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Extent of Surgery for Low Risk Thyroid Cancer in Elderly: Equipoise in Survival but Not in Short-Term Outcomes[1]

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Abstract

Background—Total thyroidectomy is more common than lobectomy for low risk papillary thyroid cancer (PTC), despite equipoise in survival. Since postoperative morbidity increases with age, we aimed to investigate how extent of thyroidectomy affects short-term outcomes among older patients.

Methods—Using the SEER-Medicare database, we identified patients ≥66 years treated for PTC ≤2 cm between 1996–2011. We used multivariable logistic regression to evaluate the effect of extent of surgery on complications, emergency department visits, and unplanned readmissions.

Results—Among 3341 selected patients, 77.3% were female, mean age was 72.9 years, and tumors averaged 0.8 cm. 67.6% underwent total thyroidectomy; 32.4% underwent lobectomy. Total thyroidectomy was associated with complications [odds ratio (OR)=1.99] and readmissions (OR=1.59); both P<0.01. Complications were higher in females (OR=1.34), blacks (vs. whites, OR=1.65), and those with ≥2 comorbidities (vs. 0, OR=1.43), all P<0.01. Black patients and those with ≥2 comorbidities had more emergency department visits (OR=1.50 and 1.92, respectively) and readmissions (OR=2.19 and 2.29), all P<0.01.

Conclusions—Total thyroidectomy for older adults with low risk PTC may lead to potentially avoidable complications and readmissions, particularly in black and female patients. In many cases, lobectomy may be a safer and less costly alternative.

[1]A portion of these data were included in a podium presentation at the 14th Annual Academic Surgical Congress, February 5–7, 2019, Houston, TX.

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COI/ DISCLOSURE STATEMENT

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INTRODUCTION

Thyroid cancer has the fastest increasing incidence of any cancer worldwide.[1] Over the past 30 years, incidence in the U.S. has tripled, reaching 64,300 in 2016.[2] Eighty-five percent of new cases are papillary thyroid cancer (PTC), for which the 10-year survival rate exceeds 95%. The American Thyroid Association (ATA) categorizes PTC as low risk when tumors are ≤4 cm in diameter, do not feature aggressive histology (e.g. tall cell, insular, or diffuse sclerosing variants), and are not associated with extrathyroidal invasion or metastasis.[3] Prior to 2015, the ATA universally recommended total thyroidectomy except in the case of subcentimeter tumors (papillary thyroid microcarcinoma, PTMC), in which thyroid lobectomy was the recommended alternative.[4–6] The current (2015) guidelines consider either procedure appropriate for all low risk tumors.[3]

Despite this equipoise in operative recommendations for low risk PTC, total thyroidectomy is still performed more commonly, even for subcentimeter tumors.[7] Extent of surgery does not impact survival,[8] but total thyroidectomy is associated with nearly doubled complication rates.[9] Older patients are particularly vulnerable: those >70 years have higher complication rates, longer lengths of stay (LOS), and greater hospital charges after any type of thyroid surgery.[10] As the Centers for Medicare and Medicaid Services (CMS) expand penalties for postsurgical complications and readmissions, extent of thyroidectomy may have financial implications as well.[11]

Our aim was to use the Surveillance, Epidemiology, and End Results (SEER)-Medicare database to investigate the association between extent of surgery and complications, emergency department (ED) visits, and readmissions among patients ≥66 years with low risk PTC ≤2 cm in diameter. This size threshold selects a majority of tumors for which current guidelines permit either total thyroidectomy or lobectomy (≤4 cm), while excluding larger tumors (2–4 cm) that many clinicians would not be comfortable treating with lobectomy. We hypothesized that total thyroidectomy is independently associated with complications, ED visits, and readmissions.

