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Characterization of Korean Male Breast Cancer Using an Online Nationwide Breast-Cancer Database

Matched-Pair Analysis of Patients With Female Breast Cancer

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Abstract: The aim of this study is to review the characteristics and the survival rate in male breast cancer (MBC) patients in Korea over a 31-year period. Additionally, we analyzed the overall survival (OS) rate of a group of MBC matched to females with breast cancer.

We retrospectively analyzed the data from 400 Korean patients who were treated for MBC from 1978 to 2009. Patient demographics and clinical information were routinely documented throughout the study period. Survival and prognostic factors were evaluated. Each MBC patient was matched with 5 female breast cancer (FBC) patients based on 7 characteristics and we compared the OS rates between the 2 groups.

For MBC cases, the median follow-up was 72 months and the 5-year OS rate was 85.9%. In univariate analyses, the prognostic factors influencing OS were age (more than 60 years, $P < 0.001$), tumor size (>2 cm, $P = 0.007$), and having a negative progesterone receptor (PR) status ($P = 0.042$). Only the age ($P = 0.028$) and tumor size ($P = 0.024$) were significant prognostic factors for OS in multivariate analysis. After matching, we had 260 male patients matched to 1300 female patients for analysis. Compared with cases among females, the rate of mastectomy was higher among MBC cases and tumors, which were almost invasive ductal carcinomas (IDCs), were more likely to be located in the central part of the breast. For MBC cases, the percentage of adjuvant radiation therapy was low compared with female cases. The primary hormone therapy agent used was tamoxifen. The 5-year OS rates were similar in MBC compared with FBC (91.0% vs. 92.6%, $P = 0.300$).

We found that only the age (more than 60 years) and tumor size were independent prognostic factors of survival in MBC. The prognosis for MBC is similar to that for FBC given similar stage and hormone-receptor status.

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Abbreviations: AI = aromatase inhibitor, AJCC = American Joint Committee on Cancer, BCS = breast conserving surgery, DCIS = ductal carcinoma in situ, ER = estrogen receptor, FBC = female breast cancer, HER2 = human epidermal growth factor receptor 2 c-erbB2, HR = hazard ratio, IDC = invasive ductal carcinoma, IHC = immunohistochemistry, KBCS = Korean Breast Cancer Society, MBC = male breast cancer, MOSPA = Ministry of Security and Public Administration, NCI = National Cancer Institute, OS = overall survival, PR = progesterone receptor, SEER = Surveillance Epidemiology and End Results, SERM = selective estrogen-receptor modulator, SLN = sentinel lymph node.

INTRODUCTION

Male breast cancer (MBC), a very rare cancer in males, accounts for less than 1% of all cases of malignancies in men and less than 1% of all breast cancers.[1] In the United States, more than 2 thousand men were diagnosed with primary breast cancer in 2012.[2] In a recent analysis of the data from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI), the annual incidence rate showed a slight increase over time from 1.0 to 1.2 per 100,000/year in the late 1970s compared with 2000 to 2004.[3] Because of the scarcity, MBC has not been conducted an extensive research like a female breast cancer. There have been no prospective randomized control trials and most studies about this disease are retrospective analysis with a small number of patients or extrapolation from breast cancer trials in women.[4] Consequently, appropriate management guidelines for MBC have not been clearly established.

At present, there are several known features of MBC, including the following. Approximately 90% of MBCs are invasive ductal carcinomas, whereas lobular carcinoma is rare, accounting for only 1.5% of MBCs. MBC cases involve high rates of estrogen and progesterone receptor expression. Similar to female breast cancer, tumor size and lymph node involvement are important prognostic factors for MBC.[1]

In this study, we retrospectively evaluated the clinicopathological features, treatments, and outcomes for MBC patients in Korea, over a 31-year period. Additionally, we investigated the differences between male and female breast cancer by using matched-pair analysis.

METHODS

Approval was granted by the Institutional Review Board of Samsung Medical Center (IRB file No. 2014-09-134). To

protect the personal information, patient records/information was anonymized and deidentified prior to analysis. Data from patients treated for breast cancer throughout Korea from 1978 to 2009 were retrospectively evaluated. All patient data were obtained from an online breast cancer registration program, collated by the Korean Breast Cancer Society (KBCS). Thirty-eight of the 41 medical schools in Korea, as well as 24 general hospitals and 6 private hospitals and special clinics, participated in the survey. We examined the following in our analysis: the number of patients, patient age, gender, year of diagnosis, surgical method, location of cancer, pathological findings (American Joint Committee on Cancer [AJCC] values for stage, tumor type, lymph node, metastasis [TNM] stage, and hormone receptor status), and postoperative adjuvant treatment.

