Title

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Low risk thyroid cancer in elderly: total thyroidectomy/RAI predominate but lack survival advantage.

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Abstract

Background—Papillary thyroid cancer (PTC) is the fastest increasing cancer in the US; incidence increases with age. It generally has a favorable prognosis but may behave more aggressively in older patients. This study aims to describe national treatment patterns for low risk PTC in older adults.

Materials and Methods—The SEER-Medicare database was used to identify patients ≥66 years treated for clinical T1N0M0 PTC between 1996 and 2011. Multivariable logistic regression was used to identify factors associated with extent of surgery (total thyroidectomy vs. lobectomy)

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DISCLOSURES

Julie A. Sosa is a member of the Data Monitoring Committee of the Medullary Thyroid Cancer Consortium Registry, supported through UBC by NovoNordisk, GlaxoSmithKline, Astra Zeneca, and Eli Lilly. The other authors have no competing financial interests.

and radioactive iodine (RAI) administration. Cox proportional hazards modeling was used to estimate the effect of treatment type on disease-specific survival (DSS).

Results—3214 patients met inclusion criteria; 77.6% were women, median age was 72 years, and mean tumor size was 0.7 cm. 42.7% had preoperatively diagnosed PTC (vs. incidental). 65.4% underwent total thyroidectomy, 29.0% lobectomy, and 5.6% lobectomy followed by completion thyroidectomy; 33.4% received postoperative RAI. Five- and ten-year DSS were 98.9% and 98.3%, respectively. After adjustment, larger tumor size (1.1-2 cm), multifocality, and a preoperative PTC diagnosis were associated with greater odds of undergoing more extensive surgery and receiving RAI (P <0.0001). DSS was not associated with extent of surgery or RAI administration (P >0.05).

Conclusions—Most older adults with PTC underwent total thyroidectomy and a third received RAI; neither treatment improved DSS. In the growing elderly population, less extensive interventions for PTC may reduce morbidity and improve quality of life while preserving an excellent prognosis.

Keywords

papillary thyroid cancer; older adults; surgery; thyroidectomy; lobectomy; disease-specific survival

INTRODUCTION

Thyroid cancer incidence is increasing faster than that of any other cancer worldwide. In the United States, this number has tripled over the past three decades, reaching 64,300 in 2016.[1,2] Papillary thyroid cancer (PTC) comprises about 85% of all new cases, and ten-year survival is excellent, exceeding 95%.[3,4] The American Thyroid Association (ATA) considers PTC low risk when tumors are ≤4 cm in diameter, do not feature aggressive histology (e.g. tall cell, insular, or diffuse sclerosing variants), and have no evidence of extrathyroidal invasion or metastasis.[5] The ATA has historically recommended total thyroidectomy (TT) for these cancers and considered thyroid lobectomy (TL) only for low risk PTC ≤1 cm in diameter (termed papillary thyroid microcarcinoma, or PTMC). Completion thyroidectomy (CT) was indicated if TL revealed an incidental tumor that would have required TT if the diagnosis had been established prior to the initial procedure. Radioactive iodine (RAI) ablation was only recommended selectively for patients with intermediate or high risk features.[6-9]

These guidelines lack specific recommendations for older adults, however. The number of Americans ≥65 years has increased by 41% since 2000; it is expected to rise to 80 million in the next two decades.[10,11] This growing segment of our population receives inconsistent, sometimes even substandard, cancer care.[12,13] In thyroid cancer, this is likely a result of conflicting evidence. On the one hand, patient age is an independent prognostic factor as PTC tends to present more aggressively in older patients, suggesting a need for more extensive intervention.[14,15] On the other, population-level studies show that, compared to younger groups, patients ≥70 years undergoing thyroid operations have more complications,

longer lengths of stay, and greater hospital charges.[16,17] In this vulnerable population, adequate and consistent treatment is paramount.

This study aims to use the SEER-Medicare database to describe national treatment patterns and survival in patients ≥66 years with low risk PTC ≤2 cm in diameter. We hypothesize that most patients undergo extensive surgery (TT or CT vs. TL alone), at least 20% undergo RAI treatment, and that neither extent of surgery nor receipt of RAI is associated with disease-specific survival (DSS).

