Disparity in the use of adjuvant radioactive iodine ablation among high-risk papillary thyroid cancer patients

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ABSTRACT

Background: We sought to identify treatment disparities existing prior to publication of the 2015 American Thyroid Association Management Guidelines in order to identify patients with papillary thyroid cancer (PTC) at risk for receiving inadequate treatment.
Methods: Patients diagnosed with PTC from 2011 to 2013 were identified using Surveillance, Epidemiology and End Results database. High-risk disease was defined as T4, N1, or M1. Chi-square tests compared characteristics of patients with and without high-risk disease and characteristics of high-risk patients who did and did not receive radioactive iodine ablation (RAI). Likelihoods of having high-risk disease, of receiving RAI, and of cause-specific death were calculated using regression analyses.
Results: Sample included 32,229 individuals; 7894 (24.5%) had high-risk disease. Mean age was 50.0 years, 24,815 (77.0%) were female, and 21,318 (66.2%) were white. Odds of high-risk disease were greater among males (OR:2.04; 95% CI:1.92–2.16), Hispanics (OR:1.67; 95% CI:1.56–1.79) and Asians (OR:1.49; 95% CI:1.37–1.62), and uninsured (OR:1.24; 95% CI:1.07–1.43), and lower among patients ages 45–64 (OR:0.57; 95% CI:0.53–0.60), and ≥65 years (OR:0.54; 95% CI:0.50–0.59), and Blacks (OR:0.46; 95% CI:0.40–0.53). Most (69.3%) high-risk patients received RAI. Odds of receiving RAI were lower among patients age ≥65 years (OR:0.67; 95% CI:0.58–0.77), uninsured (OR:0.52; 95% CI:0.41–0.67), or with Medicaid (OR:0.58; 95% CI:0.50–0.69). RAI use reduced the risk of cause-specific mortality (HR:0.29; 95% CI:0.18–0.47).
Conclusion: Knowledge of these treatment disparities will allow recognition of groups at risk for high-risk disease and receiving inadequate treatment.

Introduction

The incidence of papillary thyroid carcinoma (PTC), the predominant type of thyroid cancer, has been increasing over the past several decades, and this increase has occurred for all stages of disease [1]. The most recent American Thyroid Association (ATA) Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer have implications on the use of adjuvant radioactive iodine ablation (RAI) [2]. Specifically, it is recommended that patients with high-risk disease (e.g. gross extrathyroidal extension, distant metastasis, pathologic N1 with large metastatic nodes) routinely receive postsurgical RAI [2]. The use of adjuvant RAI in patients with intermediate and high-risk thyroid cancer has been shown to decrease mortality [3–5]. However, RAI may be underutilized in particular groups of patients, leading to unwarranted variation among patients with high-risk disease. Therefore, the aim of this study was to identify treatment disparities existing prior to publication of these ATA guidelines in order to delineate patient groups at risk for receiving inadequate treatment.

Methods

The Surveillance, Epidemiology and End Results (SEER) database was used to identify patients diagnosed with thyroid cancer from 2011 to 2013 [6]. SEER is a publicly available, de-identified database

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representing approximately 28% of the United States population that contains demographic, tumor-related, treatment-related and survival information for various cancer types [6]. This study focused on cases of thyroid cancer diagnosed between 2011 and 2013 because this was the most recent SEER data available prior to publication of the current ATA guidelines. Our goal was to assess treatment patterns, in order to identify patient groups most at risk for receiving inadequate treatment. This finding can provide an appreciation of those groups most at risk of not achieving guideline recommended treatment.

An initial sample consisting of 38,013 cases of thyroid cancer was identified. Patients were excluded if the histology of their thyroid cancer was not papillary, if they did not undergo surgery or underwent an unknown type of surgery, and if their tumor size was designated as T0 (Fig. 1). Thus the final analytic sample consisted of 32,229 cases.

The age variable was divided into the following categories: age less than 45 years, age 45–64 years, and age 65 years or older. This was done in order to be consistent with the age groups designated in thyroid cancer staging of the American Joint Committee on Cancer Staging Manual 7th edition (less than or greater than 45 years), and to denote the age at which patients may become eligible for Medicare insurance by age (65 years) [7]. The race variable contained the following categories: non-Hispanic white, non-Hispanic Black, Hispanic, non-Hispanic Asian and other/unknown. The insurance variable contained the following categories: uninsured, Medicaid, insured, and unknown. The insured category referred to patients with private insurance or Medicare. The stage variable refers to the American Joint Committee on Cancer staging, 7th edition [7].

