The influence of primary thyroid cancer to the prognosis of breast cancer: A SEER-based study

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Abstract

Purpose: Previous studies have revealed a potential link between breast cancer (BC) and thyroid cancer (TC). This study aimed to estimate the clinical characteristics of BC patients who also had primary TC, and to determine the effect of the sequence of the two malignancies on survival.

Methods: We selected female patients with BC or TC in the Surveillance, Epidemiology, and End Results (SEER) database (2000 to 2012), and classified them as four cohorts, BC patients with a second TC (BC2TC cohort), TC patients with a second BC (TC2BC cohort), BC patients without TC (BC cohort) and TC patients without BC (TC cohort). Differences in clinical characteristics were analyzed using the chi-square test. The propensity score matching (PSM) method was performed to balance the baseline characteristics. The survival outcomes were analyzed using the Kaplan-Meier log-rank test. Multivariate Cox regression analyses were used to identify risk factors associated with overall survival (OS) and disease-specific survival (DSS).

Results: After PSM, 1,260 pairs of patients with or without second primary TC were included in the survival analysis. The patients in BC2TC cohort had better OS (HR: 0.511(0.421-0.620), $P<0.001$) and DSS (HR: 0.458(0.346-0.606), $P<0.001$) than those in BC cohort. The subgroup analysis showed that OS was better in the BC2TC cohort in Luminal A and Luminal B subtypes ($P<0.05$).

Conclusion: We found a second primary TC may improve the prognosis of BC patients, especially in women with Luminal breast cancer, while there was no such trend in TC patients with second BC.

Introduction

Breast cancer is the most common malignancy among women, contributing to approximately 30% of all female cancers [1]. Emerging evidence have revealed a potential link between breast cancer and thyroid cancer, which is also a common disease in women. In terms of incidence rate, evidence showed that the incidence of secondary primary thyroid cancer (SPTC) is higher in the survivors with breast cancer than general women, especially within three years of the onset of breast cancer [2-4]. At the same time, patients with thyroid cancer have an increased risk of developing breast cancer [5].

What's more, previous reports demonstrated that breast cancer patients with SPTC have lower risk of recurrence and death compared with simple breast cancer patients, [2,3]. The authors suggested that the improvement in prognosis might be attributed to TSH (Thyroid Stimulating Hormone) -suppressive therapy for thyroid cancer. However, this mechanism cannot explain the phenomenon that BC-specific survival and overall survival rates were significantly lower in women with BC as the second primary cancer than in those with breast cancer as the prior cancer [6]. Therefore, it is urgent to figure out the relationship between thyroid cancer and breast cancer.

In the current study, we collected the data of female patients with BC or TC in the SEER database (2000 to 2012 data) to explore and the potential effect of primary thyroid cancer on the prognosis of breast cancer

patients.

Materials And Methods

Data source

We collected data from the SEER Database (<http://seer.cancer.gov/seerstat>), using the SEER*Stat software program (version 8.3.8). We chose the samples from the Incidence-SEER Research Data, 18 Registries, Nov 2019 sub (2000-2017), which covers approximately 27.8% of the U.S. population. In order to ensure that the selected data had been followed at least 5 years, we selected female BC and TC patients who had active follow-up and specific death records from 2000 to 2012. The primary tumor site codes of BC patients were C50.0–C50.9, and histology codes were 8500/3, 8501/3, 8502/3, 8503/3, 8504/3, 8507/3, 8510/3, 8512/3, 8513/3, 8514/3, 8520/3, 8521/3, 8522/3, 8523/3, 8524/3, 8525/3, 8530/3, 8540/3, 8541/3 and 8543/3. All data with unknown tumor size, lymph node (LN) status, tumor grade, TNM stage, surgical history, or estrogen receptor (ER)/ progesterone receptor (PR) status were excluded (Figure 1).

