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Use of Radioactive Iodine for Thyroid Cancer

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Abstract

Context—Substantial uncertainty persists over the indications for radioactive iodine for thyroid cancer. Use of radioactive iodine over time and the correlates of its use remain unknown.

Objective—To determine practice patterns, the degree to which hospitals vary in their use of radioactive iodine, and factors that contribute to this variation

Design, Setting, Patients—We performed time trend analysis of radioactive iodine use in a cohort of 189,219 well-differentiated thyroid cancer patients treated at 981 hospitals associated with the National Cancer Database between 1990 and 2008. We used multilevel analysis to assess the correlates of patient and hospital characteristics on radioactive iodine use in the cohort treated from 2004–2008.

Main Outcome Measure—Use of radioactive iodine after total thyroidectomy

Results—Between 1990 and 2008, across all tumor sizes, there was a significant rise in the proportion of well-differentiated thyroid cancer patients receiving radioactive iodine (1373/3397, versus 11539/20620, $P<0.001$). Multivariable analysis of patients treated from 2004 to 2008 found that there was a statistical difference in radioactive iodine use between AJCC stage I and IV (odds ratios (OR) 0.34 (0.31–0.37) but not between stage II/III versus IV (OR 0.97 (0.88–1.07), 1.06 (0.95–1.17), respectively). In addition to patient and tumor characteristics, hospital volume was associated with radioactive iodine use. Wide variation in radioactive iodine use existed, and only 21.1% of this variation was accounted for by patient and tumor characteristics. Hospital type and case volume accounted for 17.1% of the variation. After adjusting for available patient, tumor, and hospital characteristics, much of the variance, 29.1%, was attributable to unexplained hospital characteristics.

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Conclusions—Among patients treated for well-differentiated thyroid cancer at hospitals in the National Cancer Database, there was an increase in the proportion receiving radioactive iodine between 1990 and 2008; much of the variation in use was associated with hospital characteristics.

Over 40,000 Americans are diagnosed with thyroid cancer each year, and the overwhelming majority of cases are well-differentiated thyroid cancer. Standard treatment for well-differentiated thyroid cancer is thyroidectomy. To ensure full eradication of remnant thyroid tissue and to treat residual disease, in patients with visible inoperable iodine avid metastases, radioactive iodine is often administered after total thyroidectomy. Previous cohort studies have shown improved survival and reduced tumor recurrence when iodine-avid advanced stage well-differentiated thyroid cancer is treated with radioactive iodine.[1–3] There is little controversy over the value of radioactive iodine for these patients. In contrast, for very low risk disease, in which the prognosis is typically excellent, treatment with radioactive iodine is of uncertain benefit.[4–7]

Indications for use of radioactive iodine following surgery for the majority of well-differentiated thyroid cancer are hotly debated.[8–10] In the absence of randomized control trials evaluating the utility of radioactive iodine relative to disease severity, clinical guidelines have left radioactive iodine use to physician discretion in the majority of scenarios.[11–16] Proponents argue that universal use of radioactive iodine increases the ease of following the tumor marker, thyroglobulin, and may destroy microscopic metastases. In contrast, opponents counter that the mortality secondary to thyroid cancer is sufficiently low negating the need for the unnecessary health risks[17–29] and costs[30] associated with universal radioactive iodine use.

The recent rise in the incidence of small, low risk thyroid cancers[31,32] mandates an understanding of patterns of care in thyroid cancer. We hypothesized that there would be unwarranted variation in radioactive iodine use with factors other than disease severity predicting administration. In this study, we determined the recent change in practice patterns, examined the degree to which hospitals vary in their use of radioactive iodine, and assessed factors that contribute to this variation.

Methods

Data Source and Study Population

The National Cancer Database, a joint project of the American College of Surgeons Commission on Cancer and the American Cancer Society, is a nationwide, facility-based oncology data set that currently captures 70% of all newly diagnosed malignant cancers, including close to 85% of all thyroid cancers, in the United States.[33] Once diagnosed and treated at a hospital with a Commission on Cancer-accredited cancer program, the remainder of the patient's disease course and treatment are documented by the hospital registrar even when care is transferred to another facility.[33] Data are coded and reported according to nationally established protocols coordinated under the auspices of the North American Association of Central Cancer Registries.[34] No patient, physician, or hospital identifiers were examined in this study, and Institutional Review Board (IRB) exemption was granted for this study by the University of Michigan IRB.

