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Original Article

Comparison of characteristics in patients with both thyroid and breast cancer: Based on order of incidence

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Purpose: Clinicopathologic characteristics of patients with both thyroid and breast cancer during their lifetime were analyzed to investigate the association between the two malignancies according to the order of incidence.

Methods: A total of 405 patients who underwent surgery for breast and thyroid cancer at Severance Hospital between 1995 and 2014 were retrospectively selected and classified into 3 groups according to the order of incidence of the two cancers: simultaneous cancer (S), thyroid cancer followed by breast cancer (TB), and breast cancer followed by thyroid cancer (BT). Univariate analysis was conducted to compare parameters.

Results: S, TB, and BT groups were 166 (41.0%), 96 (23.7%), and 143 (35.3%) patients, respectively. In TB and BT groups, tumor size and surgical site for secondary cancer were smaller; therefore, adjuvant treatments were less frequently required for secondary cancer. ER positive rate was 77.1% in S, 75% in TB, and 63.7% in BT groups (P=0.027). The ratio of ER negative was higher in the group with BRAF mutation. Survival rate for index tumor was higher in order from TB, and BT, followed by S groups without statistical difference.

Conclusion: It is difficult to find a significant difference according to the order of occurrence except by screening test, and more studies are needed in the future. Establishing an appropriate screening program is important in order to detect secondary breast or thyroid cancer after surgery for thyroid or breast cancer.

Keywords: Breast neoplasms, Thyroid neoplasms, Second primary neoplasms, Survival rate

INTRODUCTION

Breast and thyroid cancer occur at high rates among women. In 2014, 24,632 and 18,304 Korean women developed thyroid and breast cancer, respectively, and the incidence of thyroid and breast cancer were 97 and 72.1 cases per 100,000 persons, or the highest and the second highest incidence of cancer in Korea, respectively [1].

The association between breast and thyroid cancer has been debated for some time. Since Chalstrey and Benjamin [2] reported a high incidence of breast cancer as a secondary cancer among patients treated for thyroid cancer, additional studies have reported a relatively high incidence of secondary breast cancer compared to other secondary cancers, as well as an association between thyroid cancer and breast cancer [2,3]. Studies have also reported a high incidence of secondary thyroid cancer among patients treated for breast cancer [4-6]. Factors that have been suggested to contribute to this association include genetic factors shared between the two cancer types [5,7,8], environmental factors [9], hormonal influences [2,10-13], the influence of thyroid disorders (autoimmune disease) on the incidence of breast cancer [14], the effect of radioactive iodine therapy following thyroid cancer surgery on the etiology of breast cancer [15,16], and the effect of radiation therapy after

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breast cancer surgery on the etiology of thyroid cancer [5,17,18].

However, a study has recently reported that radioactive iodine therapy after thyroid cancer surgery does not influence the incidence of breast cancer [19], while another reported that based on the differences in the incidence of thyroid and breast cancer as secondary cancers, the physiological characteristics of each type of cancer and treatment-related factors contribute to the incidence of secondary cancers more significantly than the mutual risk factors for thyroid and breast cancer, including genetic factors [20]. Therefore, the association between thyroid and breast cancer, as well as their characteristics, are still not clear [21,22].

It is important to invesigate the correlation between the types of cancer and their characteristics. The present study aimed to investigate the clinical and pathological characteristics of breast and thyroid cancer in patients who developed both types of cancer, and compare differences in the characteristics, outcomes, and causes of the two cancer types between two patient groups that differed by the order in which they developed each cancer.

METHODS

In the present study, the medical records of patients who were diagnosed with thyroid and breast cancer as primary cancers and underwent both thyroidectomy and breast surgery at the Department of Surgery of the Severance Hospital of Yonsei University College of Medicine were retrospectively analyzed. Patients who were diagnosed with distant metastasis or bilateral breast cancer, or who received treatment in a different hospital, were excluded.

The number of surgeries performed for breast cancer at the Department of Surgery of the Severance Hospital in the last 20 years was approximately 10,000, and that for thyroid cancer was around 23,000. Among all patients treated, 405 patients were included in this study. The patients' age, sex, pathological type of thyroid and breast cancer, cancer stage, surgery type and site, and postoperative adjuvant therapy were investigated. In addition, histological grade, estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) status were investigated in association with breast cancer. Extracapsular extension, multifocality, the *BRAF* V600E mutation, and histological thyroiditis were investigated in association with thyroid cancer.

