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ORIGINAL RESEARCH

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Long-term survival of male patients with invasive breast cancer in Southern Taiwan

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Abstract

This study aimed to assess the survival rates of male patients diagnosed with invasive breast cancer. A comprehensive review of medical records of 28 male breast cancer patients in Southern Taiwan from 2006 to 2017 was conducted, and Kaplan-Meier analysis was computed to estimate survival probabilities. Among the 28 patients, 22 (78.6%) were diagnosed with left-sided breast cancer, while 6 (21.4%) had right-sided breast cancer. Within the subgroup of 22 patients with left-sided breast cancer, 5 individuals succumbed to the disease during the ten-year observation period. Further analysis revealed that the estimated survival rates at both the 5-year and 10-year intervals were 57.1%, and the median survival duration was 87.7 months, with a 95% confidence interval spanning from 69.5 to 105.8 months. Univariate Cox regression analysis identified stage (p = 0.034), pathological N (p = 0.0001), and distant metastasis (p = 0.007) as significant variables associated with patient survival, but none of these were independent variables on multivariate Cox regression analysis. Taken together, despite the relatively limited sample size of this study, which reflects the rarity of male breast cancer cases, our findings underscore the critical importance of early diagnosis and timely treatment in preventing disease recurrence and improving overall survival rates in male breast cancer patients.

Keywords

Male breast cancer; Survival analyses; Follow-up study

1. Introduction

Male breast cancer (MBC) is a relatively rare malignancy, comprising less than 1% of all breast cancer cases, but its incidence has demonstrated a significant increase of approximately 26% over the past two decades [1]. In 2019, an estimated 2670 new cases of MBC were reported in the United States, with the associated mortality rate being 18% [2]. Furthermore, the incidence of MBC is expected to rise in China from 2020 to 2034 [3]. In contrast to female breast cancer patients, MBC patients have a substantially lower lifetime risk of breast cancer, with an estimated risk of approximately 1 in 1000 men compared to 1 in 8 women [4]. A minority of MBC patients carry mutations in specific genes, substantially elevating their susceptibility to the disease, and exhibit a lifetime risk ranging from 1% to 5%, signifying a significantly increased risk compared to the general male population [5]. While most MBCs are classified as invasive ductal carcinomas, research has indicated that they tend to express more estrogen or androgen receptors and are less likely to overexpress the human epidermal growth factor receptor 2 compared to female breast cancer patients [5, 6]. Furthermore, the median age at the initial diagnosis of invasive breast cancer tends to be higher in men than in women (68 years versus 62 years) [7]. There has been a sharp increase in age-adjusted breast cancer rates in both men and women during their fifth decade of life, and while this incidence stabilizes in women during the sixth decade, it continues to rise in men through the seventh decade [8]. Notably, approximately one-third of MBC cases are observed in families with a history of familial breast and ovarian cancers [7]. A positive family history of breast cancer confers an increased risk of MBC [9], with those having such a family history experiencing a relative risk of 2.5 [10].

Given the rarity of MBC cases, there is a prevailing misconception that breast cancer occurs exclusively in women. However, it should be acknowledged that men also possess mammary glands and can develop cancer in these tissues. Unfortunately, MBC awareness is limited, leading to the under-recognition of symptoms such as breast swelling, palpable lumps, chest skin changes, nipple discharge or bleeding, pus, nausea or loss of appetite. In addition, men often tend to delay seeking medical attention until systemic symptoms emerge, thereby missing the critical window for timely treatment [11]. Breast cancer screening is typically recommended, especially for individuals with a family history of breast cancer. Nevertheless, the increasing burden of breast cancer screening in low and middle-income countries has sparked debates about its cost-effectiveness for screening in men [12]. In patients with breast cancer, it is imperative to maintain a high index of sus-

picion for potential laryngeal metastasis when new laryngeal symptoms arise or when imaging studies suggest primary laryngeal cancer. Confirming the diagnosis of metastatic breast carcinoma requires a thorough histopathological analysis of laryngeal biopsies in comparison to the original breast carcinoma biopsies [13]. Previous studies, often retrospective, have failed to provide sufficient evidence concerning the efficacy of radiation therapy, adjuvant chemotherapy, and hormone therapy for MBC. While some reports suggest a less favorable prognosis for MBC compared to females [14], others have not observed significant sex-based differences [15], which have resulted in varying treatment strategies and survival outcomes. Currently, specific treatment guidelines tailored exclusively to MBC are lacking, with management primarily following the established guidelines for female breast cancer [16, 17]. It is important to emphasize that considerations for female breast cancer should still be integrated into the treatment paradigm [8, 18]. A notable research gap exists regarding the scarcity of studies investigating the long-term prognosis of male patients diagnosed with invasive breast cancer in Southern Taiwan. Thus, the primary objective of this study is to explore the survival rate among males with breast cancer in Taiwan and provide insights into the corresponding treatment modalities and patient prognosis, which could be considered for guiding future treatment options in MBC.

