39%)
Endocrine Surgery	48 (9%)
Otolaryngology	241 (44%)
Other	44 (8%)
Practice Setting	
Academic	122 (23%)
Community based academic affiliate	86 (16%)
Private practice	323 (61%)

Table 2

Multivariable analysis of hospital and surgeon characteristics associated with radioactive iodine use for AJCC Stage I thyroid cancer

	Proportion treated with RAI at hospital (Mean % $\pm$ SD)	Multivariable P value
Hospital Characteristics		
Case Volume		
Low	40.13 $\pm$ 25.66	<0.001
Low-Mod	48.63 $\pm$ 21.97	0.205
Moderate	44.29 $\pm$ 20.14	0.012
High	48.58 $\pm$ 17.75	Ref.
Practice Setting		
Academic	44.91 $\pm$ 17.34	Ref.
Community	44.09 $\pm$ 19.52	0.353
Private	46.48 $\pm$ 22.92	0.193
Surgeon Characteristics		
Number of years in practice	0.19% decrease in RAI use per year increase experience	0.033
Specialization		
General Surgery	47.73 $\pm$ 21.23	0.036
Endocrine Surgery	44.78 $\pm$ 17.24	0.363
Other	44.67 $\pm$ 16.95	0.758
Otolaryngology	44.44 $\pm$ 22.44	Ref.
Surgery preference		
More extensive	47.83 $\pm$ 21.47	0.010
Less extensive	43.08 $\pm$ 20.39	Ref.

RAI= radioactive iodine