Original Article

Matched-pair long-term survival analysis of male and female patients with breast cancer: a population-based study

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Background: Previous studies found that the long-term survival of male breast cancer patients differed from those of female patients, however, the conclusions were contradictory. We conducted the study to examine the sex disparity in breast cancer survival by carefully controlling demographic and clinical factors using data from the Shanghai Cancer Registry (SCR).

Methods: Every male breast cancer patient was matched with four female patients by the diagnosis year, age, stage, and histology. We used Kaplan-Meier survival estimates to calculate the cumulative observed overall survival (OS) and cancer-specific survival (CSS) rates and log-rank tests to compare the survival rates by sex. We used Cox proportional-hazards regression models to assess the association between sex and risk of death.

Results: A total of 50,958 patients with breast cancer (0.85% male) were registered in the SCR between 2002 and 2013. After matching, 434 male and 1,736 female patients were included in the study. With a median follow-up of 10 years, men with breast cancer showed worse OS (P<0.001) and CSS (P<0.001) than did women. The 5- and 10-year OS rates for male and female patients were 67.27% and 77.75%, and 45.95% and 62.60%, respectively; the 5- and 10-year CSS rates for male and female patients were 70.19% and 79.79%, and 50.57% and 67.20%, respectively. Compared with women, men had 65% increased risk of overall death [95% confidence interval (CI): 1.42–1.92] and 70% increased risk of cancer-specific death (95% CI: 1.44–2.00).

Conclusions: This study found male patients with breast cancer had poorer long-term survival than women in China.

Keywords: Male breast cancer; female breast cancer; long-term survival; matched-pair analysis

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Introduction

The incidence of breast cancer in males is much lower than that in females, representing 0.6–1.6% of all breast cancers (1-3). In general, men tend to be diagnosed with breast cancer approximately 10 years later than women, reaching a peak at the age older than 65 years (2-4). Data from the Surveillance, Epidemiology, and End Results (SEER) program showed that men are more likely to be diagnosed

at a higher stage of breast cancer than women (1,5). Furthermore, studies have found the biological differences between male and female breast cancer (6-8).

Previous studies found that the survival rates of male breast cancer patients differed from those of female patients; however, the conclusions were contradictory (1). Studies from North America and European countries have suggested that male patients have a similar or even better survival than female patients with breast cancer (3,9), while worse survival was observed in most studies in China (2,10-13). Moreover, because of the rarity of male breast cancer, most survival studies used data obtained from small, single-institutional, or retrospective studies in China (10-14), with only one analysis conducted at the population-based level but a small sample size of male breast cancer patients (2), which limited the interpretability. Additionally, given the distinct characteristics of male and female breast cancer cases, such as age, tumor-node-metastasis (TNM) stage, and histological subtype, which are crucial for the prediction of survival, the matched-pair method could serve as an important study design to investigate the potential sex disparity in the survival of breast cancer.

To better understand the sex heterogeneity in the survival of patients with breast cancer in China. Based on the Shanghai Cancer Registry (SCR), the oldest cancer registry in China and one of the largest single cancer registries in the world, we conducted the current sex-comparative study to explore the difference in survival between male breast cancer patients and matched female breast cancer patients. We present this article in accordance with the STROBE reporting checklist (available at https://tbcr.amegroups.org/article/view/10.21037/tbcr-24-3/rc).

Highlight box

Key findings

- This is the largest sex-specific survival study on breast cancer in China, and the results may help to better understand the sex disparity in breast cancer.

What is known and what is new?

- The incidence of breast cancer in males is much lower than that in females.
- We reported the sex heterogeneity in the survival of patients with breast cancer in China.

What is the implication, and what should change now?

- Male patients with breast cancer had poorer long-term survival than women in China.

Methods

Study population and data collection

Breast cancer cases were derived from the SCR database, one of the largest cancer registries globally, and an associate member of the International Association of Cancer Registries (IARC). The complete cancer incidence and mortality data for urban and suburban areas have been collected since the year 2002, covering an average of 14 million permanent residents in Shanghai. The vital status of cancer cases was tracked via active and passive follow-up, the death information was obtained from the Vital Statistics Section of the Shanghai Municipal Center of Disease Control and Prevention by data linkage, and the survival and treatment information were collected by the community health service through home visits. Our previous study provided detailed information on the high quality of the cancer registry data in SCR (15). Overall, the well-organized follow-up system resulted in a follow-up rate of more than 99% for Shanghai's cancer cases (16,17).

