Decreasing Use of Radioactive Iodine for Low-Risk Thyroid Cancer in California, 1999 to 2015

Ki Wan Park,[1] James X. Wu,[1] Lin Du,[2] Angela M. Leung,[3,4] Michael W. Yeh,[1] and Masha J. Livhits[1]

[1]Section of Endocrine Surgery, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California 90095; [2]Department of Biostatistics, University of California Los Angeles Fielding School of Public Health, Los Angeles, California 90095; [3]Division of Endocrinology, Diabetes, and Metabolism, Department of Medicine, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California 90095; and [4]Division of Endocrinology, Diabetes, and Metabolism, Department of Medicine, VA Greater Los Angeles Healthcare System, Los Angeles, California 90073

Context: Routine radioactive iodine (RAI) ablation for low-risk differentiated thyroid cancer (DTC) is not supported by current practice guidelines.

Objective: To assess recent stage-specific trends in use of RAI ablation.

Design, Setting, and Patients: Retrospective study of patients with DTC (1999 to 2015) identified from the California Cancer Registry. Statistical analysis included standardized differences, *P* values, and multivariable analyses using RAI as the predictor variable.

Main Outcome Measures: Trends and drivers of RAI ablation for low-risk DTC.

Results: Of 46,906 patients with DTC who underwent near-total or total thyroidectomy [mean age 48.2 ± 15.5 (standard deviation) years, 77% female], 25,457 (54%) received RAI. The proportion of patients with regional/distant disease who received RAI remained stable at 68%. Use of RAI for patients with localized disease (no extrathyroidal extension, lymph node, or distant metastases) decreased from 55% (1999) to 30% (2015), with the most substantial change occurring in tumors <1 cm (39% to 11%). The rate also decreased for localized tumors between 1 and 2 cm (62% to 34%) and 2 and 4 cm (67% to 49%) and remained stable at 59% for tumors >4 cm. In multivariable analyses, patients with localized disease were less likely to receive RAI if they were >65 years old [odds ratio (OR) 0.77, 95% confidence interval (CI): 0.71 to 0.83], had tumors <1 cm (OR 0.33, 95% CI: 0.31 to 0.35), or were treated in an academic hospital (OR 0.71, 95% CI: 0.67 to 0.75).

Conclusions: The rate of RAI ablation decreased over time, mainly attributable to decreased use for localized DTCs <2 cm. Many patients with low-risk DTC still receive RAI unnecessarily. (*J Clin Endocrinol Metab* 103: 1095–1101, 2018)

Thyroid cancer is the most common endocrine malignancy in the United States, with differentiated thyroid cancer (DTC) comprising up to 90% of cases (1, 2). Historically, patients were routinely treated with total thyroidectomy, followed by radioactive iodine (RAI) ablation. RAI ablation reduces the risk of recurrence and improves survival in patients with high-risk DTC (3, 4).

RAI ablation has not been demonstrated to improve outcomes in patients with low-risk DTC, commonly defined as tumors <4 cm with no gross lymphadenopathy or local invasion (5, 6).

Revised national guidelines from the American Thyroid Association (ATA), published in 2009, discouraged routine RAI ablation for patients with low-risk DTC, and

this was further emphasized in the 2015 updated ATA guidelines (7, 8). Adverse outcomes of RAI ablation include decreased fertility and increased risk of secondary malignancies (9, 10). Unnecessary RAI use also exposes patients to increased health care costs associated with thyroid cancer treatment (11). Prior studies have found wide variability in RAI administration as a result of uncertainty regarding its benefits and risks (12–15).

Given the increasing prevalence of low-risk DTC, ongoing analysis of appropriate and inappropriate RAI use is critical to help guide current and future practice patterns. We analyzed the time trends of RAI ablation from 1999 to 2015 on a population level in California and determined the drivers of RAI ablation in patients with low-risk DTC. We hypothesized that the rates of RAI ablation in patients with low-risk DTC decreased following publication of the 2009 ATA guidelines.

Materials and Methods

Setting and subjects

The California Cancer Registry (CCR) is a statewide cancer surveillance system that collects information on all cancers diagnosed in California. Data from patients diagnosed with thyroid cancer between 1 January 1999 and 31 December 2015 were extracted from the CCR database. Cases of DTC were identified using thyroid site code C739 in combination with ICD-O-3 histology codes 8050, 8260, 8330 to 8332, 8335, 8340, 8342 to 8344, and 9690. Patients who underwent lobectomy or near-total or total thyroidectomy were identified using the CCR variable SURGPRIM, which codes for the most extensive type of surgery during the first stage of treatment. Only patients who received near-total or total thyroidectomy were included in the analysis of RAI trends. The study was approved by the University of California, Los Angeles, Institutional Review Board.