High-risk disease was defined as T4, N1, or M1. Chi-square tests were used to compare the characteristics of patients with high-risk disease to those without high-risk disease. Chi-square tests were also used to compare the characteristics of high-risk patients who did receive RAI to those who did not receive RAI. One-way ANOVA was used to compare mean age at diagnosis between those with and without high-risk disease, and between those with high-risk disease who did and did not receive RAI.

Logistic regression was used to determine the odds ratios (OR) and respective 95% confidence intervals (CI) of having high-risk disease. The adjusted regression model included the covariates age, sex, race, and insurance type. These demographic variables were significantly associated with presenting with high-risk disease in chi-square analysis, and thus it was important to account for them in the regression model. Next, logistic regression was used to determine the odds ratios and respective 95% CI of receiving RAI for high-risk disease. The adjusted regression model included the covariates age, sex, race, insurance type, surgery type, and number of nodes removed. These demographic and clinical variables were significantly associated with high-risk disease and/or receipt of RAI in chi-square analysis. Therefore, it was important to account for them in the regression model.

Finally, Cox regression was used to determine the risk of cause-specific death associated with receipt of RAI for high-risk disease. The adjusted regression model included the covariates age, sex, race, insurance type, surgery type and number of nodes removed. These demographic and clinical variables were significantly associated with high-risk disease and/or receipt of RAI in the previous analyses. Thus, it was important to account for them in the regression model.

Statistical analysis was performed using Stata version 12.1 (StataCorp LP, College Station, TX, USA). Statistical significance was determined using a p-value of <0.05 for all tests. Because data was obtained from a publicly available, de-identified database, institutional review board approval with exempted status was received from Thomas Jefferson University.

Results

The study sample included 32,229 individuals with PTC, of who 7894 (24.5%) had high-risk disease (Table 1). The mean age was 50.0 years, while 24,815 (77.0%) were female, and 21,318 (66.2%) were white (Table 1).

The odds of presenting with high-risk disease were greater among males (OR 2.04; 95% CI 1.92–2.16), Hispanics (OR 1.67; 95% CI 1.56–1.79) and Asians (OR 1.49; 95% CI 1.37–1.62), and the uninsured (OR 1.24; 95% CI 1.07–1.43)(Table 2). In contrast, the odds of presenting with high-risk disease were lower among patients ages 45–64 (OR 0.57; 95% CI 0.53–0.60), and ≥65 years (OR 0.54; 95% CI 0.50–0.59), and Blacks (OR 0.46; 95% CI 0.40–0.53)(Table 2).

Most (69.3%) high-risk patients received RAI. The odds of receiving RAI among high-risk patients were lower among patients older than 65 years (OR 0.67; 95% CI 0.58–0.77), the uninsured (OR 0.52; 95% CI 0.41–0.67), and those with Medicaid (OR 0.58; 95% CI 0.50–0.69)(Table 3). The odds of receiving RAI among high-risk patients were higher among patients who underwent total thyroidectomy (OR 1.983; 95% CI 1.438–2.733). Odds were also higher among patients who had at least 4 lymph nodes removed (OR 1.493; 95% CI 1.151–1.938)(Table 3).

The use of RAI among high-risk patients was associated with a decreased risk of cause-specific mortality (HR 0.29; 95% CI 0.18–0.47)(Table 4). With high-risk patients stratified by age group, the use of RAI among high-risk patients was associated with a decreased risk of cause-specific mortality in each age group (Table 4).

