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Thyroid Cancer: Is the Incidence Still Increasing?

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Background: The objective of this study was to define the epidemiology of thyroid cancer in our regional population and compare results with Surveillance, Epidemiology, and End Results (SEER) Program cancer registry trends.

Methods: Thyroid cancer cases diagnosed between 1990 and 2000 were identified in the Florida Cancer Data System (FCDS). Overall, gender-specific, age-specific, and stage-specific incidence rates were calculated. All rates are per 100,000 and age-adjusted to the 2000 U.S. standard population. Estimated Annual Percent Change (EAPC) was calculated with a linear least-squares model.

Results: Patients with thyroid cancer (n = 8603) were identified in the FCDS registry. Age-adjusted incidence rates increased from 4.2 per 100,000 to 7 per 100,000 in 2000. The EAPC for this period was 5.5% ($P < .001$). The SEER incidence rates increased from 7.9 to 10.2 per 100,000, and the EAPC was 3.7% ($P < .05$). Analysis of gender-specific incidence rates showed increases from 6 and 2.2 per 100,000 in 1990 to 10.1 and 3.8 per 100,000 in 2000 among females and males, respectively, with EAPCs of 5.9% (females) and 4.5% (males) ($P < .001$). With stratification by age group, the highest incidence rates were 9 per 100,000 in the group aged 65 to 84 years and 8.4 per 100,000 in the group aged 45 to 64 years.

Conclusions: Thyroid cancer incidence rates in Florida almost doubled over the 1990–2000 period and are concordant with SEER trends. Etiologic studies addressing temporal changes in reproductive factors, more intensive diagnostic activities, and changes in histological criteria are warranted.

Key Words: Epidemiology— Incidence—Thyroid cancer.

The trend of increasing thyroid cancer has been recognized worldwide for several decades and shows considerable geographic variation. Recent studies have shown a steady increase in the United States, Canada, Sweden, and Britain.[1–4]

Zheng et al.[1] identified a strong birth cohort effect underlying the observed increase in thyroid cancer incidence in both sexes in the state of Connecticut. This study suggested that the introduction of radiation treatment for benign childhood conditions of the head and neck between the 1920s and 1950s was largely responsible for the increasing temporal trends in thyroid cancer. With the incidence three times higher among females, numerous epidemiologic studies have attempted to examine the possible associations between hormones and other reproductive factors. Unlike breast cancer, pregnancy and early menopause appear to increase the risk of thyroid cancer.[4] Changes in thyroid cancer incidence could also reflect increased use of diagnostic activity such as ultrasonography and fine-needle aspiration biopsy or changes in histologic criteria.[5]

The Surveillance, Epidemiology, and End Results Program (SEER),[6] the largest cancer registry network in North America, has only one of its cancer registries in the southeastern United States (metropolitan Atlanta). The SEER program data are thought to be representative of the entire United States population; however, the program includes only 15% of the United States population for its cancer statistics, and heterogenous populations such as Florida may not be accurately represented by the SEER data. Therefore, we sought to

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analyze Florida's thyroid cancer incidence pattern and to investigate possible contributing factors in this regional population.

The primary objective of this study was to define recent secular trends in the incidence of thyroid malignancies in Florida in comparison with the SEER cancer program data. Secondary objectives included assessment of age-specific, gender-specific, stage-specific, and histopathologic subtype–specific thyroid cancer incidence rates.

MATERIALS AND METHODS

Thyroid cancer incidence data from 1990 to 2000 were obtained from the Florida Cancer Data System (FCDS), Florida's population-based central incident statewide cancer registry. The FCDS was established in 1981 to accumulate vital statistics on cancer diagnosed in Florida. Florida statute requires acute care facilities to report basic information on all cases of invasive cancer within 6 months of diagnosis. All diagnoses of cancer are based on histopathologic examination of affected tissues. No material was obtained from autopsy. The histopathologic diagnoses in the FCDS are coded according to the International Classification of Diseases for Oncology (ICD-0–3).[7] For comparative data from the SEER[8] program (nine registries), incidence data was obtained from 1990 to 2000. To compare data to the previous decade, we also obtained thyroid incidence rates for the years 1981 to 1989 from both the FCDS and SEER databases.