2. Materials and methods

2.1 Study patients

In this retrospective study, a total of 28 male patients were included from a population of initially 4300 patients with invasive breast cancer treated at the Cancer Center of Kaohsiung Chang Gung Memorial Hospital between January 2006 and June 2017. The diagnosis of breast cancer was established through radiological diagnosis, assessment by surgical oncologists, and pathological histologic assessment, following standardized pathologic criteria. The patients were assessed based on the 2010 pathologic tumor (T), lymph node (N) and metastasis (M) staging criteria of the American Joint Committee on Cancer. Patient survival was determined by analyzing factors such as primary tumor size, characteristics of surrounding structures, number and location of regional lymph nodes, presence/absence of an extracapsular extension, and presence/absence of distant metastasis [19]. The detailed information is shown in a previous publication [20]. Approximately 99% of the patients (4272 patients) were excluded due to being female breast cancer or having carcinoma *in situ*.

2.2 Data collection

The hospital records of patients were examined by well-trained senior chart reviewers using a standardized data collection form. Information, including demographic details, pre-existing comorbidities and medications administered at admission and discharge, was extracted from nursing and medical histories. Guidelines for identifying primary MBC were followed [19]. Following the International Classification of Cancer, T was used to represent the primary tumor size and extent, N was used to indicate nearby lymph node involvement, and M denoted the presence of metastasis [19]. Information on the year of breast cancer diagnosis was collected. Surgical treatment for breast cancer comprised any surgical resection of the primary tumor, with details on tumor size, degree of violation, lymph node metastasis at diagnosis, and distant metastatic dissemination. The tumor histology was classified into five subtypes: intraductal carcinoma, mucinous carcinoma, papillary carcinoma, other specified carcinoma and carcinoma. Additional data included tumor location (left-sided or right-sided tumors), tumor size, primary site, cause of death and survival time (calculated as the difference between the date of diagnosis and the study's cut-off date (03 July 2017)).

2.3 Statistical analyses

Statistical analyses were conducted using the SPSS software (v23.0, SPSS Inc., Chicago, IL, USA). Prognostic predictors and all-cause mortality associated with discrete variables were identified using the chi-squared test, and continuous variables were assessed using the two-sample *t*-test. Cumulative survival rates among breast cancer patients across different factor strata were estimated using the Kaplan-Meier method for categorical variables. The results are presented as mean values along with their corresponding standard deviations.

3. Results

Table 1 displays the baseline characteristics of MBC patients, stratified by age: <65 years (n = 11; 39.3%) and ≥65 years (n = 17; 60.7%). Cancer stage distribution included stage I or II (n = 19; 67.9%), pathologic tumor status (T1) (n = 7; 25.0%), (T2) (n = 12; 42.9%), (T3) (n = 1; 3.6%), and (T4) (n = 5; 17.9%). Pathologic node status comprised pN0 (n = 19; 67.9%), pN1 (n = 3; 10.7%), pN2 (n = 1; 3.6%) and pN3 (n = 2; 7.1%). Distant metastasis was observed in 4 (14.3%) cases. Surgical procedures included partial mastectomy (n = 4; 14.3%), total mastectomy (n = 6; 21.4%), and modified radical mastectomy (n = 11; 39.3%). Histopathological subtypes included intraductal carcinoma (n = 17; 60.7%), mucinous carcinoma (n = 5; 17.9%), and papillary carcinoma (n = 3; 10.7%). Right-sided breast cancer was observed in 6 (21.4%) cases and left-sided breast cancer in 22 (78.6%) cases. Tumor size was classified as ≥2 cm (n = 19; 67.9%) and <2 cm (n = 7; 75.0%). The tumor's location showed single-site involvement in 16 (57.1%) cases and overlapping regions in 12 (42.9%) cases.