The patients were assigned to three different groups depending on the order of surgery they underwent for each cancer: the TB group for patients who underwent thyroidectomy then mastectomy, the S group for patients who underwent thyroidectomy and mastectomy at the same time, and the BT group for patients who underwent mastectomy followed by thyroidectomy. Characteristics of breast and thyroid cancer were compared among the three groups. Patients whose surgeries for both cancers were timed less than 6 months apart from each other were included in the S group, and the remaining patients were placed in the TB or BT group.

SPSS ver. 23.0 (IBM Inc., Armonk, NY, USA) was used for statistical analysis. A chi-square test was used to analyze the nominal variables in each group, and a one-way ANOVA or independent t-test was used to analyze the continuous variables. For multivariate analysis, the Bonferroni method was used. The Kaplan-Meier method was used for the survival analysis, and the log-rank test was used to compare variables. The nominal variables were expressed as proportions, and the continuous variables were expressed as mean and standard deviation. The level of statistical significance was set at $P < 0.05$.

The present study was approved by the Institutional Review Board of the Severance Hospital (IRB no., 4-2016-1018).

RESULTS

The mean age of the patients at the time of being diagnosed with breast cancer was 50.9 ± 9.5 years, and ductal carcinomas were the most common pathological type of breast cancer, accounting for 363 cases (89.6%). T1 and N0 were the most common stages of breast cancer accounting for 237 cases (58.5%) and 286 cases (70.6%), respectively. In the TNM classification, stage 1 was the most common, accounting for 177 cases (43.7%). In regards to histological grades, 97 patients had grade I (24.0%), 168 (41.5%) had grade II, and 61 (15.1%) had grade III breast cancer. By receptor status, 70.6%, 55.3%, and 18.8% of all patients were ER, PR, and HER2 positive, respectively, and 70.4% of all patients underwent antihormonal therapy. Around half (45.7%) of all patients underwent breast-conserving surgery, and 56.5% underwent radiation therapy after surgery (Table 1).

The mean age of the patients at the time of being diagnosed with thyroid cancer was 51.4 ± 9.7 years, and 201 patients (49.6%) were found to have other accompanying diseases such as thyroiditis on histological examination performed after thyroidectomy. Papillary carcinoma was the most common histological type, accounting for 399 cases (98.5%), and TNM stage 1 was the most common stage, accounting for 233 cases (55.1%). There were 204 cases of extracapsular extension (50.4%). Of the total 405 patents, 61 patients were tested for the BRAF V600E mutation in their thyroid cancer, and of these, 45 (73.8%) had the BRAF V600E mutation. A total of 161 patients (39.7%) underwent radioactive iodine therapy after thyroidectomy (Table 2).

The patients were divided into three groups according to the order of surgeries they underwent after being diagnosed with breast and thyroid cancer to analyze the characteristics of both cancer

Table 1. Clinicopathologic characteristics of primary breast cancer

Characteristic	Total patients (n = 405)
Age (yr)	50.9 ± 9.5
Histologic type	
Ductal	363 (89.6)
Lobular	11 (2.7)
Others	31 (7.7)
T stage	
Tis	60 (14.8)
T1	237 (58.5)
T2	100 (24.7)
T3	8 (2)
N stage	
N0	286 (70.6)
N1	89 (22)
N2	20 (4.9)
N3	10 (2.5)
TNM stage	
Stage 0	56 (13.8)
Stage 1	176 (43.5)
Stage 2	142 (35.1)
Stage 3	31 (7.7)
Histologic grade	
I/II	265 (65.4)
III	61 (15.1)
Unknown	79 (19.5)
ER	
Negative	111 (27.4)
Positive	286 (70.6)
Unknown	8 (2)
PR	
Negative	173 (42.7)
Positive	224 (55.3)
Unknown	8 (2)
HER2	
Negative	273 (67.4)
Positive	76 (18.8)
Equivocal	29 (7.2)
Unknown	27 (6.7)
Extent of surgery	
BCS	185 (45.7)
TM	220 (54.3)
Neo-adjuvant chemotherapy	
Not done	360 (88.9)
Done	45 (11.1)
Adjuvant chemotherapy	
Not done	177 (43.7)
Done	228 (56.3)
Radiation therapy	
Not done	176 (43.5)
Done	229 (56.5)
Hormone therapy	
Not done	114 (28.1)
Done	285 (70.4)
Unknown	6 (1.5)

Values are presented as mean±standard deviation or number (%).
is, *in situ*; TNM, tumor node metastasis; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; BCS, breast conserving surgery; TM, total mastectomy.

