Original Article

Sexual disparity and the risk of second primary thyroid cancer: a paradox

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Background: Despite extensive research on sex differences in primary thyroid cancer, there is a lack of data on the role of sex in the risk of developing second primary thyroid cancer (SPTC). We aimed to investigate the risk of SPTC development according to patient sex, with an emphasis concerning previous malignancy location as well as age.

Methods: Cancer survivors diagnosed with SPTC were identified from the Surveillance, Epidemiology, and End Results (SEER) database. The SEER*Stat software package obtained standardized incidence ratios (SIR) and absolute excess risks of subsequent thyroid cancer development.

Results: Data for 9,730 (62.3%) females and 5,890 (37.7%) males were extracted for a total of 15,620 SPTC individuals. Asian/Pacific Islanders had the highest incidence of SPTC [SIR =2.67, 95% confidence interval (CI): 2.49–2.86]. The risk of SPTC was higher in males (SIR =2.01, 95% CI: 1.94–2.08) than when compared to females (SIR =1.83, 95% CI: 1.79–1.88; P<0.001). Head and neck tumors had significantly higher SIRs for SPTC development in males when compared to females.

Conclusions: Survivors of primary malignancies have an increased risk SPTC, especially males. Our work suggests that oncologists and endocrinologists may consider the need for increased surveillance of both male and female patients given their increased risk of SPTC.

Keywords: Sexual disparity; second primary thyroid cancer (SPTC); Surveillance, Epidemiology, and End Results (SEER); second malignancy; thyroid cancer

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Introduction

Thyroid cancer is currently the most common endocrine malignancy. Considering increased diagnostic scrutiny secondary to increased imaging studies and genetic testing, the prevalence of thyroid cancer continues to rise and is consequently the fastest growing cancer in the United States (1-3). Importantly, reports have consistently found higher rates of primary thyroid cancer diagnoses in females than in males (4-6).

Second primary cancers are primary cancers which develop following the diagnosis of a previous primary

cancer. Second primary cancers are liable to factors which are implicated in the development of primary cancers, such as exposure to environmental carcinogens and previous treatment exposures (i.e., radiotherapy, chemotherapy). More importantly, second primary cancers could allow for heightened scrutiny of shared genetic factors considering its confinement to only a single individual. A recent 2020 work found that second primary papillary thyroid cancer was significantly elevated in 23 of 27 primary cancers (7). Interestingly, the work of Sung *et al.* found that second primary thyroid cancer (SPTC) rates tended to be slightly more elevated in males than in females (8). Though the authors did not further investigate the matter, this finding is contrary to the increased incidence rates of primary thyroid cancer typically demonstrated in females (9). To date, the development of SPTC by sex with respect to initial malignancy location as well as age has yet to be elucidated.

Given the differences in thyroid cancer incidence rates with respect to both sex and previous history of malignancy, evaluating the risk of developing SPTC may provide information regarding cancer behavior. Importantly, understanding differences in the incidence rates of SPTC according to sex may improve medical surveillance for cancer survivors and improve the treatment of SPTCs. Here, we aimed to investigate the risk of SPTC development according to patient sex, with an emphasis concerning previous malignancy location as well as age. We present the following article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-22-411/rc).

Highlight box

Key findings

- Survivors of primary malignancies have an increased risk second primary thyroid cancer, especially males.

What is known and what is new?

- Females have consistently been found to have higher rates of primary thyroid cancer diagnoses.
- Both sexes are at increased risk of second primary thyroid cancer, especially males.

What is the implication, and what should change now?

- Our work suggests that oncologists and endocrinologists may consider the need for increased surveillance of both male and female patients given their increased risk of second primary thyroid cancer.

Methods

Data source

A cohort which was population-based was identified from the National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results (SEER) database. The SEER Program provides detailed information on a multitude of malignancies, including thyroid cancer, providing cancer incidence and survival data from cancer registries (10). These registries cover approximately 30% of the United States population (10). This database is publicly available and resultantly both patient rights and Tulane University institutional review board approval were waived. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Research Data Agreement form was signed and submitted before initiating the following study. The senior authors obtained access to the database with the username 15332-Nov2019.

