Outcomes of Thyroid Cancer in African Americans

Christopher S. Hollenbeak, PhD; Li Wang, PhD; Patrick Schneider, BS; David Goldenberg, MD

Context: Thyroid cancer, the most common endocrine cancer, is on the rise. It is less common in the African American (AA) population in the United States. Few studies have looked at outcome disparities for different patient populations, particularly those involving race.

Objective: Using data from the SEER registry, we sought to determine whether five-year survival differed significantly between AA and White patients and, whether differences were due to patient or disease characteristics.

Design: Retrospective cohort analysis. Univariate comparisons were made using Student-*t* tests for continuous variables, chi-square tests for categorical variables. Survivor functions were estimated using Kaplan-Meier curves, and comparisons were made by log rank tests.

Setting and Patients: 26,902 patients (25,210 White and 1,692 AA) were diagnosed with thyroid cancer between 1992 and 2006.

Main Outcome Measure(s): Five-year survival defined as time from diagnosis to death from cancer within five years.

Results: AA had a significantly lower rate of five-year survival compared to Whites (96.5% vs 97.4%, $P=.006$). AA patients were 2.3 times more likely to be diagnosed with anaplastic disease (Risk ratio [RR] = 2.33 (95% CI: 1.52–3.58), $P=.0001$), and were also nearly 80% more likely to be diagnosed with follicular disease (RR=1.78 [95% CI: 1.59–1.99], $P<.0001$). They were nearly twice as likely to have larger tumors (≥ 4 cm) than White patients (RR = 1.94 [95% CI: 1.78–2.12], $P<.0001$).

Conclusions: AA had poorer survival from thyroid cancer relative to White patients; this difference may be explained by differences in disease characteristics such as a relatively higher rate of anaplastic thyroid cancer, follicular cancer and larger tumors at presentation. (*Ethn Dis.* 2011;21(2):210–215)

Key Words: Thyroid Cancer, Racial Disparities, Follicular Thyroid Cancer, Anaplastic, Papillary, African Americans, Caucasians

From the Department of Surgery (CSH, PS); the Department of Public Health Sciences (CSH, LW); and the Division of Otolaryngology-Head and Neck Surgery (DG); Pennsylvania State University College of Medicine; Hershey, Pennsylvania.

Address correspondence to Christopher S. Hollenbeak, PhD; Departments of Surgery and Public Health Sciences; Pennsylvania State University College of Medicine; 600 Centerview Drive, MC A210; Hershey, PA 17033; 717-531-5890; 717-531-5779 (fax); chollenbeak@hmc.psu.edu

Introduction

Thyroid cancer (TC) is the most common endocrine cancer with an estimated annual incidence of 44,670 cases in the United States in 2010.[1] Most thyroid cancers are papillary (PTC) or follicular tumors; medullary and anaplastic tumors (ATC) are rare.[2–3] Diagnosis of thyroid cancer is more common among women in their fourth decade and is far less common in African Americans than Whites.[4–5] The median age at diagnosis for all thyroid cancers as stated by the Surveillance, Epidemiology, and End Results (SEER) tumor registry is 48 years of age.

In the United States, the overall incidence of thyroid cancer is on the rise. TC has increased from a rate of 2.7 per 100,000 people in 1973 to a rate of 7.7 per 100,000 people in 2003.[6] A number of studies have attempted to identify the reason for increased incidence.[4–8] Earlier studies suspected that the increased trend was caused by the widespread use of x-ray radiation therapy for the benign conditions of the head and neck among children and adolescents until the late 1950s. Other studies suggested that the trend might be associated with atmospheric nuclear fallouts, or increased exposures to diagnostic x-rays among children in particular. A number of recent studies concluded that increasing incidence could be a result of improved diagnosis for subclinical cancers due to the increased use of ultrasound-guided fine-needle aspiration biopsy.[6,9] Many of these subclinical cancers are tumors measuring 1 cm or smaller that lie dormant in the general population, never manifesting, and usually undiagnosed.