Patients who received RAI were identified using the CCR variable RADSUM, which codes for the type of radiation received during the first course of treatment. The date of diagnosis of thyroid cancer was determined using the CCR variable DATEDX. The study cohort was subdivided by disease stage, using the CCR variable SUMSTAGE, which codes for summary stage at time of diagnosis. Summary stage categorizes disease stage as localized (confined to thyroid), regional (extrathyroidal extension or nodal metastasis), or distant.

Demographic and clinical variables extracted from CCR included age at diagnosis, sex, race/ethnicity, socioeconomic status (SES), tumor stage, tumor size, lymph node involvement, and presence of extrathyroidal extension. Patients were stratified into three age groups: 18 to 44, 45 to 65, and >65 years. Race/ethnicity was defined by the following groups: Hispanic, Non-Hispanic white, Non-Hispanic black, and Asian/Pacific Islander. SES quintiles were calculated based on the Yost index (16). Hospitals were categorized as academic vs nonacademic, based on affiliation with an academic institution, by using the CCR variable HOSPNO, which codes for a unique hospital number.

Papillary thyroid cancer was defined by histology codes 8050, 8260, 8340, and 8342 to 8344. Low-risk DTC was

classified by both tumor size and summary stage at the time of diagnosis, in accordance with the 2009 ATA guidelines (7). This included tumor size <4 cm and localized disease stage with no lymph node or distant metastasis.

Statistical analysis

Summary statistics were used to describe baseline characteristics. Standardized differences (SDi) were used to represent differences in effect sizes when comparing demographics and clinical characteristics between patients who received RAI and patients who did not receive RAI. SDi serves as an effective statistical measure for comparing effect sizes and imbalances between two groups when no hypothesis testing is being performed (17, 18). SDi of 0.2, 0.5, and 0.8 represents small, medium, and large effect sizes, respectively.

The rate of RAI ablation was analyzed annually over the study period and was additionally compared before and after 2009 to assess for a potential decrease following publication of the ATA guidelines. RAI ablation rates were also analyzed in the localized disease subgroup based on age, sex, race/ethnicity, tumor size, SES, and hospital status (academic vs nonacademic). Univariable and multivariable logistic regressions were performed using RAI as the predictor variable with stepwise selection. For the logistic regression models, the odds ratio (OR) and 95% confidence intervals (CIs) were reported. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

From 1999 to 2015, 56,622 patients were diagnosed with DTC in California. Of these, 6883 patients underwent lobectomy, and 46,906 patients underwent total or near-total thyroidectomy. Whereas the absolute volume of both procedures increased steadily over the study period, the proportion of patients who underwent lobectomy remained relatively constant, ranging between 9.7% and 16.6% annually. The rate of lobectomy did not increase over the study period (16.6% in 1999 to 13.5% in 2015).

DTC patients who underwent near-total or total thyroidectomy

The mean age was 48.2 ± 15.5 (standard deviation) years, and 77.1% of patients were female (Table 1). The mean tumor size was 2.3 ± 5.1 (standard deviation) cm. Following thyroidectomy, 54.3% of patients received RAI ablation over the entire study period. Compared with patients who did not undergo RAI, patients who received RAI were more likely to have extrathyroidal extension (25.1% vs 13.8%, $P < 0.01$) and lymph node involvement (38.2% vs 19.9%, $P < 0.01$) (Table 2).

The rate of RAI ablation decreased from 62.6% in 1999 to 43.3% in 2015 (Fig. 1). The rate of RAI ablation remained relatively stable for patients with regional or distant disease, ranging between 62.3% and 74.7%. There was a substantial decline in the rate of RAI ablation for patients with localized disease, from 54.6% in 1999 to

Table 1. Demographic Characteristics of Patients Who Underwent Near-Total or Total Thyroidectomy for DTC Between 1999 and 2015