First, all MBC patients registered during this period were analyzed. Next, each MBC case was matched with female breast cancer patients who had at least 7 characteristics in common that are relevant for prognosis: age (within ± 5 years), tumor stage, nodal stage, year of diagnosis (within ± 1 year), estrogen receptor (ER) status, progesterone receptor (PR) status, and c-erbB2 (HER2). The hormone receptor statuses were assessed using immunohistochemistry (IHC) and were scored with the Allred Score, more than 2 (from 3) of it were used to define as tumor ER and PR positivity. HER2 gene expression was defined as intensity by IHC. We excluded patients who only underwent a biopsy, or ultimately diagnosed with phyllodes tumor or lymphoma in final pathologic evaluation, or already had systemic metastasis, or younger than 20 years. This left us 260 male patients and each MBC patient was matched with 5 women who were selected from a total FBC patient population of 85,207. The matching process was blinded with no information about patient outcome. Follow-up data were derived from death statistics at the Ministry of Security and Public Administration (MOSPA); these data are the result of complete follow-up to August 10, 2011. Overall survival (OS) was defined as the time of death from any cause.

Data analyses were performed using SAS, version 9.4 (SAS Institute, Cary, NC). Categorical and continuous variables were summarized with the χ^2 test or Fisher exact test. Survival curves were produced using the Kaplan–Meier method and were compared using the log-rank test. The prognostic relevance of all variables was analyzed in univariate and multivariate Cox regressions ($P = 0.05$ for input and $P = 0.1$ for output). The stability of the model was tested by bootstrap resampling.[5,6] Statistical significance was defined as a P value < 0.05.

RESULTS

Characteristics and Survival Analysis of MBC in Korea

The number of breast cancer patients who had been newly registered in KBCS's online breast cancer registration program from 1978 to 2009 was 87,097. Approximately 0.5% of all breast cancer patients were male (n = 400). The youngest of the patients was 17-year old, and the oldest was 90-year old; the median age was 60-year old (Table 1). Distribution of male patients by age peaks among patients in their sixties (n = 109, 27.3%, Figure 1). To investigate how the number of diagnosed male patients changed over the course of the study period, we added to the sample 48 patients who were diagnosed in 2010 and then grouped cases into 5-year intervals. We observed that the occurrence increases over time. Since 1996, when KBCS

TABLE 1. Characteristics of All Male Breast Cancer in Korea

Characteristics	MBC, n = 400 (%)
Age at diagnosis, yr	
Mean $\pm$ SD	57.9 $\pm$ 14.7
Median (range)	60 (17–90)
Operation (breast)	
Mastectomy	338 (84.5)
Breast conserving surgery	42 (10.5)
Biopsy	10 (2.5)
Unknown	10 (2.5)
Operation (axilla)	
ALND	315 (78.8)
SLNB	15 (3.7)
No operation	59 (14.8)
Unknown	11 (2.7)
AJCC stage	
0	18 (4.5)
I	130 (32.5)
II	136 (34.0)
III	67 (16.8)
IV	14 (3.5)
Others	7 (1.8)
Unknown	28 (7.0)
Pathology	
Invasive ductal carcinoma	353 (88.3)
Invasive lobular carcinoma	4 (1.0)
Ductal carcinoma in situ	19 (4.8)
Lobular carcinoma in situ	1 (0.3)
Paget disease (pure form)	1 (0.3)
Sarcoma	5 (1.3)
Others	17 (4.3)
Tumor stage	
Tis	18 (4.5)
T1	188 (47.0)
T2	120 (30.0)
T3	18 (4.5)
T4	19 (4.8)
Tx	10 (2.5)
Others	4 (1.0)
Unknown	23 (5.8)
Nodal stage	
N0	192 (48.0)
N1	77 (19.3)
N2	33 (8.3)
N3	33 (8.3)
Nx	59 (14.8)
Unknown	6 (1.5)
Metastatic node	
Mean $\pm$ SD	2.7 $\pm$ 6.2
Median (range)	0 (0–41)
Total number of harvested node	
Mean $\pm$ SD	14.4 $\pm$ 9.4
Median (range)	14 (0–47)
Estrogen receptor	271
Negative	42 (10.5)
Positive	229 (57.3)
Unknown	129 (32.3)
Progesterone receptor	267
Negative	60 (15.0)
Positive	207 (51.8)
Unknown	133 (33.3)

