Adjuvant Radioactive Iodine Use Among Differentiated Thyroid Cancer Patients in the Military Health System

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ABSTRACT Objective: Adjuvant radioactive iodine (RAI) for the treatment of differentiated thyroid cancer has been associated with better prognosis, but no consensus has been reached on the best practices for RAI. Limited data on RAI use and factors associated with the receipt of postoperative RAI in the general population are available and, to our knowledge, no data on RAI use among the U.S. Department of Defense (DoD) beneficiaries. Methods: Among 3,002 beneficiaries with differentiated thyroid cancer, who underwent total/near-total thyroidectomy between 1998 and 2007, logistic regression identified factors associated with RAI and examined effect modification by age and tumor size. Results: Fifty-two percent of patients received RAI. Receipt of RAI was more likely among beneficiaries who were diagnosed between 2004 and 2007, active duty members, had indirect care, and more advanced disease, and less likely among those affiliated with the Air Force or had unknown medical coverage. In addition, receipt of RAI significantly varied by tumor size among patients with regional lymph node metastasis. Conclusion: Among DoD beneficiaries, adjuvant RAI use was associated with clinical and nonclinical factors. Although evidence of effect modification between the recipient of RAI by tumor size was apparent, future research with a larger sample size is warranted to confirm results of this study.

INTRODUCTION

Although thyroid cancer is relatively rare, incidence among men and women in the United States continues to rise.[1–3] According to the American Cancer Society, approximately 60,220 new thyroid cancer cases will be diagnosed in 2013, of which 75% will occur among women and 80% will occur among individuals younger than 65 years of age.[1] The 5-year survival rate among thyroid cancer patients is 98%; however, 1,850 individuals are estimated to die from this disease in 2013 in the United States.[1]

Total or near-total thyroidectomy is the standard treatment for most patients with differentiated thyroid cancer (DTC), the most common form of thyroid cancer that includes papillary, follicular, and Hurthle cell thyroid cancers. Postoperative radioactive iodine (RAI) remnant ablation is also recommended to destroy any residual thyroid tissue that remains after thyroidectomy.[4–7] Studies have found that adjuvant RAI is associated with increased survival[8–13] and decreased recurrence.[8,11,13–15] However, its effectiveness may vary by tumor size and/or tumor stage. Among low-risk patients (patients with small or stage I or II tumors with no distant metastasis), studies have shown little to no benefit of adjuvant RAI with regard to disease recurrence and survival.[9,12,16,17]

In the general population, the use of RAI has risen over the past 20 years for DTC patients[18] with almost two-thirds having received RAI after thyroidectomy in the most recent years.[19] To the best of our knowledge, data on the factors associated with RAI use are sparse. In one study, multivariate analysis revealed that patients who were younger, had no comorbidities, or follicular cell tumors tended to receive RAI more frequently, whereas individuals who were female, black, uninsured, used Medicare/Medicaid, or had early stage tumors were less likely to receive postoperative RAI.[18]

Although the use of RAI and factors associated with receipt of postoperative RAI have been evaluated in the general population,[18] RAI use among the military population, an equal access care system, is unclear and, to our knowledge, has not been examined. Therefore, the aim of this study was 2-fold: (1) investigate the use of adjuvant RAI among Department of Defense (DoD) beneficiaries with DTC who underwent total or near-total thyroidectomy in the Military Health System (MHS) and (2) assess the factors associated with the use of adjuvant

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RAI and examine whether receipt of RAI varied by age at diagnosis, due to recommendations varying by age,[5–7] and tumor size.

METHODS

Data Source

This study was based on linked data from the DoD's Central Cancer Registry (CCR) and the MHS Data Repository (MDR). CCR and MDR contain information on individuals who receive health care through TRICARE, the DoD's health care program, including active duty members, retirees, National Guard and Reserve members, and dependents. Data on demographic, health, and tumor characteristics of cancer cases diagnosed and/or treated at military treatment facilities (MTFs) are collected and maintained in CCR. Certified cancer registrars abstract the data from patient records and enter them into the database. Administrative and medical care claims data, which include information from in-patient and out-patient services provided either directly at MTFs (direct care) or civilian facilities (indirect care), but are paid for by the DoD, were entered and stored in MDR. The MDR data include clinical diagnosis, diagnostic procedures, treatment, health conditions, and medical prescriptions. After the CCR and MDR databases were linked, de-identified data were delivered to the research team.

