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Increased rates of advanced thyroid cancer in California

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ABSTRACT

Background: We have noted an unusually high rate of advanced thyroid cancers presenting from across California. We examined the rates of thyroid cancer presentation throughout California for potential geographic clustering.

Materials and methods: A total of 26,983 patients with a new diagnosis of thyroid cancer (1999–2008) were abstracted from the California Cancer Registry and the Office of Statewide Health Planning and Development registry. Percentages of advanced thyroid cancer rates were calculated within each county (defined as those with distant metastatic stage; regional and/or distant metastatic stage [RM]) as well as those with well-differentiated thyroid cancer diagnosed before age 30. National averages were taken from Surveillance, Epidemiology, and End Results (SEER) data.

Results: There was no obvious clustering of advanced cases within certain regions in California; however, on average, the entire state of California had significantly higher rates of distant metastatic thyroid cancer (6.73%) and RM (34.92%) than the national SEER averages (4%, 29%, respectively, $P < 0.001$). Of the 47 California counties, 20 had significantly higher percentages of distant metastatic thyroid cancer than the national SEER average (range, 6%–13% *versus* 4%, $P < 0.05$), and 20 had a higher percentage of RM than the national SEER average (range, 35%–48% *versus* 29%, $P < 0.05$). Two California counties had higher rates of young patients with well-differentiated thyroid cancer (range, 14.29%–17.9%) than the national SEER average (12%).

Conclusions: California exhibits more advanced thyroid cancers than the national SEER population average. Further studies are warranted to better understand etiologies for these disparities, which may include environmental impacts and/or delays in diagnosis.

1. Introduction

The rising incidence of thyroid cancer over the past three decades has been variably attributed to incidentally discovered thyroid nodules, demographic variables, and/or environmental impacts [1–7]. Additional known risk factors associated with an increased risk of thyroid cancer include family history of thyroid cancer, radiation exposure, Hashimoto thyroiditis, and elevated thyroid stimulating hormone [5,8–12]. Obesity, race, and socioeconomic factors also contribute to higher advanced thyroid cancer rates [4,6]. Despite our increased understanding of thyroid cancer risk factors, collectively, they do not fully explain why the incidence rates are rising worldwide.

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California has a very diverse population with a wide range of races and ethnicities as well as a wide variety of international immigrants. Geographically, the state of California also has diverse topography and is comprised of large areas of coastline, mountainous regions, valleys, vast expanses of desert or arid land, as well as a plethora of agricultural areas scattered throughout the state. It also has one of the largest collections of decommissioned nuclear reactors in the country [13].

Other than the known impact of ionizing radiation on the development of thyroid cancer, only a few studies have addressed other possible environmental exposures as contributing factors to the rise in thyroid cancer incidence. This area of research has been difficult to study owing to the geographic mobility of many area residents and the difficulty in collecting exposure data. However, there are some studies that have emerged suggesting exposure to environmental chemicals might increase one's risk of thyroid cancer [14]. A link between environmental toxins/pesticides and thyroid cancer has been suggested, but no study large enough to assess that implication has yet been done [14]. High urinary levels of the metal tungsten have also been associated with elevated thyroid stimulating hormone levels, which in turn could increase one's risk of thyroid cancer [15]. An individual's likelihood of being exposed to any of these (or other) environmental risk factors could vary with geographical location.

In our tertiary referral center, we have noted an unusually high rate of advanced thyroid cancers presenting from across the state of California. To investigate the possibility of environmental impacts as a predisposition for thyroid cancer, we sought to identify counties in California with possible geographic clustering of advanced thyroid cancer cases.

2. Materials and methods

A total of 29,258 patients with a new diagnosis of thyroid cancer (ICD-O-2/3 code C739) were abstracted from the California Cancer Registry (CCR, 1999–2008) and the Office of Statewide Health Planning and Development. We excluded patients with unknown zip codes of residence ($n = 241$), zip codes outside of California ($n = 1303$), or those with missing stage information ($n = 731$), for a final cohort size of 26,983.

Established in 1947, the CCR is California's statewide population-based cancer surveillance system and is one of the largest, most comprehensive cancer registries in the world [16]. It captures information on every patient who is newly diagnosed with cancer within the state of California and follows their progress forward. It has collected detailed information on over 3.4 million cases of cancer, and more than 162,000 new cases are added annually [16].

Thyroid cancer stage at diagnosis was defined (using the CCR SUMSTAGE variable) as localized, regional, or distant metastatic (in CCR this is designated as "remote"). Regional disease grouped the following: regional by direct extension, regional by lymph nodes, or regional by direct extension and lymph nodes. This is the same staging system as used in the national Surveillance, Epidemiology, and End Results (SEER) data set.

Surgery was defined as either thyroid lobectomy or total thyroidectomy (with or without any type of lymph node dissection). Treatment and histology codes are summarized in Supplemental Table 1.

Patients' counties of residence were defined by zip code at the time of diagnosis. Counties with sparse populations and similar geographical characteristics were combined to ensure the cumulative cancer cases greater than 15 and the aggregated total population size of at least 200,000. This resulted in 47 counties (alone or combined) from the original 58 counties. If a zip code was shared by two counties, the zip code was classified into the county with the larger patient population size.

Racial groups were defined as non-Hispanic white, non-Hispanic black, Hispanic, Asian/Pacific Islander (API), and other. Our race variable is derived from the CCR variable "RACE08" [4]. Comorbidity was scored using the Charlson comorbidity scoring system [17]. Socioeconomic score was coded as the quintiles of Yost's index of socioeconomic status (SES) level based on a principal component analysis where the lowest SES score was 1 and the highest SES score was 5 [18].

Health insurance type was categorical with three levels: private, poor and/or uninsured, and government and/or military. Private insurance included the following subtypes: managed care/health maintenance organization (HMO)/preferred provider organization, fee-for-service, Medicare administered through a managed care plan or private supplementation, insurance/not otherwise specified. Poor and/or uninsured subtypes included Medicaid, Medicaid through managed care or with Medicare supplement, and county funded not otherwise specified. Governmental insurance included TRICARE, military, Veterans Affairs.

Hospital type was defined as public, academic, HMO, government, and private. Public hospitals were defined as county hospitals without an associated surgical residency or fellowship program. Academic hospitals were defined as hospitals in California with general surgery residency and/or endocrine surgery fellowship programs. HMO hospitals were defined as those hospital systems that were somehow vertically integrated such as Kaiser Permanente and Sutter Health hospital systems.

Percentages of advanced thyroid cancer rates were calculated within each county. Advanced thyroid cancers were defined as those with distant metastatic stage (all thyroid cancer subtypes) or a combination of regional and distant metastatic stages (RM, all thyroid cancer subtypes). We also calculated the rates of well-differentiated thyroid cancer (WDTC) in patients aged <30 y, an early onset for this type of cancer.

National (US) averages were taken from SEER data [19]. SEER currently collects and publishes cancer incidence and survival data from population-based cancer registries covering approximately 28% of the US population [20]. The collection system for the SEER data is similar to that of the CCR.

We calculated the 95% confidence interval (CI), using the exact method for binomial distribution, of the rate of advanced disease for each county in California. Exact test was used to determine if the rate was significantly different from the national average. Note that we regard the national average