MATERIALS AND METHODS

Data Source

Data were obtained from the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database. SEER collects population-based demographic, clinical, and survival data for approximately 28% of the U.S. population with cancer.[18] Medicare provides health insurance for 97% of people ≥65 years in the U.S. and collects data on health care services provided throughout a person's Medicare eligibility. The biennially linked database has been used to study factors associated with cancer care, including sociodemographic characteristics, physician and hospital characteristics, diagnostics, surgery, chemotherapy, radiation, comorbid conditions, complications, screening, relapse, and costs.[19]

Study Population

The 17 SEER registries with uninterrupted data from 1997 to 2011 were used to select all patients aged ≥66 years who underwent surgery for a primary diagnosis of PTC (ICD-O-3 codes 8050, 8060, 8140, 8260, 8340, 8341, 8342, 8343, and 8344), including the classic and follicular variants and excluding aggressive variants (e.g. tall cell, insular, or diffuse sclerosing). To restrict the cohort to low risk PTC (T1N0M0) that most clinicians would feel comfortable treating 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 performed a subset analysis of unifocal PTMC, because contemporaneous ATA recommendations considered either TT or TL appropriate for tumors of this size and focality.

Minimum age was limited to 66 years to ensure continuous Medicare Part A and Part B coverage for the year before and two years after diagnosis or until death. Patients with a missing month of diagnosis, another malignant diagnosis within a year of the diagnosis of PTC, or unclear surgical treatment (e.g. a single code for CT only, code for TL after a code for TT, three separate codes for TL) were excluded. This increased the accuracy of dates and procedure types and eliminated the potential confounding effects of coexisting diagnoses on course of treatment.

To maximize completeness of Medicare claims data, only patients who had a primary diagnosis of PTC on an inpatient, outpatient, or carrier-based Medicare claim within three months of the SEER-reported month of diagnosis were included.

Study Variables

The primary outcomes were extent of surgery, postoperative administration of RAI, and disease-specific survival. Extent of surgery was classified as TL or TT, respectively, if this was the only coded thyroid surgery. CT was defined using a code for TL followed by another thyroid surgery (TL, CT, or TT). CT was treated separately to capture factors that may be uniquely related to a two-part procedure. Medicare modifier codes were used to verify that the claims of interest were associated with thyroid surgery.

Primary outcomes were correlated with clinical variables, including preoperative diagnosis of PTC (vs. incidental PTC identified postoperatively on surgical pathology), tumor size and focality. 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 for continuous variables. Comparisons were made using ANOVA and chi-square tests for continuous and categorical variables, respectively.

Unadjusted and multivariable logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CI) associated with extent of surgery and RAI administration, adjusting for clinicopathologic disease characteristics. Age-stratified Cox proportional hazards models were used to estimate the effects of tumor size, extent of surgery, and RAI administration on DSS. To maximize accuracy of cause of death data, DSS was calculated from the SEER cause-specific death classification variable, censoring deaths from other causes per the method described by Howlader et al.[20] Comparisons among OR and hazard ratios (HR) were made using the Wald test.

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). The Duke University Health System institutional review board approved this study and determined that the project meets the definition of research not involving human subjects.

RESULTS

A total of 3214 patients with PTC ≤2 cm met eligibility criteria (Figure 1). The mean age at diagnosis was 72.8 years [standard deviation (SD): 5.4; Table 1]. Most patients were white (87.2%) and female (77.6%), residing in large metropolitan areas (55.2%). Mean tumor size was 0.8 cm (SD: 0.6 cm). Overall, 29.0% of patients underwent TL only, 5.6% underwent TL followed by CT, and 65.4% underwent TT; 33.4% received postoperative RAI. PTC was diagnosed preoperatively (vs. an incidental postoperative diagnosis) in 42.7% of patients; of these, 802 (58.4%) were ≤1 cm. Histologically, 63.6% of tumors were classic PTCs; the remainder represented the follicular variant. From 2004 to 2011, the years for which focality was recorded, 817 (33.3%) of tumors were multifocal; 336 (41.1%) of these were >1 cm.

Extent of surgery

From 1996 to 2011, the percentage of patients treated with TL decreased from 54% to 23%, while the percentage treated with TT increased from 40% to 71%. This trend was present among both incidental (Figure 2a) and preoperatively diagnosed (Figure 2b) PTC, but more pronounced in the latter. The proportion of surgeries performed as CT remained below 10%. There was no difference in treatment patterns by ATA guideline era (1996-2005, 2006-2008, 2009-2011).

2994 patients had complete data on all clinically significant covariates used in multivariable regression analysis (Table 2). After adjustment, a preoperative diagnosis of PTC, larger tumor size (1.1-2 cm), and multifocality were associated with greater odds of treatment with either TT or CT, relative to TL. Female patients and those in the highest income quartile, living in large metropolitan counties, and treated at National Cancer Institute-designated comprehensive cancer centers were more likely to undergo TT than TL. Factors independently associated with CT vs. TL were race defined as “other” (including Asian and Hispanic patients) and follicular variant histology.

