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ORIGINAL ARTICLE

Independent Prognostic Factors for Overall Survival after Salvage Operation for Ipsilateral Breast Tumor Recurrence Following Breast-Conserving Surgery

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Purpose: Few studies address independent prognostic factors after ipsilateral breast tumor recurrence (IBTR) following breast-conserving surgery (BCS). Locoregional recurrence is associated with distant metastases and increased mortality rates. Therefore anticipating prognoses after IBTR and evaluating risk factors for overall survival following a second salvage operation are important. We evaluated independent prognostic factors affecting overall survival after a second operation for IBTR. **Methods:** We retrospectively identified 11,073 patients who underwent breast cancer surgery between November 1995 and December 2011. Locoregional recurrence occurred in 787 patients. Among them, IBTR developed in 165 patients selected for analysis. Excluding eight patients who refused further treatment, we analyzed 157 patients who underwent a second operation (partial mastectomy, 28 [17.8%]; total mastectomy, 129 [82.2%]) for IBTR. Excluding 26 patients with incomplete data, we evaluated the clinicopathological features influencing overall survival at the first and the second operation in the 131 patients who underwent a second operation. **Results:** The median age of patients at the first operation was 43.6 years (range, 27–69 years). The median duration from the first to the second operation was 45.0 months (range, 2.5–164.6 months). The 5-year overall survival rate after IBTR was 87.1%. In the multivariable analyses, duration from the first to the second operation, histopathology, lymph node status, and adjuvant chemotherapy, radiotherapy, and endocrine therapy at the first operation were independent prognostic factors for overall survival. Positive estrogen receptor status and endocrine therapy at the second operation were also associated with increased overall survival following salvage operations for IBTR. **Conclusion:** The time interval to IBTR following BCS is related to overall survival after salvage operation for IBTR and it is important to undergo optimal adjuvant treatments according to risk factors after the first operation because those risk factors affect overall survival for IBTR following BCS.

Key Words: *Locoregional neoplasm recurrence, Mortality, Prognostic factors, Segmental mastectomy*

INTRODUCTION

Breast-conserving surgery (BCS) for early breast cancer patients has been well established for a number of years [1-4]. Although BCS is effective in prolonging survival compared with radical mastectomy, locoregional recurrence (LRR) rates are higher after BCS than following mastectomy [5-8]. Some studies have reported rates of LRR of 11% to 16% [9,10]. Ipsilateral breast tumor recurrence (IBTR) following treatment with BCS and radiotherapy occurs in approximately 8% to 20% of patients [2-4,8,11].

If IBTR is detected during follow-up, total mastectomy is considered standard treatment because postmastectomy radiotherapy is performed after the initial BCS and the risk of further residual recurrences increases with time after partial mastectomy [12-15]. Nonetheless, in some cases, partial mastectomy may be performed instead of total mastectomy as a second operation. There is a report that suggests the type of surgery does not affect survival, therefore, BCS can be considered in selected patients with IBTR [13]. Known risk factors for IBTR include age, race, obesity, size of the pathological tumor, time interval to recurrence, lymph node status, estrogen receptor (ER) status, progesterone receptor (PR) status, and

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receipt of adjuvant radiotherapy or systemic therapy [9-11,16,17]. However, risk factors affecting survival after a second operation following IBTR are not as well understood as the risk factors related to IBTR. In this study, we analyzed independent prognostic factors affecting overall survival after a second operation for IBTR.

METHODS

We retrospectively analyzed the medical records of 11,073 patients who underwent breast cancer surgery at Samsung Medical Center between November 1995 and December 2011. LRR occurred in 787 (7.1%), of which 622 including 471 with distant metastases, 109 who underwent total mastectomy at the first operation and 42 with regional recurrences were excluded. Of the remaining 165 patients who developed IBTR, eight refused further treatment, leaving 157 eligible for analysis. These included 28 patients (17.8%) who underwent partial mastectomy and 129 patients (82.2%) who underwent total mastectomy. Of these, 26 patients with incomplete data were excluded from the survival analysis at the second operation (Figure 1).