METHODS

Data Source

Data were collected from the SEER-Medicare linked database. SEER captures population-level demographic, clinical, and survival data for approximately 28% of all cancer patients in the U.S.[12] Medicare insures 97% of the ≥65-year-old U.S. population and collects data on health care services provided throughout a person's Medicare eligibility. Medicare Part D files, available to us for the years 2008–2012 (N = 1224, 36.6% of the entire cohort), provide information on filled prescriptions. The biennially linked database has been used to study factors associated with cancer care, including the following: sociodemographic characteristics, physician and hospital characteristics, diagnostics, surgery, chemotherapy, radiation, comorbid conditions, complications, screening, relapse, and costs.

Cohort Selection

The 17 SEER registries with uninterrupted data from 1997 to 2011 were used to select all patients aged ≥66 years with a primary diagnosis of PTC (ICD-O-3 codes 8050, 8060, 8140, 8260, 8340, 8341, 8342, 8343, and 8344), including classic and follicular variants and excluding aggressive variants (e.g. tall cell, insular, or diffuse sclerosing), who underwent thyroid lobectomy (CPT codes 60210, 60212, 60220) or total thyroidectomy (CPT codes 60240 and 60271) ≤180 days following diagnosis. To select the subset of low risk PTC (T1N0M0) that most clinicians would feel could be treated with lobectomy, we excluded patients with the following: tumors >2 cm in diameter, cancer *in situ*, extrathyroidal extension, nodal or distant metastases, or a PTC diagnosis at autopsy.

We restricted the minimum patient age to 66 years to ensure continuous Medicare Part A and Part B coverage for at least one year before diagnosis; we further required coverage for two years after diagnosis (or until death). We excluded patients with a missing month of diagnosis, a second malignant diagnosis ≤1 year within the diagnosis of PTC, or procedure codes suggesting multiple thyroid surgeries (e.g. code for completion thyroidectomy, multiple codes for lobectomy). This increased the accuracy of dates and reduced the potential confounding effects of coexisting diagnoses and multiple surgical procedures.

To maximize completeness of Medicare claims data, we only included patients whose PTC diagnosis in SEER could be matched with a synchronous, primary diagnosis of PTC on an inpatient, outpatient, or carrier-based Medicare claim.

Independent Variable and Outcomes

The independent variable, extent of surgery, was dichotomized into total thyroidectomy or lobectomy, based on the thyroid surgical procedure coded within 180 days following diagnosis. Medicare modifier codes were used to verify that the claims of interest were associated with thyroid surgery.

The primary outcomes were postoperative complications and unplanned encounters. Complications were identified using ICD-9 diagnosis codes from postoperative encounters. General surgical complications (e.g. pneumonia, cystitis, wound infection) and endocrine-specific complications [e.g. hypoparathyroidism, hoarseness – a sign of recurrent laryngeal nerve (RLN) injury] were recorded during the first 30 postoperative days and are henceforth termed ≤30-day complications. To estimate rates of permanent injury to neck structures, endocrine complications also were examined between 618 months after surgery and termed ≥6-month complications.[13] Rates of filled prescriptions for calcitriol were used as the most specific measure of postoperative hypoparathyroidism.

Unplanned encounters comprised presentations to the ED not resulting in admission, henceforth termed ED visits, and postoperative hospital admissions for any cause except radioactive iodine (RAI) administration, henceforth termed readmissions. Exclusion of patients with more than one coded surgery ensured that readmissions did not include hospitalization for completion thyroidectomy. Given recent data demonstrating that up to 48% of readmissions occur after the traditional postoperative window of 30 days, these encounters were examined over 90 postoperative days.[14–16]

Other Variables

Primary outcomes were correlated with clinical variables, including comorbidity, tumor size, histology, and (multi)focality. Comorbidity was assessed using the 2014 version of the National Cancer Institute (NCI) Comorbidity Index, based on the Charlson Comorbidity Index.[17] Demographic variables included patient age, sex, race, and local census tract characteristics, such as population density and income quartile, which were obtained from the SEER data. Vital status and follow-up times were acquired from the SEER Patient Entitlement and Diagnosis Summary File.