Among the 28 patients included in the study, 5 patients died during the 10-year follow-up period, and the observed 5-year and 10-year survival rates were 57.1% (Fig. 1A). The median survival time was 87.7 months (95% confidence interval, 69.5 to 105.8 months). In the univariate Cox regression analysis, various variables were examined, including age status (p = 0.388), stage status (p = 0.034), pathological T status (p = 0.228), pathological N status (p = 0.0001), distant metastasis (p = 0.007), laterality (p = 0.312), tumor size status (p = 0.214), and primary tumor status (p = 0.117) (Fig. 1B–I).

TABLE 1. Baseline characteristics of male breast cancer patients (n = 28).

Variables	Category	N	%
Age			
	<65 years	11	39.3
	≥65 years	17	60.7
Cancer stage			
	I	8	28.6
	II	11	39.3
	III	1	3.6
	IV	5	17.9
	Unknown	3	10.7
Pathological tumor status			
	T1	7	25.0
	T2	12	42.9
	T3	1	3.6
	T4	5	17.9
	Unknown	3	10.7
Regional lymph node metastasis			
	pN0	19	67.9
	pN1	3	10.7
	pN2	1	3.6
	pN3	2	7.1
	Unknown	3	10.7
Distant metastasis			
	No	21	75.0
	Yes	4	14.3
	Unknown	3	10.7
Surgical procedure			
	Partial mastectomy	4	14.3
	Total mastectomy	6	21.4
	Modified radical mastectomy	11	39.3
	NO	7	25.0
Histopathology			
	Intraductal carcinoma	17	60.7
	Mucinous carcinoma	5	17.9
	Papillary carcinoma	3	10.7
	Other specified carcinoma	2	7.1
	Carcinoma	1	3.6
Laterality			
	Right	6	21.4
	Left	22	78.6
Tumor size			
	<2 cm	7	75.0
	≥2 cm	19	67.9
	Unknown	2	7.1
Primary site			
	Single site	16	57.1
	Overlapping regions	12	42.9

4. Discussion

4.1 Clinical implications

This retrospective study provides an analysis of 28 MBC patients treated at a single medical center. Although such as cancer stage ($p = 0.034$), pathological N stage ($p = 0.0001$) and the presence of distant metastasis ($p = 0.007$) were identified to be significant factors affecting the survival of MBC in univariate Cox regression analysis, subsequent multivariate Cox regression analysis showed that these were not independent variables.

In this study, the term "elderly" generally refers to individuals aged over 65 [1]. The median age at the diagnosis of MBC was 63.7 years. Among all MBC cases, 60.7% occurred in males aged 65 years or older, while 39.3% were below 65 years old. The Kaplan-Meier analysis revealed differences in the characteristics of MBC in Korea among patients who developed the condition at ages 60–69 (24.9%) and 70–79 years (23.5%) (log-rank test, $p = 0.388$). Univariate analyses demonstrated a significant association between mortality and older age ($p < 0.001$), indicating that older people have a greater risk of succumbing to the diseases. These findings diverge from the results of a previous study [1]. Compared to female breast cancer patients, MBC was previously considered an aggressive type of cancer with poor prognoses. However, in regards to the average age at diagnosis for MBC, the cut-off age is 67 years, which is 5 to 10 years later than that for women [21, 22]. Similar to most carcinomas, the risk of developing MBC increases with age [23]. A study population from the Portuguese Institute of Oncology of Porto included 111 cases of MBC treated at the same Cancer Center from 1980 to 2012 and surveilled them for a maximum of 23 years and reported that most cases presented with ductal carcinomas (90.1%), followed by papillary histopathology, with a rare occurrence of lobular carcinoma (9.9%). In this present study, ductal carcinoma accounted for 60.7% of the histopathological types, while others accounted for 36.3%. Both the estimated 5- and 10-year survival rates for male patients were 57.1%. MBCs were predominantly located in the left breast (78.6%) compared to the right breast (21.4%), and individuals with left breast cancer had the highest mortality rates (18.0%) (univariate Cox regression, $p = 0.312$). These findings align with those of a previously published study, which reported no significant difference in laterality between men and women ($p = 0.085$) [24]. Data from the American College of Surgeons study, comprising 109,795 breast cancer cases, found that left and right breast cancers accounted for 52.4% and 46.9%, respectively, and the highest mortality rates were observed in 2822 (52.4%) individuals with left breast cancer [25]. A retrospective study at a single institute involving a cohort of 155 breast cancer patients treated between 2009 and 2013 reported that left-sided tumors were identified in 50.3% of patients, whereas right-sided tumors were observed in 49.7% of patients. Furthermore, the study revealed that left-sided breast cancer had poorer outcomes compared to right-sided tumors (hazard ratio: 1.05; 95% CI: 1.01–1.08) [26].