Thyroid cancer has increased from a rate of 2.7 per 100,000 people in 1973 to a rate of 7.7 per 100,000 people in 2003.[6]

Few studies have looked at outcome disparities for different patient populations, particularly those involving race. This may be the result of thyroid cancer being a relatively nonlethal cancer. While a few studies have noted that African Americans are more likely to experience follicular tumors and tumors that are 4.0 cm or larger, no study has formally noted an increased mortality associated with these distinctive disease characteristics.[2,4,6–7]

We used data from the SEER tumor registry to study outcomes for thyroid cancer diagnosed between 1992 and 2006. Many existing studies base their assumptions and conclusions on data arising from 1973 onward.[4,6,7,10,11] While the inclusion of patients from the 1970s from the SEER7 registry dramatically increases the sample size and number of patients available for analysis of an otherwise relatively rare cancer, it is not a true barometer of the current state of thyroid cancer in the United States. Since 1973, detection has greatly improved due to ultrasound, fine-needle aspiration biopsy and thyroglobulin assay. Ultrasound, introduced in the 1980s, can detect nodules 0.2cm in diameter while fine-needle aspiration biopsies introduced in the

1990s can definitively confirm the disease in smaller nodules.[5–6,9,12–15] Therapy largely involves surgery followed by radioiodine treatment.[3,6,16,17]

The purpose of this study was to determine whether outcomes differed between Whites and African Americans and to determine the extent to which observed differences arise from patient or disease characteristics.

METHODS

Data

Data for this study came from the SEER program of the National Cancer Institute (NCI, www.seer.cancer.gov). We used data from the SEER13 tumor registry to study outcomes for thyroid cancer diagnosed between 1992 and 2006. The SEER17 is an expansion of the SEER13, and those additional four areas had data only starting from 2000, which is too recent for survival analysis especially considering cases diagnosed just a few years back. In contrast, the SEER13 region has data from 1992–2006 for all the areas in the SEER 13 region. The SEER program collects data on cancer incidence and survival in the United States and covers approximately 26% of the US population. The analysis was limited to adult patients (aged ≥18 yrs) diagnosed between 1992 and 2006 with a primary tumor of the thyroid gland. Variables in the data set included demographics (age, sex, race/ethnicity), stage at diagnosis (localized, regional, distant), histology, size, and survival duration (months from diagnosis until death from cancer). Since the primary interest was in whether outcomes differed between African American and White patients, we excluded other race/ethnicity groups. Our analysis contained 26,902 patients, of which 1,692 were African American and 25,210 were White.

Statistical Analysis

Statistical analysis was performed using STATA software (version 10, Stata Corp., College Station, Texas). We made comparisons between White and African American patients using Student's *t*-test for continuous variables and chi-square tests for binary and categorical variables. We estimated thyroid cancer survivor functions using the Kaplan-Meier product limit method. Log rank tests were used to compare survivor functions. We further explored survival by disease characteristics such as histology (follicular, papillary, and anaplastic) and tumor size in order to determine whether differences in survival rates were explained by differences in the distribution of these characteristics.

Patient characteristics by race

	White (*n*=25,210)	African American (*n*=1,692)	*P* value
Age (years)	45.83	47.34	<.0001
Sex (%)			
Male	23.17	18.44	<.0001
Female	76.83	81.56	
Tumor Stage (%)			
Localized	62.15	65.60	<.0001
Regional	34.18	28.96	
Distant	3.66	5.44	
Tumor Histological Class (%)			
Papillary	87.49	78.78	<.0001
Follicular	9.71	17.32	
Medullary	2.19	2.48	
Anaplastic	0.61	1.42	
Primary Tumor Size (%)			
0.0–0.9 cm	27.50	25.30	<.0001
1.0–2.9 cm	27.48	19.62	
2.0–3.9 cm	31.82	29.43	
≥4.0 cm	13.20	25.65	

RESULTS

Our analysis sample of African American and White patients with thyroid cancer diagnosed from 1992–2006 contained many more White patients than African American patients (25,210 White vs 1,692 African American patients). When compared to Whites, African American patients were more likely to have thyroid cancer at later age (47.3 vs 45.8 $P<.0001$), higher rates of anaplastic cancer (1.4% vs 0.6%, $P<.0001$) and follicular cancer (17.3% vs 9.7%, $P<.0001$), a lower incidence of papillary tumors (78.8% vs 87.5%, $P<.0001$), and larger primary tumors (≥4.0 cm, 25.6% vs 13.2%, $P<.0001$) (Table 1). All of these traits are considered to be associated with more advanced disease and higher mortality.