Statistical Analysis

Baseline patient characteristics are presented as frequencies and proportions for categorical variables and mean with standard deviation (SD) or median with interquartile range for continuous variables. Comparisons between patients undergoing total thyroidectomy vs. lobectomy were made using chi-squared tests for categorical variables and Student's t-tests for continuous variables.

Multivariable logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals associated with extent of surgery. The model for postsurgical complications and encounters was adjusted for patient age, sex, race, comorbidity index, RAI administration, tumor size and focality, and other clinicopathologic disease characteristics.

All P values are two-sided and set at a significance level of 0.05. All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC). This study was approved by the Duke University Health System institutional review board.

RESULTS

Demographic, Clinical, and Surgical Characteristics

A total of 3341 patients with PTC ≤2 cm met eligibility criteria (Figure 1). The mean age at diagnosis was 72.9 years (SD 5.5 years; Table 1). Most patients were white (86.8%) and female (77.3%). Mean tumor size was 0.8 cm (SD 0.6 cm). Histologically, 65.0% of tumors were classic PTC; the remainder represented the follicular variant. From 2004 to 2011, the years for which focality was recorded, 805 (31.7%) of tumors were multifocal.

Most patients (67.6%) underwent total thyroidectomy; 32.4% underwent lobectomy. Lobectomy was more likely than total thyroidectomy to be performed in the outpatient setting (37.7% vs. 27.6%, $P < 0.01$; Table 2). Longer LOS (≥2 days) was more likely with total thyroidectomy than lobectomy (42.2% vs. 36.9%, $P < 0.01$). Survival at one year was 98.0%.

Short-term (≤30-day) Complications

Six hundred eighty-two patients (20.4%) experienced complications in the first 30 postoperative days. Complications were more common after total thyroidectomy vs. lobectomy (23.7% vs. 13.5%, respectively, $P < 0.01$). Specifically, total thyroidectomy was followed by higher rates of hoarseness (3.1% vs. 1.8%, $P = 0.03$), hypocalcemia (12.7% vs.

4.9%, $P < 0.01$), hypoparathyroidism (4.6% vs. 2.0%, $P < 0.01$), and proportion of patients filling calcitriol prescriptions (>10.7% vs. <3.4%, $P < 0.01$). There was no significant difference in rates of general complications (e.g. pneumonia, wound infection) between total thyroidectomy and lobectomy (7.1% vs. 5.9%, respectively; $P = 0.21$).

On multivariable analysis (Figure 2), ≤30-day complications were independently associated with total thyroidectomy (OR 1.99), a comorbidity index ≥2 (OR 1.43), female sex (OR 1.34), and black vs. white race (OR 1.65); all $P < 0.01$. Sex-based differences may be explained in part by differential rates of hypocalcemia (females vs. males: 11.2% vs. 6.9%, $P < 0.01$). Potentially due to small sample sizes, race-based differences could not be attributed to any one particular complication.

Long-term (≥6-month) Complications

Three hundred eighty-six patients (11.6%) had endocrine complications recorded ≥6 months after surgery (Table 2). Complication rate was not significantly different between total thyroidectomy (11.9%) vs. lobectomy (10.8%), $P = 0.36$, although total thyroidectomy more often resulted in ≥2 complications (1.5% vs. <0.9%, $P < 0.01$). Overall, 5.1% of patients had hoarseness, 4.5% had hypocalcemia, 2.6% had hypoparathyroidism, and notably, 4.2% of patients were still filling prescriptions for calcitriol at ≥6 months after surgery. After multivariable adjustment (Figure 2), only female sex remained associated with ≥6-month complications (OR 1.37, $P = 0.03$).

Postoperative Encounters

During the first 90 postoperative days, 379 patients (11.3%) presented to the ED but did not require admission (Table 2). The median number of days between surgery and ED visit was 24. The most common reasons for these ED visits were general (non-endocrine) surgical complications (32.2%), followed by cardiac (29.3%) and endocrine complications (26.9%). ED visit rates did not vary significantly by extent of surgery (total thyroidectomy vs. lobectomy: 11.9% vs. 10.3%, $P = 0.18$).

