

Survival of Male Breast Cancer Patients: A Population-Based Study in Osaka, Japan

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Background: Little information is available on the survival of male breast cancer patients because the disease is extremely rare in men. Recent studies indicated there were no gender-differences in the 5-year survival if patients' age and stage were matched. However, this problem has rarely been studied in Japan.

Methods: Using the Osaka Cancer Registry's data, the 5-year survival was analyzed based on the reported 19 869 cases who lived in Osaka Prefecture excluding Osaka City and were diagnosed in 1975–1997, or who resided in Osaka City and were diagnosed in 1993–1997, because reliable follow-up information was available for them.

Results: Breast cancer in males accounted for 0.49% of all cases during 1975–1997. The 5-year relative survivals were 71.1% in men and 81.6% in women. The survival in males decreased over older groups due to a lower proportion of localized stage, but not in females. The survival of males in the regional stage was significantly lower than that of females (49.1 versus 73.7%, $P < 0.05$). Survival of males has increased since 1980–1984, while it has been stable in females. Compared with the survival of patients diagnosed in 1975–1979, male patients diagnosed in 1995–1997 had a noticeably lower risk of death after adjusting for age and cancer stage.

Conclusions: The results suggest male breast cancer patients at the regional stage had a worse 5-year survival rate compared to females. However, this gender-related difference seems to have disappeared with the increased survival of males during the 1990s. Further population-based studies are required with a greater number of male patients diagnosed after 1990.

Key words: male – breast cancer – survival – age – cancer stage

INTRODUCTION

Breast cancer in males is uncommon (1,2). It accounts for less than 1% of all breast cancers in Osaka, Japan (3). In contrast to the increasing age-standardized incidence rates for female breast cancer (4,5), the rates for male breast cancer have remained stable during the last three decades (3). Because of the low incidence rates in men, little information has been available on the survival of male breast cancer patients as compared with female breast cancer patients, although the number of male patients has increased.

It has long been believed that prognosis is worse for male breast cancer patients than female. As in women, an older age and a more advanced stage of disease at the time of diagnosis have consistently been associated with poor

survival in men with breast cancer (6–9). However, more recent studies, including a Japanese one where male patients were matched with female patients by age and stage, have shown almost an equal 5-year survival rate (10–12). In the Japanese study the number of subjects was less than 20 and there have been few population-based studies on the survival of male breast cancer patients in Japan (3). In the present study, therefore, we tried to estimate the 5-year survival of male breast cancer patients in Osaka, Japan, and compared it with that of a female study, taking age and stage at diagnosis into consideration.

SUBJECTS AND METHODS

DATA SOURCES

Individual data on 19 869 reported cases of breast cancer (ICD Tenth Revision, C50) were retrieved from the Osaka Cancer Registry's database for analysis of survival. The

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patients lived in Osaka Prefecture excluding Osaka City and were diagnosed with breast cancer in 1975–1997; or resided in Osaka City and were diagnosed in 1993–1997, since active follow-up information was available for them. Details of the Osaka Cancer Registry (OCR) have been described elsewhere (4). Briefly, it has been operating since 1962, covering all of the Osaka Prefecture (population: 8.8 million in 2000 census), and it has enabled the preparation of long-term trends of incidence with reliable accuracy (13). The proportion of death certificate only (DCO) cases was 6.0% in men and 3.1% in women in 1975–1997. In the case of multiple tumors, only the first was included in the survival analyses and patients diagnosed with carcinoma *in situ* were excluded. A total of 543 cases (2.7%) were lost to follow-up as of 5-years after diagnosis and were treated as censored at the latest date when they were confirmed as alive.

The cancer stage at diagnosis was classified into the following three groups (i) localized: cancer is confined to the original organ, (ii) regional: cancer spreads to regional lymph nodes and/or spreads to immediately adjacent tissues, (iii) distant: cancer metastasizes to distant organs. These stages were roughly defined as follows if expressed by the TNM system (TNM Classification of Malignant Tumors):

- i) Localized: T1–3. N0. M0.
- ii) Regional: T4, and/or N1–3. M0.
- iii) Distant: Tany. N3c (supraclavicular nodes), and/or M1.