Between 2002 and 2013, 434 men and 50,524 women were registered in the SCR as breast cancer cases. The current study included all male cases registered with primary breast cancer diagnosed between 2002 and 2013 who were followed up until death or December 31, 2019. Every male case was matched with four female cases from the original dataset. Age, the year of diagnosis, clinical stage at the time of diagnosis, and histological subtype, as confounding factors in breast cancer prognosis, could all have influenced the results of the analysis. Therefore, matching was used to control for potential confounding from, i.e., age (within ±3 years), year of diagnosis (within ±4 years), tumor stage (I, II, III, IV, and unknown), as well as histological subtype [infiltrating ductal carcinoma (IDC), others, and unknown]. If more than four female patients were eligible, the best matches were chosen by random selection; if fewer than four female patients were available for matching, all of them were selected. The matching procedure was conducted in a blinded manner without any information about the patient's outcomes.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional ethics board of Fudan University Shanghai Cancer Center (No. 2106237-19) and the data used in this study were derived from a de-identified

SCR database, and thus informed consent was exempt from the Institutional Review Board approval.

Statistical analysis

For male and all female breast cancer cases, the 5-year relative survival (RS) rates were calculated as the ratio of the net cancer-specific survival (CSS) rate to the expected rate, which was estimated from the general sex and calendar period-specific life tables for Shanghai residents using the Ederer II method (18). For male and matched female breast cancer cases, cumulatively observed overall survival (OS) and CSS rates were calculated using Kaplan-Meier survival estimates, and log-rank tests were applied to compare the survival rates of male and matched female cases. In addition, the 5-year OS and CSS rates were reported for these patients, while data of patients diagnosed during 2002–2009 who were followed for at least 10 years were used for calculating 10-year OS and CSS. Cox proportional-hazards regression models were used to assess the hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between sex and the risk of OS and CSS for male and matched female patients. Matching was accounted for in the Cox proportional hazards models by including a matching variable based on age, year of diagnosis, tumor stage, and histological subtype in the analysis. Analyses were conducted using SAS statistical software (version 9.4). All statistical tests were two-sided, and a P value <0.05 was considered "statistically" significant.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author (C.F.). The data are not publicly available due to privacy and ethical restrictions.

Results

After excluding 18 (0.035%) cases without death date and 35 (0.069%) cases that were only recognized by death certification, 434 male and 50,471 female new breast cancer cases diagnosed from 1 January 2002 to 31 December 2013 among all population in Shanghai were included in the study. Based on the matching procedure and four matching criteria, 434 male cases were 1:4 matched with 1,736 female cases were available for survival analyses. A large number of male breast cancer cases in this study had missed information regarding TNM stage (45.16%) and histologic subtype (26.50%), which may lead to the unprecise estimates of breast cancer survival. By December 31, 2019, 914 patients (231 men and 683 women) died, including 752 (196 men and 556 women) who died of cancer.

Table 1 shows the distribution of male, matched female, and all-female breast cancer cases according to the matching criteria and other characteristics. Compared with all female breast cancer cases in Shanghai, the male patients were nearly 10 years older at the time of diagnosis (mean age at diagnosis: 66.06 *vs.* 57.27 years, P<0.01), they were more frequently diagnosed with higher TNM stage (stage III–IV: 71/238 *vs.* 7,737/35,708) and more frequently with unknown TNM information (45.16% *vs.* 29.32%, P<0.01); the histology information was available for 73.5% of the male breast cancer cases, and the proportion of IDC was lower for male cases than female cases (54.38% *vs.* 70.70%, P<0.01); after matching, the difference disappeared.

The 5-year RS rates for male and all-female breast cancer patients diagnosed in Shanghai between 2002 and 2013 were 83.30% (83.22–83.37%) and 86.55% (86.55–86.56%), respectively (data not shown). After matching, men with breast cancer showed significantly worse OS (P<0.001) and CSS (P<0.001) than female patients, with a median follow-up time of 10 years (*Figures 1*,*2*).