Characteristics	MBC, n = 400 (%)
Chemotherapy	
No	96 (24.0)
Yes	173 (43.3)
Unknown	131 (32.8)
Radiation therapy	
No	189 (47.3)
Yes	66 (16.5)
Unknown	145 (36.3)
Hormone therapy	
No	57 (14.3)
Yes	200 (50.0)
Tamoxifen	166 (83.0)
Toremifene	18 (9.0)
Anastrozole	2 (1.0)
Letrozole	3 (1.5)
Unknown	11 (5.5)
Unknown	143 (35.8)
Follow-up time, mo	
Mean ± SD	82.0 ± 51.7
Median (range)	72.0 (0.1–363.6)
Status at end of follow-up	
Alive	313 (78.3)
Dead	87 (21.7)
Cause of mortality	
Breast cancer	34 (39.1)
Second primary cancer	10 (11.5)
Other causes	8 (9.2)
Unknown	35 (40.2)
5-year OS rate	85.9%
10-year OS rate	70.5%

ALND = axillary lymph node dissection, OS = overall survival, SD = standard deviation, SLNB = sentinel lymph node biopsy.

FIGURE 2. Number of newly diagnosed male breast cancer patients and the ratio of male-to-female breast cancer patients at the time of diagnosis according to the Korean Breast Cancer Society survey.

first began recording the occurrence of breast cancer patients, the number of MBC patients in the last period (2006–2010) was 184, which was an increase of 2.4 times the number from the first period (1996–2000). Meanwhile, of all breast cancer patients, the proportion of men steadily decreased by 2-year intervals from 1996 (Figure 2).

Among 400 patients, mastectomy was performed in 338 cases (84.5%), which was significantly higher than the number of breast conserving surgeries (BCS) performed (10.5%). Figure 3 shows the surgical methods employed for treatment of MBC from 1996 to 2009. Axillary lymph node dissection was
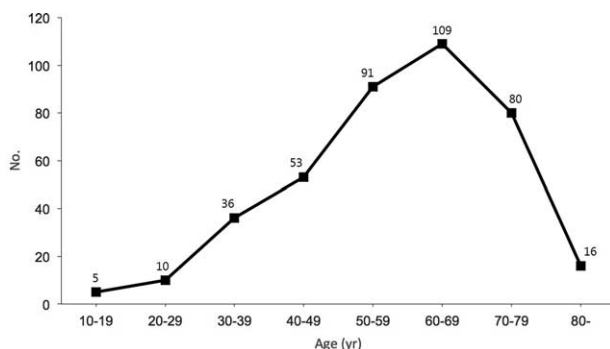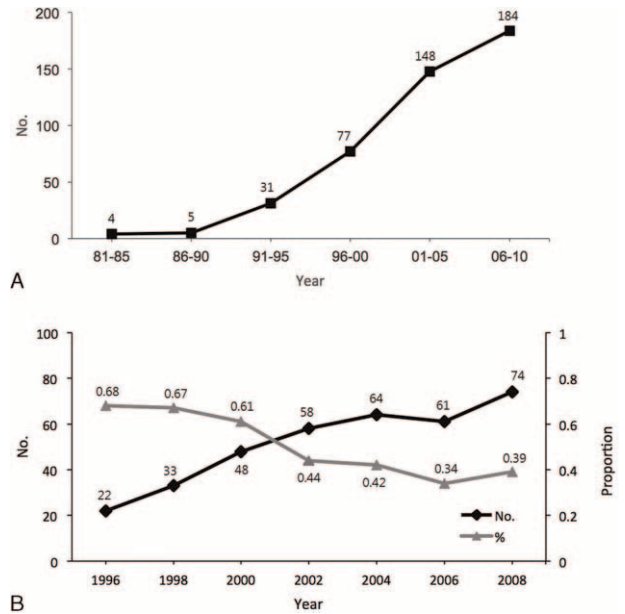
performed in 315 patients (78.8%) and sentinel lymph node (SLN) biopsy was performed in 52 patients (12.9%). There were 15 patients who underwent SLN biopsy only (3.7%). The number of patients with classifiable stages was 372 (excluding unknown patients in Table 1), 36.6% of whom were classified as stage II, followed by 34.9% at stage I, and 18.0% at stage III.