Discussion

This analysis of a large database identified particular characteristics associated with an increased likelihood of presenting with high-risk PTC. These characteristics included younger age, male sex, Hispanic and Asian race and uninsured status. Interestingly, Black patients were less likely to present with high-risk disease compared to whites. The association between race, socioeconomic status and advanced stage of thyroid cancer at presentation has been previously described [8–10]. Non-white (Black, Hispanic, Asian) patients have been reported as more likely to present with metastatic disease compared to their white counterparts [8]. Hispanic patients are more likely to have positive lymph nodes compared to whites, African Americans and Asians [10]. Similarly, low socioeconomic status and uninsured status have been associated with increased odds of having metastatic disease [8,9]. Also,
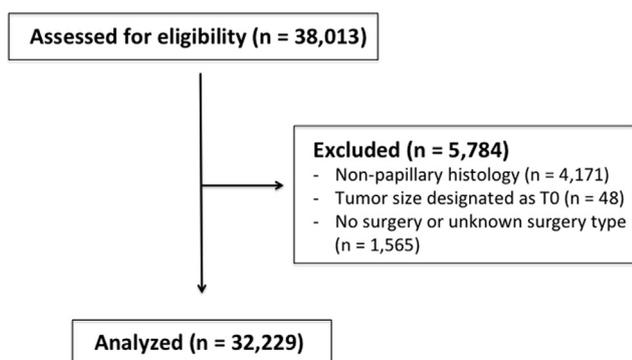

Fig. 1. Exclusion criteria and final analytic sample size.

Table 1
Demographic and clinical characteristics by risk category.

Characteristic	All, n (%)	Not High Risk, n (%)	High Risk, n (%)	p-value
Total	32,229 (100)	24,335 (75.5)	7894 (24.5)	
Mean Age in Years (standard deviation)	50.0 (14.8)	51.1 (14.3)	46.8 (15.7)	<0.001*
Age Group in Years				<0.001*
<45	11,855 (36.8)	8148 (33.5)	3707 (47.0)	
45 - 64	14,644 (45.4)	11,627 (47.8)	3017 (38.2)	
≥65	5730 (17.8)	4560 (18.7)	1170 (14.8)	
Sex				<0.001*
Female	24,815 (77.0)	19,423 (79.8)	5392 (68.3)	
Male	7414 (23.0)	4912 (20.2)	2502 (31.7)	
Race				<0.001*
White	21,318 (66.2)	16,493 (67.8)	4825 (61.1)	
Black	2016 (6.3)	1786 (7.3)	230 (2.9)	
Hispanic	4981 (15.5)	3308 (13.6)	1673 (21.2)	
Asian	3368 (10.5)	2339 (9.6)	1029 (13.0)	
Other/Unknown	546 (1.7)	409 (1.7)	137 (1.7)	
Insurance				<0.001*
Uninsured	949 (2.9)	655 (2.7)	294 (3.7)	
Medicaid	2686 (8.3)	1955 (8.0)	731 (9.3)	
Insured	27,933 (86.7)	21,179 (87.0)	6754 (85.6)	
Unknown	661 (2.1)	546 (2.2)	115 (1.5)	
Stage				<0.001*
I	23,441 (72.7)	19,787 (81.3)	3654 (46.3)	
II	1990 (6.2)	1947 (8.0)	43 (0.5)	
III	4263 (13.2)	2255 (9.3)	2008 (25.4)	
IVA	1570 (4.9)	0	1570 (19.9)	
IVB	160 (0.5)	0	160 (2.0)	
IVC	199 (0.6)	0	199 (2.5)	
IVNOS	26 (0.1)	0	26 (0.3)	
Unknown	580 (1.8)	346 (1.4)	234 (3.0)	
T Stage				<0.001*
T1	20,219 (62.7)	17,286 (71.0)	2933 (37.2)	
T2	4671 (14.5)	3465 (14.2)	1206 (15.3)	
T3	6080 (18.9)	3269 (13.4)	2811 (35.6)	
T4	856 (2.7)	0	856 (10.8)	
TX	403 (1.3)	315 (1.3)	88 (1.1)	
N Stage				<0.001*
N0	24,335 (75.5)	23,998 (98.6)	337 (4.3)	
N1	7541 (23.4)	0	7541 (95.5)	
NX	353 (1.1)	337 (1.4)	16 (0.2)	
M Stage				<0.001*
M0	31,987 (99.3)	24,335 (100)	7652 (96.9)	
M1	242 (0.8)	0	242 (3.1)	
Surgery Type				<0.001*
Lobectomy and/or Isthmectomy	4081 (12.7)	3922 (16.1)	159 (2.0)	
Partial Lobectomy	237 (0.7)	217 (0.9)	20 (0.3)	
Total/Near Total Thyroidectomy	27,911 (86.6)	20,196 (83.0)	7715 (97.7)	
Lymph Nodes Removed				<0.001*
0	14,405 (44.7)	14,141 (58.1)	264 (3.3)	
1−3	8290 (25.7)	6431 (26.4)	1859 (23.6)	
≥4	8870 (27.5)	3322 (13.7)	5548 (70.3)	
Other/Unknown	664 (2.1)	441 (1.8)	223 (2.8)	
Radiation				<0.001*
None	16,787 (52.1)	14,968 (61.5)	1819 (23.0)	
Radioactive Iodine	13,877 (43.1)	8405 (34.5)	5472 (69.3)	
Other/Unknown	1565 (4.9)	962 (4.0)	603 (7.6)	