Table 2. Clinicopathologic characteristics of primary thyroid cancer

Characteristic	Total patients (n = 405)
Age (yr)	51.4 ± 9.7
Histologic type	
Papillary	399 (98.5)
Follicular	4 (1)
Others	2 (0.5)
T stage	
T1	196 (48.4)
T2	5 (1.2)
T3	196 (48.4)
T4	8 (2)
N stage	
N0	310 (76.5)
N1a	78 (19.3)
N1b	17 (4.2)
TNM stage	
Stage 1	223 (55.1)
Stage 2	4 (1)
Stage 3	159 (39.3)
Stage 4	19 (4.7)
Capsular invasion	
Intrathyroidal	201 (49.6)
Extrathyroidal	204 (50.4)
Multifocality	
Single lesion	282 (69.6)
Multiple lesions	123 (30.4)
Tumor location[a]	
Ipsilateral	140 (68)
Bilateral	66 (32)
Operation method	
Conventional	381 (94.1)
Minimally invasive	24 (5.9)
Extent of surgery	
Less than bilateral total	199 (49.1)
Bilateral total	206 (50.9)
Postoperative RAI therapy	
None	244 (60.2)
Low dose	139 (34.3)
High dose	22 (5.4)
Thyroiditis	
Absent	309 (76.3)
Present	96 (23.7)
BRAF V600E mutation	
No mutation	16 (4)
Mutation	45 (11.1)
Unknown	344 (84.9)

Values are presented as mean±standard deviation or number (%).
TNM, tumor node metastasis; minimally invasive, endoscopic or robotic thyroidectomy; RAI, radioactive iodine; BRAF, B-type Raf kinase.
[a]Patients undergoing bilateral total thyroidectomy. n = 206.

Table 3. Clinicopathologic characteristics of primary breast cancer based on order of incidence

Characteristic	TB (n = 96)	S (n = 166)	BT (n = 143)	P-value
Age (yr)	52.7 ± 10.1	50.8 ± 9.1	49.8 ± 9.2	0.073
Histologic type of breast cancer				0.054
Ductal	82 (85.4)	145 (87.3)	136 (95.1)	
Lobular	4 (4.2)	7 (4.2)	0	
Others	10 (10.4)	14 (8.4)	7 (4.9)	
T stage				0.001
Tis–1	81 (84.4)	126 (75.9)	90 (62.9)	
T2–4	15 (15.6)	40 (24.1)	53 (37.1)	
N stage				0.002
N0	80 (83.3)	117 (70.5)	89 (62.2)	
N1–3	16 (16.7)	49 (29.5)	54 (37.8)	
TNM				< 0.001
Stage 0–1	70 (72.9)	98 (59)	64 (44.8)	
Stage 2–4	26 (27.1)	68 (41)	79 (55.2)	
Histologic grade				0.787
I/II	55 (80.9)	111 (79.9)	99 (83.2)	
III	13 (19.1)	28 (20.1)	20 (16.8)	
ER				0.027
Negative	24 (25)	38 (22.9)	49 (36.3)	
Positive	72 (75)	128 (77.1)	86 (63.7)	
PR				0.555
Negative	38 (39.6)	77 (46.4)	58 (43)	
Positive	58 (60.4)	89 (53.6)	77 (57)	
HER2				0.306
Negative	74 (77.1)	122 (74.4)	77 (65.3)	
Positive	17 (17.7)	29 (17.7)	30 (25.4)	
Equivocal	5 (5.2)	13 (7.9)	11 (9.3)	
Subtype				0.199
ER+, HER2–	63 (65.6)	113 (68.9)	62 (52.5)	
ER+, HER2+	9 (9.4)	14 (8.5)	15 (12.7)	
ER–, HER2+	8 (8.3)	15 (9.1)	15 (12.7)	
ER–, HER2–	16 (16.7)	22 (13.4)	26 (22)	
Extent of surgery				< 0.001
BCS	59 (61.5)	82 (49.4)	44 (30.8)	
TM	37 (38.5)	84 (50.6)	99 (69.2)	
Neo-adjuvant chemotherapy				0.023
Not done	89 (92.7)	139 (83.7)	132 (92.3)	
Done	7 (7.3)	27 (16.3)	11 (7.7)	
Adjuvant chemotherapy				< 0.001
Not done	61 (63.5)	72 (43.4)	44 (30.8)	
Done	35 (36.5)	94 (56.6)	99 (69.2)	
Radiation therapy				< 0.001
Not done	33 (34.4)	59 (35.5)	84 (58.7)	
Done	63 (65.6)	107 (64.5)	59 (41.3)	
Hormone therapy (n = 399)				0.074
Not done	22 (23.2)	43 (25.9)	49 (35.5)	
Done	73 (76.8)	123 (74.1)	89 (64.5)	