Data from 314,039 patients diagnosed with primary thyroid cancers between January 1, 1990, and December 31, 2008 were queried from the National Cancer Database. To ensure a stable physician cohort over the time period reviewed in this study, only currently accredited Commission on Cancer programs that had reported cases in 14 of the 19 years to the National Cancer Database were included. The patients with tumor histologies of papillary, follicular, or Hurthle cell cancer types were retained for analysis. Finally, because total thyroidectomy is recommended before radioactive iodine treatment, only the patients who had undergone total thyroidectomy (n = 189,219) at the 981 Commission on Cancer-accredited programs were selected for analysis. Correlates of radioactive iodine use were evaluated in the 85,948 patients diagnosed between 2004 and 2008 in order to define the most contemporary practice patterns.

Measures

Patient age was stratified into three biologically-relevant groups: 44 and younger, 45–59, and 60 and older. Patient race/ethnicity was categorized by the National Cancer Database as non-Hispanic white, African American, and Hispanic, Asian/ Pacific Islanders, Native American. Due to smaller numbers, Hispanic, Asian/Pacific Islanders, and Native American were collapsed into Other. Race/ethnicity was included in the analysis because race/ethnicity has been shown to influence cancer treatment.[35] With data drawn from the 2000 Census, we assigned 2008 100% poverty line, insurance type, percentage with college degree, and rural-urban continuum. We used the Charlson-Deyo Index to identify comorbid conditions within the cohort.[36,37] Tumor size was categorized according to the definitions used by the American Joint Committee on Cancer (AJCC).[38] Tumor histology was limited to International Classification of Diseases for Oncology (ICD-O) classification codes for papillary, follicular and Hurthle cell cancer types.[39] Type of cancer program consisted of the following mutually exclusive categories: community hospitals, comprehensive community, teaching/research, and National Cancer Institute/National Comprehensive Cancer Network. Hospital volume was analyzed as a continuous and categorical variable. Case volume categories were created by computing a weighted average of the annual thyroid case volume at each reporting cancer program for the years 2004 to 2008 and dividing the distribution into equal-sized quintiles of hospitals: ≤ 6, 7–11, 12–19, 20–34, and ≥ 35 cases per year.

Statistical Analysis

We performed a time trend analysis of radioactive iodine use relative to tumor size between years 1990–2008. The Chi-square test was used to assess the statistical significance of temporal trends in radioactive iodine use.

Next, we selected data from the most recent five years in this cohort, 2004-2008, for univariate analysis and multivariable logistic regression. Univariate associations between radioactive iodine use and patient and tumor characteristics were evaluated with chi-square tests.

We used hierarchical generalized linear models[40,41] to account for the clustering of thyroid cancer patients within hospitals while assessing the effect of comorbidity and sociodemographic (gender, age, race, poverty level, insurance, education, rural/urban continuum), tumor (histology, stage), and hospital (hospital type and case volume) characteristics. Specifically, we used a logit link to model the binary radioactive iodine use. Our model also included a random hospital-specific intercept to capture the heterogeneity across hospitals. Let $Y_{ij} = 1$, if the *j*th patient seen at the *i*th hospital used radioactive iodine, and $Y_{ij} = 0$ otherwise. The probability of radioactive iodine use by the *j*th patient seen at the *i*th hospital can then be modeled as follows:

Level 1: between-patients (within hospitals): $\text{logit}(P(Y_{ij}=1))=\mu_{0i}+\underline{\theta}' X_{ij}$

Level 2: between-hospitals: $\mu_{0i} = \beta_{00} + \beta_{0i} + \gamma' \text{-} Z_i$

Combined model: $\text{logit}(P(Y_{ij}=1))=\beta_{00}+\beta_{0i}+\gamma' - Z_i+\underline{\theta}' X_{ij}$

where β_{00} is the population-averaged log-odds of radioactive iodine use, β_{0i} is the hospital-specific random effect, assumed to follow a normal distribution with mean zero and variance σ^2_{hosp}, $\underline{X}_{ij}$ is the matrix of patient and tumor covariates, $\underline{\theta}$ is the corresponding vector of fixed effects representing changes in the log-odds of radioactive iodine use corresponding to each unit change in the covariate values, Z_i represents the vector of hospital-level covariates for the ith hospital, and γ is the corresponding vector of coefficients. Model estimates were obtained using likelihood based approach in SAS PROC GLIMMIX (SAS version 9.2; SAS Institute, Cary, NC). A hierarchical generalized linear model approach allows the estimation and partitioning of variance in radioactive iodine use between the patient and hospital levels. As a measure of the importance of the hospital effect on individual use of radioactive iodine, we estimated the percentage of the variance in radioactive iodine use attributable to hospital, using the intraclass correlation coefficient. The intraclass correlation coefficient was estimated based on the assumption of a threshold model that is appropriate for a binary outcome.[40]