Patient population

Patients with a diagnosis of SPTC were included in the study. No exclusion was made based on age. Patients with an initial primary cancer located in the thyroid were excluded. In accordance with the World Health Organization (WHO) guidelines, thyroid malignancies diagnosed within 2 months of an initial primary cancer diagnosis were considered synchronous cancers and were consequently excluded (11). Since increased medical surveillance by default increases the detection of incidental SPTCs, we attempted to limit our analysis to clinically relevant cancers by excluding thyroid malignancies detected on death certificates or autopsy only.

Data extraction

Primary malignancies cases were extracted from the SEER 18 registry [2000–2016] using SEER*Stat software (version 8.3.6; Surveillance Research Program, National Cancer Institute, Bethesda, MD, US; www.seer.cancer.gov/seerstat: access date: 1/15/2021). Data were subsequently imported into IBM Statistical Package for the Social Sciences (SPSS) version 27.0 (Armonk, NY, USA). An analysis was conducted to identify standardized incidence ratios (SIR) and absolute excess risks (AER) of subsequent thyroid cancer. The International Classification of Diseases for Oncology (ICD-O-3) was implemented to identify the

cancer site (i.e., thyroid).

Variables and outcomes

Outcomes were analyzed in a similar manner to previously published works (7,8). The incidence of SPTC was estimated by comparing the SPTC cohort to cancer incidence rates of the United States general population with respect to primary malignancy location. Expected cancer incidences were calculated based on the 5-year age-specific and sex-specific cancer incidence rates of the United States general population. Incidence values were reported as a SIR with its corresponding 95% confidence interval (CI). SIRs are a reported ratio of the observed value divided by the expected value. Absolute excess ratios (AERs) were determined as well and, since their calculation incorporates disease prevalence, represents the burden in consequence of SPTC. To determine the number of cases, person-years at risk were multiplied by their corresponding primary cancer incidence rates.

Statistical analysis

SIRs and AERs for SPTC were obtained by multiple Primary-SIR programs (version 8.3.6, SEER Program, National Cancer Institute, Bethesda, MD) in the SEER*Stat software package.

To compare SIRs, P values were computed by Z-score, which was calculated with the SIR value and its CI using the following equation: Z = (Y1 – Y2)/SE (Y1 – Y2), where Y1 = ln(OR), SE1 = SE (Y1) and SE (Y1 – Y2) = SQRT(SE12 + SE22). Statistical analyses were two-sided. A P value of <0.05 was considered statistically significant.

Results

Characteristics of the study population

After screening 7,586,281 records in the SEER database, 15,620 SPTC patients with 33,551 primary cancers were analyzed. The majority of these SPTC patients had cancer only at a single site (n=13,980, 89.5%), 1,443 SPTC patients (9.2%) previously had two primary cancers while 197 (1.3%) had three or more primary cancers. With respect to race, Whites accounted for the 84.2% (n=13,157) while Blacks accounted for 9.1% (n=1,422) of the study population. With respect to sex, females accounted for 62.3% (n=9,730) of the study population while males accounted for 37.7% (n=5,890).

The overall mean age at diagnosis was 62.4±13.9 years. The mean age at diagnosis for males and females were 64.7±13.2 and 61.0±14.1 years, respectively. The age of patients at SPTC diagnosis was 61.8±13.9, 66.9±12.7, and 71.2±11.9 years in patients with one, two, and three or more primary malignancies, respectively. This trend was noticeable when patients were subgrouped by sex as well, with 60.4, 65.5, and 69.4 years and 64.1, 68.7, and 73.3 years corresponding with the mean age at SPTC diagnosis in one, two, and three or more primary malignancies in females and males, respectively (Table S1). Interestingly, the most common sites of primary cancer were that of the breast (n=4,354, 13%), prostate (n=1,718, 5.1%), colon-rectum (n=1,545, 4.6%).

Prevalence of SPTC

The prevalence of SPTC from 1975 to 2016 are displayed in *Figure 1*. Since 1995, the count of SPTC has increased an average of roughly 5% each year. The most dramatic increase in SPTC incidence occurred in females aged 45–75 years.

Risk of SPTC

The risk of SPTC development in primary cancer survivors is summarized in *Table 1*. Compared to White populations, Asian/Pacific Islander populations displayed significantly higher risks of SPTC development (SIR =2.67 *vs.* 1.84, P<0.001). With respect to sex, there was a significantly higher risk of SPTC development in males when compared to females (SIR =2.01 *vs.* 1.83, P<0.001).