Values are presented as mean ± standard deviation or number (%).

TB, thyroid cancer followed by breast cancer; S, simultaneous cancer; BT, breast cancer followed by thyroid cancer; is, *in situ*; TNM, tumor node metastasis; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; BCS, breast conserving surgery; TM, total mastectomy.

Table 4. Clinicopathologic characteristics of primary thyroid cancer based on order of incidence

Characteristic	TB (n = 96)	S (n = 166)	BT (n = 143)	P-value
Age (yr)	48.6 ± 10.5	51.3 ± 9.2	53.4 ± 9.3	0.001
Histologic type				0.351
Papillary	94 (97.9)	163 (98.2)	142 (99.3)	
Follicular	2 (2.1)	1 (0.6)	1 (0.7)	
Others	0	2 (1.2)	0	
Tumor size				0.004
≤ 1 cm	60 (62.5)	119 (71.7)	117 (81.8)	
> 1 cm	36 (37.5)	47 (28.3)	26 (18.2)	
T stage				0.494
T1–2	43 (44.8)	87 (52.4)	71 (49.7)	
T3–4	53 (55.2)	79 (47.6)	72 (50.3)	
N stage				0.611
N0	70 (72.9)	128 (77.1)	112 (78.3)	
N1	26 (27.1)	38 (22.9)	31 (21.7)	
TNM stage				0.322
Stage 1-2	57 (59.4)	97 (58.4)	73 (51)	
Stage 3-4	39 (40.6)	69 (41.6)	70 (49)	
Capsular invasion				0.291
Intrathyroidal	41 (42.7)	87 (52.4)	73 (51)	
Extrathyroidal	55 (57.3)	79 (47.6)	70 (49)	
Multifocality				0.825
Single lesion	67 (69.8)	118 (71.1)	97 (67.8)	
Multiple lesions	29 (30.2)	48 (28.9)	46 (32.2)	
Tumor location				0.44
Ipsilateral	75 (78.1)	139 (83.7)	120 (83.9)	
Bilateral	21 (21.9)	27 (16.3)	23 (16.1)	
Operation method				0.02
Conventional	85 (88.5)	161 (97)	135 (94.4)	
Minimally invasive	11 (11.5)	5 (3)	8 (5.6)	
Extent of surgery				0.001
Less than bilateral total	36 (37.5)	75 (45.2)	88 (61.5)	
Bilateral total	60 (62.5)	91 (54.8)	55 (38.5)	
Postoperative RAI therapy				0.003
None	43 (44.8)	102 (61.4)	99 (69.2)	
Low (30 mCi)	48 (50)	54 (32.5)	37 (25.9)	
High	5 (5.2)	10 (6)	7 (4.9)	
Thyroiditis				0.805
Absent	71 (74)	127 (76.5)	111 (77.6)	
Present	25 (26)	39 (23.5)	32 (22.4)	
BRAF V600E mutation (n = 61)				0.649
No mutation	5 (35.7)	4 (22.2)	7 (24.1)	
Mutation	9 (64.3)	14 (77.8)	22 (75.9)	

Values are presented as mean ± standard deviation or number (%).
TB, thyroid cancer followed by breast cancer; S, simultaneous cancer; BT, breast cancer followed by thyroid cancer; TNM, tumor node metastasis; RAI, radioactive iodine; BRAF, B-type Raf kinase.

types.

In regards to the characteristics of breast cancer, the breast tumors were significantly smaller, the extent of lymphatic invasion was significantly less, and the TNM was significantly lower in the TB group. Breast-conserving surgery was the most common type of surgery performed in the TB group, and the rate of postoperative radiation therapy was also significantly higher. A small proportion of patients in the TB group underwent postoperative chemotherapy. The rate of preoperative chemotherapy was higher in the S group (Table 3).