	All Patients (N = 46,906)	No RAI (n = 21,449)	RAI (n = 25,457)	SDi
Age, y (means ± SD)	48.2 ± 15.5	49.5 ± 15.5	47.1 ± 15.4	−0.16
Sex, n (%)				0.08
Female	36,156 (77.1)	16,895 (78.8)	19,261 (75.7)	
Male	10,746 (22.9)	4551 (21.2)	6195 (24.3)	
Race/ethnicity, n (%)				0.09
White[a]	24,664 (52.6)	11,437 (53.3)	13,227 (52.0)	
Black[a]	1659 (3.5)	866 (4.0)	793 (3.1)	
Hispanic	12,468 (26.6)	5504 (25.7)	6964 (27.4)	
Asian/Pacific Islander[a]	7529 (16.1)	3323 (15.5)	4206 (16.5)	
SES quantile, n (%)				0.07
Lowest	5746 (12.9)	2850 (14.1)	2896 (12.0)	
Lower-middle	7674 (17.3)	3541 (17.5)	4133 (17.1)	
Middle	8985 (20.2)	4020 (29.9)	4965 (20.5)	
Higher-middle	10,373 (23.3)	4586 (22.7)	5787 (23.9)	
Highest	11,685 (26.3)	5245 (25.9)	6440 (26.6)	
Unknown	2443 (5.2)	1207 (5.6)	1236 (4.9)	
Hospital type, n (%)				0.13
Nonacademic	34,326 (73.2)	15,018 (70.0)	19,308 (75.9)	
Academic	12,022 (25.6)	6136 (28.6)	5886 (23.1)	

Abbreviation: SD, standard deviation.

[a]Non-Hispanic.

29.6% in 2015 ($P < 0.01$). For patients with localized disease, there was a clear point of inflection in RAI ablation after 2009 ($P < 0.01$).

Time trends of RAI ablation in patients with localized disease

Of patients with localized disease (no lymph node involvement or extrathyroidal extension), 45.3% underwent RAI ablation during the study period. Patients with localized disease who received RAI were younger (47.8 vs 50.0 years, SDi −0.15), had a larger mean tumor size (2.4 vs 1.7 cm, SDi 0.14), and were more likely to be treated in a nonacademic center (77.9% vs 71.6%, SDi 0.14) compared with patients who did not undergo RAI.

There were no significant differences in patients with localized disease who received RAI ablation compared with patients who did not with respect to SES, ethnicity, or sex.

The effect of tumor size on RAI use for localized disease over time is shown in Fig. 2. The rate of RAI ablation for tumors <1 cm decreased by 70% over the study period from 38.8% in 1999 to 11.3% in 2015 ($P < 0.01$). The rate also decreased significantly for tumors between 1 and 2 cm (61.5% to 33.6%, $P < 0.01$) and tumors between 2 and 4 cm (67.4% to 48.6%, $P < 0.01$). Use of RAI remained relatively stable for tumors >4 cm, ranging from 51.3% to 67.0%. With the specific comparison of the rate of RAI before and after publication of

Table 2. Tumor Characteristics of Patients Who Underwent Near-Total or Total Thyroidectomy for DTC Between 1999 and 2015

	All Patients (N = 46,906)	No RAI (n = 21,449)	RAI (n = 25,457)	SDi
Tumor size, cm (means ± SD)	2.3 ± 5.1	2.0 ± 5.5	2.5 ± 4.6	0.10
Summary stage, n (%)				0.46
Localized	28,475 (60.7)	15,577 (72.6)	12,898 (50.7)	
Regional/distant	18,265 (38.9)	5796 (27.0)	12,469 (49.0)	
Extrathyroidal extension, n (%)				0.29
Yes	9346 (19.9)	2959 (13.8)	6387 (25.1)	
No	37,433 (79.8)	18,428 (85.9)	19,005 (74.7)	
Lymph node involvement, n (%)				0.41
Yes	14,013 (29.9)	4278 (19.9)	9735 (38.2)	
No	31,663 (67.5)	16,480 (76.8)	15,183 (59.6)	
Histology, n (%)				0.03
Papillary	31,079 (66.3)	14,070 (65.6)	17,009 (66.8)	
Nonpapillary	15,827 (33.7)	7379 (34.4)	8448 (33.2)	