On subset analysis of unifocal PTMC (Table 3), 408 patients (33.4%) had preoperatively diagnosed PTC and thus were eligible for either TL or TT, according to contemporaneous ATA recommendations. 291 of these 408 (71.3%) underwent complete thyroid removal (TT or CT). Of those with unifocal PTMC found incidentally after lobectomy, 26 (7.2%) proceeded to undergo CT.

RAI ablation

The yearly percentage of patients undergoing postoperative RAI ablation ranged from 5 to 42%, averaging 33.4% during the study period. As with extent of surgery, there were no trends based on ATA guideline period. A larger tumor size (1.1-2 cm), multifocality, follicular variant histology, and a preoperative diagnosis of PTC were independently associated with receiving postoperative RAI therapy. Older patients and those treated at comprehensive cancer centers were less likely to undergo RAI ablation.

Survival analysis

Censoring of patients with unclear cause of death reduced the sample size for survival analysis to 2480 (Figure 1). The censored and uncensored cohorts were similar, except that patients included in survival analysis were more often female (78.7 vs. 73.8%), non-white (13.4 vs. 10.7%), and treated outside of a comprehensive cancer center (91.3 vs. 88%). Among these patients, median follow-up was 61 months (first-third quartile 35-94 months). DSS was 98.9% at five years and 98.3% at ten years. Univariate analysis showed no difference in survival based on extent of surgery ($P = 0.66$) or RAI administration ($P = 0.32$, Table 4). Even after stratification by age group and adjustment for tumor size, DSS was not associated with extent of surgery ($P = 0.75$) or RAI administration ($P = 0.40$).

DISCUSSION

To our knowledge, this is the first nationally-representative study to characterize how treatment impacts survival of older patients (≥66 years) with low risk PTC ≤2 cm (T1N0M0). Between 1996 and 2011, the proportion of patients undergoing TT increased from 40% to 71%, and 33.4% on average received postoperative RAI. Five- and ten-year DSS were 98.9% and 98.3%, respectively. Importantly, neither more extensive surgery nor RAI was associated with a survival advantage. Both were, however, associated with a preoperative diagnosis of PTC, tumor multifocality, and a larger tumor size.

The observed ten-year DSS of 98.3% is excellent, and it matches the average thyroid cancer-related mortality of 1.7% seen in age-unrestricted cohorts.[21] These data suggest that low risk PTC behaves similarly in older and younger patients, an important finding given that age is a well-established independent prognostic factor in thyroid cancer.[14,15,22] On the whole, PTC in older adults often features more aggressive histology and increased propensity for local and regional invasion, distant metastasis, as well as disease persistence and recurrence.[23] However, these small, intrathyroidal tumors appear to be low risk regardless of patient age.

One-third of patients in this study underwent postoperative RAI ablation. Considering the overall low risk nature of this cohort and the fact that RAI did not improve DSS, there are two reasons suggesting that most patients who received RAI likely did not benefit from this treatment. First, guidelines have never recommended RAI for unifocal, low risk PTC.[7-9] Per 2006 and 2009 ATA guidelines, the only indication for RAI in this cohort would have been grossly multifocal disease, but it cannot fully explain the rate of RAI use (33.4%). Though multifocality – regardless of size – was associated with RAI administration (multivariable OR 2.85, 95% CI 2.34 - 3.48, $P<0.01$), grossly multifocal tumors constitute at most 13.7% of this cohort. Even if every case of gross multifocality had undergone ablation, 59.0% (1 – 13.7/33.4) of those treated would have had unifocal or microscopically multifocal disease and therefore no indication for RAI. Second, recent literature supports our finding that RAI does not improve survival in low risk PTC, even in the presence of multifocality.[24,25] Two prospective studies by the National Thyroid Cancer Treatment Cooperative Study Group showed no overall or disease-specific survival benefit with RAI in PTC patients ≥45 years with primary tumor <4 cm and no extrathyroidal extension or nodal metastases. These results were confirmed by a 2015 systematic review of the literature.[26]

In this low risk cohort, extent of surgery was not associated with DSS. In other words, the 65.4% of patients who underwent TT may have had similar outcomes with TL alone. The observed associations of TT (vs. TL) with 1.1-2 cm tumors and CT (vs. TL) with incidental tumors, were consistent with contemporaneous guidelines. ATA recommendations from 1996, 2006, and 2009 universally recommended TT for PTC ≥1 cm to reduce risk of recurrence, improve survival, and facilitate use of RAI for remnant ablation and for detection of persistent or recurrent disease.[7-9] TL was considered sufficient only for unifocal, intrathyroidal PTMC. CT was recommended for incidental tumors which would have required TT had the diagnosis been known preoperatively.