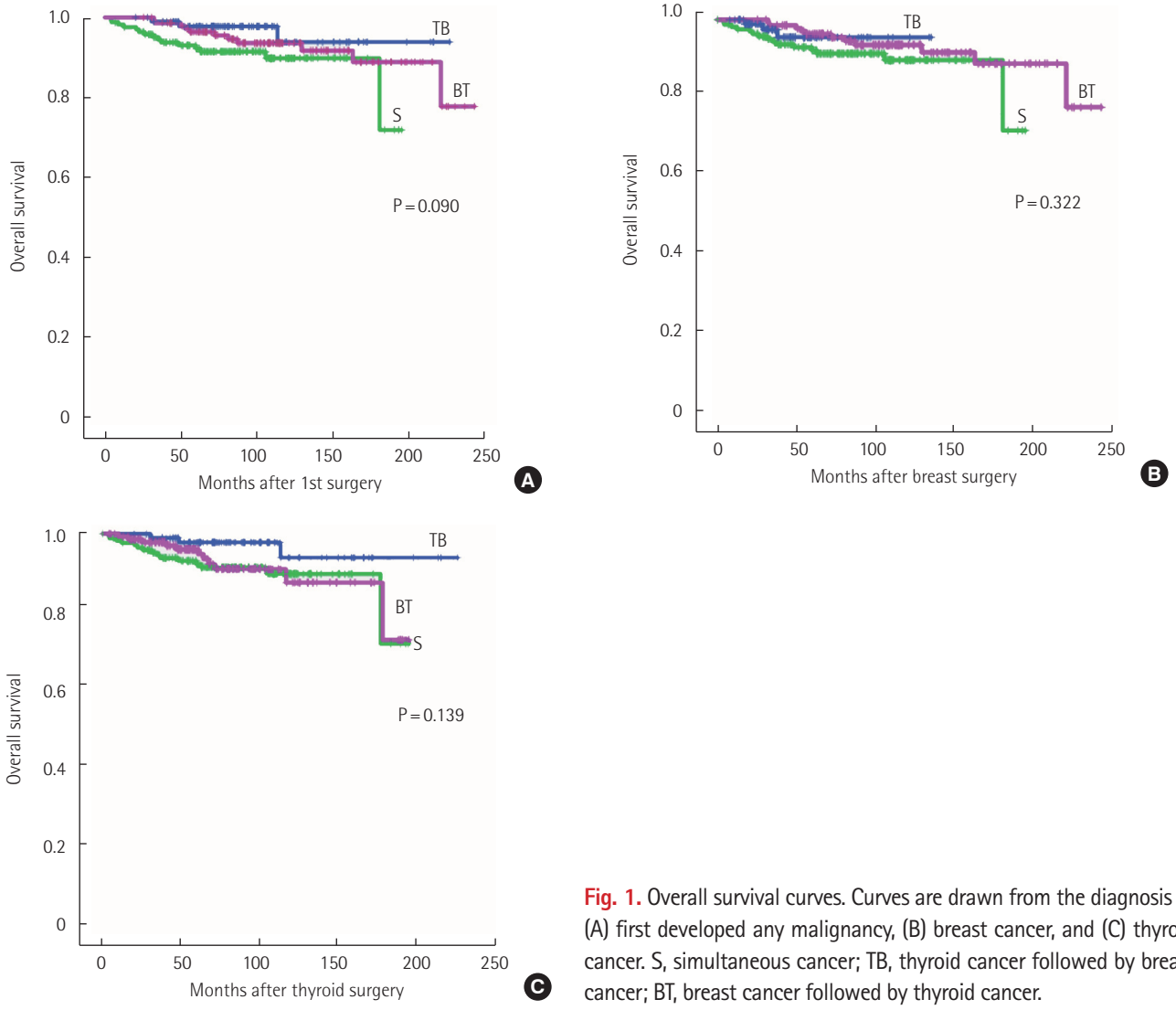

Fig. 1. Overall survival curves. Curves are drawn from the diagnosis of (A) first developed any malignancy, (B) breast cancer, and (C) thyroid cancer. S, simultaneous cancer; TB, thyroid cancer followed by breast cancer; BT, breast cancer followed by thyroid cancer.