Risk of SPTC by sex

To elucidate the risk of SPTC incidence, patients were subgrouped by sex (*Table 2*). The SIRs of SPTC development among males and females irrespective of primary malignancy site were 2.01 (95% CI: 1.94–2.08) and 1.83 (95% CI: 1.79–1.88; P<0.001), respectively. Apart from sex-specific sites, head and neck cancer risk was markedly higher in males than females in most sites analyzed (floor of mouth: SIR =4.27 *vs.* 1.75; gum: SIR =4.47 *vs.* 2.2; tonsil: SIR =2.61 *vs.* 0.52; pharynx: SIR =4.27 *vs.* 1.18; larynx: SIR =4.03 *vs.* 2.01; eye and orbit: SIR =4.6 *vs.* 2.56; and nasal cavity and middle ears: SIR =6.34 *vs.* 2.53). Males with a history of acute lymphocytic leukemia had a fourfold higher risk for SPTC than females (SIR =5.51 *vs.* 1.32). Males also

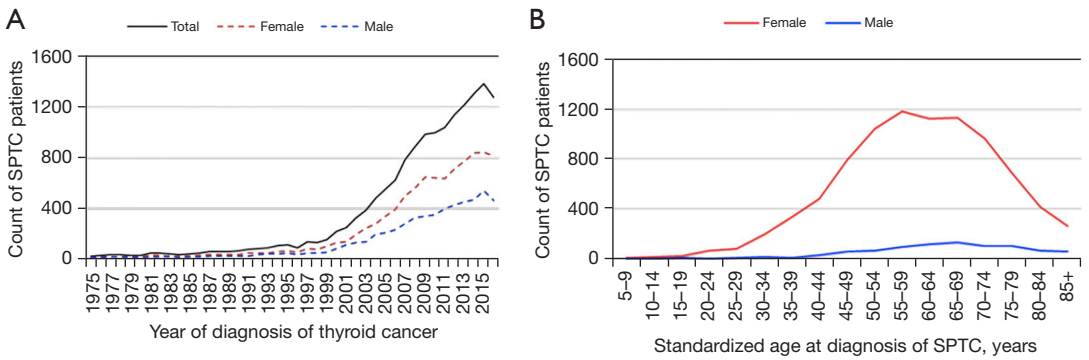

Figure 1 The annual increase in diagnosed cases of thyroid cancer. (A) Incidence by year. (B) Incidence by age. The data was retrieved from the SEER registry 9 [1975–2016]. SPTC, second primary thyroid cancer; SEER, Surveillance, Epidemiology, and End Results.

Table 1 Demographic disparities in second primary thyroid cancer risk

Characteristics at diagnosis of primary cancer	SIR	95% CI	AER	Z score
Sex				
Male	2.01	1.94–2.08	1.42	Reference
Female	1.83	1.79–1.88	2.30	−4.24***
Age, years				
<5	18.03	5.10–46.4	0.95	Reference
5–24	4.90	4.08–12.0	8.31	−1.22
25–44	2.26	2.04–2.65	11.1	−1.50
45–64	1.95	1.87–2.09	9.29	−1.53
65–84	1.67	1.51–1.79	4.46	−1.55
85+	1.22	0.97–1.53	0.23	−1.60
Race				
White	1.84	1.80–1.88	1.80	Reference
Black	1.87	1.73–2.02	1.22	0.39
American Indian/Alaska Native	2.34	1.70–3.13	2.69	1.37
Asian or Pacific Islander	2.67	2.49–2.86	3.46	8.59***
Management				
Primary site surgery	1.90	1.86–1.93	1.85	Reference
Radiotherapy	1.78	1.55–2.73	2.15	−0.40
Chemotherapy	2.10	2.03–2.18	2.58	4.74***
Surgery and radiation	1.86	1.08–5.70	2.23	−0.03

P values for the Z score: ***P<0.001. SIR, standardized incidence ratio; CI, confidence interval; AER, absolute excess risk.