Patient data, tumor characteristics, and adjuvant treatment information were stratified according to the order of diagnosis (Table 1). Patient data, tumor characteristics, and adjuvant treatment information after the second operation following IBTR were analyzed using a Fisher exact test (Table 2). Age and durations were analyzed using the Mann-Whitney U-test after applying a Shapiro-Wilk test for normality (Table 2). Univariable and multivariable analyses were conducted using Cox regression analysis model. Survival from the date of the first operation to the time of death was estimated using the Kaplan-Meier method. A 95% confidence interval (CI) for survival was generated after estimating the standard error using Greenwooding Greenwowith variables affecting overall survival. Independent prognostic factors affecting overall survival were analyzed separately for the first and second operations. Univariable and multivariable analyses used age, duration from the first to the second operation, histopathology, multiplicity, nuclear grade, tumor size, resection margin, extensive intraductal component, ER/PR/human epidermal growth factor receptor 2 statuses, in addition to, adjuvant chemotherapy, radiotherapy, and endocrine therapy as variables (Table 3). Statistical significance was established at $p < 0.05$. All statistical analyses were performed using Statistical Analysis System (SAS) Software version 9.3 (SAS Institute Inc., Cary, USA) and R Statistical Programming Language version 2.13.2 (The R Foundation, Vienna, Austria; available

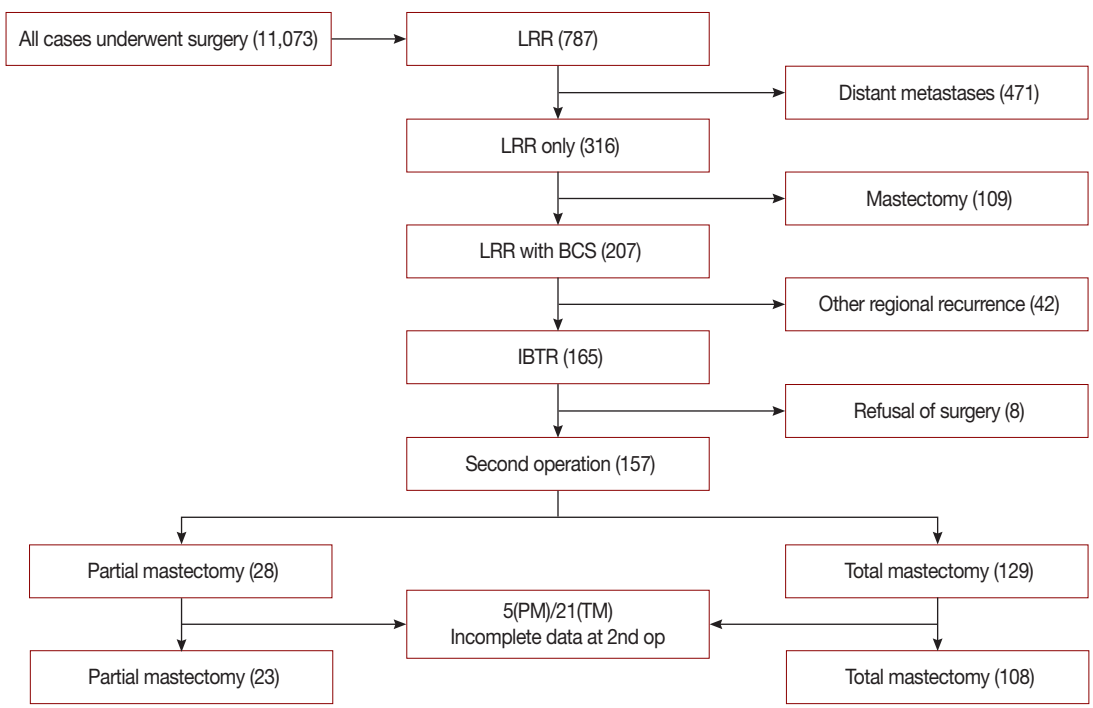

Figure 1. Consort diagram depicting the study selection process.
LRR = locoregional recurrence; BCS = breast-conserving surgery; IBTR = ipsilateral breast tumor recurrence; TM = total mastectomy; PM = partial mastectomy; op = operation.