*p-value significant at the <0.05 level.

patients of low socioeconomic status more often have stage IV disease than their counterparts of high socioeconomic status [9]. These findings are consistent with the results of our study, which suggest that particular socioeconomic variables are associated with more advanced thyroid cancer at presentation. This may be related to access to healthcare. Patients of lower socioeconomic status may have lower health literacy and access to healthcare resources, and thus may present with more advanced disease.

The suggested management of patients with high-risk thyroid cancer is described in the ATA Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer [2]. Regarding RAI use in particular, the current ATA guidelines recommend that patients with gross extra-thyroidal extension or distant metastasis routinely receive postsurgical RAI [2]. Furthermore, RAI should be considered for tumors greater than 4 cm in size, microscopic extra-thyroidal extension or lymph node metastases [2]. Thus, the current ATA guidelines are slightly more limited with recommending routine RAI use compared to the prior ATA guidelines published in 2009, which recommended that RAI be routinely administered to patients with tumors greater than 4 cm, gross extra-thyroidal extension or distant metastasis [10]. Selective RAI was suggested for patients with lymph node metastasis or minimal extra-thyroidal extension in the guidelines from 2009 [11].

Our study sought to identify factors associated with a decreased likelihood of receiving RAI for high-risk thyroid cancer, for which RAI is routinely recommended under the current ATA guidelines,

Table 2
Odds ratios for presenting with high-risk papillary thyroid cancer.

Characteristic	Crude Odds of High Risk Disease, Odds Ratio (95% CI)	Adjusted[a] Odds of High Risk Disease, Odds Ratio (95% CI)
Total		
Age in Years	0.980 (0.979—0.982)*	0.979 (0.977—0.981)*
Age Group in Years		
<45	Reference	Reference
45—64	0.570 (0.539—0.603)*	0.566 (0.534—0.599)*
≥65	0.564 (0.523—0.608)*	0.541 (0.501—0.585)*
Sex		
Female	Reference	Reference
Male	1.835 (1.733—1.942)*	2.041 (1.924—2.164)*
Race		
White	Reference	Reference
Black	0.440 (0.382—0.507)*	0.457 (0.397—0.528)*
Hispanic	1.729 (1.617—1.849)*	1.674 (1.561—1.795)*
Asian	1.504 (1.388—1.629)*	1.492 (1.375—1.619)*
Other/Unknown	1.145 (0.941—1.394)	1.123 (0.919—1.372)
Insurance		
Insured	Reference	Reference
Uninsured	1.408 (1.223—1.619)*	1.237 (1.070—1.431)*
Medicaid	1.173 (1.072—1.282)*	1.092 (0.995—1.198)
Unknown	0.660 (0.539—0.809)*	0.680 (0.552—0.836)*

*p-value significant at the <0.05 level.
CI = confidence interval.
  [a] Adjusted for age, sex, race, and insurance type.