STATISTICAL ANALYSIS

Distributions of patients' characteristics were assessed with χ^2 tests for categorical variables. The cumulative observed survival was estimated using the Kaplan–Meier method, by gender. Survival time was computed from the date of the first diagnosis to the endpoint, defined as death from any cause. The closing date was defined as the date after 5 years from the first diagnosis. The relative 5-year survival was calculated as described in the previous papers (14,15). The prognostic factors were evaluated by a Cox proportional hazards regression model. In this analysis, the dependent variable was vital status 5 years after diagnosis and independent variables were age, cancer stage (localized, regional, distant and unknown) and the diagnosed year. Differences were considered as statistically significant if *P* values were less than 0.05 in the two-sided test. Data management and statistical analyses were conducted with STATA (16).

RESULTS

The number of male breast cancer cases was 97, or 0.49% of all study subjects (19 869). A profile of the study subjects is given in Table 1. The mean age at diagnosis for males (62.5 years; median 63 years) was significantly higher than that for females (53.0 years; median 51 years). Proportions of older age groups (60 years and older) among males were remarkably more than among females. Stage distributions were not significantly different between males and females. The

distribution of histological types did not differ markedly by sex, while the proportion of Paget's disease was not seen in males.

Table 2 compares the relative 5-year survival between males and females, according to age and stage at diagnosis. The survival rates for men and women were 71.1% (95% confidence interval (CI) 69.9–72.3) and 81.6% (95%CI 81.0–82.2), respectively. The survival rate decreased with older age among males (82.6/69.6/66.9% in 50–59/60–69/70+ years), but not among females. The 5-year survival rate for cases with localized stage were more than 94.0% among both males and females, whereas the survival

Table 1. Characteristics of patients with breast cancer

	Male (n = 97)	Female (n = 19772)	<i>P</i> -value
Age (years)			<0.01
0–49	14* (14.4) [†]	9130 (46.2)	
50–59	21 (21.7)	4983 (25.2)	
60–69	34 (35.1)	3288 (16.6)	
70 +	28 (28.9)	2371 (12.0)	
Cancer stage			0.37 [‡]
Localized	47 (48.5)	9869 (49.9)	
Regional	32 (33.0)	7702 (39.0)	
Regional lymph nodes involved	27 (27.8)	7102 (35.9)	
Direct extension	5 (5.2)	600 (3.0)	
Distant	8 (8.3)	1107 (5.6)	
Unknown	10 (10.3)	1094 (5.5)	
Histological type			0.54
Invasive carcinoma	73 (75.3)	15819 (80.0)	
Invasive ductal carcinoma	13 (13.4)	1665 (8.4)	
Papillotubular carcinoma	14 (14.4)	4116 (20.8)	
Solid-tubular carcinoma	13 (13.4)	2506 (12.7)	
Scirrhus carcinoma	9 (9.3)	3474 (17.6)	
Special types	24 (24.7)	4058 (20.5)	
Paget's disease	0 (0.0)	74 (0.4)	
Others	14 (14.4)	2099 (10.6)	
Unspecified cancer	10 (10.3)	1780 (9.0)	
Diagnosed year			0.076
1975–1979	13 (13.4)	1849 (9.4)	
1980–1984	9 (9.3)	2926 (14.8)	
1985–1989	29 (29.9)	4150 (21.0)	
1990–1994	26 (26.8)	5775 (29.2)	
1995–1997	20 (20.6)	5072 (25.7)	

*Number of patients.

[†]Figures inside parentheses were proportions among total number of patients.

[‡]The distributions of cancer stage were assessed with chi-square tests excluding unknown category.

Table 2. Relative 5-year survival for patients with breast cancer

	Male		Female		P-value*
	Relative 5-year survival	Standard error	Relative 5-year survival	Standard error	
All	71.1	6.0	81.6	0.3	0.08
Age (years)					
0–49	62.4	13.6	83.2	0.4	0.13
50–59	82.6	9.0	78.3	0.6	0.63
60–69	69.6	9.5	82.0	0.8	0.19
70 +	66.9	15.7	82.5	1.2	0.32
Cancer stage					
Localized	94.1	6.1	95.4	0.3	0.83
Regional	49.1	11.4	73.7	0.5	<0.05
Distant	13.5	13.5	17.4	1.2	0.77
Unknown	48.5	19.2	78.8	1.4	0.12

*Relative 5-year survival among males was evaluated as compared with females.