Table 1. Patient, tumor characteristics, and adjuvant treatment according to order of diagnosis (1st and 2nd operation after ipsilateral breast tumor recurrence) (n = 157)

Variable	1st operation No. (%)	2nd operation No. (%)	Variable	1st operation No. (%)	2nd operation No. (%)
Age (yr)*	43.6 (27–69)	NA	ER		
Duration from 1st to 2nd operation (mo)*	NA	45.0 (2.5–164.6)	Positive	72 (45.9)	65 (41.4)
Histopathology			Negative	78 (49.7)	92 (58.6)
IDC	121 (77.1)	108 (68.8)	Unknown	7 (4.4)	0
DCIS	28 (17.8)	41 (26.1)	PR		
Mucinous	3 (1.9)	4 (2.5)	Positive	56 (35.7)	54 (34.4)
Others	5 (3.2)	4 (2.5)	Negative	91 (58.0)	103 (65.6)
Multiplicity			Unknown	10 (6.3)	0
Yes	18 (11.5)	17 (10.8)	HER2		
No	139 (88.5)	140 (89.2)	Positive	75 (47.8)	70 (44.6)
Nuclear grade			Negative	68 (43.3)	85 (54.1)
Low	59 (37.6)	74 (47.1)	Unknown	14 (8.9)	2 (1.3)
High	85 (54.1)	82 (52.2)	Molecular subtypes		
Unknown	13 (8.3)	1 (0.6)	Luminal A	33 (21.0)	46 (29.3)
Tumor size (cm)			Luminal B	35 (22.3)	21 (13.4)
≤2	122 (77.7)	133 (84.7)	HER2	33 (21.0)	49 (31.2)
>2, ≤5	34 (21.7)	22 (14.0)	TNBC	34 (21.7)	39 (24.8)
>5	1 (0.6)	2 (1.3)	Unknown	22 (14.0)	2 (1.3)
Lymph node involvement			Adjuvant chemotherapy		
Negative	115 (73.2)	NA	Yes	87 (55.4)	69 (44.0)
1–3	42 (26.8)	NA	No	70 (44.6)	88 (56.0)
>3	0	NA	Adjuvant radiotherapy		
Stage			Yes	135 (86.0)	20 (12.7)
0, I	96 (61.1)	NA	No	22 (14.0)	137 (87.3)
II	52 (33.1)	NA	Endocrine therapy		
III	9 (5.8)	NA	Yes	61 (38.9)	59 (37.6)
Resection margin			No	94 (59.9)	98 (62.4)
Positive	3 (1.9)	3 (1.9)	Unknown	2 (1.2)	0
Negative	154 (98.1)	154 (98.1)			
EIC					
Present	72 (45.9)	83 (52.9)			
Absent	72 (45.9)	74 (47.1)			
Unknown	13 (8.3)	0			

NA = not applicable; IDC = invasive ductal carcinoma; DCIS = ductal carcinoma *in situ*; EIC = extensive intraductal component; ER = estrogen receptor; PR = progesterone receptor; HER2 = human epidermal growth factor receptor 2; TNBC = triple-negative breast cancer.
*Median (range).

at http://www.R-project.org/). The study was approved by Institutional Review Committees (2015-07-150) and work was conducted according to the principles outlined in the Helsinki Declaration.