After excluding admissions for RAI administration and completion thyroidectomy, 494 (14.8%) patients were readmitted ≤90 days after surgery. The median time to readmission was 41 days. Most readmissions (57.7%) were for endocrine complications; readmissions were more common after total thyroidectomy vs. lobectomy (17.2% vs. 9.7%, $P < 0.01$). After multivariable adjustment (Figure 2), readmissions remained associated with total thyroidectomy (OR 1.59), comorbidity index ≥2 (vs. 0, OR 2.29), and black race (vs. white, OR 2.19); all $P < 0.01$.

DISCUSSION

This nationally-representative study is the first to show that rates of both complications and unanticipated readmissions are higher after total thyroidectomy vs. lobectomy for elderly patients with low risk PTC. Female sex and black race are independently associated with complications and readmissions. In the absence of evidence that extent of surgery affects survival in low risk PTC, our findings suggest that lobectomy may often be the safer surgical choice.

Higher ≤30-day endocrine complication rates following total thyroidectomy underscore the increased risk of hypoparathyroidism and RLN injury associated with a bilateral procedure. Our findings are consistent with a 2014 nationwide analysis of outcomes after 62,722 thyroid surgeries.[9] In that study, Hauch et al. demonstrated nearly doubled complication rates after total thyroidectomy relative to lobectomy (20.4% vs. 10.8%), even in the hands of high-volume surgeons. We corroborate that these differences are largely driven by higher rates of hypocalcemia following total thyroidectomy. Although the multivariable model used by Hauch et al. adjusted for diagnosis (Graves' disease vs. benign vs. malignant), it did not distinguish among cancer types or risk strata, likely increasing the proportion of complicated cases (e.g. larger or locally invasive tumors) in the total thyroidectomy group. Our data suggest that even for small, intrathyroidal tumors, total thyroidectomy vs. lobectomy is associated with doubled odds of complications and should be used judiciously.

Unlike ≤30-day complications, ≥6-month complication rates do not appear to differ by extent of surgery. This stands in contrast to prior published work. A meta-analysis examining longer-term complications of thyroid surgery found that, relative to lobectomy, total thyroidectomy resulted in 1.85 and 3.17 times higher rates of permanent RLN and parathyroid injuries, respectively.[18] As in the study by Hauch et al., the total thyroidectomy group in this meta-analysis included larger and more aggressive tumors, which would increase post-total thyroidectomy complication rates. In our cohort, fewer complicated total thyroidectomy cases likely resulted in fewer events at ≥6 months and therefore less power to detect a difference in rates of permanent injury between total thyroidectomy vs. lobectomy.

Differences in complication rates may also have been biased towards the null by the presence of hypoparathyroidism among some patients in the lobectomy group. Most likely, these patients had previously (i.e. at a time not captured in this study) undergone lobectomy. The procedure coded as "lobectomy" during our observation period would in truth have been a completion thyroidectomy, a more plausible cause of hypoparathyroidism. Alternatively, others have suggested that – even with lobectomy – exploration of the contralateral lobe, ischemia of two or more parathyroid glands, or postoperative hematoma formation may be sufficient to cause hypoparathyroidism.[19,20]

Readmission rates, another measure of postoperative morbidity, were also significantly higher for patients undergoing total thyroidectomy vs. lobectomy in this cohort. Previously published readmissions data vary, as do methodologies. Collier et al. also compared 90-day readmission rates by extent of surgery.[21] Their study of 59,427 patients found an overall readmission rate (17.6%) similar to the one we observed (14.8%), but a 32% lower adjusted risk of readmission after total thyroidectomy vs. lobectomy. Importantly, Collier et al. did not analyze unplanned readmissions separately: 98.9% of readmissions after lobectomy for thyroid cancer were for completion thyroidectomy or administration of RAI – planned treatments that exaggerate the post-lobectomy readmission rate. In contrast, and more in line with our findings, Iannuzzi et al. examined 30-day unplanned readmissions after 34,046 thyroid surgeries, demonstrating a significantly lower readmission rate after lobectomy (2.1%) vs. after total thyroidectomy (2.8%).[22] Although their cohort was not stratified by diagnosis, more complicated thyroidectomy procedures (total thyroidectomy with lymph node dissection, substernal thyroidectomy) were treated separately, increasing the likelihood