Without controlling for other characteristics, African Americans had a poorer thyroid cancer survival at five years compared to Whites (96.5% vs 97.4%, $P=.006$) (Figure 1). Although this additional risk of mortality was small, it was nonetheless significant. We sought to determine to what extent differences in disease characteristics were the underlying source of the mortality difference. African American patients were 2.3 times more likely to be diagnosed with anaplastic disease (Risk ratio [RR] = 2.33 [95% CI: 1.52–3.58], $P=.0001$), which is known to carry a higher mortality burden. African Americans were also nearly 80% more likely to be diagnosed with follicular disease (RR = 1.78 [95% CI:

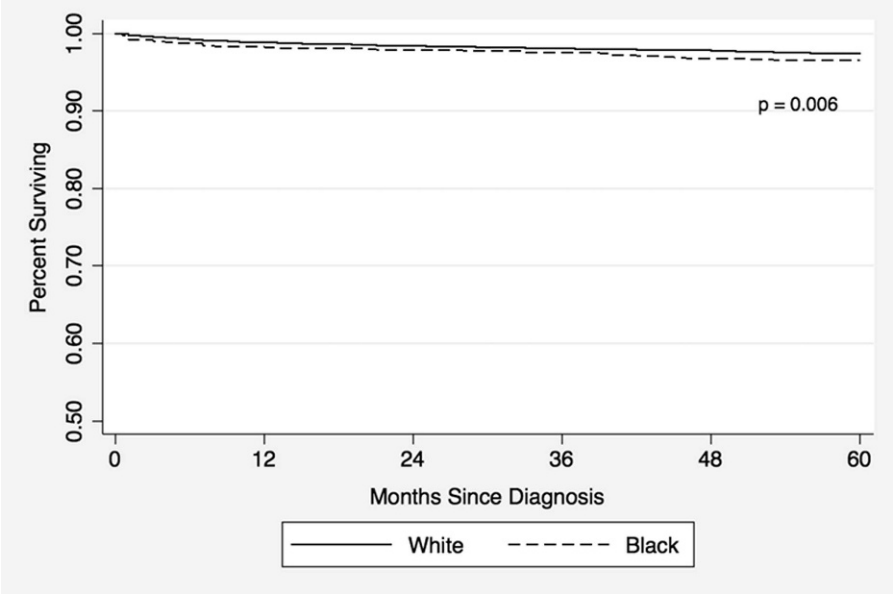

Fig 1. Five-year survival for all patients, stratified by race. Measure is time from diagnosis until death from cancer

1.59–1.99], $P<.0001$) and they were nearly twice as likely to have larger tumors (≥4 cm) than White patients (RR = 1.94 [95% CI: 1.78–2.12], $P<.0001$).

To determine whether race had an independent effect on survival, we performed stratified survival analyses on histology and tumor size. As seen in Figure 2, among patients with anaplastic disease, five-year survival for African Americans was not significantly different from White patients (12.4% vs 6.5%, $P=.79$), nor was survival significantly different by race among patients with other histology (follicular, medullary, and papillary combined) (97.9 vs 97.6, $P=.12$). Tumor size did not have a differential impact on survival by race either (Figure 3). Black patients with smaller tumors (< 4 cm) had a similar survival rate compared to White patients with smaller tumors (98.4% vs 98.8%, $P=.11$), and African American patients with larger tumor (≥4 cm) had a similar five-year survival rate compared to White patients (91.0% vs 89.0%, $P=.20$).

DISCUSSION

Thyroid cancer is the most common endocrine cancer. Unlike many other cancers, the incidence of thyroid cancer has increased over the past 3 decades and is also 1 of 4 cancer sites with an increasing death rate, showing a 13.5% increase between 1990 and 2003.[18] Prognostic factors for outcomes in thyroid cancer are well described. An important component of staging and prognosis is patient age.[19] Other prognostic factors include sex, tumor size and extracapsular spread. Prior to this study, race has not been investigated as a possible prognostic indicator.