The 5-year OS rates for male and matched female breast cancer patients were 67.27% (95% CI: 62.57–71.51%) and 77.75% (95% CI: 75.70–79.66%), respectively; and the 5-year CSS rates for male and matched female breast cancer patients were 70.19% (95% CI: 65.52–74.35%) and 79.79% (95% CI: 77.79–81.64%), respectively. Stratification analysis showed that men younger than 70 years old, with early TNM stage (stage I–II), and diagnosed as IDC subtype had better survival than men older than 70 years of age, with late TNM stage, and other histological subtypes (*Table 2*).

When restricted to cases diagnosed during 2002–2009, the median follow-up time was 13 years. The 10-year OS rate for male and female breast cancer patients was 45.95% (95% CI: 39.85–51.82%) and 62.60% (95% CI: 59.62–65.42%), respectively; and the 10-year CSS rates for male and matched female breast cancer patients were 50.57% (95% CI: 44.27–56.53%) and 67.20% (95% CI: 64.26–69.96%), respectively. The results of the stratification analysis are shown in *Table 3*.

Table 4 presents the results of a Cox proportional-hazards analysis for the association between sex and survival. Compared with women, the overall results showed that men had a 65% increased risk of overall death (95% CI: 1.42–

Table 1 Characteristics of male patients and female breast cancer patients diagnosed during 2002–2013 in Shanghai, China

Characteristics	Men	Matched women[†]	All women	P[‡]
Total, n	434	1,736	50,524	
Age at diagnosis (years), mean ± SD	66.06±13.44	65.91±13.34	57.27±12.87	<0.01
Age group (years), n (%)				<0.01
<50	50 (11.52)	201 (11.58)	15,120 (29.93)	
50–59	90 (20.74)	376 (21.66)	16,527 (32.71)	
60–69	92 (21.20)	374 (21.54)	9,096 (18.00)	
70–79	130 (29.95)	513 (29.55)	6,680 (13.22)	
≥80	72 (16.59)	272 (15.67)	3,101 (6.14)	
Diagnosed year, n (%)				0.057
2002–2005	148 (34.10)	592 (34.10)	14,599 (28.90)	
2006–2009	130 (29.95)	520 (29.95)	16,614 (32.88)	
2010–2013	156 (35.94)	624 (35.94)	19,311 (38.22)	
TNM stage, n (%)				<0.01
I	79 (18.20)	316 (18.20)	12,428 (24.60)	
II	88 (20.28)	352 (20.28)	15,543 (30.76)	
III	40 (9.22)	160 (9.22)	4,493 (8.89)	
IV	31 (7.14)	124 (7.14)	3,244 (6.42)	
Unknown	196 (45.16)	784 (45.16)	14,816 (29.32)	
Histology, n (%)				<0.01
IDC	236 (54.38)	944 (54.38)	35,718 (70.70)	
Others	83 (19.12)	332 (19.12)	6,279 (12.43)	
Unknown	115 (26.50)	460 (26.50)	8,527 (16.88)	
Vital status, n (%)				
Dead	231 (53.23)	683 (39.34)	15,576 (30.83)	<0.01
Dead due to cancer	196 (45.16)	556 (32.03)	13,627 (26.97)	<0.01
Without any follow-up, n (%)	0	0	18 (0.036)	
Cases recognized by death certificate only, n (%)	0	0	35 (0.069)	

[†], there were no significant differences among men and the matched women (all P>0.05); [‡], P value for the difference between men and all women breast cancer cases. SD, standard deviation; TNM, tumor-node-metastasis; IDC, infiltrating ductal carcinoma.

1.92) and 70% increased risk of cancer-specific death (95% CI: 1.44–2.00). In the stratification analyses, the hazard of overall or cancer-specific death was greater for men younger than 70 years old (HR: 2.02, 95% CI: 1.54–2.63; HR: 2.07, 95% CI: 1.57–2.74, respectively); men with early-stage (stage I–II) breast cancer (HR: 1.89, 95% CI: 1.40–2.56; HR: 2.00, 95% CI: 1.44–2.79, respectively); men diagnosed in early period [2002–2005] (HR: 1.91, 95% CI: 1.52–2.40; HR: 2.04, 95% CI: 1.59–2.60, respectively); and men with histology subtypes other than IDC (HR: 2.64, 95% CI: 1.84–3.79; HR: 2.55, 95% CI: 1.71–3.80, respectively).