Table 2 Risk of developing second primary thyroid cancer according to primary malignancy and identified sex

Cancer site	Male		Female	
	Mean age, years	SIR (95% CI)	Mean age, years	SIR (95% CI)
All sites	61.68	2.01 (1.94–2.08)	64.54	1.83 (1.79–1.88)
Sex-specific sites				
Prostate	69.98	1.31 (1.23–1.38)		
Testis	42.44	2.69 (2.05–3.48)		
Penis	70.45	1.14 (0.24–3.33)		
Corpus and uterus			61.43	1.73 (1.58–1.89)
Ovary			56.03	1.82 (1.55–2.12)
Vagina			59.57	3.68 (1.96–6.3)
Vulva			61.23	1.67 (1.13–2.39)
Head and neck				
Brain	42.5	3.1 (2.02–4.54)	45.43	1.82 (1.28–2.53)
Eye and orbit	62.11	4.6 (2.68–7.37)	60.05	2.56 (1.47–4.17)
Cranial nerves other nervous system	58.86	3.32 (0.9–8.5)	62.36	2.2 (0.95–4.33)
Other endocrine including thymus	51.54	10.84 (6.79–16.41)	53.68	4.33 (2.61–6.76)
Lip	63.32	1.31 (0.53–2.69)	61.26	1.28 (0.35–3.26)
Tongue	59.37	4.01 (3.11–5.09)	60.07	3.52 (2.58–4.69)
Salivary gland	55.23	4.91 (3.14–7.3)	56.87	4.07 (2.86–5.61)
Floor of mouth	61.21	4.27 (2.13–7.63)	61.68	1.75 (0.48–4.47)
Gum	64.19	4.47 (2.8–6.76)	59.62	2.2 (1.3–3.48)
Tonsil	58.87	2.61 (1.82–3.63)	58.54	0.52 (0.11–1.53)
Oropharynx	57.91	4.27 (1.72–8.79)	57.6	1.18 (0.03–6.56)
Nasopharynx	59.78	2.77 (1.19–5.45)	58.64	2.21 (0.89–4.56)
Nose, nasal cavity, and middle ear	61.82	6.34 (3.63–10.3)	61.6	2.53 (1.16–4.81)
Larynx	63.26	4.03 (3.21–4.99)	63.73	2.01 (1.21–3.13)
Bronchus and lungs	67.19	2.65 (2.28–3.06)	68.26	2.07 (1.84–2.31)
Breast	60.56	2.33 (1.12–4.29)	61.6	1.58 (1.51–1.64)
Digestive system				
Esophagus	61.16	2.25 (1.41–3.4)	60.14	2.11 (1.01–3.88)
Stomach	61.74	2.91 (2.11–3.91)	62.8	2.57 (1.93–3.37)
Small intestine	63.57	3.27 (2.08–4.91)	67	2.59 (1.78–3.64)
Colon and rectum	63.85	1.99 (1.78–2.21)	63.92	1.78 (1.63–1.94)
Liver and intrahepatic bile duct	63.27	2.56 (1.78–3.56)	63.93	2.12 (1.35–3.18)
Pancreas	59.57	4.07 (2.8–5.72)	60.71	2.28 (1.6–3.16)

Table 2 (*continued*)

Table 2 (*continued*)

Cancer site	Male		Female	
	Mean age, years	SIR (95% CI)	Mean age, years	SIR (95% CI)
Urinary system				
Urinary bladder	68.27	1.4 (1.2–1.63)	68.51	1.22 (0.97–1.53)
Kidney and renal pelvis	61.48	3.87 (3.42–4.37)	62.6	3.7 (3.3–4.13)
Ureter	70.4	2.14 (0.44–6.25)	75.69	0.69 (0.02–3.86)
Other solid tumors				
Bones and joints	45.85	5.08 (2.63–8.88)	50.65	3.07 (1.82–4.86)
Soft tissue	53.86	6.15 (4.75–7.84)	57.08	3.64 (2.86–4.58)
Skin excluding basal and squamous	58.19	2.73 (2.44–3.05)	62.19	1.89 (1.7–2.08)
Melanoma of the skin	58.09	2.73 (2.43–3.06)	61.98	1.82 (1.64–2.02)
Lymphoma				
Hodgkin lymphoma	41.41	3.61 (2.53–5)	42.36	3.01 (2.39–3.76)
Non-Hodgkin lymphoma	61.36	3.21 (2.81–3.64)	61.64	2.71 (2.43–3)
Myeloma	63.16	2.4 (1.74–3.23)	64.85	1.61 (1.18–2.14)
Leukemia				
Lymphocytic leukemia	62.23	2.13 (1.63–2.73)	61.45	1.81 (1.39–2.32)
Acute lymphocytic leukemia	32.57	5.51 (2.38–10.85)	34.85	1.32 (0.43–3.07)
Chronic lymphocytic leukemia	65.89	1.99 (1.47–2.63)	65.75	1.93 (1.45–2.5)
Myeloid and monocytic leukemia	53.92	2.25 (1.44–3.34)	60.21	1.71 (1.2–2.37)
Chronic myeloid leukemia	58.69	2.52 (1.41–4.16)	61.08	1.58 (0.9–2.56)