Of the selected data, 345,236 had breast cancer only (BC cohort), 63,620 had thyroid cancer only (TC cohort), 606 had breast cancer after a thyroid cancer diagnosis (TC2BC cohort), and 1,269 had thyroid cancer after a breast cancer diagnosis (BC2TC cohort). The following clinicopathological characteristics were collected for BC: age, race, tumor size, regional nodes status, histopathological type, tumor grade, TNM stage, history of breast surgery, ER status, PR status, Her-2 status, breast molecular subtype and survival information.

Statistical methods

The differences in clinical characteristics were analyzed using chi-square test. The propensity score matching (PSM) method with a ratio of 1:1 was performed to balance the baseline characteristics of patients in BC cohort and BC2TC cohort. Overall survival (OS) was defined as the time from the diagnosis of BC to the time of death from any cause or loss of contact. Disease-specific survival (DSS) was defined as the time from the diagnosis of BC to the time of death caused by BC. Multivariate Cox regression analyses were performed to determine independent prognostic factors for OS and DSS. The Kaplan-Meier log-rank test was used to compare differences in OS and DSS among the cohorts or subgroups for specific characteristic. Data were analyzed using SPSS, version 26.0 (IBM Corporation, Armonk, NY, USA), and figures were created with GraphPad Prism 9.0 (GraphPad Software, Inc., CA, USA). All statistical tests were two-tailed, and $p < 0.05$ was considered significant.

Statement

All methods in this study were carried out in accordance with relevant guidelines and regulations. All clinical data were from the SEER database, which we have obtained the permission to use. We complied

with the rules for the use of SEER databases, and no privacy of patients was disclosed in this research. No ethical issue was involved.

Results

Clinicopathological characteristics among the BC, TC2BC and BC2TC cohorts

The clinicopathological features of patients in BC, TC2BC and BC2TC cohorts were shown in Table 1. Among these three cohorts, we found significant differences in age, race, lymph node (LN) status, tumor grade, TNM stage, ER status and PR status ($P<0.05$). Compared with BC cohort, patients in TC2BC cohort were older and patients in BC2TC were younger when diagnosed with BC. Regarding race, TC2BC and BC2TC cohorts had fewer black women and more from other race including Asian. More patients in BC cohort had more than 10 lymph nodes involved and advanced TNM stage accordingly. More patients in TC2BC had better well differentiated tumor and hormone receptor positive compared to patients in other cohorts.

Table 1. Clinicopathological characteristics among the BC, TC2BC and BC2TC cohorts