In this study, of the 78.6% of MBC cases located in the left breast (22 cases), 5 died due to breast cancer and 2 due

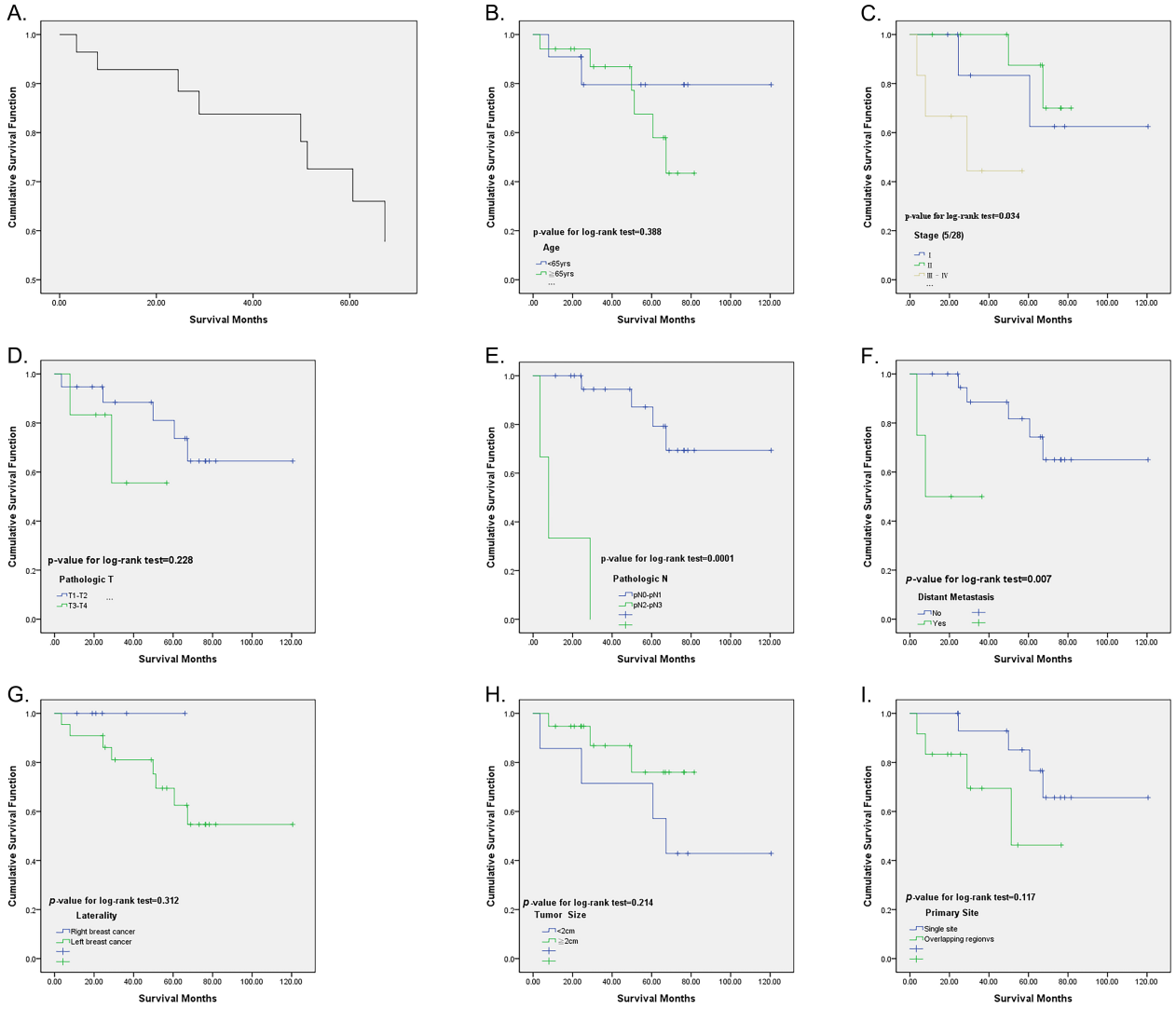

FIGURE 1. The 10-year cumulative survival rate of male breast cancer patients stratified by various factors. (A), Age (B), Stage (C), Pathological T (D), Pathological N (E), Distant metastasis (F), Laterality (G), Tumor size (H), Primary site (I).