In regards to the characteristics of thyroid cancer, the thyroid tumors were smaller in the BT group; however, no significant difference in the N and TNM stages were found between the BT and the other groups. The rates of extracapsular extension and bilateral total thyroidectomy were significantly lower in the BT group. The BT group also had the highest proportion of patients (69.2%) who did not require radioactive iodine therapy (Table 4).

A survival analysis of breast cancer, thyroid cancer, and the first cancer to occur (the index tumor) was performed for the TB, S, and BT groups. The mean length of follow-up was 83.9 months, 83.1 months, and 108.6 months, respectively, and no significant difference in survival rates was found among the groups. The relatively short follow-up period for thyroid cancer and breast cancer, which have high survival rates, limited the survival analysis. The S group included patients whose surgeries for thyroid and breast cancer were separated by less than 6 months; this included some of the patients who developed breast cancer first (18 out of 166 patients, 10.8%), and who developed thyroid cancer first (14 out of 166 patients, 8.4%) (Fig. 1).

DISCUSSION

Thyroid and breast cancer have the highest incidence among all types of cancer in women, and while studies have reported on an apparent association between these two cancers [2-6], their correlation and characteristics are still not clear [21,22]. We analyzed and compared the pathological characteristics and outcomes of breast and thyroid cancer in patients who were treated for both types of cancer at a single institution according to the occurrence order of these cancers using a database of surgeries performed in the last 20 years for thyroid and breast cancer. We found a number of significant differences among the different groups of patients.

First, the TNM stage of breast cancer decreased in the order of the TB, S, and BT groups (Table 3), and the rate of mastectomy was found to be BT (69.2%) > S (50.6%) > TB (38.5%) (P < 0.001). These results suggest that the rate of breast-conserving surgery was high among patients who were previously surgically treated for thyroid cancer possibly because breast cancer was detected early through regular medical examinations. The rate of postoperative radiation therapy according to the rate of breast-conserving surgery was the highest in the TB group (65.6%, P < 0.001), and the rate of postoperative chemotherapy was higher in the BT group, in which breast cancers were at relatively high TNM stages (69.2%) (P < 0.001). Therefore, the differences in the characteristics of breast cancer among the TB, S, and BT groups may be attributed to the different timing of discovering breast cancer during follow-up or through early screening.

However, considering the rate of ER positive breast cancer, it is possible that other factors contributed to the differences in the characteristics of breast cancer among the three groups. The rate of ER-positive breast cancer was 75%, 77.1%, and 63.7% in the TB, S, and BT groups, respectively (P = 0.027). While no significant difference in the rate of ER-positive breast cancer was found among the three groups, the higher mean age of the TB and S groups in comparison with the BT group may have translated to the slightly higher rates of ER+ breast cancer in these groups. Since a number of previous studies have suggested a correlation between thyroid cancer and ER expression [23-25], research on the effects of ER expression or estrogen on thyroid cancer is necessary. Chiappa et al. [26] previously reported a significantly high rate of ER+ breast cancer among patients with chronic thyroiditis in their study on the correlation between thyroid disorders and breast cancer. In the present study, no significant difference in the rate of thyroiditis was found among the groups. However, only a histological examination was used to assess thyroiditis after thyroid cancer surgery, and thus, our analysis on the correlation between thyroiditis and breast cancer was limited. It is important to investigate the effects of the pathways of thyroid hormones on the incidence of secondary breast cancer.

In regards to the characteristics of thyroid cancer, the rate of thyroid tumors that measured less than 1 cm was the highest at 81.8% in the BT group (TB, 62.5%; S, 71.7%; P = 0.004), and the rate of less than bilateral total thyroidectomy was also the highest at 61.5% in the BT group (TB, 37.5%; S, 45.2%; P = 0.001). In addition, the proportion of patients who did not undergo radioactive iodine therapy after thyroidectomy was the highest at 69.2% in the BT group (TB, 44.8%; S, 61.4%; P = 0.003). Therefore, the size of the thyroid tumor and the extent of surgery were less, and the rate of postoperative adjuvant therapy was lower for the patients who were diagnosed with thyroid cancer after undergoing treatment for breast cancer (Table 4). This may be the result of early detection of thyroid cancer during postoperative follow-up and regular medical examinations as was the case in the study by Zhang et al. [27]. On the contrary An et al. [28] reported that patients who were diagnosed with both types of cancer at the same time had the smallest thyroid tumor size. Different follow-up protocols for patients with breast cancer among institutions and different treatment guidelines used among countries may have affected these results, and thus, additional research is necessary.