RESULTS

Patient data, tumor characteristics, and adjuvant treatment information for the first and second operations are described in Table 1. The median age of the patients at the first operation was 43.6 years (range, 27–69 years). Median disease-free duration from the first to the second operation was 45.0 months (range, 2.5–164.6 months). Of the 131 patients analyzed who underwent a second operation, 23 patients (17.6%) underwent partial mastectomy and 108 patients (82.4%) underwent total mastectomy (Table 2). For the survival analysis, 26 patients with incomplete data for one or more variables for the first or second operations were excluded (Figure 1). Histopathology of the tumors revealed invasive ductal carcinomas in 121 patients (77.1%) with no invasive or *in situ* lobular carcinomas reported at the first operation.

At the time of the first operation, most patients had stage I (n = 96, 61.1%) or stage II (n = 52, 33.1%) breast cancer. Systemic treatments included chemotherapy for 69 patients (44.0%) and endocrine therapy for 59 patients (37.6%) after the second operation (Table 1). Patient characteristics stratified according to the second operation method following IBTR were analyzed (Table 2). Histopathology of the tumors

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Table 2. Comparison of patient characteristics by 2nd operation method after ipsilateral breast tumor recurrence (n=131)

Variable	2nd operation after IBTR		*p*-value
	TM (n=108) No. (%)	PM (n=23) No. (%)	
Age (yr)*	44.0 (27–73)	45.0 (28–61)	0.645
Duration from 1st to 2nd operation (mo)*	41.2 (2.7–164.6)	35.7(2.5–142.6)	0.486
1st operation			
Histopathology			0.587
IDC	84 (77.8)	18 (78.4)	
DCIS	20 (18.5)	3 (13.2)	
Mucinous	1 (1.0)	1 (4.2)	
Others	3 (2.7)	1 (4.2)	
Multiplicity	13 (12.0)	3 (13.2)	0.894
Nuclear grade			0.995
Low	42 (38.9)	9 (39.1)	
High	66 (61.1)	14 (60.9)	
Tumor size (cm)			0.306
≤2	57 (52.8)	14 (60.9)	
>2, ≤5	41 (38.0)	9 (39.1)	
>5	10 (9.2)	0	
Lymph node involvement			0.634
Negative	77 (71.3)	16 (69.6)	
1–3	31 (28.7)	7 (30.4)	
>3	0	0	
Stage			0.448
0, I	67 (62.0)	11 (47.8)	
II	34 (31.5)	11 (47.8)	
III	7 (6.5)	1 (4.2)	
Resection margin positive	1 (1.0)	0	0.643
EIC present	56 (52.0)	10 (43.6)	0.466
ER positive	47 (43.5)	12 (52.2)	0.449
PR positive	38 (35.2)	10 (43.6)	0.454
HER2 positive	63 (58.3)	8 (34.8)	0.040
Molecular subtypes			0.019
Luminal A	23 (21.3)	5 (21.8)	
Luminal B	27 (25.0)	7 (30.4)	
HER2	36 (33.3)	1 (4.2)	
TNBC	22 (20.4)	10 (43.6)	
Adjuvant chemotherapy	58 (53.7)	16 (69.6)	0.164
Adjuvant radiotherapy	93 (86.1)	20 (87.0)	0.915
Endocrine therapy	41 (38.0)	13 (56.5)	0.101
2nd operation			
Histopathology			0.192
IDC	72 (66.7)	19 (82.6)	
DCIS	32 (29.6)	3 (13.2)	
Mucinous	1 (1.0)	1 (4.2)	
Others	3 (2.7)	0	
Multiplicity	11 (10.2)	1 (4.2)	0.378
Nuclear grade			0.875
Low	50 (46.3)	12 (52.2)	
High	58 (53.7)	11 (47.8)	
Tumor size (cm)			0.292
≤2	74 (68.5)	19 (82.6)	
>2, ≤5	28 (26.0)	4 (17.4)	
>5	6 (5.5)	0	
Resection margin positive	3 (2.7)	0	0.419
EIC present	63 (58.3)	6 (26.1)	0.003
ER positive	39 (36.1)	12 (52.2)	0.151
PR positive	35 (32.4)	7 (30.4)	0.854
HER2 positive	52 (48.1)	8 (34.8)	0.243
Molecular subtypes			0.024
Luminal A	30 (27.8)	6 (26.1)	
Luminal B	12 (11.1)	6 (26.1)	
HER2	40 (37.0)	2 (8.7)	
TNBC	26 (24.1)	9 (39.1)	
Adjuvant chemotherapy	43 (40.0)	12 (52.2)	0.276
Adjuvant radiotherapy	3 (2.7)	13 (56.5)	<0.001
Endocrine therapy	34 (31.5)	11 (47.8)	0.134