Discussion

To the best of our knowledge, this is the largest sex-specific survival study that considered the major established cancer

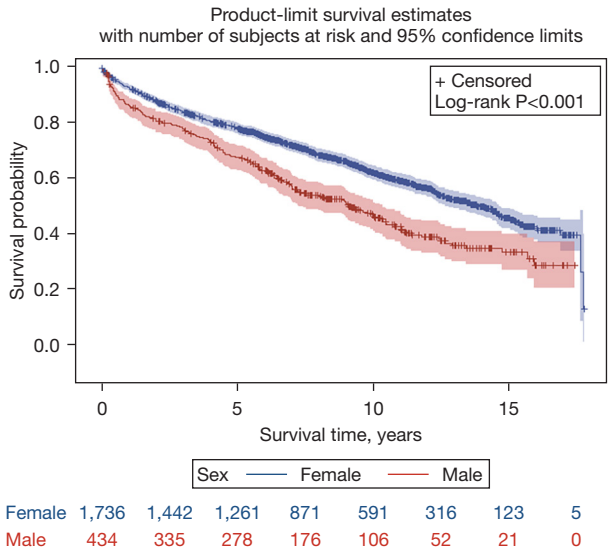

Figure 1 Observed OS of breast cancer patients diagnosed during 2002–2013 by sex. OS, overall survival.

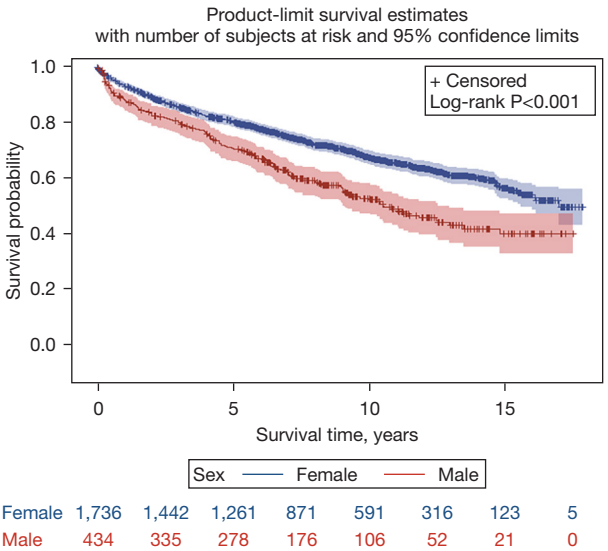

Figure 2 CSS of breast cancer patients diagnosed during 2002–2013 by sex. CSS, cancer-specific survival.

Table 2 Five-year observed OS and CSS rates of male and matched female breast cancer patients diagnosed during 2002–2013 by different characteristics

Characteristics	5-year OS rate (95% CI), %		5-year CSS rate (95% CI), %	
	Men	Women	Men	Women
All	67.27 (62.57–71.51)	77.75 (75.70–79.66)	70.19 (65.52–74.35)	79.79 (77.79–81.64)
Age group (years)				
<70	79.57 (73.69–84.28)	88.69 (86.47–90.56)	80.65 (74.81–85.27)	89.39 (87.22–91.21)
≥70	52.78 (45.59–59.45)	64.58 (61.09–67.85)	57.48 (50.13–64.14)	68.04 (64.58–71.25)
TNM stage				
I–II	84.99 (78.44–89.68)	90.86 (88.34–92.86)	86.75 (80.40–91.16)	93.28 (91.05–94.97)
III–IV	50.24 (37.89–61.37)	62.98 (57.01–68.37)	52.10 (39.50–63.29)	65.78 (59.79–71.11)
Unknown	57.31 (50.03–63.93)	69.66 (66.28–72.78)	62.45 (55.10–68.95)	73.69 (70.41–76.67)
Diagnosed year				
2002–2005	58.11 (49.74–65.58)	75.42 (71.73–78.69)	62.11 (53.58–69.52)	78.02 (74.43–81.17)
2006–2009	72.72 (64.13–79.59)	78.91 (75.13–82.18)	74.03 (65.46–80.78)	80.63 (76.92–83.80)
2010–2013	70.87 (62.78–77.51)	78.22 (74.64–81.35)	73.90 (65.91–80.30)	80.03 (76.54–83.06)
Histology				
IDC	75.62 (69.52–80.67)	84.55 (82.03–86.74)	77.43 (71.39–82.35)	85.56 (83.10–87.69)
Other	66.25 (54.74–75.48)	84.06 (79.61–87.61)	70.46 (58.92–79.32)	87.01 (82.83–90.23)
Unknown	48.98 (39.51–57.78)	57.30 (52.59–61.72)	52.97 (43.21–61.80)	60.97 (56.23–65.36)