Our initial null model contained only a hospital-specific random effect term. Next we fitted a series of adjusted models which, in addition to the hospital-specific random effect, included fixed patient characteristics (comorbidity, sociodemographic covariates), tumor characteristics and hospital covariates (each covariate group at a time). These models were used to calculate the percentage of total variance attributable to patient, tumor and hospital characteristics. The denominator for this calculation was the total variance, which included the variance attributable to random (unmeasured) hospital effects after adjustment for the corresponding fixed effect covariates in a given model, the variance attributable to the corresponding measured covariates (i.e. fixed effects), and the variance attributable to unmeasured patient or tumor characteristics plus error. In this way, the relative importance of each component could be examined. Finally, a fully adjusted model was fitted incorporating the available patient and hospital characteristics as fixed effects covariates in the model. The residual intraclass correlation coefficient was calculated based on the fully adjusted model and represents the percentage of variance attributable to hospital after adjustment for available patient and hospital characteristics. The denominator in the calculation of this percentage was composed of the variance attributable to unmeasured hospital effects, after adjustment for available patient and hospital variables, and the variance attributable to unmeasured patient or tumor characteristics plus error.

As another measure of hospital variation in use of radioactive iodine, hospital-specific radioactive iodine administration rates were calculated based on a hierarchical generalized linear model that was adjusted for patient and tumor characteristics. Hospital-specific rates were obtained using empirical Bayes predictions[42] and then plotted by hospital rank, from lowest to highest according to the empirical Bayes predictions. This method shrinks the estimate of hospital-specific radioactive iodine administration rate towards the average rate, as a factor of the number of thyroid cancer patients treated at the hospital. Hospitals treating a large number of thyroid cancer patients will have less shrinkage whereas hospitals treating a small number of thyroid cancer patients will have more shrinkage towards the average rate.

All statistical analyses were performed using SAS software (SAS version 9.2; SAS Institute, Cary, NC). Two-sided tests were used, with p values <0.05 considered statistically significant.

Results

Between 1990 and 2008 there was a significant increase in the proportion of well-differentiated thyroid cancer patients receiving radioactive iodine as adjuvant therapy after total thyroidectomy (P<0.001). In 1990, 1,373/3,397 (40.4%) patients received radioactive iodine whereas in 2008 11,539/20,620 (56.0%) received radioactive iodine. For tumors 1.1 to 2 cm, 2.1 to 4 cm, and over 4 cm there was a 55–67% increase in the percentage of patients treated in 2008 compared to those treated in 1990. The proportion of tumors ≤ 1 cm treated with radioactive iodine was lower but has also climbed steadily over time (Figure 1).

Table 1 summarizes the study population and proportion receiving radioactive iodine as adjuvant therapy following total thyroidectomy in 2004–2008. In multivariable analyses, younger age and absence of comorbidity were associated with a small but significantly greater likelihood of receiving radioactive iodine after total thyroidectomy (odds ratio (OR) 2.15 (2.04–2.26), 1.19 (1.07–1.35), respectively). Female gender, African American race, and absence of private/government insurance was associated with significantly less likelihood of receiving radioactive iodine (OR 0.87 (0.84–0.91), 0.83 (0.77–0.89), and 0.84 (0.81–0.88), respectively). There was a statistical difference in radioactive iodine use between AJCC stage I and IV (OR 0.34 (0.31–0.37), but not between stage II and III versus stage IV (OR stage II, 0.97 (0.88–1.07), stage III, 1.06 (0.95–1.17)). When hospital case volume was analyzed as a categorical variable, there was an increased likelihood of radioactive iodine use as the volume category increased. There was a significant difference between low and low-medium versus high case volume (respectively OR 0.44 (0.33–0.58) and 0.62 (0.48–0.80)). The effect of continuous case volume was also statistically significant in both the unadjusted and adjusted models. The adjusted OR (95% CI) was 1.006 (1.003 – 1.008), p-value=0.0001 suggesting that with every one additional case a hospital treats, the odds of radioactive iodine use increases by 0.6% after adjusting for patient and tumor characteristics and hospital type.

The subgroup analysis of patients treated between 2004 and 2008 demonstrates substantial variation in use of radioactive iodine. Patient characteristics explain 21.1% of this variance and measured hospital characteristics 17.1%. These partitioned variances were obtained from a series of adjusted models so the relative importance of each component could be examined. After controlling for gender, age, race, comorbidity, poverty level, insurance, education, degree of rural/urbanism, tumor histology, size, stage, and hospital type, case volume, the residual intraclass correlation coefficient was 29.1% indicating that substantial variation in radioactive iodine use still exists across hospitals.