Invasive ductal carcinoma (IDC) was the most common diagnosis (n = 353, 88.3%), followed by ductal carcinoma in situ (DCIS; n = 19, 4.8%). The number of patients whose tumor stage could be confirmed was 377 (excluding unknown patients in Table 1), 49.9% of whom were at T1, and 31.8% of whom were at T2. N0 was the most common nodal stage (n = 192, 57.3%, excluding Nx and unknown patients in Table 1), followed by N1 (n = 77, 23.0%), N2, and N3, respectively.

The proportions of ER and PR positivity among MBC patients were 84.5% and 77.5%, respectively. For most cases, the expression of other receptors, such as HER2, p53, and Ki-67, was not investigated. The median follow-up period was 72
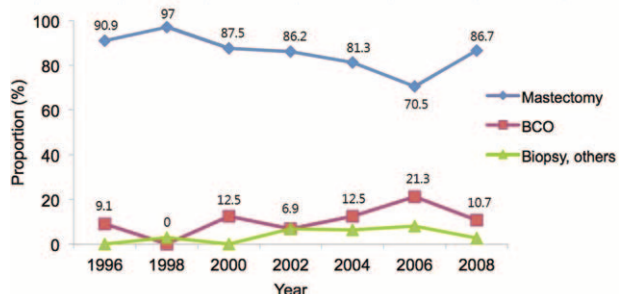

FIGURE 1. Age distribution of Korean male breast cancer patients.

FIGURE 3. Surgical trends in Korean male breast cancer patients.

TABLE 2. Multivariate Analysis of Factors Predicting Overall Survival for MBC

Characteristics	Hazard Ratio (95% CI)	P Value
Age at diagnosis, yr		
<60	1.00	0.028
≥60	2.41 [1.10−5.30]	
Tumor size, cm		
≤2	1.00	
>2	2.28 [1.11−4.65]	0.024
PR status		
Positive	1.00	0.329
Negative	1.45 [0.69−3.09]	

CI = confidence interval, PR = progesterone receptor.

TABLE 3. Matching Criteria of Male and Female Breast Cancer Patients

Characteristics	MBC, n = 260 (%)	FBC, n = 1300 (%)	P Value
Year of diagnosis			
1981−1990	4 (1.5)	21 (1.6)	
1991−2000	67 (25.8)	326 (25.1)	
2001−2009	189 (72.7)	953 (73.3)	0.970
Age at diagnosis, yr			
Mean ± SD	56.2 ± 12.0	56.2 ± 11.9	
Median (range)	57.0 (29−83)	57.0 (28−86)	0.928
Tumor stage			
Tis	15 (5.8)	75 (5.8)	
T1	152 (58.5)	760 (58.5)	
T2	87 (33.5)	435 (33.5)	
T3	5 (1.9)	25 (1.9)	
T4	1 (0.4)	5 (0.4)	ns
Nodal stage			
pN0	156 (60.0)	780 (60.0)	
pN+	94 (36.2)	470 (36.2)	
Unknown	10 (3.8)	50 (3.8)	ns
AJCC stage			
0−I	114 (43.8)	570 (43.8)	
II−III	136 (52.3)	680 (52.3)	
Unknown	10 (3.8)	50 (3.8)	ns
ER status			
Negative	22 (8.5)	110 (8.5)	
Positive	161 (61.9)	805 (61.9)	
Unknown	77 (29.6)	385 (29.6)	ns
PR status			
Negative	36 (13.8)	180 (13.8)	
Positive	147 (56.5)	735 (56.5)	
Unknown	77 (29.6)	385 (29.6)	ns
c-erbB2 (IHC)			
0	63 (24.2)	315 (24.2)	
1+	40 (15.4)	200 (15.4)	
2+	24 (9.2)	120 (9.2)	
3+	21 (8.1)	105 (8.1)	
Unknown	112 (43.1)	560 (43.1)	ns

AJCC = American Joint Committee on Cancer, ER = estrogen receptor, IHC = immunohistochemistry, ns = not significant, PR = progesterone receptor, SD = standard deviation.

months and the mortality rate was 21.7% at the end of the follow-up period (Table 1).