Characteristic	BC (n=345236)		TC2BC (n=606)		BC2TC (n=1269)		P value
	n	%	n	%	n	%	
Age diagnosed with BC							<0.001
≤40	22100	6.4	25	4.1	109	8.6	
40-60	164968	47.8	287	47.4	753	59.3	
>60	158168	45.8	294	48.5	407	32.1	
Race							0.014
White	281666	81.6	500	82.5	1038	81.8	
Black	34141	9.9	49	8.1	100	7.9	
Other	29429	8.5	57	9.4	131	10.3	
Tumor size							0.777
≤20mm	210571	61.0	374	61.7	795	62.6	
20-50mm	110122	31.9	189	31.2	384	30.3	
>50mm	24543	7.1	43	7.1	90	7.1	
Positive LN							<0.001
0	223459	64.7	386	63.7	820	64.6	
1-3	82817	24.0	160	26.4	423	33.3	
4-9	26400	7.6	40	6.6	89	7.0	
10	12560	3.6	20	3.3	36	2.8	
Histology							0.103
Duct carcinoma	278515	80.7	475	78.4	1020	80.4	
Lobular carcinoma	25048	7.3	57	9.4	85	6.7	
Mixed	38137	11.0	73	12.0	151	11.9	
Other	3536	1.0	1	0.2	13	1.0	
Tumor grade							0.012
□ (well differentiated)	68499	19.8	125	20.6	235	18.5	
□ (moderately differentiated)	148149	42.9	296	48.8	551	43.4	
□ (poorly differentiated)	125030	36.2	180	29.7	464	36.6	
□ (undifferentiated)	3558	1.0	5	0.8	19	1.5	
TNM stage							0.028
0	61	0.0	0	0.0	2	0.2	
□	164212	47.6	292	48.2	606	47.8	
□	133354	38.6	236	38.9	499	39.3	
□	43154	12.5	70	11.6	152	12.0	
□	4455	1.3	8	1.3	10	0.8	
ER							0.013
Positive	273760	79.3	512	84.5	1023	80.6	
Negative	70916	20.5	93	15.3	244	19.2	
Borderline	560	0.2	1	0.2	2	0.2	
PR							0.006
Positive	235316	68.2	445	73.4	900	70.9	
Negative	108150	31.3	158	26.1	360	28.4	
Borderline	1770	0.5	3	0.5	9	0.7	
HER-2							0.257
Positive	13991	4.1	51	8.4	52	4.1	
Negative	79810	23.1	244	40.3	223	17.6	
Borderline*	2000	0.6	8	1.3	5	0.4	
Unknow	249435	72.3	303	50.0	989	77.9	
Subtype							0.096
HR+/HER2- (Luminal A)	68791	19.9	215	35.5	192	15.1	
HR+/HER2+ (Luminal B)	9834	2.8	41	6.8	32	2.5	
HR-/HER2+ (HER2	4157	1.2	10	1.7	20	1.6	

enriched)						
HR-/HER2- (Triple Negative)	11019	3.2	29	4.8	31	2.4
Unknow	251435	72.8	311	51.3	994	78.3
History of breast surgery						0.097
Yes	343656	99.5	604	99.7	1268	99.9
No	1580	0.5	2	0.3	1	0.1

*The algorithm used to derive HER-2 information is detailed in the following link (<https://seer.cancer.gov/seerstat/databases/ssf/her2-derived.html>).

Abbreviation: BC, breast cancer; TC, thyroid cancer; LN, lymph node; HER2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor.

Impact of clinicopathological characteristics on survival

Multivariate Cox regression analyses were performed to determine independent prognostic factors for OS and DSS of breast cancer (Table 2). We found that the patients in BC2TC cohort had better OS (HR: 0.483 (0.412-0.567), $P<0.001$) and DSS (HR: 0.390 (0.307-0.495), $P<0.001$) than those in BC cohort.

Furthermore, it is also demonstrated that all these clinicopathological characteristics, including age, race, tumor size, LN status, tumor grade, histologic type, TNM stage, surgical treatment for breast cancer, ER/PR status, Her-2 status and breast cancer molecular subtype, were significantly associated with OS and DSS($P<0.05$).