Table 3. Relative 5-year survival stratified by stage and age for breast cancer

	Male			Female			P-value*
	No	Relative 5-year survival	Standard error	No	Relative 5-year survival	Standard error	
Localized stage							
0–59	21	91.8	6.6	6949	94.8	0.3	0.65
60+	26	91.9	10.1	2920	96.8	0.7	0.63
Regional stage							
0–59	11	51.2	16.5	5675	73.8	0.6	0.17
60+	21	47.5	15.3	2027	73.6	1.2	0.09
Distant stage							
0–59	1	—	—	742	17.0	1.4	—
60+	7	15.5	15.4	365	18.5	2.2	0.85
Unknown stage							
0–59	2	—	—	747	80.5	1.5	—
60+	8	47.3	22.3	347	75.2	3.0	0.21

*Relative 5-year survival among males was evaluated as compared with females.

for cases with the regional stage was significantly lower among males than females (49.1 versus 73.7%, $P < 0.05$). There was no significant difference in the survival for cases with the distant stage.

Table 3 compares the gender-specific relative 5-year survival between younger (0–59 years old) and older age (60+ years old) groups according to the stage. Within the same gender and stage, there was no remarkable difference in the survival between the two age groups. The survivals of

male breast cancer patients with regional stage were 51.2% for younger age group and 47.5% for older age group, respectively.

Figure 1 indicates the trends of relative 5-year survival by sex during 1975–1997. The survival of males has increased since 1980–1984, while it has been stable in females. Considering age and stage, male patients diagnosed in 1995–1997 had notably low risk of death as compared with the survival of patients diagnosed in 1975–1979 (Table 4).

DISCUSSION

Breast cancer in males accounted for not more than 0.5% of all breast cancer occurrences in Osaka during 1975–1997. Its relative 5-year survival was generally lower than that of breast cancer in females. However, the survival has increased since 1980–1984. The risk of death among male patients has decreased remarkably. The improvement of male breast cancer survival may be explained by the fact that the superficial and rudimentary nature of male breast tissue makes the diagnosis of palpable breast disease easier. In addition, men

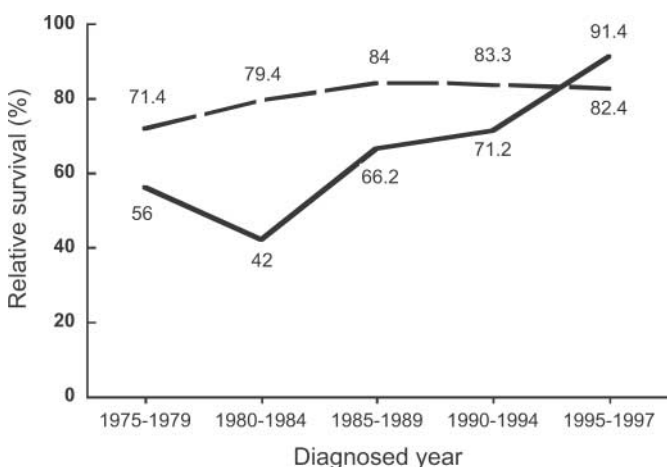


Figure 1. Trends of relative 5-year survival by gender during 1975–1997. Survival in males (solid line) has increased, while it in females (dashed line) has been stable.

might seek treatment earlier in the disease course, as implied in the increased number of male breast cancer cases.

More recent studies have indicated that survival of male breast cancer patients is almost equivalent to female breast cancer patients if age and stage at diagnosis are matched (10–12). However, this study suggests that male breast cancer patients with regional stage had a notably worse relative 5-year survival compared with females at the corresponding stage. Survivals of breast cancer patients with both ipsilateral regional lymph nodes involved and regional direct extension, classified as regional stage in males, also tended to be lower than in females. The worse survival in males has been attributed to the advanced stage at presentation and a higher incidence of lymph node involvement (7,17,18). Joshi et al. (19) reported that the gender-difference effect on prognosis might be the result of anatomical differences between male and female breasts: sparseness of breast tissue in men might facilitate dermal lymphatic spread and early regional and distant metastasis in tumors in close proximity to both the overlying skin and the underlying pectoral fascia. Dermal lymphatic involvement is much more common in male breast cancer compared with female breast cancer. Therefore, further investigation is required on gender-difference in the study of lymph node metastases in the stages II or III through to a more detailed cancer staging, which usually is not available in the population-based cancer registries.