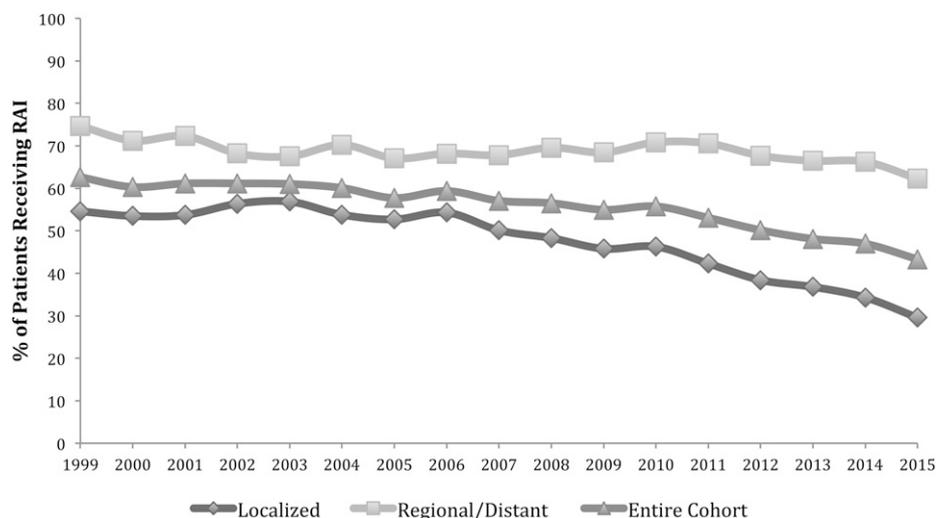Abbreviation: SD, standard deviation.

Figure 1. Rates of RAI ablation by year of diagnosis and disease stage. Disease stage was defined as localized (confined to the thyroid), regional (extrathyroidal extension or nodal metastasis), or distant.

the 2009 revised ATA guidelines, there was a decrease in RAI ablation in patients with tumors <1 cm (31.5% in 2009 to 11.3% in 2015, $P < 0.01$) and tumors between 1 and 2 cm (54.6% in 2009 to 33.6% in 2015, $P < 0.01$). However, the rates of RAI ablation for tumors larger than 2 cm did not change significantly following 2009. Overall, 36.6% of patients with localized tumors <1 cm received RAI from 1999 to 2009 compared with 19.3% of patients from 2010 to 2015 ($P < 0.01$).

The rate of RAI ablation decreased in both academic and nonacademic centers for patients with localized disease. RAI ablation in academic centers decreased from 47.2% in 1999 to 23.6% in 2015 ($P < 0.01$) and in nonacademic centers, from 56.4% in 1999 to 31.6% in 2015 ($P < 0.01$; Fig. 3). After 2009, academic centers had a greater decrease in the rate of RAI ablation (43.0% in 2009 to 23.6% in 2015, $P < 0.01$) compared with

nonacademic centers (46.8% in 2009 to 31.6% in 2015, $P < 0.01$).

Predictors of RAI ablation for patients with localized disease

In univariable analysis, clinical factors associated with decreased rates of RAI ablation for patients with localized disease included older age, smaller tumor size, treatment at an academic center, and papillary histology (Table 3). In multivariable analysis, tumor size <1 cm was predictive against RAI (OR 0.33, 95% CI: 0.31 to 0.35 vs tumor size 1 to 2 cm). Age >65 years was also predictive of decreased use of RAI (OR 0.77, 95% CI: 0.71 to 0.83 vs age 18 to 44 years), as was treatment in an academic hospital (OR 0.71, 95% CI: 0.67 to 0.75 vs nonacademic hospital). Year of diagnosis, papillary histology, and lowest SES were also independent predictors of decreased
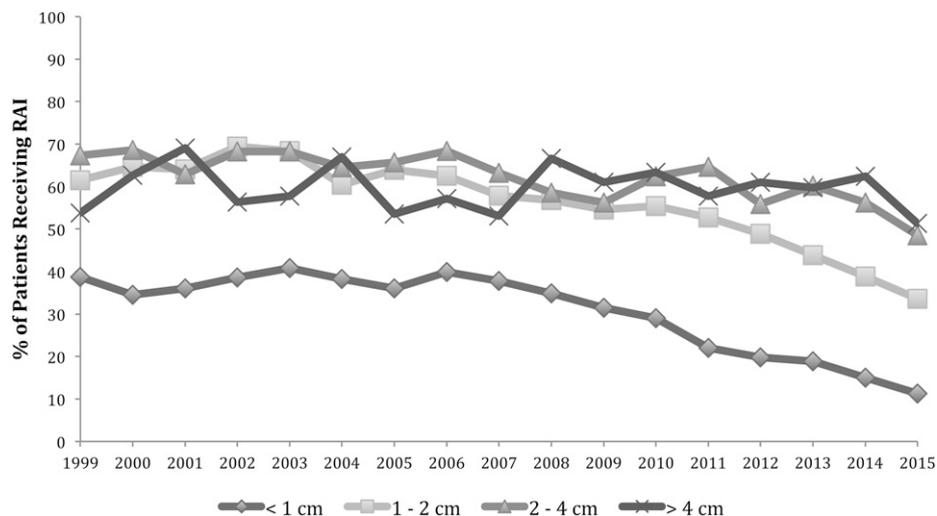