African Americans are, overall, more likely to develop cancer, and to die from it, than any other racial or ethnic group in the United States. Most human cancers, including colorectal, lung, prostate, gastric, and head and neck cancer, are more common in African American than White Americans.[2] The cancer death rate of African American is 1.4 times higher for men and 1.2 times higher for women than White Americans.[20] The incidence of thyroid cancer in African Americans is actually lower than in White Americans, and significantly so. In fact, thyroid cancer is half as common in the African American population as in the White population.[21] That being stated, as in Whites, an increased incidence of thyroid cancer in African Americans across time has been observed in a number of studies.[21,22]

There are a few risk factors for the development of thyroid cancer. These include radiation exposure in childhood for benign or malignant conditions or exposure to nuclear fallout. Other risk factors for the development of thyroid cancer include a history of goiter, family history of thyroid disease, female sex, and certain Asian groups.[23–25] Iodine deficiency appears to be protective against papillary (but not follicular) cancer.[26]

Adverse prognostic factors in thyroid cancer included age older than 45 years, follicular histology, primary tumor larger than 4 cm (T2–T3), extrathyroid extension (T4), and distant metastases.[27,28]

A number of studies have investigated the disparity in incidence and outcome in thyroid cancer among various racial groups. The results have not been uniform. Mitchell et al found that, although African American patients were more likely to harbor larger neoplasms, the mortality and survival in African Americans was not significantly different from White patients.[2]

Recently Yu et al concluded that African American patients had a lower 5-year survival rate from PTC than other ethnic groups but not from other thyroid cancer histologies.[29]

In light of this large African-American-White disparity in the rate of thyroid cancer, the question arises: is this a true population difference with a biological explanation? Or, is it possible that, despite improved detection of thyroid cancer, we fail to diagnose a large number of thyroid cancers in the African American population? Morris et al highlighted this point by asking whether the racial