utilizing a national dataset from a time period when guidelines for this condition were established. The factors associated with a decreased likelihood of receiving RAI for high-risk thyroid cancer included, older age, uninsured status, and Medicaid. Therefore, these patient groups were undertreated according to the prior ATA guidelines and continued to be undertreated according to the most recent ATA guidelines. Reasons for undertreatment among patients without insurance or with Medicaid may be related to inability to afford treatment. As for patient age, it is an important factor that physicians use to determine who should receive RAI [12]. The decreased use of RAI in older patients may be due to concern regarding the ability of older patients, who often have many co-morbid conditions, to tolerate RAI treatment. We also found a decreased likelihood of the use of RAI among patients with distant metastasis, patients who underwent lobectomy rather than total thyroidectomy and patients who had zero lymph nodes rather than four or more lymph nodes removed. The latter findings may be explained by the fact that all thyroid tissue should be removed before administering RAI, and that RAI should be considered for lymph node involvement rather than lack of involvement. The reasons for patients with distant metastasis being less likely to receive RAI is unclear. Possibly the presence of distant metastatic disease or the patient's overall condition was deemed not treatable, so maybe palliative care was used instead of RAI.

Factors associated with the receipt of ATA-compliant care for advanced thyroid cancer have been investigated [13,14]. Wenaas et al. examined whether the treatments (surgery, central neck lymph node dissection, RAI) received by patients with stages III and IV PTC complied with the 2006 ATA recommendations and deter-mined that age 45—64 years and higher income were predictive of receipt of ATA-compliant care [13]. Studies specifically investi-gating factors impacting the use of RAI for thyroid cancer have also been reported [9,14—18]. Similar to the results of the current study, Goffredo et al. found that older age, in addition to residing in the Northeast region of the United States and undergoing partial thy-roidectomy versus total thyroidectomy, were associated with a decreased likelihood of receiving RAI in accordance with ATA guidelines [14]. In contrast, having more than one lymph node examined was associated with an increased likelihood of receiving RAI [14]. Likewise, Haymart et al. used the National Cancer

Database to assess the use of RAI and found that, among patients with high-risk thyroid cancer (stage III or IV), United States region (West North Central), higher case volume (≥35 cases per year), younger patient age (45—59 years versus > 59 years), private in-surance versus Medicare, and lymph node involvement were significantly associated with RAI use [15].

Race also appears to play a role. Shah et al. analyzed the National Cancer Database and found that Blacks, Hispanics and Asians had an increased likelihood of being undertreated with radioactive iodine compared to their white counterparts [16]. However, appropriate use of RAI was more likely in Blacks, and less likely in Hispanics, compared to whites [16]. Race-related differences in receipt of RAI may be related to access to care. Minority patients are more likely to be of lower socioeconomic status compared to their White counterparts, and thus may have limited access to treatment. However, although our study found that certain racial groups were more likely to present with high-risk disease, there were no sig-nificant differences in the likelihood of receiving RAI based on race among high-risk thyroid cancer patients.

The use of post-surgical RAI in patients with intermediate and high-risk thyroid cancer has been shown to decrease mortality [3—5]. RAI use in patients with intermediate PTC has been associ-ated with a 29% decreased risk of death (HR 0.71; 95% CI 0.62—0.82) [3]. Similarly, patients with stages III or IV thyroid cancer who received RAI had a 46% increased likelihood of disease-specific survival compared to those who did not receive RAI (relative risk 1.46; 95% CI 1.13—1.87) [5]. Those results are consistent with our study results, in which survival analysis revealed a significantly decreased risk of cause-specific death among patients with high-risk disease who received RAI compared to those who did not. Moreover, this survival benefit was seen for all age groups. Because RAI use in patients with high-risk disease improves outcomes, it is important that all patients receive this therapy as indicated under the ATA guidelines.

Limitations of this study include that data was obtained from a national database that may be subject to chance coding errors and missing data. Further, this database only represents about 28% of the population and may be subject to inclusion bias. Also, survival analysis may be premature given the number of years available to assess events. By design, this study focused on cases of thyroid

Table 3
Characteristics of high-risk patients by radioactive iodine (RAI) category.