Our findings reinforce the most recent (2015) ATA guidelines, which consider either TL alone or TT adequate for ≤4 cm PTC, but do not offer specific recommendations for older patients.[6] The decision to expand the scope of TL in the 2015 version is largely based on a 2014 study by Adam et al., which examined a National Cancer Database (NCDB) cohort of 61,775 patients with 1-4 cm PTC and a median follow-up of 82 months. After adjustment for comorbidities, multifocality, extrathyroidal extension, and completeness of resection – factors known to be associated with mortality in thyroid cancer – the study showed that TT was not associated with an overall survival advantage over TL.[27] Deciding extent of surgery is more complex when it comes to older patients, who were not studied separately by Adam et al. Accordingly, the ATA identifies patient age >45 years as a reason to consider TT but does not offer more specific age-based guidance.[6-8] The present findings show that, even in patients well over 45 years, TL preserves an excellent prognosis for low risk PTC ≤2 cm, and therefore age may not be a useful criterion for deciding extent of surgery.

A potential explanation for the high rates of TT could be the frequency of incidental PTC in this cohort (57.3%). Surgeons and patients anticipating a procedure for a benign diagnosis, such as multinodular goiter, may prefer TT over TL. However, when the PTC diagnosis was known preoperatively, patients were still more likely to undergo TT than TL [OR 1.88; 95% CI (1.57, 2.24); P <0.01]. It is possible that some preoperative diagnoses of PTC were made concurrently with a benign condition (such as multinodular goiter or hypothyroidism), which may prompt surgeons and patients to select TT as a definitive procedure. Another reason for the observed rates of TT could be that contemporaneous guidelines only held TT vs. TL in equipoise for intrathyroidal, unifocal PTMC. Even in these very low risk cases, however, surgeons erred on the side of more extensive surgery 71.3% of the time. Including the 26 patients who underwent CT for incidentally-discovered, unifocal PTMC, a total of 317 patients (25.9% of the unifocal PTMC cohort) could potentially have undergone less extensive surgery while adhering to contemporaneous guidelines, limiting the complications of a bilateral operation, and preserving an excellent prognosis.

More generally, less extensive treatment of low risk thyroid cancer has the potential to improve safety and quality of life. The North American Thyroid Cancer Survivorship Study demonstrated compromised quality of life for patients with thyroid cancer compared to patients with breast or colorectal cancer, despite a significantly better prognosis.[28] This is due, at least in part, to postoperative complications from thyroid surgery, which include hoarseness/loss of voice, hypocalcemia, and lifelong need for thyroid hormone replacement. These risks are doubled (14.5% vs. 7.6%), even for high-volume surgeons performing TT vs. TL.[29] RAI carries its own risk profile, including salivary gland dysfunction, pneumonitis, myelosuppression, and cystitis, among others. Reducing the need for lifelong thyroid hormone replacement, RAI ablation, and associated testing could substantially improve quality of life. To more completely characterize patient outcomes, future work should examine how extent of surgery and RAI ablation impact postoperative complications and cost.

This study has several limitations. First, large administrative databases such as SEER-Medicare are prone to coding errors. Some patients were excluded from analysis because their Medicare claims represented unclear courses of treatment, such as three separate

lobectomies. Second, a relatively small number of events (30 patients in this cohort succumbed to their thyroid cancer) limits power in survival analysis. We were careful to limit covariates and not over-interpret results. Third, because data on number and size of involved lymph nodes were unavailable, we restricted the cohort to N0 tumors to ensure low risk status for all patients. This criterion may have inadvertently excluded a small number of tumors that would be considered low risk despite the presence of lymph node micrometastases. Finally, decisions about extent of surgery and RAI administration include consideration of patient preference, size of the thyroid gland, a history of radiation and preexisting dependence on thyroid supplementation – factors that are difficult to capture using retrospective data analysis.

This study demonstrates that between 1996 and 2011, an increasing majority of older adults with PTC ≤2 cm underwent more extensive treatment than necessary to improve their survival. While elderly patients may indeed harbor aggressive PTC, age alone should not be an indication for more extensive surgery or RAI administration. In fact, a study from Japan with long followup suggests that selected patients may even be eligible for active surveillance; this is an important area for further research.[30] In the growing population of older adults, less extensive interventions for PTC may reduce morbidity and improve quality of life while preserving an excellent prognosis.