Figure 2. Rates of RAI ablation by tumor size in the localized disease group. Localized disease was defined as tumors confined to the thyroid with no extrathyroidal extension, lymph node, or distant metastasis.
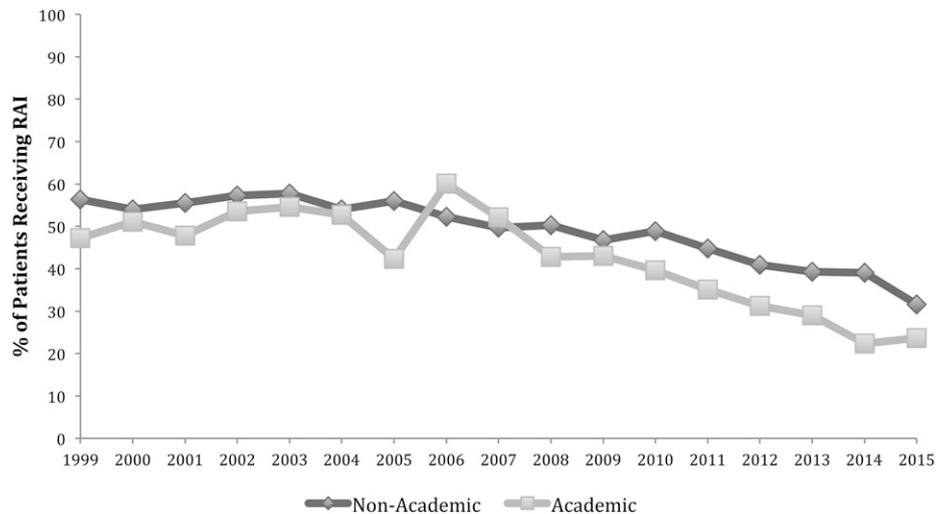
Figure 3. Rates of RAI ablation by hospital type in the localized disease group. Localized disease was defined as tumors confined to the thyroid with no extrathyroidal extension, lymph node, or distant metastasis.

RAI rates (Table 3). The analysis was repeated with age as a continuous variable, and no changes in the findings were observed.

Discussion

We found a decreasing rate of RAI ablation for patients with low-risk DTC in California from 1999 to 2015. This is a departure from previous studies that have found increases in RAI ablation across all tumor sizes from 1990 to 2008 (12). The routine use of RAI ablation for low-risk DTC was explicitly discouraged in the 2009 ATA guidelines. This population-level study assesses the potential impact of the 2009 ATA guidelines on RAI use. We found that the rate of RAI decreased significantly following 2009 for patients with localized tumors <2 cm, but many patients still underwent potentially unnecessary RAI ablation for tumors >2 cm.

Before publication of the 2009 ATA guidelines, studies reported an increase in RAI ablation over time. In a study of 189,219 patients from 1990 to 2008 using the US National Cancer Database, Haymart *et al.* (12) reported an increase in RAI ablation across all tumor sizes. This trend was attributed to an overestimation of RAI efficacy and subsequent overtreatment. In a similar study of 37,136 patients from 1973 to 2007 using the Surveillance, Epidemiology, and End Results database, Iyer *et al.* (19) also reported an increase in RAI ablation across all cases of DTC. In this study, the rates of RAI ablation for low-risk thyroid cancer patients also increased consistently over time, with no changes in overall survival.

In contrast, we found a decreased rate of RAI ablation, particularly following 2009. We observed that the greatest decrease in RAI ablation occurred in localized tumors smaller than 2 cm. The decrease in the rate of RAI

ablation for localized tumors between 2 and 4 cm was less pronounced. Although the ATA definition of low-risk DTC includes tumors up to 4 cm, many patients with tumors between 2 and 4 cm still received potentially unnecessary RAI ablation. The more contemporary database likely explains the main difference in our findings compared with earlier studies. There may also be differences in our study as a result of the use of a state-wide rather than national database. However, given the large size of the CCR database and heterogeneity of the population in California, it is likely that this reflects national trends. Indeed, previous studies using CCR showed no differences in RAI ablation trends compared with studies using national databases (20).