The data linkage project, which this analysis was based on, was reviewed and approved by the institutional review boards of the Walter Reed National Military Medical Center, TRICARE Management Activity, and the National Institutes of Health Office of Human Subjects Research.

Study Subjects

Between 1998 and 2007, there were 3,016 eligible patients diagnosed with primary, histologically confirmed DTC not reported first via death certificate or autopsy. Poorly DTC, which include medullary and anaplastic carcinomas and account for about 5% of all thyroid cancers, do not absorb RAI readily; therefore, adjuvant RAI is generally not recommended for these patients,[20,21] so they were not eligible for inclusion in this study. Patients were excluded if they did not undergo total or near-total thyroidectomy ($N = 6$) or received radioiodine before undergoing surgery ($N = 8$).

Study Variables

Demographic variables were obtained from CCR, with supplemental information obtained from MDR if values were missing. If information were missing from both CCR and MDR, then the value was considered to be unknown. Year of diagnosis included the following categories: 1998–1999, 2000–2001, 2002–2003, 2004–2005, and 2006–2007. Age at diagnosis was classified into five groups: 20 to 34 years, 35 to 44 years, 45 to 54 years, 55 to 64 years, and 65+ years. Race and ethnicity categories were based on the definitions used in the 2000 U.S. Census and were classified as non-Hispanic white, non-Hispanic black, non-Hispanic Asian/Pacific Islander, Hispanic, and other/unknown (American Indian/Alaskan Native or unknown). Marital status at diagnosis included never married, married, other (separated, divorced, or widowed), and unknown. Duty status at diagnosis was categorized as active duty or non–active duty, which included retirees and dependents. Affiliated military service branch was classified into six groups: Army, Air Force, Navy, Marines, other (Coast Guard or Public Health service), and unknown. Benefit type was classified as TRICARE Prime (HMO component), TRICARE non-Prime, or unknown medical coverage.

Treatment information was obtained from CCR and MDR. If either database recorded a patient as having surgery within 12 months after diagnosis, then surgery was classified as "yes." Source of care during a 3-year period around surgery (1.5 years before 1.5 years after surgery) was categorized as direct care, indirect care, both direct and indirect care, and unknown. It is recommended that RAI be administered within 3 months of total or near-total thyroidectomy[5,6]; therefore, the receipt of RAI was considered "yes" if CCR or MDR recorded the occurrence within this timeframe.

Data on tumor characteristics were obtained from CCR. Tumor histology was classified as papillary, follicular, or Hurthle cell, based on the third version of the International Classification of Diseases (ICD-3) codes (8050, 8052, 8260, 8290, 8330–8332, 8335, 8340, 8341–8344, 8350). Tumor size, in centimeters, was categorized as <1, 1.0 to 4, and >4, based on more recent RAI recommendations.[6,7] Lymph node involvement was categorized as none, metastasis in regional lymph nodes, and unknown ("regional lymph nodes cannot be assessed"). Metastasis classification was none, distant, or unknown. Tumor stage at diagnosis was defined according to the recommendations of the American Joint Committee on Cancer.[22] Disease recurrence was categorized as either no or yes.

Comorbidity information was obtained from MDR and was based on ICD-9 diagnosis codes. If a diagnosis was recorded in inpatient and/or outpatient data during the year before thyroid cancer diagnosis and was recorded at least three times (to reduce the possibility of false diagnoses), then the comorbidity was considered present. The Charlson comorbidity index, which is a weighted measure of comorbidity, was categorized as none, one, or greater than one;[23] thyroid cancer diagnosis was excluded from the calculation.