After selecting patients without comorbidity and with consistent sociodemographic variables (white race, income above 100% poverty, private insurance, areas where over 12% of the population have a college education, and metropolitan residence) evaluation of radioactive iodine use in both lower risk, young, female patients with tumor size ≤ 1 cm and stage I disease and in higher risk, older, male patients who have tumor size over 2 cm and have stage III or IV disease, showed wide hospital-level variation. For the lower risk profile, 246 (64.9%) of the 379 hospitals treating such patients had a radioactive iodine administration rate that was statistically significantly different from the average of 37.4%, with 79 (20.8%) of the 379 hospitals having a rate below the average rate, and 167 (44.1%) of the hospitals having a rate above the average (Figure 2). For the higher risk profile, 63 (64.3%) of the 98 hospitals treating such patients had a radioactive iodine administration rate that was statistically significantly different from the average rate of 74.9%, with 17 (17.4%) of the 98 hospitals having a rate below the average rate, and 46 (46.9%) of the hospitals having a rate above the average (Figure 3).

Discussion

The results of this study provide insight into the use of radioactive iodine for management of well-differentiated thyroid cancer. Between 1990 and 2008, there was a rise in radioactive iodine use across all tumor sizes. In addition to tumor characteristics, other patient and hospital characteristics were also associated with radioactive iodine use. There was wide between-hospital variation in radioactive iodine use and much of the variance was attributable to unexplained hospital characteristics.

Previous studies have evaluated between-hospital variation in rates of surgical procedures[43,44] and the role of discretionary decision making on treatment intensity.[45,46] Germane to our study is a single-institution study that evaluated use of radioactive iodine over time and found a rise in use between 1940 and 1999[47] and a study with Surveillance, Epidemiology, and End Results data that found increased radioactive iodine use between 1973 and 2006.[21] However, our study is novel as it investigates not only treatment trends but also correlates of radioactive iodine use and variation in use in a large and recently treated multicenter cohort of thyroid cancer patients.

The explanation for the rise in radioactive iodine use across all tumor sizes is not entirely clear, but it has been hypothesized that increased detection of low risk disease can lead to overestimation of treatment efficacy and a subsequent rise in use of therapy.[48] We know from previous population studies that well-differentiated thyroid cancer is increasing at a faster rate than any other malignancy with a 2.4-fold rise in incidence over the past 30 years.[31,32,49] The majority of the increase is due to detection of small, low risk tumors,[31,50] and, in light of the 10–36% incidence of occult well-differentiated thyroid cancer in autopsy studies,[51,52] over diagnosis of clinically irrelevant cancers may be occurring.[48,53] Thus, there is potential for increased detection of low risk disease spurring a rise in thyroid cancer treatment intensity.

In addition to identifying trends in radioactive iodine use and correlates of use, this study also found large hospital-based variation with patient and tumor characteristics accounting for 21% of the variation and unknown hospital factors accounting for 29% of the variation. These findings suggest disease severity is not the sole determinant of radioactive iodine use.

Wide variation in radioactive iodine use was seen in both lower and higher risk patients. The low risk patient profile depicted in Figure 2 is a profile in which the use of radioactive iodine was left to physician discretion[12–14,16] until the most recent clinical guidelines.[11] In contrast, almost all clinical guidelines would strongly recommend radioactive iodine post thyroid surgery in the high risk patient profile depicted in Figure 3.[11–16] The variation demonstrated in both low and high risk patients suggests clinical uncertainty.[54,55] Some of this uncertainty may be explained by the lack of clinical trials evaluating the efficacy of radioactive iodine use for thyroid cancer and the conflicting single institution studies. Because of limited clinical evidence, clinical guidelines have left radioactive iodine use to physician discretion in many cases.[11,12] A recent study has shown that when clinical guideline treatment recommendations are not supported by strong evidence there is less guideline-concordant care.[56]

Studies using a large database such as the National Cancer Database have inherent limitations. Specific to thyroid cancer, presence of extrathyroidal extension, post-operative serum thyroglobulin level, and tumor iodine-avidity are not recorded. In addition, treatment details such as dose of radioactive iodine and addition of prophylactic central lymph node dissection are not known. These missing details may be important as they can impact the indications for radioactive iodine[57] and, in the case of radioactive iodine dosing, affect our assessment of intensity of care.