IBTR=ipsilateral breast tumor recurrence; PM=partial mastectomy; TM=total mastectomy; IDC=invasive ductal carcinoma; DCIS=ductal carcinoma *in situ*; EIC=extensive intraductal component; ER=estrogen receptor; PR=progesterone receptor; HER2=human epidermal growth factor receptor 2; TNBC=triple-negative breast cancer.
*Median (range).

revealed mainly invasive ductal carcinomas in both groups. Adjuvant radiotherapy was administered to 13 patients (56.5%) after partial mastectomy in contrast to three patients (2.7%) after total mastectomy (Table 2).

Univariable analyses showed duration from the first to the second operation, multiplicity, nuclear grade, lymph node status, tumor stage, ER/PR/human epidermal growth factor receptor statuses, and adjuvant radiotherapy at the first operation, in addition to, nuclear grade, ER/PR statuses, and endocrine therapy at the second operation to be significantly associated with survival outcome (Table 3). In the multivariable analyses, duration from the first to the second operation (hazard ratio [HR], 0.98; 95% CI, 0.97–0.99; $p<0.001$), histopathology (HR, 0.42; 95% CI, 0.23–0.78; $p=0.006$), and adjuvant chemotherapy (HR, 0.38; 95% CI, 0.21–1.06; $p=0.002$), and radiotherapy (HR, 0.47; 95% CI, 0.24–0.89; $p=0.022$) at the first operation, in addition to, positive ER status (HR, 0.46; 95% CI, 0.22–0.96; $p=0.039$) and endocrine therapy (HR, 0.52; 95% CI, 0.30–0.91; $p=0.022$) at the second operation were found to be significantly associated with an overall increase in survival following IBTR. Conversely, positive lymph node status (HR, 3.71; 95% CI, 1.51–9.10; $p=0.004$) and en-

Table 3. Univariable and multivariable Cox regression analysis of overall survival after second operation (n=131)