The FCDS utilizes the SEER Summary Staging guide, which is based on a combination of pathologic, operative, and clinical assessments. For this analysis, tumor staging was categorized as (1) local if the lesion was described as in situ or was confined to the organ of origin; (2) regional if local invasion or lymph node metastasis was present; (3) distant if metastatic dissemination to other organs was evident; and (4) unstaged if information was insufficient to assign a stage.

Statistical Analysis

The primary outcome was age-adjusted incidence. All rates reported are per 100,000 per year. Age-adjusted incidence rates were calculated by means of direct standardization with the United States standard 2000 population. Other outcomes included age-specific (stratified into 4 age groups: 10–24, 25–44, 45–64, and 65–84 years), gender-specific, stage-specific, and histopathologic subtype–specific thyroid cancer incidence rates. The incidence of thyroid cancer per public health region in Florida was also calculated.

The EAPC is a summary statistic that indicates the trend over a defined time period.[8] The EAPC values were calculated by linear regression to fit a weighted least-squares model to the log of age-adjusted rates for the period. The slope of the line is tested for significant increases or decreases (95% confidence intervals were recorded, and $P < .05$ was considered significant). The SEER Stat 5.1.14 software was utilized.[9]

RESULTS

Overall Age-Adjusted Incidence Rates

A total of 8603 incident cases of thyroid cancer were registered in Florida between 1990 and 2000. Of these, 6235 (72.5%) were diagnosed in women and 2368 (27.5%) in men. The overall age-adjusted incidence rates increased from 4.2 per 100,000 in 1990 to 7 per 100,000 in 2000. Age-adjusted incidence rates are increasing with time in Florida. These trends are concordant with SEER program data (Fig. 1). The EAPC increased from 3.1% in the 1981–1989 period to 5.5% per year ($P < .001$) in the 1990–2000 period (Table 1). The EAPC for the SEER registries also increased from 2.4% to 3.6% ($P < .05$) in the 1981–1989 and 1990–2000 periods, respectively.

Gender and Age-Specific Group Trends

The female and male incidence rates increased from 6 to 10.1 cases per 100,000 and 2.2 to 3.8 per 100,000, respectively (Fig. 1). The EAPCs (1990–2000) were 5.9% ($P < .05$) and 3.9% ($P < .05$) per year for females and males, respectively. The age-specific incidence rates for four age group cohorts are illustrated in Figure 2. The highest incidence rates for females and males were 11.4 per 100,000 in the group aged 45 to 64 years (6.3 per 100,000 in the 1981–1989 period) and 7.1 per 100,000 in the group aged 65+ years, respectively.

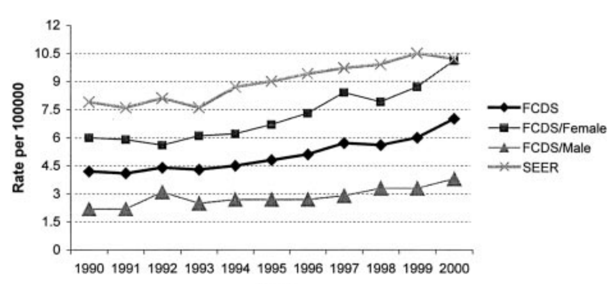

FIG. 1. Age-adjusted incidence rates for the Florida Cancer Data System (FCDS) and Surveillance, Epidemiology, and End Results (SEER) Program are illustrated (rates are number of cases per 100,000). Female and male thyroid cancer incidence rates for the years 1990 to 2000 are also shown.

TABLE 1. *Change in thyroid cancer incidence: estimated annual percent change (EAPC), Florida Cancer Data System (FCDS) versus Surveillance, Epidemiology, and End Results (SEER) Program*

	EAPC (95% confidence interval)	
Time Period	FCDS	SEER
1981–1990	3.1[a] [2.1,4.2]	2.4[a] [1.3,3.5]
1990–2000	5.5[b] [4.3,6.7]	3.6[a] [3.0,4.1]

[a] $P < .05$
[b] $P < .001$

Stage at Diagnosis

The majority of patients presented with cancer at localized stage (Fig. 3). Rates of cancer presenting at localized stage increased from 2.4 per 100,000 in 1990 to 4.8 per 100,000 in 2000; among females, the rate increased from 3.6 (1990) to 7.3 (2000). There were no changes in the rates of regional, distant disease, or unstaged patients.