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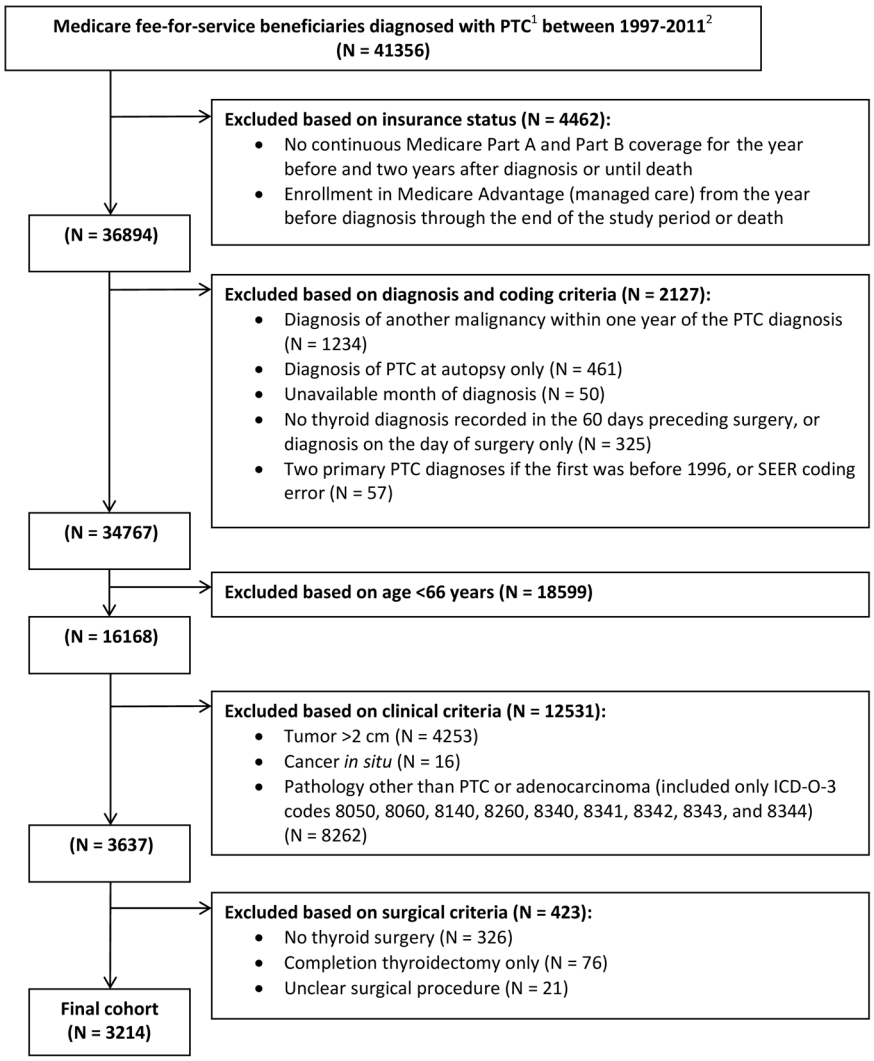

FIGURE 1.

CONSORT diagram for patient selection from the SEER-Medicare linked database. *PTC*, papillary thyroid cancer; *SEER*, Surveillance, Epidemiology, and End Results.

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

2 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.