OS, overall survival; CSS, cancer-specific survival; CI, confidence interval; TNM, tumor-node-metastasis; IDC, infiltrating ductal carcinoma.

Table 3 Ten-year observed OS and CSS rates of male and matched female breast cancer patients diagnosed during 2002–2009 by different characteristics

Characteristics	10-year OS rate (95% CI), %		10-year CSS rate (95% CI), %	
	Men	Women	Men	Women
All	45.95 (39.85–51.82)	62.60 (59.62–65.42)	50.57 (44.27–56.53)	67.20 (64.26–69.96)
Age group (years)				
<70	64.51 (55.85–71.90)	81.83 (78.41–84.77)	66.96 (58.32–74.21)	83.61 (80.28–86.42)
≥70	25.31 (18.10–33.14)	40.79 (36.46–45.07)	30.72 (22.44–39.37)	46.89 (42.30–51.35)
TNM stage				
I–II	64.57 (53.91–73.37)	83.95 (79.77–87.34)	69.31 (58.68–77.72)	87.08 (83.16–90.14)
III–IV	26.75 (15.19–39.75)	45.61 (38.62–52.31)	27.05 (15.21–40.35)	49.75 (42.45–56.61)
Unknown	37.81 (29.23–46.34)	53.42 (48.93–57.71)	43.52 (34.20–52.47)	57.22 (52.62–61.55)
Diagnosed year				
2002–2005	41.08 (33.10–48.88)	62.08 (58.00–65.89)	43.91 (35.56–51.94)	65.55 (61.47–69.32)
2006–2009	47.92 (38.40–56.80)	61.87 (57.37–66.05)	57.04 (47.38–65.58)	67.88 (63.46–71.89)
Histology				
IDC	56.36 (47.59–64.22)	68.76 (64.66–72.49)	59.89 (51.03–67.66)	75.11 (71.21–78.56)
Other	47.52 (34.26–59.64)	73.63 (67.47–78.81)	55.57 (41.46–67.56)	76.81 (70.72–81.79)
Unknown	23.15 (14.05–33.59)	41.73 (36.05–47.30)	25.73 (15.64–37.03)	45.81 (39.91–51.51)

OS, overall survival; CSS, cancer-specific survival; CI, confidence interval; TNM, tumor-node-metastasis; IDC, infiltrating ductal carcinoma.

and patient characteristics in breast cancer to elucidate potential sex-specific differences in the survival of breast cancer patients in China within a time span of more than 15 years. We found that the long-term survival rate of male patients with breast cancer is significantly lower compared to female patients after matching for age, year of diagnosis, TNM stage, and histological subtype.

Similar to previous reports, male patients in this study accounted for 0.85% of all patients with breast cancer and were more likely to receive a diagnosis at a later age and higher stage than female cases (1,3,19). Men in this study were less likely to be diagnosed with a ductal histologic type (54.38%), which is not consistent with previous findings reported by studies in the SEER database and from European countries (>75%) (1,20). A large number of missing histological cases in this study (26.50%) and the population difference might partially contribute to this gap.