The 5-year OS rate was 85.9% and the 10-year OS rate was 70.5%. The hazard ratio (HR) for OS in patients older than 60 years that is a median age, who had a tumor greater than 2 cm, and who were PR negative was significantly higher than for patients who did not have these characteristics. In multivariate analyses, age and tumor size were prognostic factors of OS in MBC cases (Table 2).

Matched-Pair Analysis With MBC and FBC Cases

According to the above-mentioned matching procedure that is based on 7 matching criteria, 260 male patients were matched to 1300 female patients for survival analysis. Table 3 shows the tumor characteristics for matching. The median age at diagnosis was approximately 57 years (29−83 years for men and 28−86 years for women). Almost 60.0% of the male patients had early tumor stages (pTis, pT1). Lymph node metastases were found in 36.2% of male patients. ER and PR expression among MBC patients was positive in 61.9% and 56.5% of cases, respectively. In many cases, we do not know the HER2 receptor status, but the negative ratio was approximately 24%. In Table 4, we present a list of nonmatched tumor characteristics and treatment features that were also obtained from the database (Table 4). There were significant differences between male and female patients for operation method, tumor location, pathology, radiation therapy, and hormone therapy agent. MBCs were primarily treated with mastectomy, whereas the proportion of mastectomies in females was 57.7% (P <0.001). There was no significant difference in the frequency of axillary surgery between the 2 groups. Tumors were located in the center of the breast in 41.5% of MBC cases and 9.2% of FBC cases; about 65% of the tumors in FBC were located in the peripheral quadrant (P <0.001).

Less than 15% of males patients received adjuvant radiotherapy, whereas more than 30% of female patients did (P <0.001). No significant differences according to adjuvant systemic treatment were observed between male and female patients (Table 4). Adjuvant hormone therapy was carried out for 53.5% of male patients; these treatments consisted of selective estrogen-receptor modulators (SERMs, tamoxifen, or toremifene) in 50.4% of cases and aromatase inhibitors (AI) were given to 1 patient. Most of the MBC patients who received hormone therapy were given SERMs (about 94%),

which is significantly higher than the SERMs treatment rate for FBC patients (about 68%) (P <0.001).

The median follow-up time for men and women was 78 and 80 months, respectively. We found no differences in OS among the matched pair comparisons of male and female breast cancer patients (Figure 4). The 5-year OS rates were 91.0% and 92.6% in men and women, respectively. The influence of the gender, patient's age, tumor stage, lymph node status, hormone receptor status, HER2 status, hormone therapy, and chemotherapy on OS was examined by univariate analysis. In the current study, more than 60 years of age, higher tumor stage, the lymph node positive status, negative PR status, HER2 status (3+ in IHC), and the patients without hormone therapy showed a trend to a decreased OS in the univariate analysis. To confirm the difference of gender on OS, in the multivariate analysis, the factors that were included were found to be a trend or significant prognostic factors in the univariate analysis. When MBC cases

TABLE 4. Nonmatched Tumor Characteristics and Treatment Features of Male and Female Breast Cancer Patients