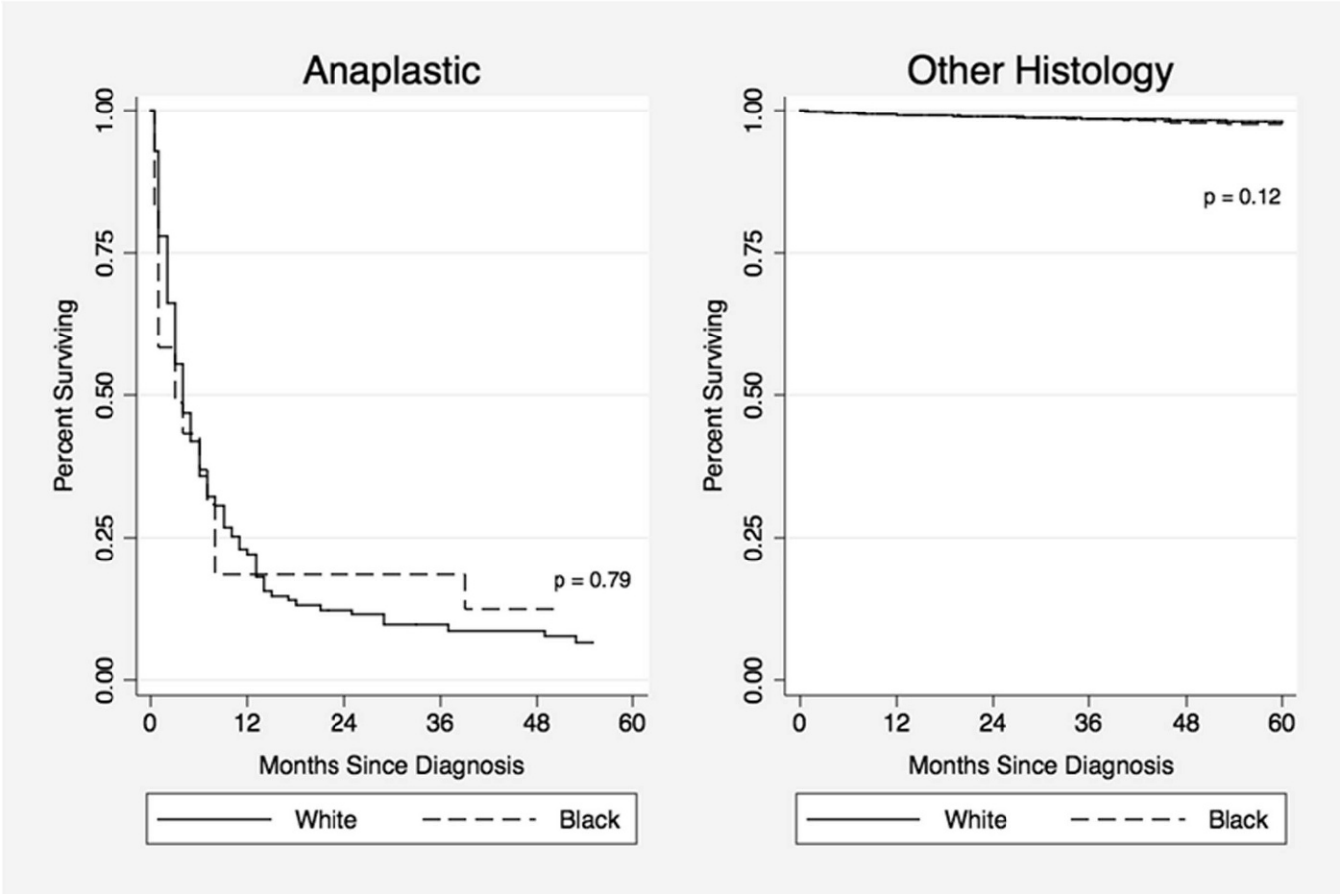

Fig 2. Five-year survival stratified by race and histology. Other histology included follicular, medullary, and papillary disease. Measure is time from diagnosis until death from cancer

disparity of thyroid cancer between African Americans and Whites was: a) under diagnosis of African American, b) lower incidence in African Americans; or c) less or more aggressive disease in African Americans.[30]

We found AA with thyroid cancers to be slightly older than their White counterparts (47.34 years AA vs 45.83 years, respectively). Age plays a role in both staging and outcome in patients with papillary and follicular thyroid cancer. For example; in stage I papillary carcinoma, the 10-year survival rate is slightly better for patients younger than 40 years than for patients older than 40 years. Stage II, III and IV papillary and follicular carcinoma are all upstaged if the patient is older than 45 years. We found the African American population more likely to present with larger primary tumors as compared with Whites. The RR of a tumor >4 cm in size in African Americans was 1.94 ($P<.0001$). This finding was consistent with other studies[2] and can be explained by either late diagnosis or aggressive tumor biology.

Our results show less regional disease (regional lymph node metastasis) in AA (28.96% AA vs 34.18% Whites). While rates of distant metastasis were greater in AA than in Whites (5.44% vs 3.66%, respectively). The prognostic significance of lymph node status is controversial while distant metastases are a typically poor prognostic sign.

We found African Americans were more likely to have follicular thyroid cancer than Whites. This finding has been shown in other studies as well.[2,25] Many investigators have reported a less favorable outcome in patients with follicular cancer[31–32] when compared to papillary disease. Loh et al reported a 3.4-fold higher cancer mortality risk in patients with follicular thyroid cancer as compared to papillary thyroid cancer.[33]

In our study we found the incidence of anaplastic thyroid carcinoma to be higher (1.4% vs 0.6%, $P<.0001$) in African Americans than in Whites. Although anaplastic disease constitutes only 2% of all thyroid cancer, it is typically lethal with no effective systemic therapy. The mean survival time is usually less than 6 months from the time of diagnosis and, unfortunately, this outcome is not fundamentally altered by available treatments.[34] While