Our matched-pair study showed that the survival rate of male breast cancer was significantly lower compared to female breast cancer, which was in line with the observations reported in the single-institute studies from Guangdong, Tianjin, and Shandong, showing a worse prognosis for male breast cancer patients both in overall and disease-free survival (10-13). Still, the population-based study from Hong Kong showed that male patients had poorer OS in an early stage but better breast-CSS compared with their female counterparts (2), however, given the limited number of male cases (n=132) and breast cancer-specific deaths (n=12), these results need to be further confirmed. The sample size is crucial in the analysis of population-based survival data. For instance, most US studies before the year 2015 showed similar OS rates for male and female breast cancer patients (9,21-23). However, the recent updated analysis in the SEER programs, and in the National Cancer Database, which comprised 16,025 men with breast cancer, revealed a significant survival disadvantage for male patients (19,24,25). The results from a worldwide study including 2,665 men diagnosed with breast cancer from five European countries and one country from southeast Asia were different from the findings of the present study, which revealed a better survival for male breast cancer patients than females after adjusting for region, time since diagnosis, age, and year of diagnosis, stage, and treatment (relative excess risk: 0.78, 95% CI: 0.62–0.97) (3), thus

Table 4 Cox proportional hazards regression analysis for the OS and CSS of male patients (*vs.* female patients)

Characteristics	Total, n	OS		CSS	
		Death, n	HR (95% CI)	Death, n	HR (95% CI)
Overall	434	231	1.65 (1.42–1.92)	196	1.70 (1.44–2.00)
Age subgroup (years)					
<70	232	81	2.02 (1.54–2.63)	75	2.07 (1.57–2.74)
≥70	202	150	1.55 (1.29–1.88)	121	1.52 (1.23–1.88)
TNM subgroup					
I–II	167	61	1.89 (1.40–2.56)	52	2.00 (1.44–2.79)
III–IV	71	54	1.73 (1.26–2.39)	49	1.84 (1.31–2.59)
Unknown	196	116	1.52 (1.23–1.88)	95	1.52 (1.20–1.91)
Diagnosed year					
2002–2005	148	103	1.91 (1.52–2.40)	91	2.04 (1.59–2.60)
2006–2009	130	66	1.43 (1.08–1.90)	54	1.46 (1.07–1.99)
2010–2013	156	62	1.55 (1.15–2.07)	51	1.50 (1.09–2.07)
Histology					
IDC	236	103	1.50 (1.20–1.88)	86	1.61 (1.26–2.07)
Others	83	47	2.64 (1.84–3.79)	38	2.55 (1.71–3.80)
Unknown	115	81	1.51 (1.17–1.95)	72	1.53 (1.16–2.00)

OS, overall survival; CSS, cancer-specific survival; HR, hazard ratio; CI, confidence interval; TNM, tumor-node-metastasis; IDC, infiltrating ductal carcinoma.

suggesting the regional diversity in the sex disparity of breast cancer survival. Several possible factors might explain the sex disparity in the breast cancer survival rate. First, the mutation prevalence, population-based studies have shown that the prevalence of breast cancer susceptibility gene 2 (*BRCA2*) mutations in men with breast cancer was 4–16% (26,27), which is slightly higher than that in women with breast cancer (around 4%) (28). A meta-analysis showed that *BRCA2* mutations are associated with worse OS among breast cancer patients (29). Second, the treatment patterns for men differed from that for women, although male breast cancer patients' management was mainly extrapolated from the knowledge about female breast cancer (30,31), compared with women, the compliance of adjuvant radiotherapy was lower for men among many countries (3), and more than 50% of men who were treated with breast-conserving surgery did not receive radiotherapy (4,32), which could explain the more obvious sex disparity among patients with early-stage breast cancer in our study. In addition, our results on the changes in risk of death for male breast cancer patients over time suggest the advancement of breast cancer treatment could narrow the survival gap between men and women but could not eliminate it. Third, the lifestyle risk factors that closely related to breast cancer survival, such as smoking and obesity, might be differently distributed among male and women breast cancer patients (33-35).