that their lobectomy and total thyroidectomy groups were similar to ours. Lower average age (54 years) and a shorter readmission window likely contributed to lower overall readmission rates relative to our cohort.

Increased readmission rates following total thyroidectomy vs. lobectomy have three major implications. First, most readmissions were prompted by endocrine complications, emphasizing that even the increased risk of “short-term” complications with total thyroidectomy warrants careful consideration. In fact, unplanned readmissions may portend poor survival outcomes. In a cohort that included all stages of thyroid cancer, Tuggle et al. found that unplanned hospitalizations were significantly associated with death at one year, compared with nonhospitalization.[23] A low mortality rate in our cohort precluded a similar analysis. Second, half of all readmissions occurred after postoperative day 41; this supports recent findings that events during the first 30 postoperative days do not fully capture surgical outcomes.[14–16] Instead, a 60- or 90-day postoperative period may better define a complete “episode of care” if CMS bundled payments expand to include thyroid surgery. Third, as the CMS Hospital Readmission Prevention Program increases penalties for readmissions following a broader range of surgeries, avoiding total thyroidectomy when lobectomy is sufficient may have a cost benefit as well.

Two demographic factors are independently associated with both complications and readmissions: female sex and black race. Sex-based differences are chiefly a result of higher rates of postoperative hypocalcemia in women. This may be because postmenopausal women have a smaller calcium “reserve” relative to male counterparts, increasing the likelihood that parathyroid ischemia causes symptomatic hypocalcemia, which could in turn prompt readmission. As Wang and Yen have summarized, up to a third of readmissions after thyroid surgery are driven by symptomatic hypocalcemia, which can be addressed with postoperative counseling and implementation of algorithms for inpatient and outpatient management.[24] Race-based differences are more concerning because a biological explanation likely does not exist. Sosa et al. have previously shown that, on a national level, >50% of black and Hispanic patients have thyroid surgery by the lowest-volume surgeons (1–9 cases per year), compared to 44% of whites.[25] It is likely that in our study as well, race-based differences in complications and resulting readmissions were driven by inequity in access to high quality care. Dedicated health disparities research would better address race-based differences in thyroidectomy outcomes.

The main limitations of this study stem from the nature of administrative databases such as SEER-Medicare, which do not indicate the intent of clinical or coding decisions. For example, the multifactorial decision about extent of surgery depends on the possibility of concomitant benign thyroid disease, patient preference, size of the thyroid gland, radiation history, and preexisting dependence on thyroid supplementation – factors that SEER-Medicare does not fully capture. Furthermore, diagnosis codes may be imprecise measures of complications such as surgical hypoparathyroidism. Rates of hypocalcemia likely overestimate this value (due to low specificity), while rates of hypoparathyroidism or filled calcitriol prescriptions are likely underestimates (due to sparse documentation and limited sensitivity, respectively). Unlike other databases, however, SEER-Medicare allows us to examine all three measures. Therefore, while a precise rate of surgical hypoparathyroidism

may be inaccessible, the observed consistency in trends across all three measures of this complication lends internal validity to the conclusion that surgical hypoparathyroidism is more common after total thyroidectomy.

To our knowledge, this is the first nationally-representative study of the effect of extent of surgery on postoperative complications, ED visits, and unplanned readmissions in older adults (≥66 years) with low risk PTC ≤2 cm (T1N0M0). Complications, often severe enough to warrant readmission, are independently associated with total thyroidectomy, female sex, and black race. Among older adults, more judicious use of total thyroidectomy and an increased vigilance for postoperative hypocalcemia may mitigate the morbidity of a disease with an otherwise excellent prognosis.