Even with the limitations inherent in a large database, the results of this study have implications for patients, physicians, and payers. Although appropriate therapy for select well-differentiated thyroid cancer, the benefit of radioactive iodine may not always exceed the risks. There is a clear role for adjuvant therapy with radioactive iodine in iodine-avid advanced stage well-differentiated thyroid cancer.[1–3,58] however, there is unclear benefit to radioactive iodine use in low risk disease.[4–6,59–64] as patients with low risk disease have an excellent prognosis regardless of intervention.[5,65,66]

In addition to clear cost saving benefits associated with not using radioactive iodine for low risk disease,[30] limiting radioactive iodine use would decrease patients' risks of side effects. Not only are there transient adverse effects on quality of life with the hypothyroidism typically required pre-radioactive iodine treatment,[67] radioactive iodine has long term health risks. Recent studies have found increased risk for second primary malignancies after radioactive iodine treatment, even in the lowest risk patients,[21] with the greatest risk for leukemia, which increases 2.5-fold.[18,19,68,69] Radioactive iodine is also associated with additional adverse systemic effects, [26,17,27,70,29,16,71] and damage to local tissue, such as the salivary glands and nasolacrimal ducts.[20,22,24,25] There are also potential public health risks if appropriate safety precautions are not taken at the time of radioactive iodine administration.[72] In contrast to the potential for over treatment and greater harm than good when using radioactive iodine for low risk disease, the spectrum of radioactive iodine use in the high risk patient profile, suggest there may be under treatment of some high risk patients. This has potential implications for patient health, such as increased risk of disease recurrence and mortality.[3,5]

The fact that disease severity appears to have a small influence on radioactive iodine use after thyroid surgery is concerning. In the interest of curbing the rising health care costs and preventing both over- and under treatment of disease, indications for radioactive iodine should be clearly defined, and disease severity should become the primary driver of radioactive iodine use.

In summary, in the United States, the incidence of small, low risk thyroid cancers is growing at a faster rate than any other malignancy.[49] Paradoxically, use of radioactive iodine is climbing in patients with all tumor sizes. The significant between-hospital variation in radioactive iodine use suggests clinical uncertainty over the role of radioactive iodine in thyroid cancer management. Of concern, for patients with thyroid cancer, the hospital where care is received has a substantial influence on treatment with radioactive iodine after total thyroidectomy, even after accounting for patient and tumor characteristics.

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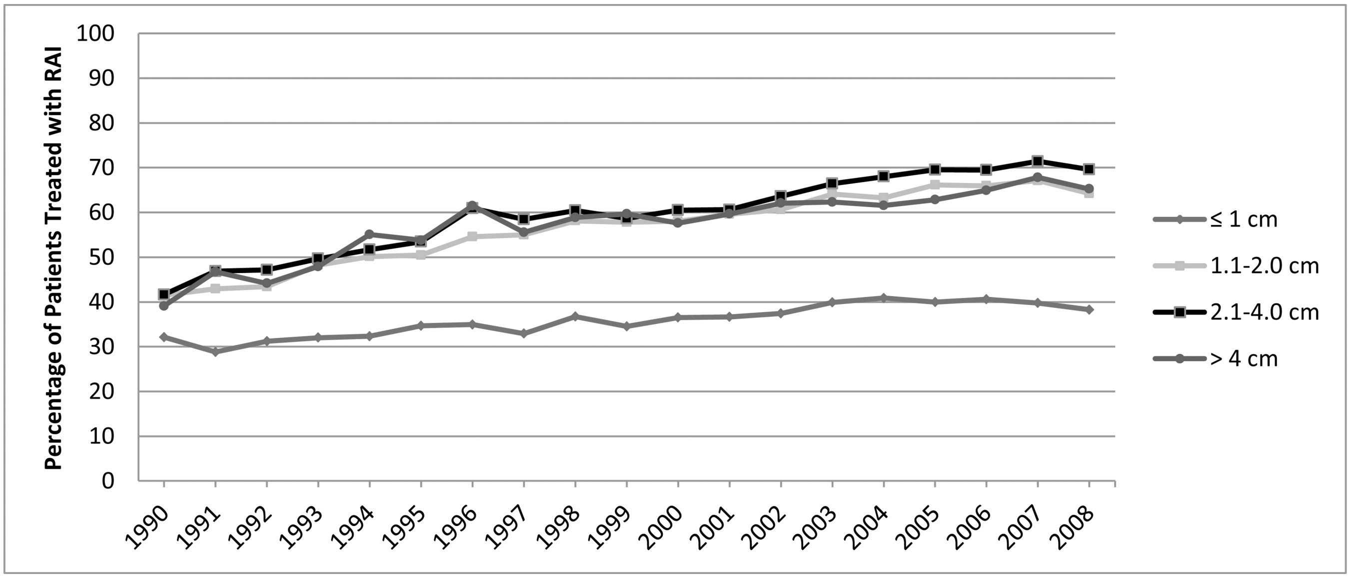

Figure 1.
Proportion of patients treated with radioactive iodine (RAI) based on tumor size between 1990 and 2008.