Variable	Univariable		Multivariable	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Age (yr)	1.01 (1.00–1.03)	0.099	1.01 (0.99–1.04)	0.341
Duration from 1st to 2nd operation (mo)	0.98 (0.97–0.98)	<0.001	0.98 (0.97–0.99)	<0.001
1st operation				
Histopathology				
IDC	0.95 (0.63–1.43)	0.795	0.42 (0.23–0.78)	0.006
Non-IDC	NA	NA	NA	NA
Multiplicity	2.01 (1.21–3.32)	0.007	1.21 (0.63–2.30)	0.565
High nuclear grade	1.71 (1.22–2.42)	0.002	0.93 (0.53–1.64)	0.805
Lymph node involvement				
Negative	NA	NA	NA	NA
1–3	1.14 (0.77–1.69)	0.510	2.26 (1.22–4.18)	0.009
>3	2.33 (1.16–4.67)	0.017	3.71 (1.51–9.10)	0.004
Stage				
0, I	NA	NA	NA	NA
II	1.34 (0.95–1.89)	0.089	NA	NA
III	2.52 (1.25–5.08)	0.010	NA	NA
Resection margin positive	0.49 (0.15–1.56)	0.229	5.72 (0.55–59.37)	0.144
EIC present	1.35 (0.96–1.90)	0.086	1.67 (0.95–2.93)	0.073
ER positive	0.43 (0.31–0.60)	<0.001	0.55 (0.25–1.18)	0.125
PR positive	0.71 (0.51–1.00)	0.049	1.11 (0.58–2.09)	0.756
HER2 positive	0.48 (0.34–0.69)	<0.001	0.53 (0.27–1.06)	0.075
Adjuvant chemotherapy	1.17 (0.85–1.61)	0.328	0.38 (0.21–0.70)	0.002
Adjuvant radiotherapy	0.35 (0.22–0.57)	<0.001	0.47 (0.24–0.89)	0.022
Endocrine therapy	1.31 (0.94–1.82)	0.112	1.91 (1.09–3.35)	0.024
2nd operation				
Histopathology				
IDC	0.95 (0.66–1.36)	0.767	0.70 (0.38–1.29)	0.256
Non-IDC	NA	NA	NA	NA
Multiplicity	0.89 (0.54–1.47)	0.648	1.04 (0.47–2.26)	0.256
High nuclear grade	1.47 (1.07–2.02)	0.017	1.01 (0.67–1.82)	0.688
Tumor size (cm)*				
≤2	NA	NA	NA	NA
>2, ≤5	0.75 (0.47–1.20)	0.228	NA	NA
>5	1.18 (0.29–4.77)	0.820	NA	NA
Resection margin positive	3.11 (0.98–9.86)	0.054	2.26 (0.52–9.75)	0.274
EIC present	1.09 (0.79–1.51)	0.606	1.20 (0.71–2.04)	0.486
ER positive	0.51 (0.36–0.71)	<0.001	0.46 (0.22–0.96)	0.039
PR positive	0.66 (0.47–0.92)	0.015	1.31 (0.64–2.66)	0.453
HER2 positive	0.78 (0.57–1.07)	0.128	0.55 (0.29–1.04)	0.068
Adjuvant chemotherapy	0.82 (0.59–1.13)	0.218	0.73 (0.43–1.22)	0.234
Adjuvant radiotherapy	1.60 (0.99–2.57)	0.053	1.62 (0.83–3.18)	0.158
Endocrine therapy	0.58 (0.42–0.80)	0.001	0.52 (0.30–0.91)	0.022

HR=hazard ratio; CI=confidence interval; IDC=invasive ductal carcinoma; NA=not applicable; EIC=extensive intraductal component; ER=estrogen receptor; PR=progesterone receptor; HER2=human epidermal growth factor receptor 2.
*It was impossible to analyze all variables using multivariate analysis by Cox regression model since 26 patients among 131 patients underwent salvage operation, in which causes the number of events in subgroups depending on certain variables to be 0.

docrine therapy (HR, 1.91; 95% CI, 1.09–3.35; $p=0.024$) at the first operation were found to be significantly associated with an overall decrease in survival after salvage operation following IBTR (Table 3).

Overall survival rates were estimated for the 131 patients who experienced IBTR using the Kaplan-Meier method (Figure 2). One-, 3-, and 5-year overall survival rates were 98.2% (95% CI, 0.927–0.996), 90.6% (95% CI, 0.827–0.950), and 87.1% (95% CI, 0.774–0.928), respectively. The Kaplan-Meier method was also used to estimate overall survival rates of pa-

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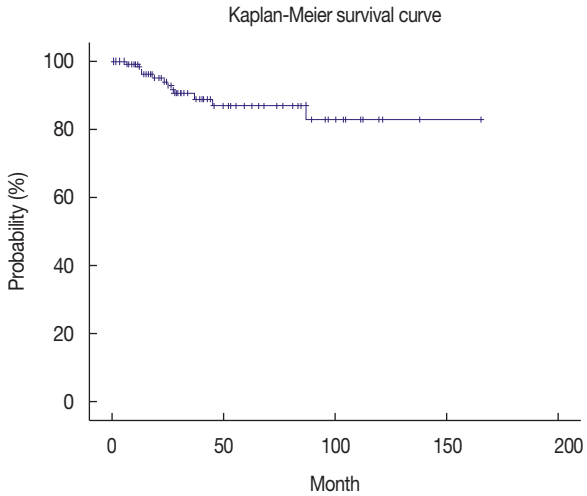

Figure 2. Overall survival after salvage operation for ipsilateral breast tumor recurrence.