There were 1043 patients diagnosed with lesions of 1 cm or less, comprising 12% of the study population. The incidence rates of tumors <1 cm at presentation increased from 0.4 cases per 100,000 in 1994 to 1.4 cases per 100,000 in 2000. This corresponded to an EAPC of 17.7 % (95% CI, 9.3–26.7; $P < .05$).

Histopathologic Subtypes

The changes in EAPC for each histologic subtype for the 1981–1989 and 1990–2000 periods are outlined in Table 2. For the 1990–2000 period, the follicular variant of papillary cancer showed the highest increase (EAPC, 12.4%). There was also an increase in pure papillary carcinoma (EAPC, 4.8%) and Hurthle cell carcinoma (EAPC, 4.7%), but this increase was less than in the 1981–1989 period. The observed changes in annual incidence were all statistically significant ($P < .05$). The incidence of medullary carcinoma remained constant. There was a decreasing trend in follicular carcinoma, but this was not statistically significant. Other thyroid malignancies have decreased in incidence during both time periods.

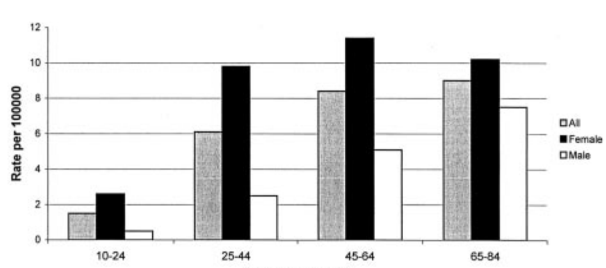

FIG. 2. Age was stratified according to the following age group cohorts: 10 to 24, 25 to 44, 45 to 64, and 65 to 84 years. The changes in incidence rates observed for females and males for the years 1990 to 2000 are illustrated. For females, the age-specific incidence rates were 2.6 (10–24 years), 9.8 (25–44 years), 11.4 (45–64), and 10.2 (65–84). For males, the rates were 0.5 (10–24), 2.5 (15–44), 5.1 (45–64), and 7.5 (65–84).

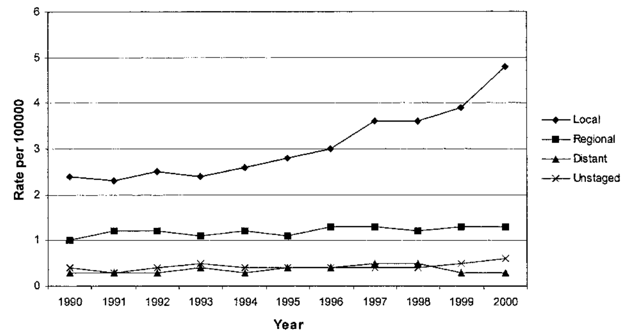

FIG. 3. Stage at presentation for all cases of thyroid cancer diagnosed in Florida for the period 1990 to 2000.

Geographic Patterns

The thyroid cancer incidence rates per public health region in Florida were calculated. The highest rates were in the Palm Beach region (6.4 per 100,000) and Miami Dade region (5.5 per 100,000). The lowest rate was 4.2 per 100,000 in the South Central region.

DISCUSSION

The overall age-adjusted incidence rates of thyroid cancer have been increasing in Florida among both females and males. The increasing time trends in thyroid cancer incidence in Florida are concordant with SEER data and extend the results of earlier publications.[1–5] There is a striking increase in the female incidence rates, which are almost twice the male incidence rates. For the 1990–2000 period, thyroid cancer incidence in Florida continued to show a statistically significant annual percent increase of 5.5% per year.

Environmental and genetic factors are thought to contribute to an increased risk of thyroid carcinoma; these include epidemic goiter, radiation, and autosomal dominant inheritance for medullary carcinoma.[10] The Connecticut Tumor Registry study from 1935 to 1992 associated this primary increase in papillary carcinoma with radiation exposure during childhood for benign medical conditions.[1] When we analyzed our data by age-specific incidence, the highest rates were observed in the age cohort of 65+ years, but a high incidence was also observed in the cohort aged 45–64 years. Furthermore, age-specific analysis by 10-year age groups identified that thyroid cancer incidence among young females in-

TABLE 2. *Estimated annual percent change (EAPC) for histopathologic subtypes of thyroid cancer*

Histologic subtype	1981–1989	1990–2000
Papillary	5.2[a]	4.8[a]
Papillary (follicular variant)	1.4	12.4[a]
Follicular	3.7[a]	0.7
Hurthle	18.2[a]	4.7[a]
Medullary	1.8	4
Other	−3.6	−21.4

[a] *P* value <.05

creased over the 1990–2000 period (2.9 to 3.9 per 100,000 for 20–29-year-olds and 5.2 to 8.4 per 100,000 for 30–39-year-olds). Radiation effects on birth cohorts in the 1930s to1950s, therefore, cannot alone explain the increased incidence in thyroid cancer.