Statistical Analysis

χ^2 tests of significance were used to compare demographic, tumor, and health characteristics between patients who received and did not receive RAI. Backwards stepwise logistic regression was implemented and variables that met the entry/stay criteria of having a p value ≤ 0.1 were then included in an overall model. On the basis of the final overall

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TABLE I. Pattern of Radioactive Iodine Therapy Among Thyroid Cancer Patients Who Underwent Near-Total or Total Thyroidectomy in the Military Health System (N = 3,002)

	Radioiodine Use				
	No (N = 1,431)		Yes (N = 1,571)		
Characteristic	N	%	N	%	p Value[a]
Year of Diagnosis					<0.01
1998–1999	267	52	243	48	
2000–2001	252	47	279	53	
2002–2003	315	55	253	45	
2004–2005	301	44	384	56	
2006–2007	296	42	412	58	
Age at Diagnosis (Years)					<0.01
20–34	412	44	528	56	
35–44	393	46	470	54	
45–54	282	48	309	52	
55–64	238	55	191	45	
65+	106	59	73	41	
Sex					0.05
Women	1,120	49	1,181	51	
Men	311	44	390	56	
Race/Ethnicity					0.06
Non-Hispanic White	847	48	935	52	
Non-Hispanic Black	170	46	199	54	
Non-Hispanic API	173	51	169	49	
Hispanic	75	39	115	61	
Other/Unknown	166	52	153	48	
Marital Status at Diagnosis					<0.01
Married	1,200	48	1,292	52	
Never Married	81	37	138	63	
Other	91	47	103	53	
Unknown	59	61	38	39	
Active Duty Status at Diagnosis					<0.01
No	1,148	50	1,126	50	
Yes	283	39	445	61	
Service Branch at Diagnosis[b]					0.02
Army	484	44	611	56	
Air Force	511	52	475	48	
Marines	76	46	91	54	
Navy	312	47	348	53	
Other	31	52	29	48	
Unknown	17	50	17	50	
Benefit Type at Diagnosis					<0.01
TRICARE Prime "HMO"	1,237	46	1,426	54	
TRICARE Non-Prime	89	52	81	48	
Unknown	105	62	64	38	
Source of Care					0.07
Direct	706	49	738	51	
Indirect	189	45	228	55	
Direct and Indirect	82	40	124	60	
Unknown	454	49	481	51	
Tumor Histology					0.03
Papillary	1,327	48	1,416	52	
Follicular	93	41	133	59	
Hurthle Cell	11	33	22	67	
Tumor Size (cm)					<0.01
<1.0	655	71	262	29	
1.0–4.0	536	34	1,033	66	
>4.0	240	47	276	53	
Tumor Stage					<0.01
Stage I	1,028	51	987	49	
Stage II	109	41	160	59	
Stage III	52	25	152	75	

(continued)

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TABLE I. Continued

Characteristic	Radioiodine Use				
	No (N = 1,431)		Yes (N = 1,571)		
	N	%	N	%	p Value[a]
Stage IV	18	31	40	69	
Unknown	224	49	232	51	
Lymph Node Involvement					<0.01
No Regional Lymph Node Metastasis	832	50	831	50	
Metastasis in Regional Lymph Nodes	64	23	211	77	
Regional Lymph Nodes Cannot be Assessed	535	50	529	50	
Metastasis					0.11
No Distant Metastasis	1,292	48	1,412	52	
Distant Metastasis	6	26	17	74	
Unknown	133	48	142	52	
Comorbidity Index[c]					0.44
None	1,233	47	1,364	53	
One	131	69	59	31	
Two or More	67	53	60	47	
Recurrence					0.06
No	1,329	48	1,430	52	
Yes	102	42	141	58	

[a]2-sided p value. [b]Service branch of active duty member or sponsor. [c]Charlson comorbidity index. Thyroid cancer was not included in calculation.

model, we further conducted analyses stratified by age at diagnosis (<45 or >45, the recommended cut point for RAI use[5–7]) and tumor size. Odds ratios (OR) and 95% confidence intervals (CI) were calculated for overall and stratified analyses. The likelihood ratio test, comparing models with and without interaction terms, was conducted to identify significant interactions between risk factors identified in the final overall model and age at diagnosis and tumor size. Tests of significance were two-tailed and conducted at an alpha of 0.05 using Statistical Analysis System (SAS) software, Version 9.3 for Windows (SAS Institute, Cary, North Carolina).