Characteristics	MBC, n = 260 (%)	FBC, n = 1300 (%)	P Value
Operation (breast)			
Mastectomy	233 (89.6)	750 (57.7)	
Breast conserving surgery	26 (10.0)	533 (41.0)	
Unknown	1 (0.4)	17 (1.3)	<0.001
Operation (axilla)			
ALND	236 (90.8)	1113 (85.6)	
SLNB	12 (4.6)	56 (4.3)	
No operation	10 (3.8)	50 (3.8)	
Unknown	2 (0.8)	81 (6.2)	0.986
Laterality			
Right	106 (40.8)	504 (38.8)	
Left	111 (42.7)	530 (40.8)	
Unknown	43 (16.5)	266 (20.5)	0.978
Tumor location			
Central	108 (41.5)	119 (9.2)	
Peripheral quadrant	81 (31.2)	856 (65.8)	
Whole breast	0 (0.0)	3 (0.2)	
Unknown	71 (27.3)	322 (24.8)	<0.001
Pathology			
Invasive ductal carcinoma	234 (90.0)	974 (74.9)	
Invasive lobular carcinoma	4 (1.5)	21 (1.6)	
Ductal carcinoma in situ	12 (4.6)	58 (4.5)	
Others	10 (3.8)	5 (0.4)	
Unknown	0 (0.0)	242 (18.6)	<0.001
Metastatic node			
Mean ± SD	2.0 ± 4.6	1.9 ± 4.6	
Median (range)	0 (0–41)	0 (0–43)	0.998
Total harvest node			
Mean ± SD	15.5 ± 8.6	13.6 ± 8.6	
Median (range)	15.0 (0–47)	13.0 (0–68)	0.003
Adjuvant radiotherapy			
No	132 (50.8)	418 (32.2)	
Yes	38 (14.6)	409 (31.5)	
Unknown	90 (34.6)	473 (36.4)	<0.001
Adjuvant systemic therapy			
Chemotherapy[*]	122 (46.9)	561 (43.2)	0.297
Hormone therapy[*]	139 (53.5)	676 (52.0)	0.974
SERMs	131 (94.2)	461 (68.2)	
AI	1 (0.7)	106 (15.7)	
Unknown	7 (5.0)	109 (16.1)	<0.001
No therapy	7 (2.7)	46 (3.5)	
Unknown	77 (29.6)	397 (30.5)	
Follow-up time, mo			
Mean ± SD	88.0 ± 52.7	90.1 ± 55.1	
Median (range)	78.3 (8.8–363.6)	80.0 (2.7–363.7)	0.744
Status at end of follow-up			
Alive	226 (86.9)	1158 (89.1)	
Dead	34 (13.1)	142 (10.9)	0.316
Cause of mortality			
Breast cancer	13 (38.2)	64 (45.1)	
Second primary cancer	3 (8.8)	14 (9.9)	
Other causes	4 (11.8)	14 (9.9)	
Unknown	14 (41.2)	50 (35.2)	0.855

AI = aromatase inhibitor, ALND = axillary lymph node dissection, SD = standard deviation, SERMs = selective estrogen receptor modulators, SLNB = sentinel lymph node biopsy.
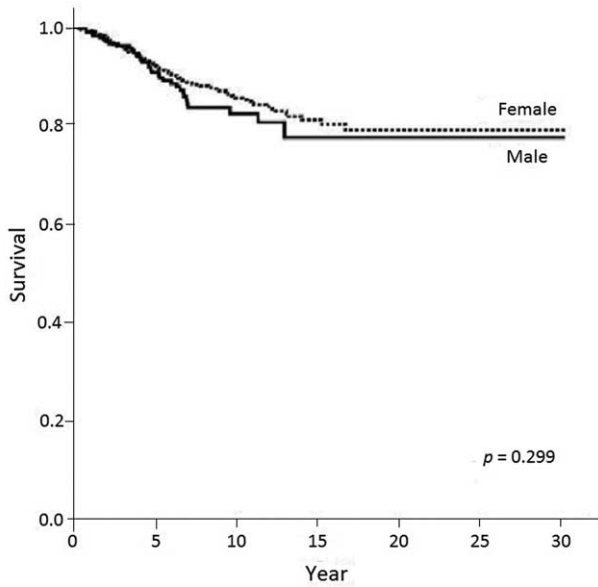[*]Contains duplicates performed.

FIGURE 4. Gender-specific overall survival of the matched-pair study group.

were compared to FBC cases, we found that the HR of male patients was not significantly different from 1.0; thus, there was no significant association between the sex of the patient and OS (Table 5).

DISCUSSION

Male breast cancer accounts for less than 1% of all breast cancers worldwide and is known to account for approximately 0.5% of all breast cancers according to previous reports. Since 1996, the Korean Breast Cancer Society (KBCS) has managed a nationwide breast cancer database through an online registration program, which has fostered an active increase in breast cancer studies based in Korea. In this study, examining previously published papers, we compared the features and the prognosis of MBC to those of FBC among Korean patients. Men accounted for about 0.4% of all breast cancer patients in Korea who received treatment during the study period. Rates of MBC vary greatly between countries. In Europe, the prevalence is approximately 1 per 100,000/year men,[7] while in the United States, MBC accounts for less than 1% of all breast cancers.[2,8] However, the prevalence is much higher in Nigeria at 8.6% of all breast cancers in men[9] and among Jewish men the preva-

TABLE 5. Survival Analysis by Cox Regressions and Stability of the Models Was Examined by Bootstrap Resampling