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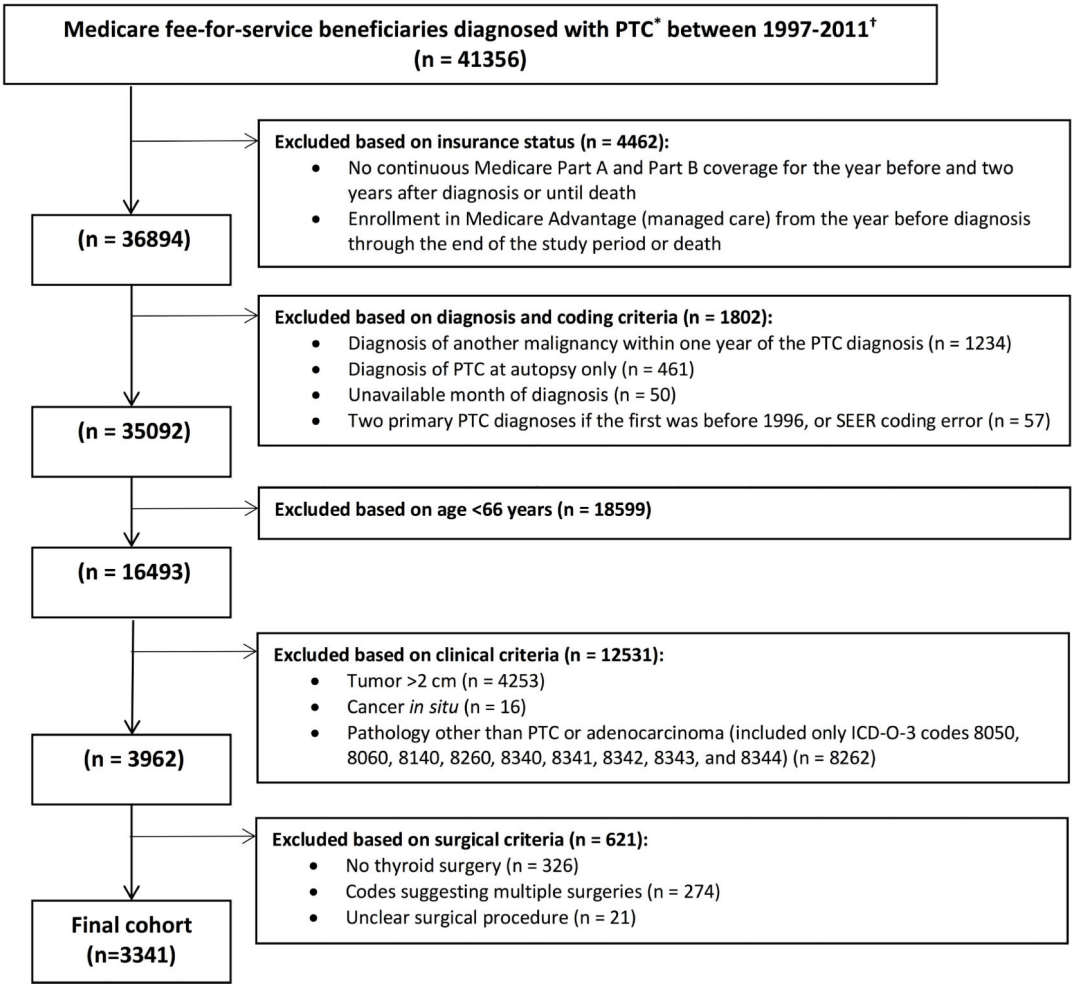

Figure 1.

Patient selection diagram. *PTC,* papillary thyroid cancer; *SEER,* Surveillance, Epidemiology, and End Results.

* Defined as a primary diagnosis of PTC on an inpatient, outpatient, or carrier-based Medicare claim within three months of the SEER-reported diagnosis.