This study has several limitations that need to be pointed out. The major limitation is the lack of information on the specific cause of death (breast cancer, other cancers, cardiovascular disease, and others) and factors closely related to breast cancer survival, such as treatment strategies [breast surgery, (neo)adjuvant chemotherapy, adjuvant radiotherapy, adjuvant endocrine therapy, etc.], molecular subtypes [estrogen receptor (ER), progesterone receptor (PR), androgen receptor, human epidermal growth factor receptor 2 (HER2), etc.]. The linkage of population-based cancer registry database and hospital-based treatment database is expected in the future to eliminate this limitation. Currently, our work on the hospital-based cancer follow-up

in Fudan University Shanghai Cancer Center indicated that compared to females with breast cancer, males are more likely to be ER positive (91% *vs.* 70%), more likely to be PR positive (86% *vs.* 63%), less likely to be HER2 positive (5% *vs.* 24%). However, this hospital-based information is not linked to the current population-based data, and we believe that it would provide additional evidence to explain the sex disparity on breast cancer survival once they are linked. Also, lifestyle factors (smoking, body mass index, etc.) were not available in this study due to the deficiencies of cancer registry data. Second, by adjusting for multi-confounders, the relationship between sex and breast cancer survival may also be impacted by overmatching bias. Because of biological and genetic differences between male and female (such as less breast tissue in male), male breast cancer is typically associated with advanced stage and higher grade, which leads to a worse prognosis. After matching, the study may have reduced the effect of sex on prognosis, and the effect of sex on prognosis may be greater than the results of our study. The strengths of this study include the coverage of all residents in Shanghai, the well-established follow-up system of SCR, and the 17-year follow-up for overall and cancer-specific death, which enabled us to examine the differences in long-term survival rates among men and women diagnosed with breast cancer in Shanghai, China. Additionally, the analysis was conducted using the matched-pair approach and considering the established factors that could affect breast cancer survival (age, year of diagnosis, TNM stage, and histological subtype), reducing the major clinical and demographic bias in the survival analysis.

Conclusions

Our study provided further evidence that male patients with breast cancer have lower long-term survival rates than women in China, particularly younger patients and those at an early clinical stage. Future studies with more detailed clinical treatment, cancer subtype, and lifestyle information are needed to deepen the understanding of male breast cancer biology and identify the factors that could eliminate this sex disparity.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional ethics board of Fudan University Shanghai Cancer Center (No. 2106237-19) and the data used in this study were derived from a de-identified SCR database, and thus informed consent was exempt from the Institutional Review Board approval.