RESULTS

A total of 3,002 thyroid cancer patients were included in this study, of which 1,571 (52.3%) received RAI. The percentages of use for the population recommended for RAI were 57, 61, 75, and 69 for stage II and <45 years of age, stage II and ≥45 years of age, stage III, and stage IV, respectively. Table I shows demographic, tumor, and disease characteristics of DTC patients by RAI treatment status. Patients diagnosed with thyroid cancer in later years and those who were younger, never married, or active duty members were more likely to receive RAI compared to those who were diagnosed with thyroid cancer in earlier years, older, had other marital status, or non–active duty status (p value: <0.01). Patients whose sponsors were in the Air Force tended to be less likely to have RAI than those in other service branches (p value: 0.02). In addition, patients with TRICARE Prime, Hurthle cell histologies, larger tumors, regional lymph node involvement, or later tumor stage were more likely to receive RAI than those with TRICARE non-Prime or unknown medical coverage, other tumor histologies, smaller tumors, no or unknown lymph node involvement, and early tumor stage (p value ≤ 0.03).

The results from the backwards stepwise regression are presented in Table II. Receipt of RAI was more likely among those diagnosed with thyroid cancer between 2004 and 2007 (2004–2005: OR = 1.41, 95% CI = 1.01–1.97; 2006–2007: OR = 1.53, 95% CI = 1.09–2.14) compared to those diagnosed from 1998 to 2001. RAI was also more likely among active duty beneficiaries than non–active duty beneficiaries (OR = 1.47, 95% CI = 1.21–1.79). In addition to, the receipt of RAI was also more likely among beneficiaries who had some form of indirect care (indirect care: OR = 1.28, 95% CI = 1.01–1.64; direct/indirect care: OR = 1.65, 95% CI = 1.19–2.30), large tumors (1.0–4.0 cm: OR = 4.49, 95% CI = 3.71–5.43; >4.0 cm: OR = 2.43, 95% CI = 1.91–3.09), or stage III (OR = 3.21, 95% CI = 2.21–4.66), and unknown stage tumors (OR = 1.65, 95% CI = 1.29–2.12) than patients with direct care, smaller tumors, or stage I cancer. Furthermore, regional lymph node involvement was also associated with increased receipt of RAI (OR = 2.42, 95% CI = 1.73–3.37). Conversely, beneficiaries affiliated with the Air Force (OR = 0.73, 95% CI = 0.61–0.89) or had unknown benefit type (OR = 0.57, 95% CI = 0.39–0.83) were less likely to receive RAI compared to those who were affiliated with the Army or had TRICARE Prime.

In general, receipt of RAI did not vary consistently by age at diagnosis (Table III) or tumor size (Table IV). Although there was some variation between subgroups, CIs overlapped between the subgroups defined by age at diagnosis or tumor size for most variables. However, the receipt of RAI in relation to lymph node involvement varied by tumor size (p interaction: 0.03; Table IV). In comparison to patients without regional lymph node involvement, patients with

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TABLE II. Stepwise Logistic Regression Assessing the Association Between Radioactive Iodine Therapy and Demographic, Health, and Tumor Characteristics Among Thyroid Cancer Patients Who Underwent Near-Total or Total Thyroidectomy in the Military Health System (N = 3,002)