The BRAF V600E mutation is the most commonly observed genetic change in papillary thyroid carcinomas, and it is an important factor in cell proliferation, differentiation, and apoptosis [29]. While it is known to be associated with not only thyroid cancer, but also malignant melanoma and other types of cancer [8], its association with breast cancer has not been clear, and thus, we conducted an additional analysis. Among all of the patients, 58 patients who were tested for the BRAF V600E mutation and had ER and HER2 test results were divided into 16 patients who did not have the mutation, and 42 patients who did. The rate of ER+ breast cancer was higher in the group without the BRAF mutation (88% vs. 81%). When the patients were further divided into four groups according to their ER and HER2 results, the rate of luminal breast cancer was slightly lower and the rate of triple negative breast cancer was slightly higher in the group with the BRAF V600E mutation than the group without. However, because BRAF V600E testing was only initiated recently and only thyroid cancer tissues were tested, it is difficult to explain the association between the BRAF V600E mutation and breast cancer based on these results. Therefore, further research is needed to test for BRAF mutations in breast cancer tissue and ER and HER2 expression in thyroid cancer tissue to investigate the association between the BRAF V600E mutation and breast cancer. In a recent study published by Jung et al. [30], 230 patients with thyroid and breast cancer were screened for the BRAF V600E mutation in breast tissue, and an association was found between the BRAF mutation and ER+ breast cancer. However, the study reported no association between the BRAF mutation and cancer prognosis, indicating additional research is necessary.

The survival analysis of the first cancer among the two types of cancer (index tumor) showed that the length of the survival period was in the order of TB > BT > S, and the survival period was predicted to be longer for the patient groups in which the two cancers developed at different times (TB or BT) than the group in which they developed simultaneously (S). Differences in outcomes due to different pathogeneses of the two cancers, and the higher likelihood of developing a secondary cancer among long-term survi-

vors than short-term survivors due to time-related reasons may explain why the survival period was shorter in the S group. In addition, differences in the outcomes between the two cancers may have contributed to the longer survival rate of the TB group compared to the BT group. Because thyroid cancer generally has a better prognosis than breast cancer, breast cancer may have affected the prognoses of both the BT and TB groups more significantly than did thyroid cancer. Breast cancers showed the smaller breast tumor size, less lymphnode invasion, and the lower TNM stage in the BT than the TB group, thus prognoses was better in the BT than the TB group. No significant differences were found between the survival curves of breast and thyroid cancer. However, as the survival analysis was limited due to the small sample size and the relatively short follow-up period, additional investigation is necessary.

The present study has a number of limitations. First, it is a retrospective study, and as a result, there were some missing clinical data. Moreover, this study may have been affected by selection bias because the data were collected from a single institution only. In addition, the relatively short follow-up period for thyroid cancer and breast cancer, which have high survival rates, limited the survival analysis. Lastly, a multivariate survival analysis in which the data were adjusted for cancer stage was not performed, and the 30,000 patients who underwent treatment for breast cancer or thyroid cancer only were not analyzed. After a longer period of follow-up, there will eventually be patients who develop secondary cancers, and thus, long-term follow-up is necessary. We minimized omission bias by thoroughly reviewing medical records, and the results of our study will be useful to guide future research.

This study divided the patients with breast cancer and thyroid cancer, which are the most common cancers among women, into three groups according to those cancers' occurrence order and compared the characteristics of the two cancer types. The rate of early detection of secondary cancer was significantly high for both patients who developed secondary breast cancer following thyroid cancer and patients who developed breast cancer followed by secondary thyroid cancer, highlighting the importance of postoperative follow-up and regular medical examinations. However, the significant differences in the rate of ER+ breast cancer and the different proportions of patients who underwent preoperative chemotherapy among the groups suggests the need for additional investigation into the pathological mechanism of secondary breast and thyroid cancer associated with primary breast and thyroid cancer. Although interpretation of the results of this study may be limited due to the small sample size used, the differences in the length of survival between the TB and BT groups suggests that thyroid cancer and breast cancer develop via different mechanisms and result in different outcomes depending on the order in which they develop. Analysis of the characteristics of patients who experienced both thyroid cancer and breast cancer may contribute to the development of cancer patient screening and follow-up programs and the establishment of guidelines for national cancer policies.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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