Variables	Univariate Analysis			Multivariate Analysis		
	Exp (B)	95% CI	P	Exp (B)	95% CI	P
Gender			0.300			0.436
Female	1			1		
Male	1.22	0.84−1.77		1.18	0.81−1.72	
Age at diagnosis, yr			0.002			0.010
<60	1			1		
≥60	1.60	1.19−2.16		1.95	1.42−2.68	
Tumor stage			<0.001			
pTis	1			1		
pT1	2.08	0.76−5.68		2.35	0.85−6.53	0.050
pT2	3.62	1.32−9.88		3.67	1.31−10.32	0.030
pT3	8.45	2.60−27.47		6.99	2.05−23.91	0.010
pT4	15.96	3.98−63.90		22.58	4.67−109.21	0.010
Nodal stage			<0.001			0.020
pN0	1			1		
pN+	2.01	1.49−2.70		1.54	1.10−2.15	
ER status			0.200			
Positive	1					
Negative	1.36	0.85−2.19				
PR status			0.032			0.644
Positive	1			1		
Negative	1.57	1.04−2.36		1.11	0.70−1.75	
c-erbB2 (IHC)			0.034			0.238
0−2+	1			1		
3+	1.83	1.05−3.21		1.38	0.73−2.60	
Hormone therapy			0.069			0.050
Yes	1			1		
No	1.50	0.97−2.33		1.60	0.99−2.59	
Chemotherapy			0.856			
Yes	1					
No	0.97	0.66−1.42				

CI = confidence interval.

lence is 2 to 3 per 100,000/year.[10] The average age of diagnosis for men worldwide varies among studies, although most patients are in their sixties or seventies, which is 5 to 10 years older than the average age of women when they are first diagnosed.[4,8,11] The median age of Korean male breast cancer patients was 60; among female Korean breast cancer patients, the median age at the time of first diagnosis was 50 in 2011.[12] The difference in peak age for FBC by region is dramatic: in Asian countries the median age for FBC is 40 to 50, while it is 60 to 70 in Western countries.[13] The age distributions for MBC and FBC in Korea are drastically different as well: there is a difference of more than 10 years between the peak age for MBC (60–69) and FBC (40–49) (Figure 1).[12,14]

Breast cancer is the second most common malignancy among Korean women. While FBC incidence has increased rapidly, an increasing trend was also seen in MBC occurrences by 2 or 5-year increments (Figure 2). However, because FBC incidence rates are increasing so rapidly compared with MBC rates, the proportion of men among all patients has actually decreased slightly. In a recent study of a Western population, the overall incidence of breast cancer decreased but the number of MBC cases, specifically, increased over the study period.[3,4] Social awareness of breast cancer has increased through efforts such as the pink-ribbon campaign, and this has raised awareness among men to pay attention to potential signs of breast cancer, to facilitate early diagnoses. Additionally, obesity and alcohol intake among men have been found to be associated with breast cancer risk because both of these activities can induce hyper-estrogenism, through local estrogen biosynthesis in adipocytes and alcohol-induced liver damage.[15] Patients' stages of MBC differed between reports. In general, male patients' prognoses were poorer than female patients because men have typically reached a higher stage by the time they receive a diagnosis.[16–18] When comparing the MBC stages from our study of Korean men to those from previous reports and other populations, the proportion of patients with cases lower than stage II was high among Korean men. In the paper on male breast cancer it was published in Korea, the ratio of lower than stage II was shown 63% to 84% and lower than T2 (Tis, T1, T2) was reported 75% to 100%.[19–23] This is slightly higher than what was announced in the West. Since the incidence of breast cancer is the top cancer in women, 10 years ago in Korea (current is the 1st excluding thyroid cancer), interest in breast cancer has increased rapidly. In addition, even men became concerned about breast cancer by actively promoting Pink-Ribbon Campaign in every year. Time of diagnosis in MBC was faster because of these causes, and we are guessing as higher the proportion of early breast cancer, the prognosis would have been even better. In fact, the 5- and 10-year survival rates of MBC have been reported in 1990 and 2008 in Korea, were improved from 57% to 85.6% and from 28% to 76%, respectively.[19] Total mastectomy was performed on more than 80% of male patients. Until recently, mastectomy was the strongly favored therapy for male breast cancer. This is in stark contrast to the rate of breast conserving surgeries (BCS) compared with mastectomy performed on female patients. For women, the proportion of BCS was only 18.7% in 1996, but by 2010, BCS was performed in 60% of FBCs, which was 20% more than mastectomies.[14] In response to patient demand, BCS and radiation therapy could be attempted when appropriate for MBC cases, but no studies have reported on treatment outcome.