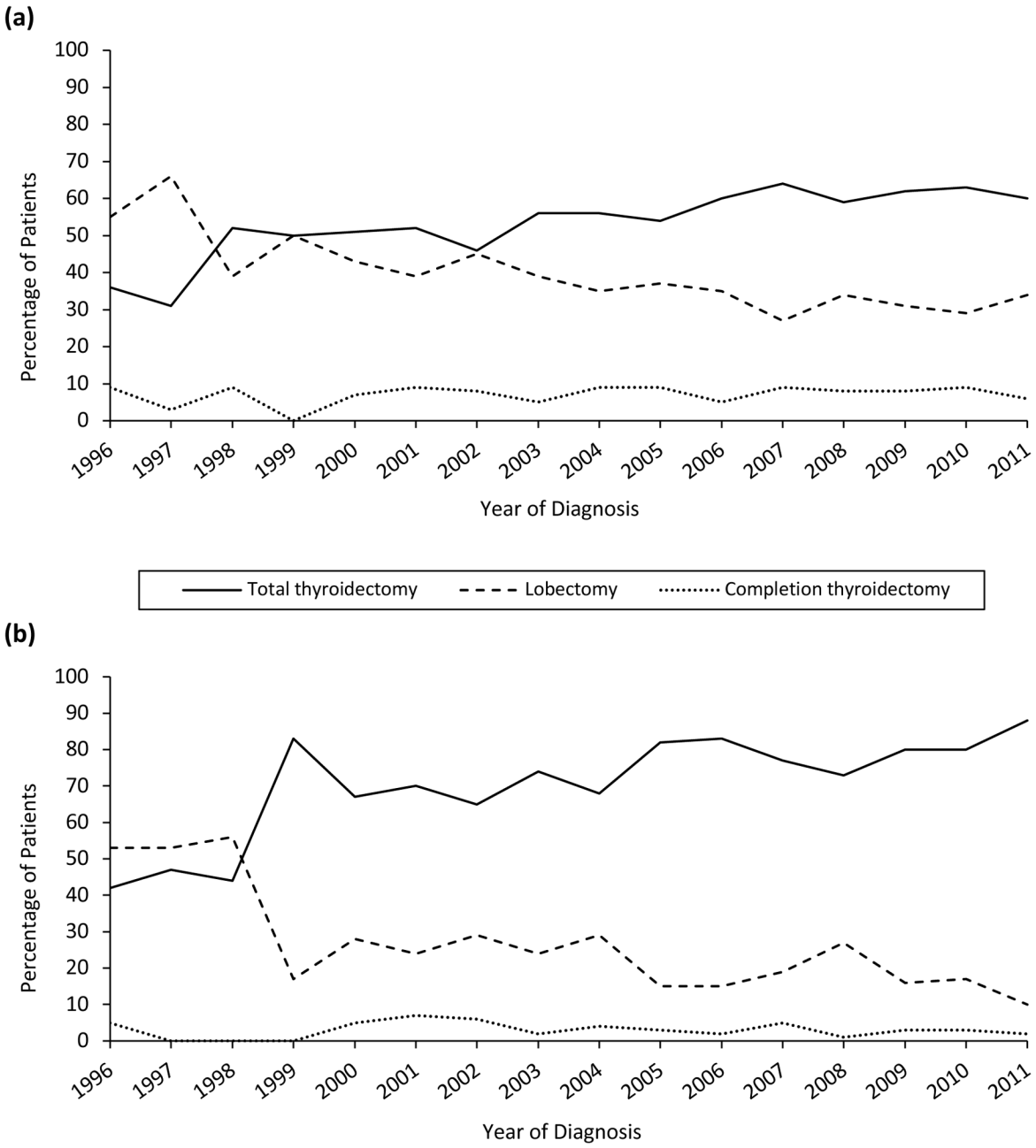

FIGURE 2.

Yearly trends in extent of surgery for patients ≥66 years with (a) incidental and (b) preoperatively diagnosed T1N0M0 papillary thyroid cancer, 1996-2011.

TABLE 1.

Characteristics of patients ≥66 years who underwent surgery for T1N0M0 PTC between 1996-2011.