Most studies describing the increasing incidence of thyroid carcinoma attribute this entirely to the increase in papillary carcinoma.[1–5,11] In the FCDS, papillary carcinoma increased 4.8% in the 1990–2000 period. The most dramatic increase was seen in the follicular variant of papillary carcinoma (12.4%), which is thought to behave clinically as pure papillary carcinoma.[12] Follicular carcinoma may be declining, with only a 0.7% increase, compared with the prior 3.7% increase in 1981–1989. The observed increase in papillary cancer of the follicular variant may be attributed in part to the new pathologic criteria for diagnosis of papillary carcinoma established in 1988.[13] Conversely, reclassification by pathologists may account for the observed decline in follicular carcinoma.[14] Hurthle cell (oxyphilic) cancer increased 4.7% per year in the 1990–2000 period, but this is less than the previous 18.2% increase in EAPC noted in 1981 to 1989. Medullary and other thyroid malignancies had no statistically significant change in annual incidence.

Given the threefold higher incidence of thyroid carcinoma among females, numerous epidemiologic studies have examined the possible associations between reproductive factors, hormones, and the risk of thyroid cancer. A pooled analysis of 14 case-control studies of thyroid cancer suggested that miscarriage of the first pregnancy posed a high risk for developing papillary carcinoma, with a pooled odds ratio of 1.7.[15] Therapeutic abortion rates increased significantly from 5 per 1000 live births to more than 20 per 1000 live births in the 1990s in the United States.[16] Controversial findings regarding hormones and reproductive factors require further study controlling for potential confounders. Anthropometric factors and thyroid cancer risk have been assessed, and an elevated body mass index was directly related to thyroid cancer risk in females (odds ratio = 1.2) but not in males.[17]

A variety of nonetiologic factors such as new diagnostic technologies may affect the incidence of thyroid cancer. A recent study in France showed that evolution in clinical practices in 1980 to 2000 in that country led to the increase in thyroid cancer reported.[18] A significant increase in the use of ultrasound (3% to 84.8%), changes in cytological practices (4.5% to 23%), and a decrease (89.4% to 49.6%) in radionuclide scan procedures were observed over time in that study. We have noticed an increase in the number of patients presenting to our clinic with incidentally found nonpalpable thyroid nodules. Invariably, many of these nodules are subjected to needle biopsy, and some of the patients may have cancer. Interestingly, the rate of clinically "occult" thyroid tumors has increased significantly since the mid 1990s in Florida. The FCDS did not collect data on <1-cm tumors until 1994; therefore, a comparison between the 2 decades to determine the impact that such tumors have on our data cannot be made. However, only 12% of patients in the study period had tumors <1 cm, and this trend cannot alone explain the overall increase in incidence. Moreover, with changing patterns of clinical care, such as increased use of ultrasonography to detect clinically nonpalpable cancers, one would expect the incidence of all thyroid cancer subtypes to increase, and this was not the case in this study. These data would support the notion that the increase in incidence is not entirely due to increased screening and detection. Such changes in medical as well as surgical and pathological practices must be taken into account in incidence measurement.

We acknowledge that the interpretation of time trends in incidence with use of data obtained from cancer registries may be distorted by the completeness of registration or other registry practices. The FCDS has received gold certification by the North American Association of Central Cancer Registries (NAACCR) for highest standard of quality, which includes completeness of 95% or more as one criterion.[19] The FCDS permits analysis of large numbers of patients with a rare neoplasm, thyroid cancer. Further analysis of FCDS patients addressing radiation exposure, occupational exposure, and reproductive factors in a population-based case-control interview study may offer further insights into this increasing incidence.

Cancer statistics form the basis of our progress. Identification of changing epidemiological patterns in thyroid cancer is paramount in formulating future health care clinical tools, evaluating prognostic and therapeutic models, and generating new hypotheses on disease etiology and prevention.

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