The reported proportion of MBC cases who were positive for hormone receptor is in the range of 75% to 85% and, because this proportion was higher than women, and though their

proportion of ER positivity has been increasing, adjuvant hormone therapy after surgery has been shown to be effective.[1] However, according to recent several studies of the MBC, the molecular subgroup differed from the intrinsic subgroups described in FBC. Despite ER positive by immunohistochemistry (IHC), each subgroup showed a different correlation to genes associated with ER signaling and displayed unlike phenotype and prognosis. These findings suggest that men diagnosed with breast cancer may require novel treatment approaches than women.[24,25] In this study, the proportion of ER positivity for men was relatively high compared with that for women (84.5% and 77.5%, respectively), but we must consider that it was not possible to know the hormone receptor status of many cases. Hormone therapy was performed in approximately 87% of the total ER-positive MBC cases and about 80% of these patients were treated with tamoxifen. Although there is limited data regarding the efficacy of tamoxifen in the adjuvant setting of hormone therapy in patients with MBC, the OS in MBC was significantly better with tamoxifen compared with an aromatase inhibitor (AI) in Germany in 2013.[26,27] In men, 80% of the estrogen is derived from peripheral aromatization of androgens and 20% is produced directly in the testes. This is the reason the insufficient suppression of estrogen level in men after treatment with AI. Given the rarity of MBC and the relative absence of research, there are no results about therapy efficacy but some researchers have reported that the survival rate improved in lymph-node positive patients after receiving adjuvant chemotherapy.[1] About 40% of MBC patients in Korea in our study received adjuvant chemotherapy.

We also compared MBC and FBC cases based on time of diagnosis, age at diagnosis, TN stage, and ER, PR, and HER2 IHC status. Among MBC cases, mastectomy was performed more often, the tumor was more likely to be located in the center of the breast, and the rate of IDC was significantly higher, compared with FBC cases. The percentage of adjuvant radiation therapy was significantly lower for men than women, which is thought to be due to the higher proportion of mastectomies performed for men. Adjuvant chemotherapy and hormone therapy between 2 groups were approached similarly.

In the past, the survival rate for MBC was lower than for FBC and many studies still find a lower survival rate for men.[28–31] However, other recent studies have found no statistically significant differences in survival between men and women.[19,32–34] Previous studies found that the significant prognostic factors for MBC were age at diagnosis, tumor size, and, most importantly, metastatic status of the axillary lymph node.[1,35] In our univariate analysis, we found that age at diagnosis, tumor size, and status of PR were the significant associations for Korean MBC cases. In multivariate analysis, the hazard ratios of survival in men, older than 60 years at diagnosis or who had tumors >2 cm were significantly greater, compared with lower than 60 years men or men with smaller tumors. Additionally, we found no significant relationship between prognosis and lymph node status. Results from a matching multivariate analysis with MBC and FBC in Germany found that advanced tumor size and a lack of PR expression were correlated with poor patient outcome and lower OS.[34] In a study published on Florida patients, there was no statistical relevance between OS and lymph node status, which is consistent with our study.[36] On the other hand, a recent study from Turkey found that the T stage and N stage were significant prognostic factors for OS.[37] To examine the differences in prognosis for MBC and FBC, we analyzed the survival rate by matching prognostic factors that were previously found to be

significant and other possible risk factors for poor prognosis of MBC. Not only were the corrected survival rates statistically different between the 2 matched groups; the survival rates before correction were not significantly different. Nevertheless, the HR tended to be higher in men than women.

The main limitations of the present study are its retrospective design and that there were many pieces of incomplete data, especially regarding hormone receptor and HER2 status. Therefore, many cases were excluded from our matching analyses. In addition, there is no variety of survival analysis to the lack of other significant data such as Ki-67. In the future, we want that more in-depth studies would be conducted by supplementation of these data. Another limitation is that other factors like smoking, drinking, and family history may affect the OS was insufficient. However, this study has several advantages. First, it offers a nationwide representation of Korean MBC cases that were registered by KBCS and it is the largest study of MBC in Asia. Second, the cohort is relatively homogenous.

CONCLUSION

We found that breast cancer for men is increasing, and the peak age of incidence is older in men than women. Only age at diagnosis and tumor size were independent prognostic factors for survival. There were no differences in OS in the matched pair comparison between male and female breast cancer patients, regardless of whether we corrected for stage and hormone receptor status. Based on the current study, further research is required to establish standard treatment guidelines of MBC in the future.

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