		Extent of Surgery				RAI Administered		
	Entire Cohort	**Lobectomy**	**Lobectomy + Completion**	**Total Thyroidectomy**	***P***	**No**	**Yes**	***P***
Number of patients	3214	931 (29.0%)	180 (5.6%)	2103 (65.4%)		2139 (66.6%)	1075 (33.4%)	
Mean age (SD), years	72.8 (5.4)	73.1 (5.5)	72.0 (5.2)	72.8 (5.4)	0.05	73.2 (5.6)	72.1 (5.0)	<0.01
Female sex	2493 (77.6%)	713 (76.6%)	136 (75.6%)	1644 (78.2%)	0.50	1675 (78.3%)	818 (76.1%)	0.16
Race					0.10			<0.01
White	2802 (87.2%)	809 (86.9%)	154 (85.6%)	1839 (87.4%)		1866 (87.2%)	936 (87.1%)	
Black	168 (5.2%)	*	*	106 (5.0%)		126 (5.9%)	42 (3.9%)	
Other	244 (7.6%)	*	*	158 (7.5%)		147 (6.9%)	97 (9.0%)	
Income Quartile[1]					<0.01			0.52
Highest	807 (25.1%)	187 (20.1%)	38 (21.1%)	582 (27.7%)		529 (24.8%)	278 (25.9%)	
Third	799 (24.9%)	234 (25.1%)	37 (20.6%)	528 (25.1%)		521 (24.4%)	278 (25.9%)	
Second	785 (24.4%)	235 (25.2%)	55 (30.6%)	495 (23.6%)		527 (24.7%)	258 (24.0%)	
Lowest	820 (25.5%)	275 (29.5%)	50 (27.8%)	495 (23.6%)		560 (26.2%)	260 (24.2%)	
Residence					<0.01			0.01
Metropolitan, pop. ≥1 million	1773 (55.2%)	486 (52.2%)	101 (56.1%)	1186 (56.4%)		1147 (53.6%)	626 (58.2%)	
Metropolitan, pop. <1 million	965 (30.0%)	272 (29.2%)	41 (22.8%)	652 (31.0%)		650 (30.4%)	315 (29.3%)	
Non-metropolitan	476 (14.8%)	173 (18.6%)	38 (21.1%)	265 (12.6%)		342 (16.0%)	134 (12.5%)	
Treated at NCI comprehensive cancer center[2]	286 (9.4%)	*	*	224 (11.4%)	<0.01	188 (9.4%)	98 (9.5%)	0.95
Charlson comorbidity index					0.56			0.11
1	825 (25.7%)	236 (25.3%)	44 (24.4%)	545 (25.9%)		540 (25.2%)	285 (26.5%)	
≥2	556 (17.3%)	168 (18.0%)	24 (13.3%)	364 (17.3%)		391 (18.3%)	165 (15.3%)	
PTC diagnosed preoperatively	1373 (42.7%)	286 (30.7%)	42 (23.3%)	1045 (49.7%)	<0.01	771 (36.0%)	602 (56.0%)	<0.01
Tumor size					<0.01			<0.01
Mean (SD), cm	0.8 (0.6)	0.6 (0.5)	1.0 (0.6)	0.9 (0.6)		0.6 (0.5)	1.1 (0.5)	
≤1 cm	2238 (69.6%)	774 (83.1%)	99 (55.0%)	1365 (64.9%)		1750 (81.8%)	488 (45.4%)	
1.1-2 cm	976 (30.4%)	157 (16.9%)	81 (45.0%)	738 (35.1%)		389 (18.2%)	587 (54.6%)	
Histology					<0.01			<0.01
Classic papillary	2044 (63.6%)	583 (62.6%)	80 (44.4%)	1381 (65.7%)		1405 (65.7%)	639 (59.4%)	

		Extent of Surgery				RAI Administered		
	Entire Cohort	**Lobectomy**	**Lobectomy + Completion**	**Total Thyroidectomy**	***P***	**No**	**Yes**	***P***
Follicular variant	1170 (36.4%)	348 (37.4%)	100 (55.6%)	722 (34.3%)		734 (34.3%)	436 (40.6%)	
Multifocal disease, 2004-2011[3]	817 (33.3%)	123 (19.1%)	68 (49.6%)	626 (37.5%)	<0.01	379 (24.2%)	438 (49.5%)	<0.01

Percentages based on column totals, except in first row. P-values computed by ANOVA and chi-square tests for continuous and categorical variables, respectively. *PTC,* papillary thyroid cancer; *RAI,* radioactive iodine; *SD,* standard deviation; *NCI,* National Cancer Institute.

[*] Suppressed due to small cell size (N <11), per data use agreement.

[1] Data were missing for 31 patients (1.0%), who were excluded from percentage calculations.

[2] NCI designations of treatment center were missing for 187 patients (5.8%), who were excluded from percentage calculations.

[3] Focality was not recorded prior to 2004 [731 patients (23.0%)]. Percentages in this row are based on remaining 2452 patients with complete focality data.

TABLE 2.

Multivariable regression analysis of treatment patterns for patients ≥66 years with T1N0M0 PTC, 1996-2011 (N = 2994[1]).