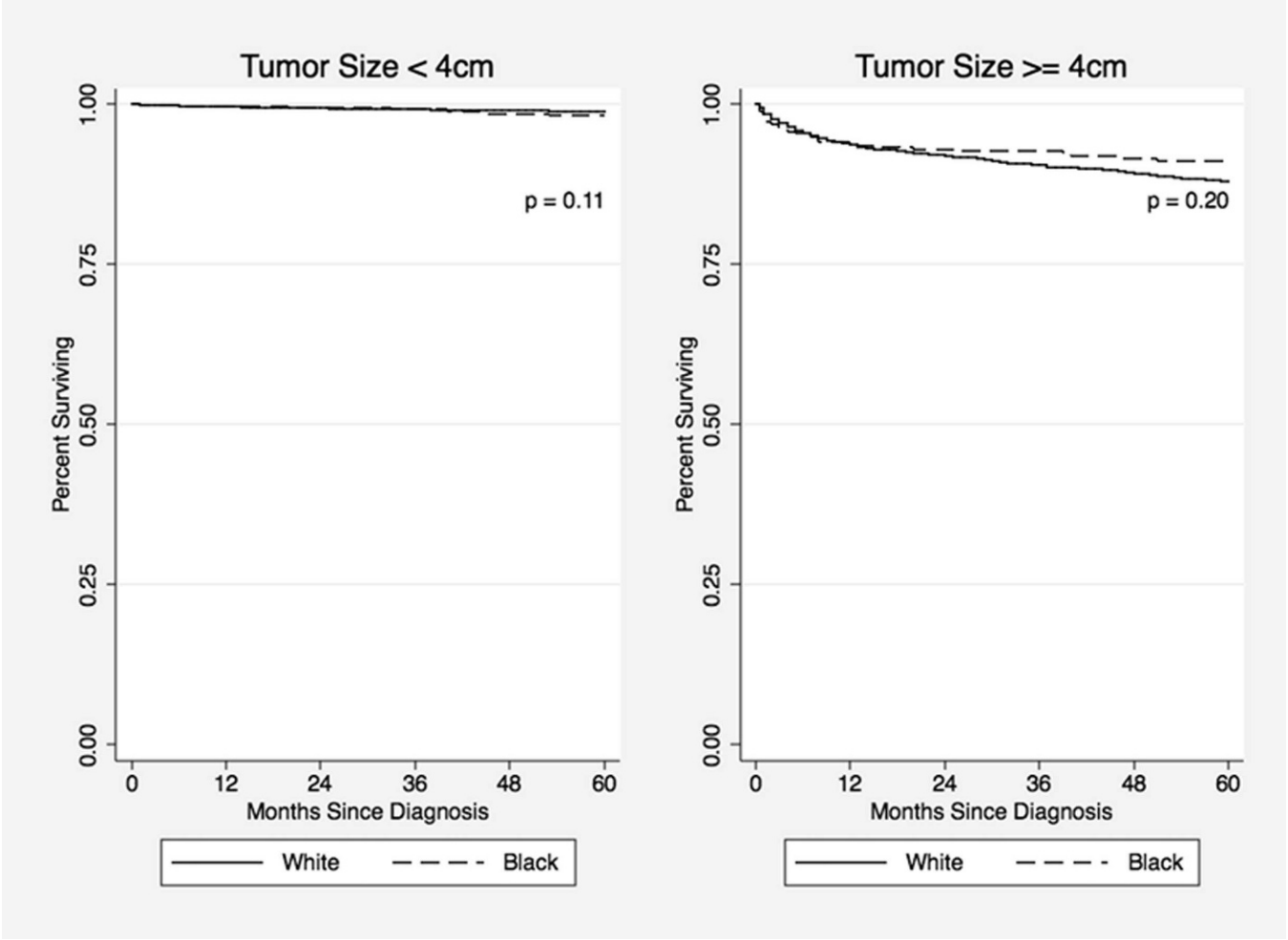

Fig 3. Five-year survival stratified by race and tumor size. Measure is time from diagnosis until death from cancer

it is possible that anaplastic disease may arise *de novo*, it is generally accepted that it can develop from pre-existing differentiated thyroid cancer (papillary or follicular).[35] This finding may suggest that African Americans are less likely to seek or receive care and therefore they will have a greater chance of presenting with an anaplastic transformation of long standing differentiated thyroid cancer.

We found African Americans had a poorer thyroid cancer survival at five years compared to Whites.

We found African Americans had a poorer thyroid cancer survival at five years compared to Whites (96.5% vs 97.4%, P=.006). Although this additional risk of mortality was small, it was nonetheless significant. This is particularly telling in light of the fact that thyroid cancer is relatively nonlethal cancer and is far less common in AA then in Whites.