Characteristic	OR	95% CI[a]
Age at Diagnosis (Years)	0.99	(0.98–1.00)
Year of Diagnosis		
1998–1999	1.00	Reference
2000–2001	1.14	(0.87–1.49)
2002–2003	0.72	(0.51–1.01)
2004–2005	1.41	(1.01–1.97)
2006–2007	1.53	(1.09–2.14)
Active Duty Status at Diagnosis		
No	1.00	Reference
Yes	1.47	(1.21–1.79)
Service Branch at Diagnosis[b]		
Army	1.00	Reference
Air Force	0.73	(0.61–0.89)
Marines	1.07	(0.74–1.53)
Navy	0.94	(0.76–1.17)
Other	0.96	(0.54–1.69)
Unknown	1.16	(0.55–2.48)
Benefit Type at Diagnosis		
TRICARE Prime "HMO"	1.00	Reference
TRICARE Non-Prime	0.99	(0.68–1.44)
Unknown	0.57	(0.39–0.83)
Source of Care		
Direct	1.00	Reference
Indirect	1.28	(1.01–1.64)
Direct and Indirect	1.65	(1.19–2.30)
Unknown	1.07	(0.89–1.29)
Tumor Size (cm)		
<1.0	1.00	Reference
1.0–4.0	4.49	(3.71–5.43)
>4.0	2.43	(1.91–3.09)
Tumor Stage		
Stage I	1.00	Reference
Stage II	1.32	(0.99–1.76)
Stage III	3.21	(2.21–4.66)
Stage IV	1.46	(0.72–2.93)
Unknown	1.65	(1.29–2.12)
Lymph Node Involvement		
No Regional Lymph Node Metastasis	1.00	Reference
Metastasis in Regional Lymph Nodes	2.42	(1.73–3.37)
Regional Lymph Nodes Cannot be Assessed	0.91	(0.69–1.19)
Metastasis		
No Distant Metastasis	1.00	Reference
Distant Metastasis	1.91	(0.65–5.61)
Unknown	0.77	(0.58–1.02)

[a]95% CI adjusted for all other variables listed. [b]Service branch of active duty member or sponsor.

<1 cm tumors, were 7.6 times more likely to receive RAI compared to 1.7 times more likely for patients with 1 to 4 cm tumors (95% CIs = 3.58–16.17 and 1.06–2.57, respectively). In addition, although the p values for interactions were not significant, the CIs did not overlap for stage II tumors by age at diagnosis (Table III) or tumor size (1.0–4.0 cm vs. >4.0 cm; Table IV) and indirect care by tumor size (<1.0 cm vs. 1.0–4.0 cm; Table IV).

DISCUSSION

According to the common guidelines,[5–7] RAI is recommended for stages III and IV DTC as well as those patients with stage II thyroid cancer depending on an age cutoff of 45 years. On the basis of the available data, this study showed that MHS beneficiaries were more likely to use RAI than the general population for most groups recommended for RAI (61% vs. 52% for stage II and 45 years or older, 75% vs. 61% for stage III, and 69% vs. 64% for stage IV).[19] This study also found that receipt of RAI was more common among beneficiaries diagnosed with thyroid cancer in later years, and those with active duty status, indirect or direct/indirect care, tumors ≥1 cm, stage III or unknown tumors, and regional lymph node involvement, but less common among beneficiaries who were in the Air Force or had unknown insurance. Furthermore, the use of RAI varied by tumor size for lymph node involvement, where the receipt of RAI significantly varied by tumor size among patients with regional lymph node metastasis. It may also be possible that RAI use varied by age at diagnosis for tumor stage as well as tumor size for source of care and tumor stage.