Table 2. Multivariate Cox regression analyses on OS and DSS of breast cancer

Characteristic	OS (overall survival)		DSS (disease-specific survival)	
	HR (95%CI)	P value	HR (95%CI)	P value
Cohort		<0.001		<0.001
BC	Reference		Reference	
TC2BC	1.087 (0.909-1.300)	0.361	1.125 (0.878-1.440)	0.352
BC2TC	0.483 (0.412-0.567)	<0.001	0.390 (0.307-0.495)	<0.001
Age at diagnosis		<0.001		<0.001
≤40	Reference		Reference	
40-60	0.876 (0.849-0.905)	<0.001	0.861 (0.832-0.890)	<0.001
>60	2.812 (2.726-2.900)	<0.001	1.323 (1.279-1.369)	<0.001
Race		<0.001		<0.001
White	Reference		Reference	
Black	1.301 (1.275-1.329)	<0.001	1.319 (1.284-1.354)	<0.001
Other	0.732 (0.711-0.754)	<0.001	0.828 (0.797-0.859)	<0.001
Tumor size		<0.001		<0.001
≤20mm	Reference		Reference	
20-50mm	1.582 (1.548-1.617)	<0.001	1.703 (1.655-1.752)	<0.001
>50mm	1.884 (1.827-1.942)	<0.001	2.227 (2.145-2.312)	<0.001
Positive LN		<0.001		<0.001
0	Reference		Reference	
1-3	1.428 (1.396-1.460)	<0.001	1.817 (1.764-1.872)	<0.001
4-9	2.051 (1.993-2.111)	<0.001	3.034 (2.925-3.147)	<0.001
10	3.071 (2.975-3.171)	<0.001	4.777 (4.594-4.967)	<0.001
Tumor grade		<0.001		<0.001
I	Reference		Reference	
II	1.164 (1.139-1.189)	<0.001	1.808 (1.733-1.887)	<0.001
III	1.372 (1.340-1.404)	<0.001	2.534 (2.425-2.647)	<0.001
IV	1.365 (1.283-1.451)	<0.001	2.543 (2.339-2.764)	<0.001
Histologic type		<0.001		<0.001
Duct carcinoma	Reference		Reference	
Lobular carcinoma	0.957 (0.932-0.982)	<0.001	1.029 (0.990-1.070)	0.141
Mixed	0.951 (0.930-0.972)	<0.001	0.973 (0.942-1.005)	0.092
Other	0.903 (0.850-0.960)	0.001	0.849 (0.787-0.916)	<0.001
TNM stage		<0.001		<0.001
0	Reference		Reference	
I	1.526 (0.762-3.057)	0.233	1.768 (0.441-7.083)	0.421
II	1.524 (0.760-3.055)	0.235	2.584 (0.645-10.351)	0.180
III	1.898 (0.947-3.806)	0.071	3.145 (0.785-12.605)	0.106

	6.031 (3.006-12.100)	<0.001	11.878 (2.963-47.622)	<0.001
History of breast surgery (Yes vs. No)	0.562 (0.522-0.606)	<0.001	0.481 (0.442-0.523)	<0.001
ER Status (Negative vs. Positive)	1.101 (1.076-1.127)	<0.001	1.228 (1.191-1.266)	<0.001
PR Status (Negative vs. Positive)	1.201 (1.179-1.225)	<0.001	1.382 (1.345-1.420)	<0.001
HER2 (Negative vs. Positive)	0.894 (0.799-1.000)	0.050	0.858 (0.738-0.999)	0.048
Breast cancer molecular subtype		<0.001		<0.001
HR+/HER2- (Luminal A)	Reference		Reference	
HR+/HER2+ (Luminal B)	0.899 (0.845-0.957)	0.001	0.804 (0.742-0.870)	<0.001
HR-/HER2+ (HER2 enriched)	0.953 (0.881-1.031)	0.230	0.800 (0.729-0.879)	<0.001
HR-/HER2- (Triple Negative)	1.690 (1.613-1.771)	<0.001	1.676 (1.584-1.774)	<0.001

Abbreviation: OS, overall survival; DSS, disease-specific survival; BC, breast cancer; TC, thyroid cancer; LN, lymph node; HER2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor.

Survival analysis of BC patients among three cohorts

The KM curves for OS and DSS among the BC, TC, TC2BC and BC2TC cohorts were shown in Figure 2. The 10-year OS rate of patients in TC cohort was 93%, compared to 89%, 73%, and 74%, respectively, for patients in BC2TC, TC2BC and BC cohorts ($P<0.001$). OS was much better in the BC2TC cohort than in the BC cohort (Figure 2A). OS showed no statistical difference between the TC2BC cohort and BC cohort (Figure 2A), and a similar trend was observed in terms of DSS (Figure 2B).