SIR, standardized incidence ratio (observed/expected). Mean age at event is reported.

experienced higher than expected rates of SPTC following malignancies in the brain (SIR =3.12 *vs.* 1.80), soft tissue (SIR =6.15 *vs.* 3.64), and bones and joints (SIR =5.08 *vs.* 3.07). As demonstrated in *Figure 2*, males were consistently at higher risk SPTC development than females.

Risk of SPTC by age

To further investigate the differences in SPTC risk incidence, we also grouped patients by age. Understandably, the SIR for SPTC development was highest for patients diagnosed with primary cancer under the age of 5 years (SIR =26.7 in boys and 15.2 in girls). Acute lymphocytic leukemia was the most common cancer in that age group (<5 years), presenting more commonly among boys than girls (SIR =31.6 in boys and 5.09 in girls). Interestingly, SPTC development in primary cancer survivors younger than 25 years was nearly twice as high in males (SIR =6.62) than it was in females (SIR =3.47). Soft tissue (SIR =6.25), lymphoma (SIR =6.09), bone (SIR =6.03), brain (SIR =5.84), salivary glands (SIR =5.26), and leukemia (SIR =4.1) cancers were the most common sites of primary cancer in these young (<25 years) patients. In middle-aged patients (25–44 years), primary malignancies in the pancreas (SIR =8.9), salivary glands (SIR =6.97), kidney (SIR =5.32), larynx (SIR =5.19), and soft tissue (SIR =5.10) were the most common. In general, SPTC risk declined with increasing age, though the risk of second thyroid malignancy following primary brain (SIR =16.60) and liver (SIR =8.45) malignancy peaked exclusively in females over 85 years (Table S2).

Discussion

Primary cancer survivors are at an increased risk of

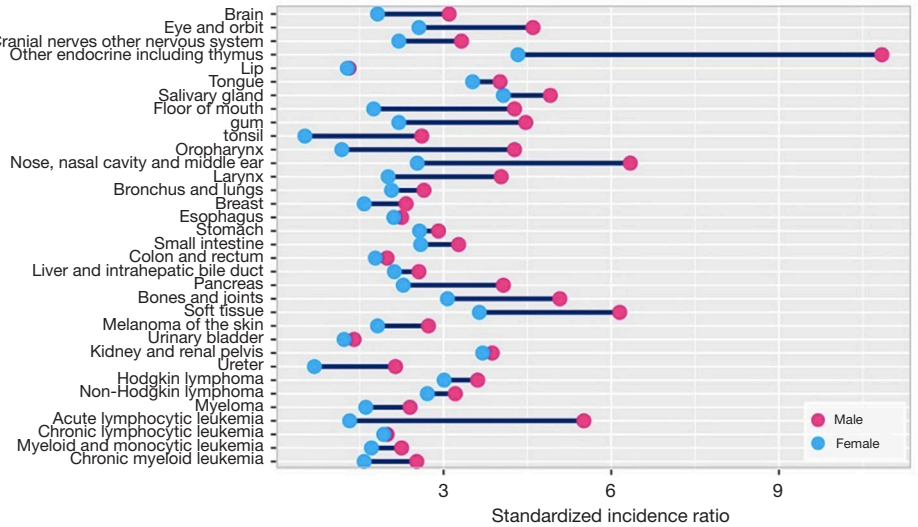

Figure 2 Standardized incidence ratios in second primary thyroid cancer according to primary malignancy location and patient sex.

developing a SPTC. Contrary to their decreased risk in primary thyroid cancers, males also have an increased risk of developing SPTC (8). To our best knowledge, this is the first work to expand on the risk of SPTC development stratified by sex with an emphasis on previous primary malignancy location and age.