† SEER records from 1997 to 2011 were searched for the incident diagnosis of PTC; Medicare claims spanning 1996 to 2013 were used to verify diagnosis-related procedures and to determine insurance status.

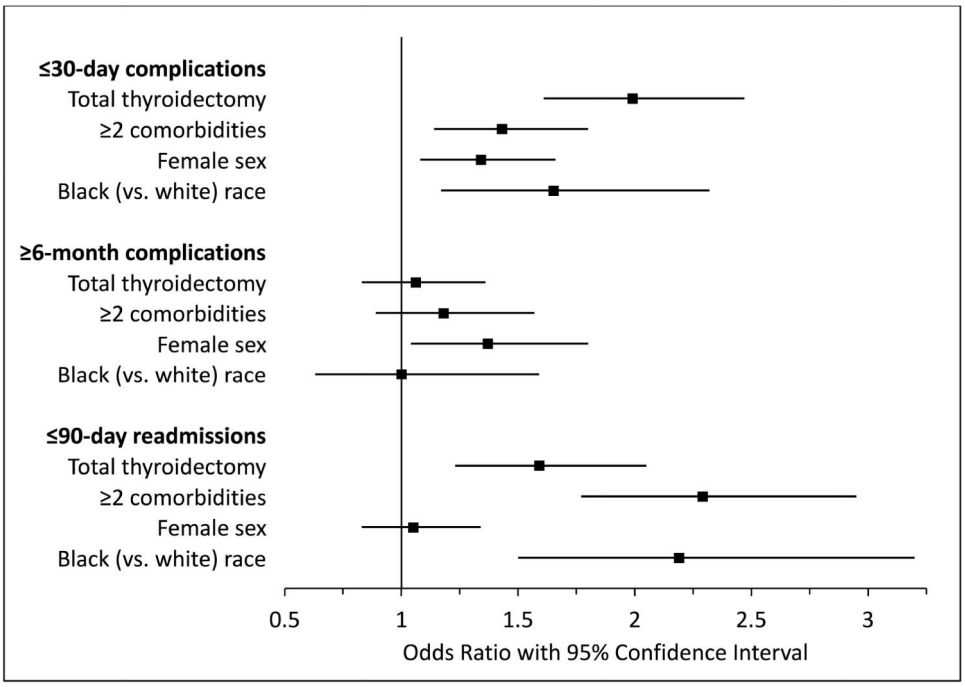

FIGURE 2.

Multivariable regression analysis of postoperative complications and réadmissions for patients >66 years with T1N0M0 papillary thyroid cancer, 1996–2011 (N = 3307*).

The <30-day period includes both general complications (e.g. pneumonia, cystitis, wound infection) and endocrine complications (e.g. hypoparathyroidism, hoarseness, vocal cord paralysis). The >6-month period only includes endocrine complications.

Aside from variables shown, analysis adjusts for the following: age, radioactive iodine administration, tumor size, (multi)focality, income, residence, year of diagnosis, and National Cancer Institute designation of treatment center. These variables did not have clinically significant effects on outcomes.

* Sample size is reduced in multivariable analysis due to exclusion of 34 patients (1.0%) with missing values.

TABLE 1.

Characteristics of patients ≥66 years who underwent surgery for T1N0M0 PTC, 1996–2011 (N = 3341).