to other diseases. When examining patients who underwent radiotherapy, other studies did not find any significant impact on mortality from cardiovascular disease, irrespective of the cancer side and its association with radiotherapy (p = 0.672). However, our study at the Korea Medical Center revealed a notable increase in cardiovascular events among patients who received radiation on the left side, especially when combined with anthracycline therapy. Specifically, this risk was higher for those who exceeded a cumulative doxorubicin-equivalent dose of 250 mg/m^2 over an average follow-up period of 47.1 months. Previous research has indicated that the risk of cardiovascular disease significantly rises at least 10 years after exposure to radiation [27]. A meta-analysis from 1966 to 2015, focusing on breast cancer patients, found that individuals who underwent radiotherapy had a greater risk of coronary heart disease and cardiac mortality compared to those who did not receive radiotherapy. Furthermore, patients who underwent left-sided radiotherapy had a higher risk of developing coronary heart disease and experiencing cardiac-related deaths compared to those who underwent right-sided radiotherapy [28]. However, the lack of a clear link between radiotherapy and cardiovascular disease mortality in MBC patients may be because individuals with left-sided breast cancer are less likely to be selected for radiotherapy due to the proximity of the tumor to the heart [29]. Evaluating breast stiffness pathology relies on breast compression during mammography, necessitating more frequent screenings to improve the early detection of breast cancer [30]. Consequently, further research on radiation dosage to the heart and its connection to cardiovascular disease mortality is essential to better understand a safe radiation threshold that enhances cancer treatment response while simultaneously minimizing the risk of cardiovascular disease in breast cancer patients. The occurrence of MBC observed in our study mirrored the global occurrence pattern, with most of our patients presenting with early breast cancer and estrogen receptor-positive disease. The predominant treatment approach involved modified radical mastectomy followed by adjuvant systemic therapy [31]. Regarding treatment, recent studies have indicated the efficacy of melatonin in breast cancer; however, the optimal dosage and timing have not been fully elucidated, necessitating further investigation. Nonetheless, melatonin remains a promising

candidate in this regard [32].

4.2 Strengths and limitations

This study focuses on the long-term survival of MBC patients from Southern Taiwan. Among the 28 MBC patients, three were diagnosed in other hospitals and were excluded owing to incomplete information (1 received chemotherapy at our hospital, 2 did not receive treatment). A higher proportion of male patients presented with more advanced disease compared to their female counterparts. It should be noted that there is still a significant concern among the general public regarding MBC. Owing to a lack of awareness, men tend to disregard symptoms such as breast swelling. Additionally, a breast cancer diagnosis can induce psychological anxiety, fear of future disease prognosis and life-related issues, leading to negative emotions. Therefore, the best prognosis is attainable when breast cancer is diagnosed at an early stage. Interventions that focus on raising awareness and providing psychological support through breast cancer education among men could greatly contribute to improving treatment outcomes and patient prognosis.

5. Conclusions

In conclusion, this retrospective study highlights that MBC is not a common disease, as evidenced by the small sample size. Furthermore, the location of tumors differed between men and women, which should be considered by healthcare professionals as a prognostic factor. Compared to female patients, MBC should be recognized as having a distinct disease. However, further research is necessary to assess various aspects of MBC, encompassing molecular pathology, risk factors and diagnostic and therapeutic approaches.

ABBREVIATIONS

MBC, Male Breast Cancer.

AVAILABILITY OF DATA AND MATERIALS

The data are contained within this article.

AUTHOR CONTRIBUTIONS

SCW, ZLJ, THT and HHC—designed the research study; wrote the manuscript. SCW, ZLJ and HHC—performed the research. SCW and HHC—analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Access to hospital records was approved by the human subjects review board at Kaohsiung Chang Gung Memorial Hospital (No. 201700844B0C601). The requirement for informed consent was waived by the Kaohsiung Chang Gung Memorial Hospital due to the retrospective nature of this study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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