In order to validate the prognostic effect of thyroid cancer, a 1:1 PSM was performed to balance the baseline characteristics of patients in BC cohort and BC2TC cohort. After matching, 1,260 pairs of patients were selected for the analysis (Table 3), and the survival curves of data after PSM were presented in Figure 3. The 10-year OS rate were 89% vs. 78%, respectively. (HR: 0.511(0.421-0.620), $P<0.001$, Figure 3A). The 10-year DSS rate were 94% vs. 88%, respectively. (HR: 0.458(0.346-0.606), $P<0.001$, Figure 3B).

Table 3. Clinical characteristics of patients in BC group and BC2TC group before and after PSM

Characteristic	before PSM		P value	after PSM		P value
	BC (n=345236)	BC2TC (n=1269)		BC (n=1260)	BC2TC (n=1260)	
Age			<0.001			0.999
≤40	22100	109		108	108	
40-60	164968	753		746	747	
>60	158168	407		406	405	
Race			0.007			0.997
White	281666	1038		1037	1036	
Black	34141	100		100	100	
Other	29429	131		123	124	
Tumor size			0.442			0.963
≤20mm	210571	795		795	790	
20-50mm	110122	384		381	383	
>50mm	24543	90		84	87	
Positive lymph node			<0.001			0.976
0	223459	820		816	816	
1-3	82817	423		328	322	
4-9	26400	89		82	86	
10	12560	36		34	36	
Histology			0.708			0.976
Duct carcinoma	278515	1020		1014	1012	
Lobular carcinoma	25048	85		86	84	
Mixed	38137	151		149	151	
Other	3536	13		11	13	
Grade			0.272			0.838
I	68499	235		237	235	
II	148149	551		547	549	
III	125030	464		463	458	
IV	3558	19		13	18	
TNM stage			0.002			0.855
0	61	2		0	1	
I	164212	606		606	603	
II	133354	499		499	497	
III	43154	152		144	150	
IV	4455	10		11	9	
ER			0.511			0.954
Positive	273760	1023		1023	1017	
Negative	70916	244		236	242	
Borderline	560	2		1	1	
PR			0.052			0.965
Positive	235316	900		899	896	
Negative	108150	360		353	355	
Borderline	1770	9		8	9	
HER-2			0.167			0.972
Positive	13991	52		50	51	
Negative	79810	223		225	222	
Borderline	2000	5		2	3	
Unknow	249435	989		983	984	
Subtype			0.119			0.986
HR+/HER2- (Luminal A)	68791	192		194	191	
HR+/HER2+ (Luminal B)	9834	32		34	32	

HR-/HER2+ (HER2 enriched)	4157	20	16	19
HR-/HER2- (Triple Negative)	11019	31	31	31
Unknown	251435	994	985	987
History of breast surgery	0.045			
Yes	343656	1268	1260	1260
No	1580	1	0	0

Abbreviation: PSM, propensity score matching; BC, breast cancer; TC, thyroid cancer; LN, lymph node; HER2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor.

Subgroup survival analysis of BC patients in BC2TC group and BC group

To explore the effect by tumor characteristics, we performed subgroup analysis for the OS and DSS in patients between BC and BC2TC cohorts based on all the clinicopathological characteristics (Figure 4, S1 and S2). Patients in BC2TC cohort had longer OS than those in BC cohort in all subgroups except for the Her2-positive subgroup (Figure 4A). DSS was better in BC2TC group except for the other race, Her2-positive and Her2-negative subgroup (Figure 4B).

Interestingly, in the subgroup analysis for BC subtypes (Figure 5), luminal BC patients with SPTC may yield longer survival than luminal BC patients (Figure 5A and 5B), but no such trend was found in Her-2 enriched or triple negative breast cancer patients (Figure 5C and 5D).

Discussion

Over the last 40 years, many studies have revealed that there is a bidirectional causative relationship between BC and TC [5]. Our results were consistent with previous studies, indicating that SPTC can improve the prognosis of BC patients [2,6,3]. We demonstrated that most of the clinicopathological characteristics in patients in BC2TC cohort were matched with those in BC cohort before PSM. In general, patients in the BC2TC cohort were younger at the time of diagnosis, had fewer positive LNs, and had earlier AJCC TNM staging.