The large variability in RAI administration and guideline adherence is likely multifactorial and includes unexplained hospital characteristics (12). In keeping with prior reports (13–15), we found that patients in academic hospitals were less likely to receive RAI ablation compared with nonacademic centers, particularly after 2009. This suggests that academic centers were more likely to be early adopters of the ATA guidelines. Previous studies have shown that strong clinical evidence correlates with higher rates of clinical guideline adherence (12, 21). In other words, the lack of definitive evidence, despite expert consensus, reduces guideline adherence. The evidence base supporting a lack of benefit for RAI ablation is strongest in patients with microcarcinomas (7). Prior studies have reported a decreased risk of tumor recurrence and mortality following RAI ablation for tumors larger than 1 to 1.5 cm but no benefit for smaller tumor sizes (22, 23).

We examined additional clinical factors that influenced the rate of RAI ablation for patients with low-risk DTC. Our finding that patients >65 years were less likely

Table 3. Univariable Analyses and Multivariable Regression for RAI Ablation in the Localized Disease Group

	Univariable Analysis OR (95% CI)	Multivariable Regression OR (95% CI)
Tumor size		
<1 cm	0.34 (0.32–0.36)	0.33 (0.31–0.35)
1–2 cm	1 (Reference)	1 (Reference)
2–4 cm	1.38 (1.29–1.47)	1.31 (1.22–1.41)
>4 cm	1.27 (1.16–1.4)	1.26 (1.14–1.39)
SES		
Lowest	1 (Reference)	1 (Reference)
Lower-middle	1.16 (1.06–1.27)	1.23 (1.12–1.36)
Middle	1.20 (1.10–1.31)	1.25 (1.14–1.38)
Higher-middle	1.26 (1.16–1.37)	1.35 (1.23–1.48)
Highest	1.17 (1.08–1.27)	1.29 (1.17–1.42)
Hospital		
Academic	0.72 (0.68–0.76)	0.71 (0.67–0.75)
Nonacademic	1 (Reference)	1 (Reference)
Age, years		
18–44	1 (Reference)	1 (Reference)
45–65	0.87 (0.83–0.91)	1.04 (0.98–1.1)
>65	0.67 (0.62–0.72)	0.77 (0.71–0.83)
Year of treatment	0.93 (0.93–0.94)	0.94 (0.93–0.94)
Tumor histology		
Papillary	0.79 (0.76–0.83)	0.91 (0.87–0.96)
Nonpapillary	1 (Reference)	1 (Reference)
Race/ethnicity		
Black[a]	0.88 (0.78–0.99)	0.89 (0.78–1.01)
White[a]	1 (Reference)	1 (Reference)
Hispanic	1.06 (1–1.13)	1.06 (0.99–1.13)
Asian/Pacific Islander[a]	1.07 (1–1.15)	1.04 (0.96–1.12)
Sex		
Female	0.87 (0.82–0.93)	0.96 (0.89–1.02)
Male	1 (Reference)	1 (Reference)

[a]Non-Hispanic.

to undergo RAI compared with younger patients is consistent with previous studies (12, 20, 24, 25). Physicians are more likely to pursue aggressive treatment in younger patients (20, 26). The distribution of race/ethnicity and SES categories in our study was similar between patients who underwent RAI and those who did not. However, in multivariable analysis after accounting for other clinical factors, SES but not race/ethnicity was significantly associated with RAI use. Lowest SES was an independent predictor of decreased RAI use in our study. Patients with low SES have been previously found to present with more advanced disease compared with high SES patients but are less likely to receive RAI ablation (25, 27, 28). Although lack of health care access may result in delayed or undertreatment, our study indicates that patients in higher SES groups are being overtreated for low-risk DTC.