		Extent of Surgery		
	Entire Cohort	**Lobectomy**	**Total thyroidectomy**	***P* value**
Number of patients	3341	1081	2260	
Mean age (SD)	72.9 (5.5)	73.2 (5.6)	72.81 (5.5)	0.05
Female sex	2,583 (77.3%)	828 (76.6%)	1,755 (77.7%)	0.49
Race				0.20
White	2,901 (86.8%)	930 (86.0%)	1,971 (87.2%)	
Black	188 (5.6%)	72 (6.7%)	116 (5.1%)	
Other	252 (7.5%)	79 (7.3%)	173 (7.7%)	
Charlson comorbidity index				0.82
1	850 (25.4%)	270 (25.0%)	580 (25.7%)	
≥2	600 (18.0%)	200 (18.5%)	400 (17.7%)	
Tumor size				<0.01
Mean (SD), cm	0.8 (0.6)	0.6 (0.5)	0.8 (0.6)	
≤1 cm	2,396 (71.7%)	906 (83.8%)	1,490 (65.9%)	
1.1–2 cm	945 (28.3%)	175 (16.2%)	770 (34.1%)	
Histology				0.12
Classic papillary	2,170 (65.0%)	682 (63.1%)	1,488 (65.8%)	
Follicular variant	1,171 (35.0%)	399 (36.9%)	772 (34.2%)	
Multifocal disease, 2004–2011 *	805 (31.7%)	138 (18.5%)	667 (37.2%)	<0.01

Percentages based on column totals; may not add to 100% due to rounding. P-values computed by t-test and chi-square tests for continuous and categorical variables, respectively. *PTC*, papillary thyroid cancer; *RAI*, radioactive iodine; *SD*, standard deviation; *NCI*, National Cancer Institute; *LOS*, length of stay.

* Focality was not recorded prior to 2004. Percentages based on the 2681 patients (75.9%) who had complete focality data.

TABLE 2.

Frequency of postoperative complications and encounters in patients ≥66 years with T1N0M0 PTC, 1996–2011 (N = 3341).

		Extent of Surgery		
	Entire Cohort (N = 3341)	**Lobectomy (N = 1081)**	**Total thyroidectomy (N = 2260)**	***P* value**
Surgical setting (LOS in days)				<0.01
Outpatient	1032 (30.9%)	408 (37.7%)	624 (27.6%)	
Inpatient (1)	1371 (41.0%)	425 (39.3%)	946 (41.9%)	
Inpatient (≥2)	938 (28.1%)	248 (22.9%)	690 (30.5%)	
≤30-day complications	682 (20.4%)	146 (13.5%)	536 (23.7%)	<0.01
General complications	224 (6.7%)	64 (5.9%)	160 (7.1%)	0.21
Hoarseness	88 (2.6%)	19 (1.8%)	69 (3.1%)	0.03
Vocal cord paralysis	36 (1.1%)	13 (1.2%)	23 (1.0%)	0.63
Hypoparathyroidism	127 (3.8%)	22 (2.0%)	105 (4.6%)	<0.01
Taking calcitriol *	107 (8.7%)	<11 (<3.4%) †	>96 (>10.7%) †	<0.01
≥6-month endocrine complications	386 (11.6%)	117 (10.8%)	269 (11.9%)	0.36
Hoarseness	171 (5.1%)	46 (4.3%)	125 (5.5%)	0.12
Vocal cord paralysis	43 (1.3%)	<11 (<1.0%) †	>32 (>1.4%) †	0.11
Hypoparathyroidism	86 (2.6%)	26 (2.4%)	60 (2.7%)	0.67
Taking calcitriol *	51 (4.2%)	14 (4.3%)	37 (4.1%)	0.86
90-day postoperative encounters				
ED visits	379 (11.3%)	111 (10.3%)	268 (11.9%)	0.18
Readmissions	494 (14.8%)	105 (9.7%)	389 (17.2%)	<0.01

Percentages based on column totals; may not add to 100% due to rounding. “Outpatient” surgical setting is defined as discharge on the same calendar day as the surgery; overnight observation stays are categorized as inpatient (LOS 1 day). General complications include cardiovascular, pulmonary, renal, infectious, and wound-related etiologies. P-values were computed by Wald test.

PTC, papillary thyroid cancer; *LOS*, length of stay; *SD*, standard deviation; *ED*, emergency department.

* Analysis limited to patients with Medicare part D (N = 1224, 36.6% of the entire cohort).

† True values suppressed due to small cell size (N <11), per data use agreement.