Lei et al. found the phenomenon that SPTC improved prognosis of BC patients was not significant in the SEER data from 1980 to 1994, suggesting this improvement in prognosis may be related to TSH inhibition therapy with exogenous levothyroxine after 2000 [2]. Additionally, the application of levothyroxine has been shown to be associated with a significant reduction in the risk of colorectal cancer [7]. Before 2000, it has been proposed that thyroid extract can be used for the treatment of BC [8], and the administration of thyroid hormone therapy could prevent the occurrence of BC [9]. However, in recent years, the effect of thyroid hormone on breast cancer was controversial. Some studies revealed that patients with hyperthyroidism had an increased risk of BC [10-13], and primary hypothyroidism is associated with a reduced incidence of BC [14,11,13]. However, other studies found that thyroid function status cannot predict the incidence of BC [15,16]. There are two main forms of thyroid hormones in the

human body, 3,5,3',5' -tetraiodothyronine or thyroxine (T4) and 3,5,3' -triiodothyronine (T3) [17]. In a clinical trial targeting advanced tumors, endogenous T4 was found to promote the development of cancers, and exogenous T3 inhibited T4, prolonging the survival time of patients with advanced cancers, including BC [18,19], which suggested that the use of exogenous thyroid hormone has a potential positive effect on the suppression of BC.

As shown in our results, the improvement of SPTC on OS of BC patients was more obvious in luminal breast cancer. Evidence showed that SPTC could also improve the prognosis of ovarian cancer [20]. Ovarian cancer and luminal BC are both estrogen-dependent cancers, so we speculated that SPTC may improve the prognosis by targeting estrogen. Although no study directly revealed the interaction between thyroid hormone and estrogen in vivo, it can be inferred from various studies that there was an antagonistic relationship between thyroid hormone and estrogen. For example, it was found that patients under the age of 65 years on L-thyroxine had an increased risk of ischaemic heart disease [21]. Besides, the patients and the mice with postpartum depression showed elevated serum levels of T3, T4 along with diminished estradiol (E2) and progesterone (P) and TSH levels. The administration of E2 and P decreased thyroid hormone [22]. A study in goldfish proved that T3 acts to diminish estrogen signaling by decreasing estrogen synthesis from androgens and decreasing sensitivity to estrogen by down-regulating the ER subtypes [23]. However, both positive and negative relationship between thyroid hormone and estrogen can be observed in different species [24]. In experiments of human tumor cell lines, T3 and T4 have been demonstrated to have different inhibitory effects on various breast and ovarian cancer cell lines [25]. T-47D cells represent estrogen-sensitive human ductal cancer cell lines, which can be promoted by a low concentration of T3 and inhibited by a high concentration of T3. T4 has a significant inhibitory effect on the proliferation of T-47D and OVCAR-3 cells [25]. Another study expressed that both E2 and T3 promoted the proliferation of MCF-7 and T47-D cells in a dose-dependent manner, and T3 can enhance the effect of E2 on the proliferation of T47-D cells [26]. A.H. et al suggested that endogenous T4 is beneficial to the ER positive cancer cells, but Tamoxifen and Fulvestrant could weaken the support of T4 for ER-positive cancer cells [18]. Tamoxifen and Fulvestrant are both standard agents for the Luminal BC patients, and this might be the reason why the influence of thyroid hormones on BC prognosis is more significant in luminal BC patients.

Studies have confirmed high level of TSH can promote the progression of thyroid cancer [27], which is one of the reasons for TSH suppressive therapy after TC surgery. However, there is no direct evidence that TSH level is related to the prognosis of BC. TSH is a member of the glycoprotein hormone family that includes luteinizing hormone (LH), follicle stimulating hormone (FSH), and human chorionic gonadotropin (hCG), and the α -subunit of hCG displays homologies with TSH, LH, and FSH [28]. Therefore, we hypothesized that TSH might harbor similar effects to gonadotropins and influence the prognosis of BC patients by affecting estrogen.