Our study has several limitations, including those inherent to the retrospective analysis of a large database. Risk factors, such as family history and prior radiation exposure, are not included in the database. Potential coding errors in tumors characteristics, such as extrathyroidal extension, may explain the use of RAI in otherwise low-risk patients. However, our main outcome was the use of RAI over time, and coding errors would be unlikely to account for the decrease in RAI use over the study period. Another limitation is the inability to assess the dose of RAI ablation given to patients. Previous studies have suggested that there is no difference in outcomes for low-risk DTC with RAI doses between 30 and 100 mCi (29, 30). We were unable to assess trends in the dose of RAI used for low-risk patients, as this variable is also unavailable in CCR. Furthermore, the updated 2015 ATA guidelines modified the stratification criteria for low-risk DTC (8). In this update, the low-risk DTC group was expanded to include intrathyroidal DTC of any size with ≤5 lymph node micrometastases. Given this change, some patients that were not previously categorized as low risk would now be included in this category. As the rate of RAI ablation in our study was higher for patients with larger tumors or regional disease, this would increase the rate of RAI in patients now considered to be in the low-risk category. However, the retrospective application of the 2015 ATA updates would be inappropriate, as a different set of guidelines was used to guide clinical practice.

In conclusion, RAI ablation for patients with low-risk DTC has decreased following the 2009 ATA guidelines. This is mostly attributable to a substantial decrease in RAI ablation for thyroid cancers <2 cm. Academic hospitals have adopted recommended treatment guidelines earlier than nonacademic centers. Despite the 2009 ATA guidelines, many patients still receive unnecessary RAI for low-risk DTC between 2 and 4 cm.

References

1. Davies L, Welch HG. Current thyroid cancer trends in the United States. *JAMA Otolaryngol Head Neck Surg.* 2014;**140**(4):317–322.
2. Gilliland FD, Hunt WC, Morris DM, Key CR. Prognostic factors for thyroid carcinoma. A population-based study of 15,698 cases from the Surveillance, Epidemiology and End Results (SEER) program 1973–1991. *Cancer.* 1997;**79**(3):564–573.
3. Carhill AA, Litofsky DR, Ross DS, Jonklaas J, Cooper DS, Brierley JD, Ladenson PW, Ain KB, Fein HG, Haugen BR, Magner J, Skarulis MC, Steward DL, Xing M, Maxon HR, Sherman SI. Long-term outcomes following therapy in differentiated thyroid carcinoma: NTCTCS registry analysis 1987–2012. *J Clin Endocrinol Metab.* 2015;**100**(9):3270–3279.

4. Mazzaferri EL, Jhiang SM. Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. *Am J Med*. 1994;**97**(5):418–428.

5. Nixon IJ, Ganly I, Patel SG, Palmer FL, Di Lorenzo MM, Grewal RK, Larson SM, Tuttle RM, Shaha A, Shah JP. The results of selective use of radioactive iodine on survival and on recurrence in the management of papillary thyroid cancer, based on Memorial Sloan-Kettering Cancer Center risk group stratification. *Thyroid*. 2013;**23**(6):683–694.

6. Hay ID, Thompson GB, Grant CS, Bergstralh EJ, Dvorak CE, Gorman CA, Maurer MS, McIver B, Mullan BP, Oberg AL, Powell CC, van Heerden JA, Goellner JR. Papillary thyroid carcinoma managed at the Mayo Clinic during six decades (1940–1999): temporal trends in initial therapy and long-term outcome in 2444 consecutively treated patients. *World J Surg*. 2002;**26**(8):879–885.

7. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B, Pacini F, Schlumberger M, Sherman SI, Steward DL, Tuttle RM; American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer. Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer [erratums appear in *Thyroid*. 2010;**20**(6):674–675 and *Thyroid*. 2010;**20**(8):942]. *Thyroid*. 2009;**19**(11):1167–1214.

8. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, Pacini F, Randolph GW, Sawka AM, Schlumberger M, Schuff KG, Sherman SI, Sosa JA, Steward DL, Tuttle RM, Wartofsky L. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid*. 2016;**26**(1):1–133.

9. Brown AP, Chen J, Hitchcock YJ, Szabo A, Shrieve DC, Tward JD. The risk of second primary malignancies up to three decades after the treatment of differentiated thyroid cancer. *J Clin Endocrinol Metab*. 2008;**93**(2):504–515.

10. Vini L, Hyer S, Al-Saadi A, Pratt B, Harmer C. Prognosis for fertility and ovarian function after treatment with radioiodine for thyroid cancer. *Postgrad Med J*. 2002;**78**(916):92–93.

11. Goffredo P, Thomas SM, Dinan MA, Perkins JM, Roman SA, Sosa JA. Patterns of use and cost for inappropriate radioactive iodine treatment for thyroid cancer in the United States: use and misuse. *JAMA Intern Med*. 2015;**175**(4):638–640.