Access to Care

While we were unable to directly glean access to medical care, financial barriers, quality and quantity of healthcare providers in underserved areas from SEER data, one could speculate as to this being a central issue. Our data show that AA were more likely to have larger tumors at diagnosis and more likely to have ATC. As mentioned, ATC often will represent transformation of a longstanding differentiated thyroid cancer. Brown et al studied the effect of race on thyroid cancer care in an equal access healthcare system. They performed a retrospective study of both White and AA patients treated in a US Department of Defense facility. They found no difference between Black and White patients in regard to age at presentation, tumor size and overall 5-year survival rate.[19]

Study Limitations

One limitation of this study is that it has been noted that minorities are not well-represented in the SEER database.[4]

The 13 cancer registries from which data are collected represent approximately 13.8% of the US population. Therefore, this sample may not reflect accurately the incidence of cancer in minority populations in the United States.[3] Other potential limitations include absent data on extracapsular disease and treatment protocols.

CONCLUSIONS

Thyroid cancer is on the rise in both Whites and AA. Although African Americans have poorer survival relative to White patients, much of this difference is explained by differences in disease characteristics. The large tumors, follicular histology, older age and relatively high rate of anaplastic cancer among African Americans may explain the poorer outcomes.

REFERENCES

1. National Cancer Institute. Thyroid Cancer. http://www.cancer.gov/cancertopics/types/thyroid. Last accessed July 22, 2010.
2. Mitchell I, Livingston EH, Chang AY, et al. Trends in thyroid cancer demographics and surgical therapy in the United States. *Surgery*. 2007;142(6):823–828; discussion 828 e821.
3. Bilimoria KY, Bentrem DJ, Linn JG, et al. Utilization of total thyroidectomy for papillary thyroid cancer in the United States. *Surgery*. 2007;142(6):906–913; discussion 913 e901–902.
4. Morris LG, Sikora AG, Myssiorek D, DeLacure MD. The basis of racial differences in the incidence of thyroid cancer. *Ann Surg Oncol*. 2008;15(4):1169–1176.
5. Shaha A. Treatment of thyroid cancer based on risk groups. *J Surg Oncol*. 2006;94(8):683–691.
6. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973–2002. *JAMA*. 2006;295(18):2164–2167.
7. Hodgson NC, Button J, Solorzano CC. Thyroid cancer: is the incidence still increasing? *Ann Surg Oncol*. 2004;11(12):1093–1097.
8. Sprague BL, Warren Andersen S, Trentham-Dietz A. Thyroid cancer incidence and socioeconomic indicators of health care access. *Cancer Causes Control*. 2008;19(6):585–593.
9. Kent WD, Hall SF, Isotalo PA, Houlden RL, George RL, Groome PA. Increased incidence of differentiated thyroid carcinoma and detection of subclinical disease. *CMAJ*. 2007; 177(11):1357–1361.
10. McNeil C. Annual cancer statistics report raises key questions. *J Natl Cancer Inst*. 2006;98(22):1598–1599.
11. Hayat MJ, Howlader N, Reichman ME, Edwards BK. Cancer statistics, trends, and multiple primary cancer analyses from the Surveillance, Epidemiology, and End Results (SEER) Program. *Oncologist*. 2007;12(1):20–37.
12. McCoy KL, Jabbour N, Ogilvie JB, Ohori NP, Carty SE, Yim JH. The incidence of cancer and rate of false-negative cytology in thyroid nodules greater than or equal to 4 cm in size. *Surgery*. 2007;142(6):837–844; discussion 844 e831–833.
13. Frates MC, Benson CB, Doubilet PM, et al. Prevalence and distribution of carcinoma in patients with solitary and multiple thyroid nodules on sonography. *J Clin Endocrinol Metab*. 2006;91(9):3411–3417.
14. Iannuccilli JD, Cronan JJ, Monchik JM. Risk for malignancy of thyroid nodules as assessed by sonographic criteria: the need for biopsy. *J Ultrasound Med*. 2004;23(11):1455–1464.