Primary thyroid cancers diagnoses are almost 3 times (2.9-fold) more likely in females than they are in males (12). Though a myriad of explanations have arisen including dietary and behavioral, hormonal, and reproduction-related differences, a single leading factor has yet to be recognized (12-14). In contrast, recent literature suggests that males, as opposed to their female counterparts, are at increased risk of developing SPTC (8,15). Our study supported this notion, finding males significantly more likely to develop a SPTC irrespective of primary tumor location ($P<0.001$). In specific, some head and neck (e.g., tonsil, pharynx) as well as hematological malignancies (e.g., acute lymphoblastic leukemia) had greater than three-fold higher SIRs in males than in females. Importantly, our work found that primary malignancies which are more common in males, such as lung and colorectal cancers, had similar SPTC risks, strongly suggesting a lack of selection bias (16,17).

The role of thyroid cancer overdiagnosis, especially in females, impacts the incidence of primary thyroid malignancy. A recent 2021 meta-analysis found no difference in the presence of subclinical papillary thyroid cancer on autopsy report in male and female patients (9). Accordingly, an interplay of thyroid cancer underdiagnosis in males and overdiagnosis in females is at hand. Importantly, a SEER database analysis found that, though there was a 3-times higher incidence of thyroid cancer in females, mortality ratios were nearly identical between the two sexes (9). Accordingly, the overdiagnosis of subclinically-relevant thyroid malignancies in females appears to the stronger driver. In general, females are over-surveilled than their male counterparts. Females are reported to have higher healthcare utilization rates and comprise the majority of referrals to endocrine specialists, likely due to primary care providers attributing female unwellness/fatigue to hormonal etiology (18-20). Such issues perpetuate and exacerbate the issue of overdiagnosis with respect to thyroid cancer in the United States.

There are a multitude of factors which increase the risk of SPTC development in males. Autoimmune diseases, which are more common in females, are associated with an increased prevalence of thyroid cancer (21,22). However, since the current work investigates SPTC patients with a primary malignancy beyond the thyroid gland, this factor can now be ignored. In addition, reproductive and hormonal factors such as menopause, exogenous hormone use, and the number of pregnancies may not play such an important role in thyroid cancer (23-26). Furthermore, females are more likely to be undertreated for head and neck cancers, receiving less radiation treatment, and in consequence are at less risk for developing subsequent primary thyroid cancer (27). Finally, male sex is associated with later staged tumors and consequently males are more

likely to have their thyroid cancer detected at a later time than their female counterparts (both of which have similar incidences of subclinical cases) (28,29). As a result, late thyroid cancer diagnosis in males allows for an increased likelihood of its detection following a primary cancer diagnosis. Still, however, no robust literature elucidates the genetic and molecular mechanisms which place males at an increased risk of SPTC (30). Altogether, however, primary care providers, oncologists, and endocrinologists may look to consider the need for increased surveillance of both male and female cancer survivors given their increased risk of SPTC.

We acknowledge that our study is not without limitation. Though our work shed light on the incidence risks, data with regards to tumor aggressiveness could not be analyzed according to patient sex. The SEER database is retrospective in nature, which allowed for inherent biases in reporting. Data on healthcare utilization and referrals to relevant specialists such as oncology or endocrinology were unavailable. In addition, our work (as are all second primary cancer investigations) is liable to slightly artificially over-report the incidence of SPTC detection due to increased medical surveillance in patients being treated for primary cancers. This would theoretically inflate the incidence reports in both sexes, however. Finally, the work does not analyze for absolute risk of SPTC nor does it account for potential confounding variables such as period latency. The authors acknowledge this limitation, and encourage readers to read their previous publication which addresses latency in SPTC (31). Despite this, our study analyzed a database of over 7 million records, allowing a considerably robust analysis investigation.