12. Haymart MR, Banerjee M, Stewart AK, Koenig RJ, Birkmeyer JD, Griggs JJ. Use of radioactive iodine for thyroid cancer. *JAMA*. 2011;**306**(7):721–728.

13. Haymart MR, Banerjee M, Yang D, Stewart AK, Doherty GM, Koenig RJ, Griggs JJ. The relationship between extent of thyroid cancer surgery and use of radioactive iodine. *Ann Surg*. 2013;**258**(2):354–358.

14. Papaleontiou M, Banerjee M, Yang D, Sisson JC, Koenig RJ, Haymart MR. Factors that influence radioactive iodine use for thyroid cancer. *Thyroid*. 2013;**23**(2):219–224.

15. Schuessler KM, Banerjee M, Yang D, Stewart AK, Doherty GM, Haymart MR. Surgeon training and use of radioactive iodine in stage I thyroid cancer patients. *Ann Surg Oncol*. 2013;**20**(3):733–738.

16. Yost K, Perkins C, Cohen R, Morris C, Wright W. Socioeconomic status and breast cancer incidence in California for different race/ethnic groups. *Cancer Causes Control*. 2001;**12**(8):703–711.

17. Thomas LE, Pencina MJ. Do not over (P) value your research article. *JAMA Cardiol*. 2016;**1**(9):1055.

18. Wasserstein RL, Lazar NA. The ASA's Statement on *p*-Values: context, process, and purpose. *Am Stat*. 2016;**70**(2):129–133.

19. Iyer NG, Morris LG, Tuttle RM, Shaha AR, Ganly I. Rising incidence of second cancers in patients with low-risk (T1N0) thyroid cancer who receive radioactive iodine therapy. *Cancer*. 2011;**117**(19):4439–4446.

20. Semrad TJ, Semrad AM, Farwell DG, Chen Y, Cress R. Initial treatment patterns in younger adult patients with differentiated thyroid cancer in California. *Thyroid*. 2015;**25**(5):509–513.

21. Greenberg CC, Lipsitz SR, Neville B, In H, Hevelone N, Porter SA, Weeks C, Jha AK, Gawande AA, Schrag D, Weeks JC. Receipt of appropriate surgical care for Medicare beneficiaries with cancer. *Arch Surg*. 2011;**146**(10):1128–1134.

22. DeGroot LJ, Kaplan EL, McCormick M, Straus FH. Natural history, treatment, and course of papillary thyroid carcinoma. *J Clin Endocrinol Metab*. 1990;**71**(2):414–424.

23. Mazzaferri EL. Thyroid remnant 131I ablation for papillary and follicular thyroid carcinoma. *Thyroid*. 1997;**7**(2):265–271.

24. Goldfarb M, Sener SF. Comparison of radioiodine utilization in adolescent and young adult and older thyroid cancer patients. *Endocr Pract*. 2014;**20**(5):405–411.

25. Zevallos JP, Xu L, Yiu Y. The impact of socioeconomic status on the use of adjuvant radioactive iodine for papillary thyroid cancer. *Thyroid*. 2014;**24**(4):758–763.

26. Patel A, Jhiang S, Dogra S, Terrell R, Powers PA, Fenton C, Dinauer CA, Tuttle RM, Francis GL. Differentiated thyroid carcinoma that express sodium-iodide symporter have a lower risk of recurrence for children and adolescents. *Pediatr Res*. 2002;**52**(5):737–744.

27. Lim II, Hochman T, Blumberg SN, Patel KN, Heller KS, Ogilvie JB. Disparities in the initial presentation of differentiated thyroid cancer in a large public hospital and adjoining university teaching hospital. *Thyroid*. 2012;**22**(3):269–274.

28. Harari A, Li N, Yeh MW. Racial and socioeconomic disparities in presentation and outcomes of well-differentiated thyroid cancer. *J Clin Endocrinol Metab*. 2014;**99**(1):133–141.

29. Fatima N, Zaman MU, Zaman A, Zaman U, Tahseen R. Comparable ablation efficiency of 30 and 100 mCi of I-131 for low to intermediate risk thyroid cancers using triple negative criteria. *Asian Pac J Cancer Prev*. 2016;**17**(3):1115–1118.

30. Mäenpää HO, Heikkonen J, Vaalavirta L, Tenhunen M, Joensuu H. Low vs. high radioiodine activity to ablate the thyroid after thyroidectomy for cancer: a randomized study. *PLoS One*. 2008;**3**(4):e1885.