Associations between RAI use and demographics and tumor characteristics were examined in a study based on the National Cancer Data Base, a program of the Commission of Cancer of the American College of Surgeons and the American Cancer Society.[18] Consistent with this study, we found that younger patients were more likely to receive RAI. However, our multivariate analysis did not show significant associations between the receipt of RAI and sex, race/ethnicity, comorbidity, or tumor histology. Lack of an association between RAI use and race/ethnicity among DoD beneficiaries might result from equal access to medical care regardless of racial/ethnic background. Therefore, different racial/ethnic groups might have equal opportunity to receive RAI. Although comorbidities may be related to the doctor's recommendation and the patient's receipt of RAI, this study suggests that the presence of comorbidities were not associated with RAI use among DoD beneficiaries. Though the reasons for this finding are not clear, reduced comorbidity-related differences in the access and use of medical care might play a role. Although RAI recommendations based on tumor histology are not consistent,[7] our study suggests that the use did not vary by histologic type among DoD beneficiaries. Unlike the aforementioned study, we found that larger, more advanced tumors were associated with the increased receipt of RAI among DoD beneficiaries. This might be related to treatment recommendations. The receipt of RAI as adjuvant treatment is recommended for all patients with advanced stage disease and tumors >4 cm, as well as selective use for patients with tumors between 1 and 4 cm.[6,7] These treatment recommendations might be more closely followed within the MHS.

This study also showed that DoD-specific demographic characteristics influence the receipt of RAI among its beneficiaries. In particular, this study found that being an active duty member and at least some indirect care were associated

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TABLE III. Logistic Regression Assessing the Association Between Radioactive Iodine Therapy and Demographic, Patient, and Tumor Characteristics by Age Among Thyroid Cancer Patients Who Underwent Near-Total or Total Thyroidectomy in the Military Health System (N = 3,002)

	Age at Diagnosis			
	<45 Years		≥45 Years	
Characteristic	OR	95% CI[a]	OR	95% CI[a]
Year of Diagnosis				
1998–1999	1.00	Reference	1.00	Reference
2000–2001	1.11	(0.80–1.55)	1.15	(0.72–1.84)
2002–2003	0.57	(0.37–0.89)	0.94	(0.54–1.62)
2004–2005	1.08	(0.69–1.69)	1.91	(1.12–3.25)
2006–2007	1.03	(0.66–1.61)	2.58	(1.49–4.45)
Active Duty Status at Diagnosis				
No	1.00	Reference	1.00	Reference
Yes	1.55	(1.25–1.93)	1.39	(0.84–2.31)
Service Branch at Diagnosis[b]				
Army	1.00	Reference	1.00	Reference
Air Force	0.76	(0.59–0.97)	0.69	(0.51–0.93)
Marines	0.95	(0.63–1.43)	1.63	(0.73–3.62)
Navy	1.01	(0.76–1.34)	0.81	(0.57–1.15)
Other	0.76	(0.36–1.58)	1.28	(0.52–3.14)
Unknown	1.88	(0.73–4.86)	0.42	(0.09–1.83)
Benefit Type at Diagnosis				
TRICARE Prime "HMO"	1.00	Reference	1.00	Reference
TRICARE Non-Prime	0.93	(0.42–2.06)	0.93	(0.62–1.40)
Unknown	0.56	(0.30–1.02)	0.60	(0.37–0.98)
Source of Care				
Direct	1.00	Reference	1.00	Reference
Indirect	1.21	(0.88–1.65)	1.46	(0.99–2.15)
Direct and Indirect	2.26	(1.43–3.57)	1.24	(0.75–2.06)
Unknown	0.94	(0.75–1.19)	1.29	(0.96–1.74)
Tumor Size (cm)				
<1.0	1.00	Reference	1.00	Reference
1.0–4.0	4.93	(3.85–6.30)	3.72	(2.72–5.08)
>4.0	2.71	(1.97–3.71)	1.95	(1.33–2.88)
Tumor Stage				
Stage I	1.00	Reference	1.00	Reference
Stage II	0.84	(0.51–1.38)	2.08	(1.40–3.08)
Stage III	2.55	(1.14–5.74)	4.59	(2.85–7.38)
Stage IV	2.97	(0.28–31.23)	1.98	(0.83–4.72)
Unknown	1.24	(0.89–1.73)	2.43	(1.64–3.60)
Lymph Node Involvement				
No regional lymph node metastasis	1.00	Reference	1.00	Reference
Metastasis in Regional Lymph Nodes	2.60	(1.77–3.83)	1.69	(0.83–3.43)
Regional Lymph Nodes Cannot be Assessed	0.75	(0.52–1.07)	1.08	(0.71–1.66)
Metastasis				
No Distant Metastasis	1.00	Reference	1.00	Reference
Distant Metastasis	2.31	(0.24–22.17)	1.87	(0.51–6.79)
Unknown	1.05	(0.73–1.49)	0.45	(0.28–0.74)