According to our results, the patients in the TC2BC cohort expressed higher level of ER/PR than those in the other two cohorts. Previous studies have also revealed a lower incidence of hormone receptor negative tumors in patients with primary hypothyroidism [14], which is consistent with our results. It was

notable that there was no difference in prognosis between the TC2BC cohort and the BC cohort, even though the TC2BC cohort had higher ER/PR expression. This suggested that thyroid hormone level before the onset of BC cannot affect the BC prognosis, which is consistent with the conclusion of a long-term observational study that found no evidence of the prognostic role of thyroid function in moderate-to-high-risk early BC [29]. In addition, BC-specific survival and OS rates were significantly lower in women with BC as the second primary cancer than in those with BC as the prior cancer, especially among hormone receptor-positive women [6]. The patients who underwent chemotherapy for prior cancer may not respond well to systemic treatment for their second primary cancer due to decreased efficacy and tolerability after prior systemic treatment. However, the chemotherapy is rarely used in the treatment of TC, so we speculated that what will affect the prognosis of BC is the change of the level of TSH and thyroid hormones after the development of BC, rather than the original level of TSH and thyroid hormones. Or it may be that the BC occurring after the TSH suppressive therapy has unknown different characteristics from the naturally occurring BC, which lead the prognosis of BC no longer dependent on the level of thyroid hormone, but all these hypotheses need to be verified in later experiments.

Our study has some limitations. First, as a retrospective study, it has selection bias. We decreased bias through performing PSM, but residual confounding factors cannot be entirely ruled out. Second, we cannot get the information of exogenous thyroid hormone treatment from the SEER database, so we assumed that TSH inhibition therapy was used in all TC patients, which might be different from the real world. Third, in order to ensure a 5-year follow-up for patients, we selected BC patients before 2012. Therefore, the sample size in the subgroup analysis might not big enough, which may cause no statistical difference of DSS between the BC2TC cohort and the BC cohort in Luminal BC patients.

Conclusions

In conclusion, a second primary thyroid cancer may improve the prognosis of patients with breast cancer, especially in women with luminal breast cancer. We speculate that endocrine therapy combined with TSH inhibition treatment may act as a potential protective mechanism to improve the prognosis of patients with luminal breast cancer followed by a second thyroid cancer.

Declarations

Author contributions

In this study, Chen and Li were responsible for writing the article, Wu was responsible for data analysis and calculation, Liu was responsible for checking the grammars and calculations, and Yuan and Sun were responsible for proposing ideas and guiding research progress.

Conflicts of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest. The manuscript was not under consideration for publication elsewhere, in whole or in part.

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Figures

Figure 1

Flowchart for selection of patients Abbreviation: BC, breast cancer; TC, thyroid cancer; LN, lymph node; ER, estrogen receptor; PR, progesterone receptor.

Figure 2

Comparison of overall survival (OS) and disease-specific survival (DSS) among breast cancer (BC), thyroid cancer (TC), breast cancer after a thyroid cancer diagnosis (TC2BC) and thyroid cancer after a breast cancer diagnosis (BC2TC). Abbreviation: BC, breast cancer; TC, thyroid cancer;

Figure 3

Comparison of OS and DSS between BC and BC2TC groups before and after propensity score matching (PSM). Abbreviation: BC, breast cancer; TC, thyroid cancer.

Figure 4

The forest plot of subgroup survival analysis of patients in the BC2TC and BC groups (BC2TC vs BC). Abbreviation: BC, breast cancer; TC, thyroid cancer; HER2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor.

Figure 5

The OS of patients between BC2TC and BC groups in the subgroup survival analysis for breast cancer subtypes. Abbreviation: BC, breast cancer; TC, thyroid cancer.

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