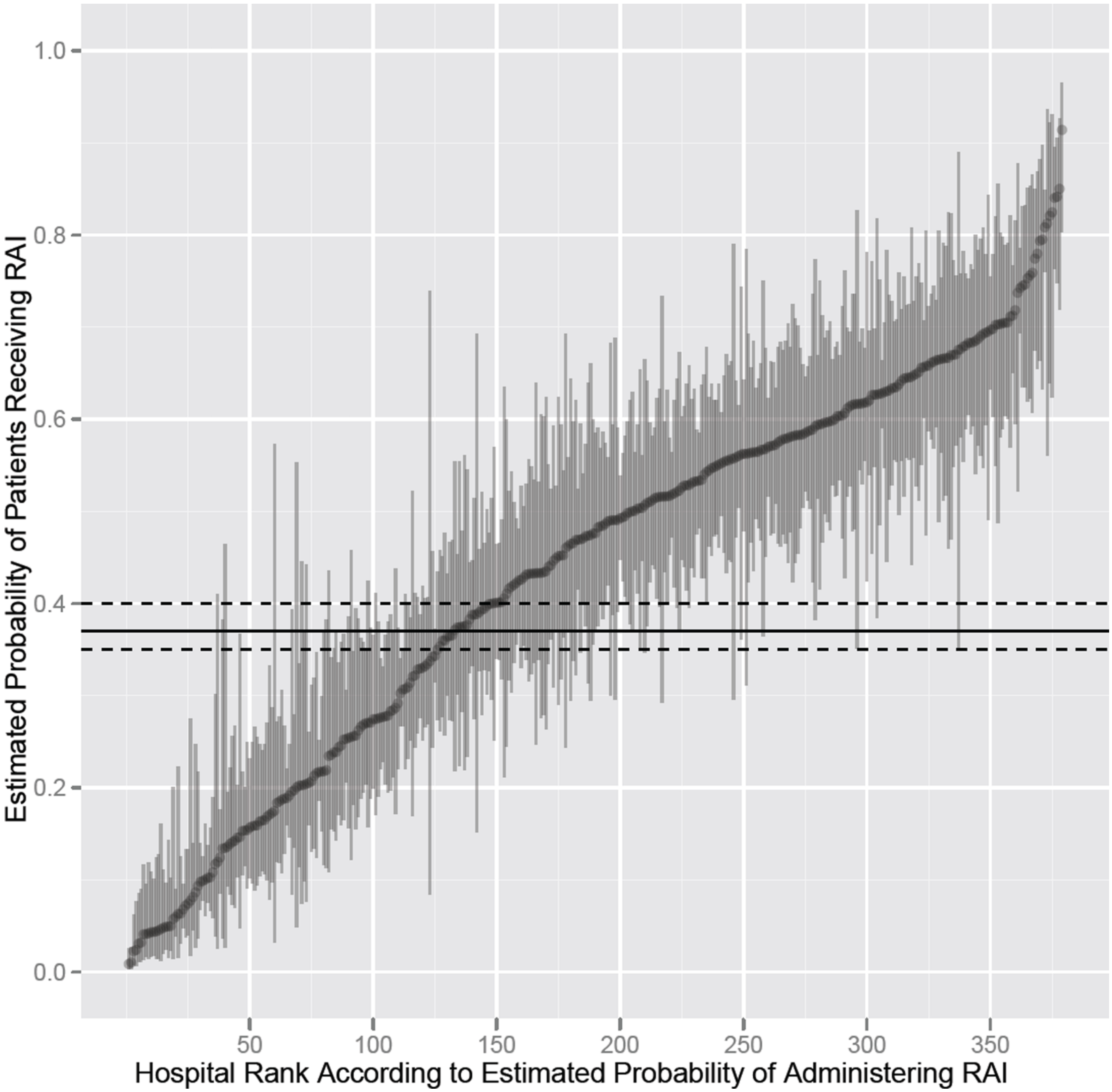

Figure 2.
When papillary thyroid cancer patients with characteristics associated with low risk of death were selected, there was tremendous variation in hospital-level radioactive iodine use. The horizontal line is the population average (37.4%) and the dashed lines represent the 95% confidence interval for the average. The vertical lines represent the 95% confidence intervals for the hospital-specific estimated probabilities of radioactive iodine use.