[a]95% CI adjusted for all other variables listed. [b]Service branch of active duty member or sponsor.

with receipt of RAI. Active duty members of the military receive free care while nonactive duty beneficiaries may be required to pay a minimal fee for services depending on the benefit type. Therefore, active duty members might be more likely to use health care services and in turn, more likely to receive RAI. Having both direct and indirect care may increase one's exposure to different health care providers, which could possibly influence treatment decisions, and thus receiving RAI. Conversely, receipt of RAI was less likely among patients affiliated with the Air Force. We are not aware of differing treatment guidelines for RAI use among the various services branches of the military; however, we cannot exclude the possibility that different service branches have differing practice patterns with regards to the utilization of adjuvant RAI. Having unknown medical coverage was also related to beneficiaries receiving less RAI. It is possible that these beneficiaries have supplemental health insurance and may obtain treatment through health care services not

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TABLE IV. Logistic Regression Assessing the Association Between Radioactive Iodine Therapy and Demographic, Patient, and Tumor Characteristics by Tumor Size Among Thyroid Cancer Patients Who Underwent Near-Total or Total Thyroidectomy in the Military Health System (N = 3,002)

	Tumor Size					
	<1.0 cm		1.0–4.0 cm		>4.0 cm	
Characteristic	OR	95% CI[a]	OR	95% CI[a]	OR	95% CI[a]
Age at Diagnosis (Years)	0.99	(0.98–1.00)	1.00	(0.99–1.01)	0.98	(0.96–1.00)
Year of Diagnosis						
1998–1999	1.00	Reference	1.00	Reference	1.00	Reference
2000–2001	1.15	(0.70–1.89)	1.36	(0.92–1.99)	0.91	(0.49–1.69)
2002–2003	0.69	(0.35–1.37)	0.75	(0.46–1.21)	0.90	(0.42–1.94)
2004–2005	1.95	(1.01–3.76)	1.43	(0.88–2.31)	1.01	(0.48–2.15)
2006–2007	2.31	(1.21–4.41)	1.62	(0.98–2.66)	0.83	(0.40–1.74)
Active Duty Status at Diagnosis						
No	1.00	Reference	1.00	Reference	1.00	Reference
Yes	1.26	(0.87–1.81)	1.41	(1.07–1.87)	2.00	(1.23–3.25)
Service Branch at Diagnosis[b]						
Army	1.00	Reference	1.00	Reference	1.00	Reference
Air Force	0.83	(0.59–1.16)	0.75	(0.57–0.98)	0.64	(0.41–1.00)
Marines	1.04	(0.56–1.93)	1.66	(0.91–3.05)	0.52	(0.23–1.15)
Navy	1.01	(0.68–1.49)	0.96	(0.70–1.32)	0.90	(0.54–1.49)
Other	1.75	(0.77–3.98)	0.69	(0.30–1.61)	0.26	(0.04–1.73)
Unknown	0.46	(0.07–2.84)	1.00	(0.29–3.54)	2.59	(0.59–11.28)
Benefit Type at Diagnosis						
TRICARE Prime "HMO"	1.00	Reference	1.00	Reference	1.00	Reference
TRICARE Non-Prime	1.08	(0.57–2.03)	0.68	(0.38–1.21)	2.15	(0.93–4.93)
Unknown	0.54	(0.23–1.23)	0.48	(0.28–0.81)	0.82	(0.38–1.77)
Source of Care						
Direct	1.00	Reference	1.00	Reference	1.00	Reference
Indirect	2.12	(1.40–3.22)	0.92	(0.65–1.30)	1.17	(0.68–2.03)
Direct and Indirect	2.50	(1.51–4.14)	1.50	(0.90–2.50)	1.17	(0.49–2.82)
Unknown	1.30	(0.93–1.81)	1.02	(0.78–1.33)	0.88	(0.57–1.37)
Tumor Stage						
Stage I	1.00	Reference	1.00	Reference	1.00	Reference
Stage II	2.76	(0.99–7.71)	0.88	(0.62–1.25)	2.66	(1.27–5.60)
Stage III	4.38	(1.88–10.22)	2.90	(1.56–5.38)	3.07	(1.64–5.74)
Stage IV	0.42	(0.03–6.11)	1.80	(0.61–5.29)	1.89	(0.63–5.62)
Unknown	1.68	(1.09–2.59)	1.55	(1.07–2.25)	1.66	(0.92–2.98)
Lymph Node Involvement						
No Regional Lymph Node Metastasis	1.00	Reference	1.00	Reference	1.00	Reference
Metastasis in Regional Lymph Nodes	7.60	(3.58–16.17)	1.65	(1.06–2.57)	1.60	(0.79–3.23)
Regional Lymph Nodes Cannot be Assessed	1.22	(0.71–2.09)	0.87	(0.60–1.28)	0.74	(0.41–1.33)
Metastasis						
No Distant Metastasis	1.00	Reference	1.00	Reference	1.00	Reference
Distant Metastasis	—[c]	—	3.35	(0.39–28.88)	1.35	(0.32–5.66)
Unknown	0.48	(0.26–0.86)	0.79	(0.53–1.18)	1.34	(0.72–2.49)