Conclusions

Survivors of primary malignancies have an increased risk SPTC, especially males. Our work suggests that oncologists and endocrinologists may consider the need for increased surveillance of both male and female patients given their increased risk of SPTC.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-22-411/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-22-411/coif). EK serves as an Editor-in-Chief of *Gland Surgery* from May 2022 to April 2024. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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Supplementary

Table S1 Characteristics and treatment of SPTC patients according to the number of previous primary cancers

Characteristics	Levels	1 PC	2 PC	≥3 PC	Total
Sex	Female	8,794 (62.9)	832 (57.7)	104 (52.8)	9,730 (62.3)
	Male	5,186 (37.1)	611 (42.3)	93 (47.2)	5,890 (37.7)
Age	Mean ± SD, years	61.8±13.9	66.9±12.7	71.2±11.9	62.4±13.9
	<25 years	155 (1.1)	3 (0.2)	2 (1)	160 (1)
	<45 years	1,458 (10.4)	78 (5.4)	5 (2.5)	1,541 (9.9)
	<65 years	6,251 (44.7)	505 (35)	41 (20.8)	6,797 (43.5)
	<85 years	5,674 (40.6)	771 (53.4)	135 (68.5)	6,580 (42.1)
	85+ years	442 (3.2)	86 (6)	14 (7.1)	542 (3.5)
Race	White	11,746 (84)	1,241 (86)	170 (86.3)	13,157 (84.2)
	Black	918 (6.6)	90 (6.2)	11 (5.6)	1,422 (9.1)
	Other	1,297 (9.3)	109 (7.6)	16 (8.1)	22 (0.1)
Primary site surgery	No	1,491 (10.7)	210 (14.6)	45 (22.8)	1,746 (11.2)
	Yes	12,031 (86.1)	1,183 (82)	143 (72.6)	13,357 (85.5)
Radiotherapy	No	9,010 (64.4)	1,005 (69.6)	137 (69.5)	10,152 (65)
	Yes	4,882 (34.9)	433 (30)	59 (29.9)	5,374 (34.4)
Chemotherapy	No	13,667 (97.8)	1,420 (98.4)	193 (98)	15,280 (97.8)
	Yes	313 (2.2)	23 (1.6)	4 (2)	340 (2.2)

Data is represented as a number and percentage or mean ± SD. SPTC, second primary thyroid cancer; PC, primary cancer; SD, standard deviation.

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Table S2 Standardized incidence ratios for SPTC in males versus females across various age groups

Tumor site	<25 years		<45 years		<65 years		<85 years		85+ years	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Overall analysis	6.62	3.47	3.69	2.05	2.21	1.83	1.64	1.70	1.36	1.15
Sex-specific										
Uterus				2.45		1.68		1.57		1.13
Ovary		3.47		1.96		1.84		1.54		
Prostate					1.42		1.20		1.12	
Hematological tumors										
Lymphoma	7.64	5.75	4.20	2.66	3.16	2.69	2.88	2.56	1.89	1.88
Leukemia	6.56	3.43	2.09	1.97	2.39	1.62	1.56	1.60	1.45	1.69
Head and neck										
Brain	13.21	4.22	2.83	2.00	1.95	1.28	3.82	0.81		16.6
Salivary	33.33	2.86	10.20	6.30	4.70	3.29	3.66	3.48		
Larynx			8.20	3.23	3.71	1.60	4.26	2.47		
Breast			7.14	1.60	1.97	1.61	2.49	1.52		0.75
Lung			3.05	2.32	2.68	1.99	2.54	2.10	4.53	2.44
Other GIT										
Colon			4.18	2.35	2.36	1.94	1.43	1.53	0.94	0.70
Liver					2.85	3.00	2.27	0.77		8.45
Pancreas			11.76	8.33	4.47	1.58	2.86	1.74		2.99
Other solid tumors										
Kidney			6.49	4.82	4.23	3.94	2.94	2.86		3.49
Bladder			2.54	1.12	1.56	1.55	1.26	0.98	0.84	0.49
Bone	6.67	4.00	5.26	2.60	6.48	2.92	2.27			
Skin			2.66	2.21	2.94	1.75	2.36	1.83	3.15	0.99
Soft tissue	9.52	5.61	9.52	3.77	6.31	3.57	4.08	2.31	5.83	4.22

Values represent the SIR. Most frequent cancer types are shown. No data is available for blank cells. SPTC, second primary thyroid cancer; GIT, gastrointestinal tract; SIR, standardized incidence ratio.

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