Characteristic	All, n (%)	No RAI, n (%)	RAI, n (%)	p-value	Crude Odds of Receiving RAI, Odds Ratio (95% CI)	Adjusted[a] Odds of Receiving RAI, Odds Ratio (95% CI)
Total	7894 (100)	2422 (30.7)	5472 (69.3)			
Mean Age in Years (standard deviation)	46.8 (15.7)	48.3 (16.6)	46.2 (15.2)	<0.001*	0.992 (0.989–0.995)*	0.992 (0.989–0.995)*
Age Group in Years				<0.001*		
<45	3707 (47.0)	1082 (44.7)	2625 (48.0)		Reference	Reference
45–64	3017 (38.2)	887 (36.6)	2130 (38.9)		0.990 (0.891–1.100)	0.990 (0.889–1.103)
≥65	1170 (14.8)	453 (18.7)	717 (13.1)		0.652 (0.569–0.748)*	0.670 (0.580–0.773)*
Sex				0.22		
Female	5392 (68.3)	1631 (67.3)	3761 (68.7)		Reference	Reference
Male	2502 (31.7)	791 (32.7)	1711 (31.3)		0.938 (0.847–1.039)	0.940 (0.846–1.045)
Race				0.03*		
White	4825 (61.1)	1449 (59.8)	3376 (61.7)		Reference	Reference
Black	230 (2.9)	83 (3.4)	147 (2.7)		0.760 (0.577–1.002)	0.846 (0.638–1.121)
Hispanic	1673 (21.2)	543 (22.4)	1130 (20.7)		0.893 (0.793–1.006)	0.958 (0.845–1.087)
Asian	1029 (13.0)	296 (12.2)	733 (13.4)		1.063 (0.916–1.233)	1.047 (0.901–1.218)
Other/Unknown	137 (1.7)	51 (2.1)	86 (1.6)		0.724 (0.509–1.029)	0.809 (0.563–1.161)
Insurance Type				<0.001*		
Insured	294 (3.7)	125 (5.2)	169 (3.1)		Reference	Reference
Uninsured	731 (9.3)	298 (12.3)	433 (7.9)		0.541 (0.427–0.686)*	0.525 (0.412–0.669)*
Medicaid	6754 (85.6)	1930 (79.7)	4824 (88.2)		0.581 (0.497–0.680)*	0.585 (0.498–0.688)*
Unknown	115 (1.5)	69 (2.9)	46 (0.8)		0.267 (0.183–0.389)*	0.279 (0.191–0.408)*
Stage				<0.001*		
I	3654 (46.3)	1068 (44.1)	2586 (47.3)		Reference	Reference
II	43 (0.5)	10 (0.4)	33 (0.6)		1.363 (0.669–2.775)	1.470 (0.716–3.018)
III	2008 (25.4)	607 (25.1)	1401 (25.6)		0.953 (0.846–1.074)	1.156 (0.304–4.393)
IVA	1570 (19.9)	485 (20.0)	1085 (19.8)		0.924 (0.812–1.051)	1.160 (0.307–4.381)
IVB	160 (2.0)	73 (3.0)	87 (1.6)		0.492 (0.358–0.677)*	0.779 (0.199–3.051)
IVC	199 (2.5)	94 (3.9)	105 (1.9)		0.461 (0.346–0.615)*	0.692 (0.178–2.692)
IVNOS	26 (0.3)	9 (0.4)	17 (0.3)		0.780 (0.347–1.756)	1.101 (0.228–5.308)
Unknown	234 (3.0)	76 (3.1)	158 (3.0)		0.859 (0.647–1.139)	1.131 (0.290–4.413)
T Stage				<0.001*		
T1	2933 (37.2)	947 (39.1)	1986 (36.3)		Reference	Reference
T2	1206 (15.3)	360 (14.9)	846 (15.5)		1.121 (0.969–1.296)	1.120 (0.966–1.299)
T3	2811 (35.6)	756 (31.2)	2055 (37.6)		1.296 (1.157–1.452)*	1.352 (1.203–1.519)*
T4	856 (10.8)	324 (13.4)	532 (9.7)		0.783 (0.668–0.917)*	0.999 (0.839–1.190)
TX	88 (1.1)	35 (1.5)	53 (1.0)		0.722 (0.468–1.114)	0.897 (0.574–1.401)
N Stage				<0.001*		
N0	337 (4.3)	138 (5.7)	199 (3.6)		Reference	Reference
N1	7541 (95.5)	2274 (93.9)	5267 (96.3)		1.606 (1.286–2.007)*	1.190 (0.890–1.591)
NX	16 (0.2)	10 (0.4)	6 (0.1)		0.416 (0.148–1.171)	0.523 (0.181–1.507)
M Stage				<0.001*		
M0	7652 (96.9)	2318 (95.7)	5334 (97.5)		Reference	Reference
M1	242 (3.1)	104 (4.3)	138 (2.5)		0.577 (0.445–0.747)*	0.712 (0.543–0.933)*
Surgery Type				<0.001*		
Lobectomy and/or Isthmectomy	159 (2.0)	78 (3.2)	81 (1.5)		Reference	Reference
Partial Lobectomy	23 (0.3)	9 (0.4)	11 (0.2)		1.177 (0.462–2.996)	1.485 (0.568–3.886)
Total/Near Total Thyroidectomy	7715 (97.7)	2335 (96.4)	5380 (98.3)		2.219 (1.620–3.039)*	1.983 (1.438–2.733)*
Lymph Nodes Removed				<0.001*		
0	264 (3.3)	111 (4.6)	153 (2.8)		Reference	Reference
1–3	1859 (23.6)	622 (25.7)	1237 (22.6)		1.443 (1.110–1.876)*	1.230 (0.939–1.612)
≥4	5548 (70.3)	1593 (65.8)	3955 (72.3)		1.801 (1.401–2.316)*	1.493 (1.151–1.938)*
Other/Unknown	223 (2.8)	98 (4.0)	127 (2.3)		0.960 (0.670–1.376)	0.869 (0.600–1.257)