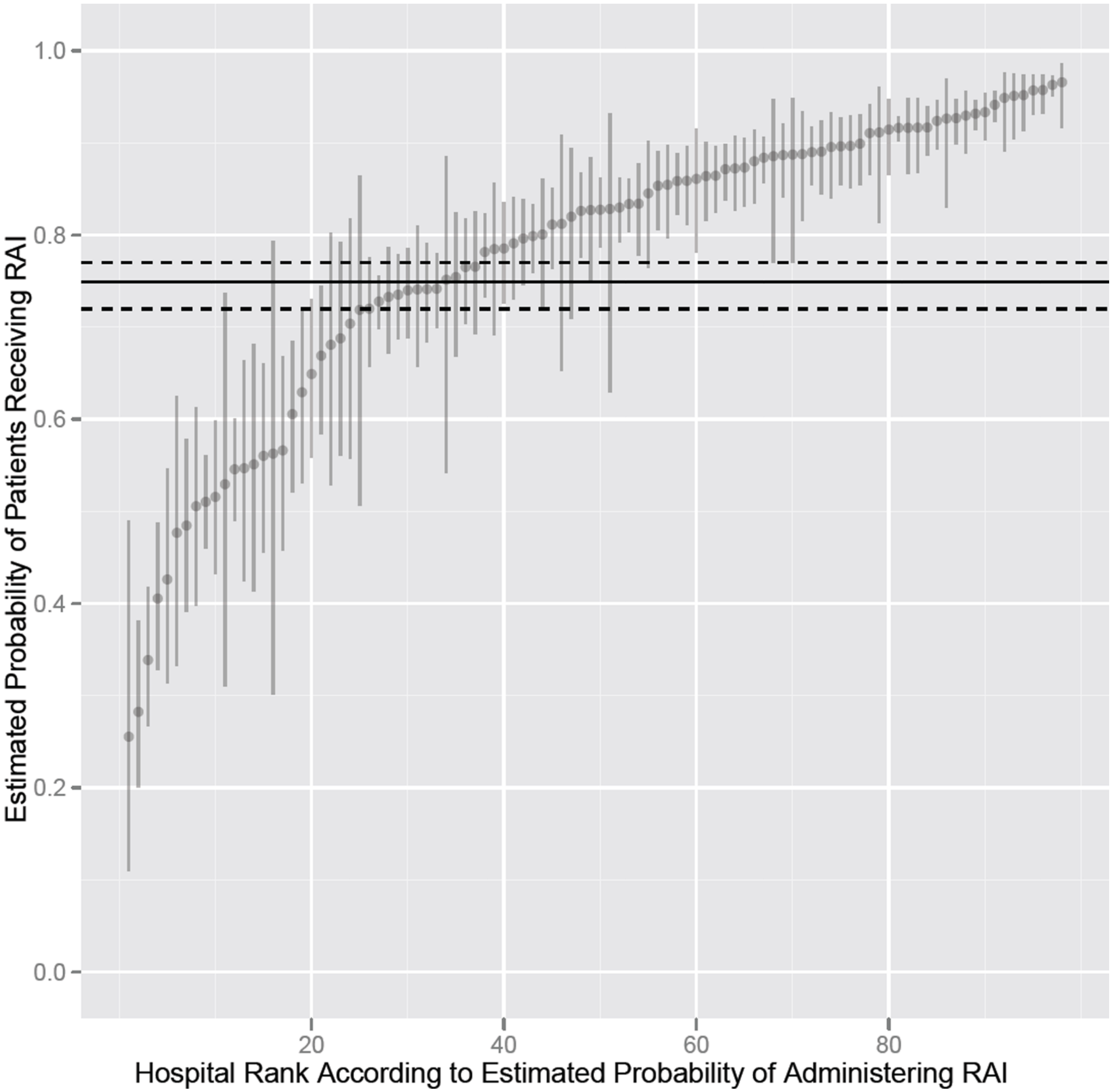

Figure 3.

When papillary thyroid cancer patients with characteristics associated with a higher risk of death were selected, variation in use of radioactive iodine still existed. The horizontal line is the population average (74.9%) and the dashed lines represent the 95% confidence interval for the average. The vertical lines represent the 95% confidence intervals for the hospital-specific estimated probabilities of radioactive iodine use.