References

1. Liu N, Johnson KJ, Ma CX. Male Breast Cancer: An Updated Surveillance, Epidemiology, and End Results

Data Analysis. Clin Breast Cancer 2018;18:e997-e1002.
2. Kwong A, Chau WW, Mang OW, et al. Male breast cancer: a population-based comparison with female breast cancer in Hong Kong, Southern China: 1997-2006. Ann Surg Oncol 2014;21:1246-53.
3. Miao H, Verkooijen HM, Chia KS, et al. Incidence and outcome of male breast cancer: an international population-based study. J Clin Oncol 2011;29:4381-6.
4. Cardoso F, Bartlett JMS, Slaets L, et al. Characterization of male breast cancer: results of the EORTC 10085/ TBCRC/BIG/NABCG International Male Breast Cancer Program. Ann Oncol 2018;29:405-17.
5. Wang B, Wang H, Zhao A, et al. Poor prognosis of male triple-positive breast Cancer patients: a propensity score matched SEER analysis and molecular portraits. BMC Cancer 2021;21:523.
6. Vermeulen JF, Kornegoor R, van der Wall E, et al. Differential expression of growth factor receptors and membrane-bound tumor markers for imaging in male and female breast cancer. PLoS One 2013;8:e53353.
7. Gucalp A, Traina TA, Eisner JR, et al. Male breast cancer: a disease distinct from female breast cancer. Breast Cancer Res Treat 2019;173:37-48.
8. Fentiman IS. Male breast cancer is not congruent with the female disease. Crit Rev Oncol Hematol 2016;101:119-24.
9. Greif JM, Pezzi CM, Klimberg VS, et al. Gender differences in breast cancer: analysis of 13,000 breast cancers in men from the National Cancer Data Base. Ann Surg Oncol 2012;19:3199-204.
10. Liu D, Xie G, Chen M. Clinicopathologic characteristics and survival of male breast cancer. Int J Clin Oncol 2014;19:280-7.
11. Liu TT, Tong ZS, Hao CF, et al. Male breast cancer: a pairing comparison of survival with women breast cancer. Zhonghua Yi Xue Za Zhi 2010;90:3135-9.
12. Chen X, Liu X, Zhang L, et al. Poorer survival of male breast cancer compared with female breast cancer patients may be due to biological differences. Jpn J Clin Oncol 2013;43:954-63.
13. Baojiang L, Tingting L, Gang L, et al. Male breast cancer: A retrospective study comparing survival with female breast cancer. Oncol Lett 2012;4:642-6.
14. Xia LP, Zhou FF, Guo GF, et al. Chinese female breast cancer patients show a better overall survival than their male counterparts. Chin Med J (Engl) 2010;123:2347-52.
15. Huang Z, Zheng Y, Wen W, et al. Incidence and mortality of gynaecological cancers: Secular trends in urban Shanghai, China over 40 years. Eur J Cancer 2016;63:1-10.
16. Zhang M, Wu C, Gong Y, et al. Survival analysis of patients with lung cancer in Shanghai. China Oncology 2017;27:326-33.
17. Gong Y, Wu C, Zhang M, et al. Colorectal cancer survival analysis in major areas in Shanghai China. China Oncology 2015;25:497-504.
18. Ederer F, Axtell LM, Cutler SJ. The relative survival rate: a statistical methodology. Natl Cancer Inst Monogr 1961;6:101-21.
19. Wang F, Shu X, Meszoely I, et al. Overall Mortality After Diagnosis of Breast Cancer in Men vs Women. JAMA Oncol 2019;5:1589-96.
20. Foerster R, Foerster FG, Wulff V, et al. Matched-pair analysis of patients with female and male breast cancer: a comparative analysis. BMC Cancer 2011;11:335.
21. Hill TD, Khamis HJ, Tyczynski JE, et al. Comparison of male and female breast cancer incidence trends, tumor characteristics, and survival. Ann Epidemiol 2005;15:773-80.
22. El-Tamer MB, Komenaka IK, Troxel A, et al. Men with breast cancer have better disease-specific survival than women. Arch Surg 2004;139:1079-82.
23. Scott-Conner CE, Jochimsen PR, Menck HR, et al. An analysis of male and female breast cancer treatment and survival among demographically identical pairs of patients. Surgery 1999;126:775-80; discussion 780-1.
24. Wang Y, Chen K, Yang Y, et al. Incidence and survival outcomes of early male breast cancer: a population-based comparison with early female breast cancer. Ann Transl Med 2019;7:536.
25. Wang X, Liu S, Xue Y. Clinicopathological features and prognosis of male breast cancer. J Int Med Res 2021;49:3000605211049977.
26. Giordano SH. Breast Cancer in Men. N Engl J Med 2018;378:2311-20.
27. Pritzlaff M, Summerour P, McFarland R, et al. Male breast cancer in a multi-gene panel testing cohort: insights and unexpected results. Breast Cancer Res Treat 2017;161:575-86.
28. Kwong A, Shin VY, Ho JC, et al. Comprehensive spectrum of BRCA1 and BRCA2 deleterious mutations in breast cancer in Asian countries. J Med Genet 2016;53:15-23.
29. Zhu Y, Wu J, Zhang C, et al. BRCA mutations and survival in breast cancer: an updated systematic review and meta-analysis. Oncotarget 2016;7:70113-27.
30. Sousa B, Moser E, Cardoso F. An update on male breast cancer and future directions for research and treatment.

Eur J Pharmacol 2013;717:71-83.
31. Korde LA, Zujewski JA, Kamin L, et al. Multidisciplinary meeting on male breast cancer: summary and research recommendations. J Clin Oncol 2010;28:2114-22.
32. Leone JP, Leone J, Zwenger AO, et al. Locoregional treatment and overall survival of men with T1a,b,cN0M0 breast cancer: A population-based study. Eur J Cancer 2017;71:7-14.
33. Duan W, Li S, Meng X, et al. Smoking and survival of breast cancer patients: A meta-analysis of cohort studies. Breast 2017;33:117-24.
34. Jiralerspong S, Goodwin PJ. Obesity and Breast Cancer Prognosis: Evidence, Challenges, and Opportunities. J Clin Oncol 2016;34:4203-16.
35. Fox S, Speirs V, Shaaban AM. Male breast cancer: an update. Virchows Arch 2022;480:85-93.

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