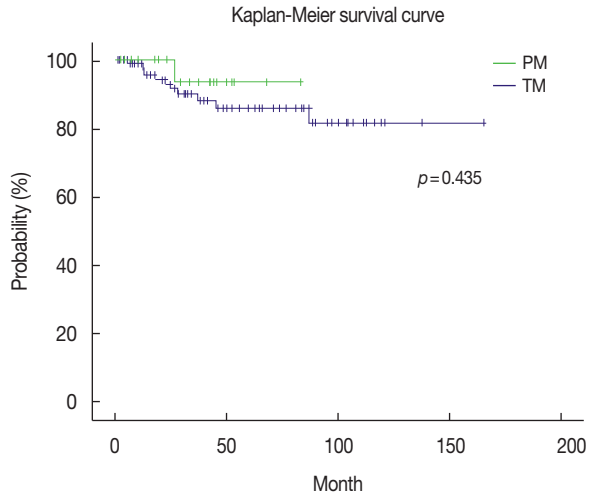

Figure 3. Overall survival according to second operation methods. TM=total mastectomy; PM=partial mastectomy.

tients stratified according to the method of the second operation (Figure 3). One-, 3-, and 5-year overall survival rates of patients who underwent total mastectomy were 97.8% (95% CI, 0.918–0.994), 90.0% (95% CI, 0.808–0.949), 85.8% (95% CI, 0.748–0.923), respectively. Conversely, 1-, 3-, and 5-year overall survival rates of patients who underwent partial mastectomy were 93.3% (95% CI, 0.618–0.990), 93.3% (95% CI, 0.618–0.990), 93.3% (95% CI, 0.618–0.990), respectively. Analysis of survival between the two patient groups reported the HRs not to be significantly different according to the method of the second operation using a Cox regression analysis model ($p=0.435$).

DISCUSSION

This retrospective analysis of patients treated with BCS for early breast cancer revealed independent prognostic factors affecting overall survival after a second salvage operation. Several previously published reports have defined IBTR as recurrent invasive carcinoma in either the skin or parenchyma of the ipsilateral breast after BCS in the absence of clinical and radiological evidence of regional or distant metastases [9,10]. Reported rates of LRR after BCS are 11% to 16% [9,10]. IBTR rates are generally reported at 8% to 20% [1-4,8,10,11,18]. In this study, the rate of IBTR was 21% (n=165), which is similar to other studies.

Previously identified risk factors known to affect overall survival after IBTR include age, race, body mass index, size of the pathological tumor, ER status, diploidy, a *BRCA1/2* mutation, lymph nodal status at relapse, and adjuvant therapy [9,10,12,15,19-22]. Anderson et al. [9] have reported that IBTR has a greater impact on mortality in ER-negative than ER-positive patients and that older patients with larger tumors (>2.0 cm) have significantly higher mortality rates compared to younger patients with smaller tumors. Body mass index and black ethnicity were also reported to be significantly associated with mortality. Adjuvant therapy after IBTR significantly influences overall survival. The use of adjuvant radiotherapy and systemic treatments, such as adjuvant chemotherapy or endocrine therapy, has reduced the incidence of IBTR and increased the overall survival following IBTR [12,23]. Histopathology, lymph node status at the first operation, hormonal receptor status, and adjuvant chemotherapy were also significantly associated with overall survival in this study. Furthermore, we also identify disease-free durations between the first and the second operations as factors affecting overall survival after a second operation following IBTR in our study. Data are limited on resection margins for second operations in other studies because total mastectomy is usually performed for IBTR [9,10,12,13,24]. Resection margins were also not associated with survival rates in our study. Time intervals between treatment of the primary breast cancer and IBTR greatly affected overall survival [10,11,19,21,22,25]. Our results on overall survival after IBTR were in concordance with previous studies.