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Table 1

Multivariate Analysis with Patient and Hospital Characteristics, 2004–2008

	Total No. (%)	No. treated with RAI (%)	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Patient Characteristics				
Patient Gender				
Male	19 754 (23.0)	12 079 (61.2)	1.00	1.00
Female	66 194 (77.0)	37 346 (56.4)	0.82 (0.79–0.85)	0.87 (0.84–0.91)
Patient Age				
Age ≤44 years	34 432 (40.1)	21 090 (61.3)	1.43 (1.38–1.48)	2.15 (2.04–2.26)
Age 45–59 years	30 267 (35.2)	17 159 (56.7)	1.18 (1.14–1.22)	1.19 (1.14–1.26)
Age ≥ 60 years	21 249 (24.7)	11 176 (52.6)	1.00	1.00
Charlson/Deyo Comorbidity Index Score				
0	73 943 (86.0)	42 942 (58.1)	1.26 (1.15–1.39)	1.19 (1.07–1.35)
1	10 303 (12.0)	5 593 (54.3)	1.08 (0.98–1.20)	1.07 (0.95–1.21)
≥ 2	1 702 (2.0)	890 (52.3)	1.00	1.00
Patient Race/Ethnicity				
White	67 528 (78.6)	39 104 (57.9)	1.00	1.00
African American	5 539 (6.4)	2 816 (50.8)	0.75 (0.71–0.79)	0.83 (0.77–0.89)
Other	12 881 (15.0)	7 505 (58.3)	1.02 (0.98–1.05)	1.06 (1.00–1.12)
Household Income				
Above 100% Poverty	41 877 (52.4)	24 011 (57.3)	0.99 (0.96–1.02)	1.04 (0.99–1.08)
Below 100% Poverty	38 054 (47.6)	21 897 (57.5)	1.00	1.00
Insurance				
Private/Gov	64 070 (75.9)	38 013 (59.3)	1.00	1.00
Medicare/Medicaid/Uninsured	20 359 (24.1)	10 776 (52.9)	0.77 (0.75–0.79)	0.84 (0.81–0.88)
Percentage with College Degree				
< 12%	33 906 (42.4)	19 335 (57.0)	0.97 (0.94–1.00)	1.01 (0.97–1.05)
≥ 12%	46 021 (57.6)	26 572 (57.7)	1.00	1.00
Rural-Urban Continuum				

	Total No. (%)	No. treated with RAI (%)	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Metropolitan population	67 852 (85.7)	38 810 (57.2)	0.94 (0.89–0.97)	1.02 (0.96–1.08)
Other	11 364 (14.4)	6 685 (58.8)	1.00	1.00
Tumor Characteristics				
Tumor Histology				
Papillary	78 651 (91.5)	44 850 (57.0)	1.00	1.00
Follicular	4 893 (5.7)	3 084 (63.0)	1.29 (1.21–1.36)	1.09 (1.01–1.18)
Hurthle	2 404 (2.8)	1 491 (62.0)	1.23 (1.13–1.34)	1.03 (0.92–1.14)
Tumor Size				
≤ 1 cm	29 941 (36.4)	11 900 (36.4)	0.36 (0.34–0.38)	-
1.1–2 cm	24 771 (30.1)	16 201 (65.4)	1.04 (0.98–1.09)	-
2.1–4 cm	20 024 (24.3)	13 952 (69.7)	1.26 (1.19–1.33)	-
> 4 cm	7 524 (9.1)	4 862 (64.6)	1.00	-
Lymph Node				
N0	66 137 (77.0)	35 019 (53.0)	1.00	-
N1	18 691 (21.7)	13 570 (72.6)	2.36 (2.72–2.44)	-
Nx	1 120 (1.3)	836 (74.6)	2.62 (2.29–3.00)	-
Distant Metastases				
M0	85 388 (99.3)	49 076 (57.5)	1.00	-
M1	560 (0.7)	349 (62.3)	1.22 (1.03–1.45)	-
AJCC TNM Stage				
I	64 166 (75.6)	34 539 (53.8)	0.56 (0.52–0.59)	0.34 (0.31–0.37)
II	9 018 (10.6)	6 113 (67.8)	1.01 (0.93–1.09)	0.97 (0.88–1.07)
III	7 843 (9.2)	5 407 (68.9)	1.06 (0.98–1.15)	1.06 (0.95–1.17)
IV	3 886 (4.6)	2 630 (67.7)	1.00	1.00
Hospital Characteristics				
Hospital type				
Community/Comprehensive Community	48 532 (56.5)	27 773 (57.2)	0.93 (0.78–1.11)	1.18 (0.97–1.44)
Teaching-Research/NCI-NCCN	37 416 (43.5)	21 652 (57.9)	1.00	1.00

	Total No. (%)	No. treated with RAI (%)	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Hospital case volume				
Low (<6 cases/year)	2 415 (2.8)	1 064 (44.1)	0.49 (0.38–0.64)	0.44 (0.33–0.58)
Low-Med (7–11 cases/year)	6 109 (7.1)	3 098 (50.7)	0.69 (0.54–0.86)	0.62 (0.48–0.80)
Medium (12–19 cases/year)	10 261 (11.9)	5 604 (54.7)	0.87(0.69–1.09)	0.82 (0.64–1.06)
Med-High (20–34 cases/year)	19 235 (22.4)	11 440 (59.5)	1.03 (0.82–1.29)	0.99 (0.79–1.27)
High (≥ 35 cases/year)	47 928 (55.8)	28 214 (58.9)	1.00	1.00