[a]95% CI adjusted for all other variables listed. [b]Service branch of active duty member or sponsor. [c]The number of beneficiaries who did not receive radioiodine therapy was too small for this strata, resulting in an infinite OR and 95% CI. Therefore, stratified results are not available.

paid for by the DoD; therefore, RAI use among these patients were less likely compared to those who have TRICARE Prime.

Our study further indicated that the relationship between receipt of RAI and lymph node metastasis varied by tumor size. There is a possibility that RAI is more likely used for lymph node metastasis when tumor size is small and RAI is selective. Although more affirmative evidence is needed on whether the relationship between RAI and care source varies by tumor size, it is also possible that when the tumor is small and RAI is selective, civilian medical facilities (indirect care) may be more likely to use RAI than military medical facilities (direct care). The possible increased association between RAI use and stage II tumors among patients aged 45 years and older is in line with common guidelines.[5–7] As far as we know, research is limited in this area. Future research assessing whether the receipt of RAI varies by these factors in a larger population is needed to confirm our results.

To the best our knowledge, this is the first study that has examined the use of adjuvant RAI and related factors among MHS beneficiaries. Caution should be taken in the interpretation of our study results, however, as limitations in this study exist. Although treatment information was relatively

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complete through the use of data from both CCR and MDR, some information may not be included. If patients had additional health care insurance, and received services that were not paid by the DoD and thus not recorded in the MDR data, the receipt of RAI might be underestimated and the results on related factors might be affected if the underestimation was differential between different levels/categories of a variable. However, we found that benefit type, which likely affects the possibility of having and using additional non-DoD insurance, was not related to receipt of RAI. Thus, the effects on the results of having additional non-DoD insurance are likely limited. Insufficient sample size for certain stratified analyses is another potential limitation. Additional research with larger numbers of patients is warranted. Furthermore, our data is several years old; therefore, we cannot exclude the possibility that the current patterns of RAI use may differ due to the possible changes in TRICARE coverage or treatment guidelines.

CONCLUSION

Among DoD beneficiaries, use of adjuvant RAI was associated with year of diagnosis, age at diagnosis, duty status, military service branch, source of care, tumor size, tumor stage, and lymph node metastasis. Although evidence of effect modification between the receipt of RAI by age at diagnosis and tumor size was apparent, future research with a larger sample size is warranted to confirm the results of this study.

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