The current study has shown differences of age factor for breast cancer survival between men and women: the 5-year survival decreased with increasing age only in men. The proportion of cases with localized stage also decreased with older

Table 4. Hazard ratios by the characteristics of patients with breast cancer

	Crude hazard ratio	95% CI*	Adjusted hazard ratio [†]	95% CI	Adjusted hazard ratio [‡]	95% CI
<i>Male</i>						
Diagnosed year						
1975–1979	1.0		1.0		1.0	
1980–1984	1.5	0.5–4.6	1.0	0.3–3.1	1.0	0.3–3.4
1985–1989	0.8	0.3–2.1	0.7	0.2–1.8	0.6	0.2–1.8
1990–1994	0.7	0.2–1.9	0.5	0.2–1.4	0.7	0.2–1.9
1995–1997	0.3	0.1–1.2	0.2	0.1–0.9	0.2	0.05–0.8
<i>Female</i>						
Diagnosed year						
1975–1979	1.0		1.0		1.0	
1980–1984	0.7	0.6–0.8	0.7	0.6–0.8	0.8	0.7–0.9
1985–1989	0.6	0.5–0.6	0.6	0.5–0.6	0.6	0.5–0.7
1990–1994	0.6	0.5–0.6	0.5	0.5–0.6	0.6	0.6–0.7
1995–1997	0.6	0.6–0.7	0.6	0.5–0.6	0.6	0.6–0.7

*Confidence interval.

[†]Hazard ratio adjusted by age.

[‡]Hazard ratio adjusted by age and cancer stage.

age among men, while it was stable among women. The stage of disease (e.g. tumor size and lymph node status) has been shown to be a significant prognostic factor in both men and women with breast cancer, and lymph node involvement is a significant negative prognostic factor in male breast cancer. A previous series (8,20) reported seemingly higher breast cancer-specific survivals in males compared with the overall survival. El-Tamer et al. (6) also reported that men had a significantly better disease-specific survival than women, as with increasing age other diseases and malignancies are more prevalent and result in more deaths in male than in female patients of a similar age and stage of disease at diagnosis. We suggest that an advanced stage at the time of diagnosis could explain the worse survival. However, it is also possible that in older age groups the worse survival is the result of co-morbidities, which accumulate with advancing age and therefore are more likely to kill a patient before breast cancer.

The study limitations should be considered before accepting any of our conclusions. First, the gender-difference of survival might have been influenced by stage migration as well as insufficient adjustment for cancer stage distribution: the proportion of an unknown stage was about 10/5% among male/female breast cancer patients and our staging system was not based on the TNM classification. A former study (21) reported that age-corrected relative survival was equivalent for men and women with stages 0, I and II, but was worse for men with stages III and IV than for women. Part of the regional stage in our study matches with the stage III considered as locally advanced breast cancer (22), therefore, stage III should be taken into consideration in analysis of the gender-difference of survival. In addition, the 5-year survival time may be too short. In our study, the survival curve in 46 males diagnosed with breast cancer in 1980–1992 becomes stable five years after the diagnosis, while the survival curve in 9801 females continues to decrease with increased time from the diagnosis. Therefore, we need further study to consider longer survival times using data that includes a higher number of male patients. As we reported some limitations of analyzing the OCR's database in a prior study, we also need to take into consideration the co-morbidities, completeness of reporting to the cancer registry and using only OCR's data – not the national population-based cancer registry data.

In conclusion, the results indicate that there were statistically significant differences of survivals for breast cancer with regional stage between men and women regardless of their age. This gender-difference, however, might have disappeared as a result of increase of the survival in males in the 1990s. We believe that population-based studies should be carried out with a higher number of male patients diagnosed after 1990 in order to further analyze the gender-difference of survivals, where more consideration will be given to detailed staging and matching with the regional stage.

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