*p-value significant at the <0.05 level.
RAI = radioactive iodine ablation; CI = confidence interval.
 [a] Adjusted for age, sex, race, insurance type, surgery type and number of nodes removed.

cancer diagnosed immediately prior to publication of the most recent ATA guidelines in order to assess current treatment patterns. Because of this, survival time is limited. Information on patients treated after publication of the 2015 ATA guidelines were not available in the SEER database at the time our study was conducted. Once this data becomes available, future research may focus on disparity in the use of RAI among high-risk patients after publication of the 2015 ATA guidelines. This study was also limited by the fact that, because it is retrospective in nature and relied on an administrative database, we were unable to infer causality.

However, the strengths of this study include that it is based on a large sample size that is representative of the United States. Thus, the results are generalizable. Furthermore, this study identifies particular variables that are predictive of having high-risk PTC and

receiving inadequate treatment. This information is highly relevant to clinical practice and patient care. Physicians should be aware that patients who are older, uninsured or have Medicaid have a decreased likelihood of receiving RAI, even though it is recommended. Increased awareness may allow for adjustment in treatment patterns in an effort to decrease the unwarranted variation in receipt of RAI for high-risk disease and improve patient outcomes. Future studies may evaluate if publication of the newer guidelines had any effect on changing treatment patterns.

Conclusion

High-risk thyroid cancer patients were more likely to be of a younger age, male sex, Hispanic and Asian ethnicity, and uninsured

Table 4
Risk of cause-specific death among high-risk patients.

Characteristic	Crude Risk of Death, Hazard Ratio (95% CI)	Adjusted[a] Risk of Death, Hazard Ratio (95% CI)
Overall		
No RAI	Reference	Reference
RAI	0.210 (0.131–0.337)*	0.289 (0.178–0.470)*
By Age Group in Years		
< 45		
No RAI	Reference	Reference
RAI	0.129 (0.013–1.241)	0.093 (0.009–0.928)*
45–64		
No RAI	Reference	Reference
RAI	0.235 (0.092–0.597)*	0.262 (0.100–0.683)*
≥ 65		
No RAI	Reference	Reference
RAI	0.275 (0.156–0.485)*	0.301 (0.168–0.538)*

*p-value significant at the <0.05 level.

RAI = radioactive iodine ablation; CI = confidence interval.

[a] Adjusted for age, race, sex, insurance type, surgery type and number of nodes removed.

status. High-risk thyroid cancer patients were less likely to receive RAI if they were older, uninsured, or had Medicaid. Receipt of RAI in patients with high-risk thyroid cancer is associated with significantly improved survival. Knowledge of these risks and treatment disparities will allow recognition of groups at risk for high-risk disease and receiving inadequate treatment, so that all patients will have the best opportunity for optimal outcomes.

Conflicts of interest

There are no known conflicts of interest associated with this manuscript and there has been no significant financial support for this work that could have influenced its outcome.

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