15. Paramo JC, Mesko T. Age, tumor size, and in-office ultrasonography are predictive parameters of malignancy in follicular neoplasms of the thyroid. *Endocr Pract*. 2008;14(4):447–451.
16. Haigh PI, Urbach DR, Rotstein LE. Extent of thyroidectomy is not a major determinant of survival in low- or high-risk papillary thyroid cancer. *Ann Surg Oncol*. 2005;12(1):81–89.
17. Bilimoria KY, Bentrem DJ, Ko CY, et al. Extent of surgery affects survival for papillary thyroid cancer. *Ann Surg*. 2007;246(3):375–381; discussion 381–374.
18. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2008. *CA Cancer J Clin*. 2008; 58(2):71–96.
19. Brown SR, Lee S, Brown TA, Waddell BE. Effect of race on thyroid cancer care in an equal access healthcare system. *Am J Surg*. 2010;199(5):685–689.
20. Ward E, Jemal A, Cokkinides V, et al. Cancer disparities by race/ethnicity and socioeconomic status. *CA Cancer J Clin*. 2004;54(2):78–93.
21. Miller BA, Scoppa SM, Feuer EJ. Racial/ethnic patterns in lifetime and age-conditional risk estimates for selected cancers. *Cancer*. 2006;106(3):670–682.
22. Mulla ZD, Margo CE. Primary malignancies of the thyroid: epidemiologic analysis of the Florida Cancer Data System registry. *Ann Epidemiol*. 2000;10(1):24–30.
23. Haselkorn T, Stewart SL, Horn-Ross PL. Why are thyroid cancer rates so high in southeast asian women living in the United States? The bay area thyroid cancer study. *Cancer Epidemiol Biomarkers Prev*. 2003;12(2):144–150.
24. Clark JR, Eski SJ, Freeman JL. Risk of malignancy in Filipinos with thyroid nodules–a matched pair analysis. *Head Neck*. 2006;28(5):427–431.
25. Iribarren C, Haselkorn T, Tekawa IS, Friedman GD. Cohort study of thyroid cancer in a San Francisco Bay area population. *Int J Cancer*. 2001;93(5):745–750.
26. Belfiore A, La Rosa GL, La Porta GA, et al. Cancer risk in patients with cold thyroid nodules: relevance of iodine intake, sex, age, and multinodularity. *Am J Med*. 1992;93(4): 363–369.
27. Shah JP, Loree TR, Dharker D, Strong EW, Begg C, Vlamis V. Prognostic factors in differentiated carcinoma of the thyroid gland. *Am J Surg*. 1992;164(6):658–661.
28. Andersen PE, Kinsella J, Loree TR, Shaha AR, Shah JP. Differentiated carcinoma of the thyroid with extrathyroidal extension. *Am J Surg*. 1995;170(5):467–470.
29. Yu GP, Li JC, Branovan D, McCormick S, Schantz SP. Thyroid cancer incidence and survival in the national cancer institute surveillance, epidemiology, and end results race/ethnicity groups. *Thyroid*. 2010;20(5):465–473.
30. Mandelblatt JS, Yabroff KR, Kerner JF. Equitable access to cancer services: A review of barriers to quality care. *Cancer*. 1999; 86(11):2378–2390.
31. DeGroot LJ, Kaplan EL, Shukla MS, Salti G, Straus FH. Morbidity and mortality in follicular thyroid cancer. *J Clin Endocrinol Metab*. 1995;80(10):2946–2953.
32. Lang BH, Lo CY, Chan WF, Lam AK, Wan KY. Classical and follicular variant of papillary thyroid carcinoma: a comparative study on clinicopathologic features and long-term outcome. *World J Surg*. 2006;30(5):752–758.
33. Loh KC, Greenspan FS, Gee L, Miller TR, Yeo PP. Pathological tumor-node-metastasis (pTNM) staging for papillary and follicular thyroid carcinomas: a retrospective analysis of 700 patients. *J Clin Endocrinol Metab*. 1997; 82(11):3553–3562.
34. Neff RL, Farrar WB, Kloos RT, Burman KD. Anaplastic thyroid cancer. *Endocrinol Metab Clin North Am*. 2008;37(2):525–538, xi.
35. Kitamura Y, Shimizu K, Nagahama M, et al. Immediate causes of death in thyroid carcinoma: clinicopathological analysis of 161 fatal cases. *J Clin Endocrinol Metab*. 1999;84(11): 4043–4049.

AUTHOR CONTRIBUTIONS

Design concept of study: Hollenbeak, Wang, Schneider, Goldenberg

Acquisition of data: Hollenbeak, Wang, Schneider, Goldenberg

Data analysis and interpretation: Hollenbeak, Wang, Schneider, Goldenberg

Manuscript draft: Hollenbeak, Wang, Goldenberg

Statistical expertise: Hollenbeak, Wang, Schneider

Supervision: Hollenbeak, Goldenberg