Recurrent cancer is generally treated by total mastectomy after IBTR because curative resection is regarded as the standard treatment [10,14,15,26]. Approaches that use partial mastectomy for reoperation with repeated radiation exposure to the residual breast are an emerging problem. Alpert et al. [12] reported that while mastectomy remains the standard of treatment for in-breast relapse after BCS and radiotherapy,

partial mastectomy appears to be feasible for selected patients with favorable tumor biology and early detection of local relapse. They also suggested that partial mastectomy may be acceptable as a second operation for selected patients with tumors < 3 cm in diameter, tumors confined to the biopsy site without skin or lymphovascular invasion, and fewer than three positive lymph nodes. According to Alpert et al. [12] approximately 20% of patients with IBTR received partial mastectomy as a second operation. In our study, partial mastectomy was performed on 17.6% (n = 23) of patients as a second operation after IBTR, similar to the previous study. Most patients in other studies had early T stage tumors at diagnosis with no multiplicity. In our study, 82.6% of tumors were < 2 cm, 17.4% were 2 to 5 cm and 95.8% were tumors without multiplicity in the second partial mastectomy group (Table 2). Alpert et al. also reported 20.5% T1 and T2 stage tumors because surgeons do not usually select patients with large tumor or tumors with multiple sites for second BCS. Comparing partial mastectomy and total mastectomy groups for overall survival is difficult because of differences in median follow-up durations. However, partial mastectomy can be done instead of total mastectomy for second operations for IBTR in selected patients with a long disease-free follow-up period and patients given endocrine therapy whose ER status is positive.

Due to its retrospective design, our study has several limitations. First, randomization was not applied when patients with IBTR underwent a second operation. The size of subgroup populations and conduct at a single center limited the statistical power for determining prognostic factors. Second, partial mastectomy as a second operation after IBTR is a recent surgical intervention. This meant relatively few patients underwent partial mastectomy. Further randomized controlled studies are needed on partial mastectomy as a standard treatment instead of total mastectomy. Third, we could not include genetic information and race, which are important prognostic factors for overall survival after a second operation, because genetic analysis was not prevalent in Korea at the time of the operations and because most patients were Asian. Published data on second operations for IBTR were limited and few published reports addressed survival outcomes of patients with second operations. Consequently, second operations for IBTR were unfamiliar and prognostic factors affecting overall survival after second operations were not well understood [12,13,19]. The strength of this study was that we evaluated IBTR and independent factors affecting survival and identified disease-free duration, histopathology, lymph node status and adjuvant therapy at the first operation, and ER status, and endocrine therapy at the second operation as important prognostic factors. Furthermore, this study was conducted using large numbers of patients with IBTR (131 patients) as compared to existing studies and we assessed predictors affecting overall survival through the analysis of multiple variables. In future, additional studies are needed to evaluate recurrence rates and prognoses according to surgery type after second operations for IBTR.

We evaluated prognostic factors affecting overall survival after a second operation following IBTR. The time interval to IBTR after BCS, histopathology, lymph node status, and adjuvant therapy at the first operation, and ER status and endocrine therapy at the second operation were related to overall survival after surgical intervention for IBTR. We could see better prognoses after a second operation following IBTR in patients with a long disease-free interval and recognized the importance of performing optimal treatment, such as adjuvant chemotherapy, radiotherapy, and endocrine therapy according to pathologic status, lymph node status, and hormonal receptor status after the first operation because those risk factors affect overall survival after a second operation for IBTR following BCS.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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