	Extent of Surgery[2]				
	Completion	Total Thyroidectomy		RAI Administered	
	OR (95% CI)	OR (95% CI)	*P*	OR (95% CI)	*P*
Age, years			0.21		<0.01
66-70	REF	REF		REF	
71-75	0.81 (0.54, 1.21)	1.13 (0.92, 1.39)		0.90 (0.73, 1.09)	
76-80	0.69 (0.43, 1.12)	0.85 (0.67, 1.08)		0.62 (0.48, 0.79)	
81-97	0.72 (0.39, 1.34)	0.98 (0.73, 1.32)		0.41 (0.30, 0.57)	
Female sex	0.95 (0.65, 1.37)	1.30 (1.06, 1.59)	0.02	0.93 (0.76, 1.14)	0.50
Race			0.04		0.10
White	REF	REF		REF	
Black	0.49 (0.18, 1.28)	0.89 (0.61, 1.30)		0.78 (0.52, 1.18)	
Other	2.00 (1.15, 3.48)	1.00 (0.72, 1.39)		1.32 (0.96, 1.81)	
Income Quartile			<0.01		0.43
Lowest	REF	REF		REF	
Second	1.11 (0.68, 1.80)	0.98 (0.77, 1.26)		0.82 (0.63, 1.05)	
Third	0.69 (0.40, 1.18)	0.97 (0.75, 1.25)		0.86 (0.66, 1.11)	
Highest	0.91 (0.52, 1.60)	1.44 (1.10, 1.90)		0.83 (0.63, 1.09)	
Residence			0.01		0.17
Non-metropolitan	REF	REF		REF	
Metropolitan, pop. <1 million	0.80 (0.46, 1.38)	1.49 (1.13, 1.97)		1.25 (0.93, 1.68)	
Metropolitan, pop. ≥1 million	1.12 (0.66, 1.90)	1.41 (1.07, 1.85)		1.33 (0.99, 1.78)	
Treated at NCI comprehensive cancer center	0.40 (0.16, 1.03)	1.57 (1.14, 2.16)	<0.01	0.70 (0.52, 0.94)	0.02
Charlson comorbidity index			0.61		0.37
0	REF	REF		REF	
1	0.78 (0.52, 1.18)	0.97 (0.79, 1.19)		0.96 (0.79, 1.18)	
≥2	0.69 (0.43, 1.16)	0.94 (0.74, 1.19)		0.84 (0.66, 1.07)	
Year of diagnosis			0.09		0.01
1996-2005	REF	REF		REF	
2006-2008	1.05 (0.62, 1.78)	1.26 (0.96, 1.65)		1.25 (0.96, 1.64)	
2009-2011	1.16 (0.70, 1.93)	1.45 (1.12, 1.89)		0.92 (0.71, 1.19)	
PTC diagnosed preoperatively	0.52 (0.35, 0.77)	1.88 (1.57, 2.24)	<0.01	1.64 (1.38, 1.96)	<0.01
Tumor size, 1.1-2 cm vs. ≤1 cm	3.96 (2.75, 5.70)	2.34 (1.90, 2.89)	<0.01	5.12 (4.27, 6.13)	<0.01
Histology			<0.01		<0.01
Classic papillary	REF	REF		REF	
Follicular variant	1.83 (1.30, 2.57)	0.87 (0.73, 1.03)		1.27 (1.07, 1.52)	
Multifocal disease, 2004-2011[3]	3.51 (2.35, 5.27)	2.23 (1.77, 2.82)	<0.01	2.85 (2.34, 3.48)	<0.01

P-values computed by Wald test. *PTC,* papillary thyroid cancer; *RAI,* radioactive iodine; *OR,* odds ratio; *CI,* confidence interval; *REF,* reference category/value; *NCI,* National Cancer Institute.

[1] Sample size is reduced in multivariable analysis due to exclusion of patients with missing data.

[2] Lobectomy is the reference procedure.

[3] Focality was not recorded prior to 2004.

TABLE 3.

Subset analysis of patients ≥66 years with unifocal PTMC, 2004[1]-2011 (N = 1220).

	PTC Diagnosis		Overall
	Preoperative	**Incidental**	
Lobectomy	117 (28.7%)	334 (41.1%)	451 (37.0%)
Completion or total thyroidectomy	291 (71.3%)	478 (58.9%)	769 (63.1%)
Overall	408	812	1220

Percentages are based on column totals; may not add up to 100 due to rounding. *PTMC,* papillary thyroid microcarcinoma.

[1]Focality was not recorded prior to 2004.

TABLE 4.

Disease-specific survival analysis for patients ≥66 years with T1N0M0 PTC, 1996-2011 (N = 2480[1]).

	Unadjusted		Adjusted[2]	
	HR (95% CI)	***P***	**HR (95% CI)**	***P***
Tumor size		0.06		0.19
1.1-2 cm	REF		REF	
≤1 cm	0.50 (0.24,1.03)		0.66 (0.30,1.45)	
Extent of surgery		0.66		0.75
Lobectomy	REF		REF	
Completion thyroidectomy	0.62 (0.08, 4.93)		0.50 (0.06, 4.16)	
Total thyroidectomy	1.30 (0.58, 2.94)		1.08 (0.46, 2.55)	
RAI administered	1.44 (0.70, 2.97)	0.32	1.41 (0.62, 3.23)	0.42

P-values computed by Wald test. *PTC,* papillary thyroid cancer; *RAI,* radioactive iodine; *HR,* hazard ratio; *CI,* confidence interval; *REF,* reference category/value.

[1]Sample size is reduced in survival analysis due to exclusion of patients with uncertain cause of death.

[2]This age-stratified multivariable model adjusts for tumor size, extent of surgery, and RAI administration.