

Comparison between Male Breast Cancer and Female Breast Cancer, Retrospective Study

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Abstract: Background Male breast cancer (MBC) is a rare disease compared to female breast cancer (FBC). It accounts less than 1% of all breast cancer and less than 1% of all men cancer. Male patients with breast cancer are treated according to treatment guidelines of FBC specifically the guidelines of post-menopausal FBC based on the high expression of estrogen receptor (ER) which found in the tumor of MBC and post-menopausal FBC patients and low estrogen expression in their bodies. In this retrospective study, we aimed to compare MBC to FBC to understand the biological behavior of MBC and the outcome of this disease. **Patients and methods** Patients diagnosed between 2005-2012 with breast cancer were included in this study, their number was 477 cases. Patients were classified according to sex into male (number=17) and female (number=460) breast cancer. We compared the incidence, tumor characters, adjuvant treatment, the 5-years disease free survival (DFS), and Overall survival (OS) of MBC to FBC. **Results** MBC cases were 3.6% compared to 96.4% FBC cases which were highly significant. As regarding to the stage of the tumor at diagnosis, no differences were seen between MBC and FBC, 82.4% stage I & II for MBC versus 77.4% for FBC and 17.3% stage III & IV for MBC versus 22.6% for FBC. No significant difference between MBC and FBC as regarding the type of pathology, ductal carcinoma in situ (DCIS) was found in 5.9% versus 1.3%, invasive ductal carcinoma (IDC) was found in 94.1% versus 96.7%, and invasive lobular carcinoma was found in 2% of FBC only. Most of patients expressed positive estrogen receptor (ER), 88.2% for MBC versus 75% in FBC ($P<0.04$) while 70.6% of MBC were progesterone receptor (PR) positive versus 71.1% in FBC. As regarding to HER2/neu status 23.5% was positive in MBC versus 66.7% positive in FBC ($P<0.04$). According to adjuvant treatment there were significant differences between MBC and FBC. There was no difference between MBC and FBC as regarding DFS. The median DFS was 3.9 years for FBC versus 3.4 years for MBC. In term of OS, the MBC had poor OS compared to FBC. **Conclusion** MBC outcome was inferior compared to FBC that may be due to the differences in the biological behavior of MBC. More studies are needed for further understand the differences between MBC and FBC.

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1. Introduction

Breast cancer in males is a rare disease, representing less than 1% of all breast cancer and less than 1% of all cancer in men [1]. In United States (US), about 2470 new cases of male breast cancer (MBC) will be diagnosed in 2017, and about 460 men will die due to breast cancer [2,3]. Due to this small number of cases, no randomized clinical trials have been carried out. Most data has been collected from retrospective studies and treatment strategies have been extrapolated from trials of female breast cancer. MBC shares many similarities with female breast cancer (FBC) however; important differences are present [4]. MBC predisposing risk factors include estrogen administration and diseases associated with increase estrogen level as liver cirrhosis or Klinefelter's syndrome, patients have XXY chromosomes [5]. Positive family history (FH) is the main predisposing factor for MBC, male with first degree FH has 2 times greater risk which suggesting an important role of genetic factors in the incidence of

MBC [6]. An increased risk of MBC has been reported in families with BRCA mutations [7, 8]. Other genes as mutation in the PTEN tumor suppressor gene, TP 53 (Li-Fraumeni syndrome), PALB2 mutations, and mismatch repair mutations associated with hereditary nonpolyposis colorectal cancer (Lynch syndrome) may be involved in predisposing to male breast cancer [9-11]. About 85-95% of male breast cancer is invasive ductal carcinoma (IDC) [12, 13]. Lymphatic and hematogenous spreads are similar to those found in FBC. Most of MBC are estrogen receptor (ER) positive about 90% and 80-96% are progesterone receptor (PR) positive [16, 17].

The TNM staging system for male breast cancer is identical to the staging system for female breast cancer. The most common sign of male breast cancer is palpable painless mass at the sub areolar region. Patients may present with other symptoms as, involvement of nipple (retraction and/or ulceration and/or bleeding), gynecomastia and enlarged axillary

lymphadenopathy [14]. Overall survival (OS) of MBC is similar to that of FBC [15, 16].

This retrospective study evaluated the clinic-pathological features, treatments and outcomes for MBC patients and the differences between MBC and FBC.

2. Patients and Methods

This retrospective study was conducted at the department of Clinical Oncology and Nuclear Medicine, Assiut University Hospital. Patients with breast cancer between 2005 and 2012 were included in the study, their number was 477 cases. The study was reviewed and approved by the Ethics Committee of Faculty of Medicine, Assiut University before data collection. About 17 cases of MBC and 460 cases of FBC were included in the study. The inclusion criteria were male and females patients' ≥ 18 years with pathologic confirmed breast cancer. All patients' data were collected from the register included, age of patients, stage of tumor according to American Joint Committee on Cancer (AJCC) staging system [18], hormonal receptor status, HER2/neu status, adjuvant treatment, and outcome of the disease. The exclusion criteria were patients who missed after diagnosis.

Statistical analysis: Clinico-pathological characteristics were compared between the two groups by Chi-square test. Disease-free survival (DFS) and OS were calculated and compared using Kaplan-Meier curves (DFS is defined as from initial diagnosis to the diagnosis of local or distant recurrence, while OS defined as from initial diagnosis to death). P values less than 0.05 was considered significant.

3. Results

The baseline demographic data and the pathologic data of our patients were summarized in Table 1. The incidence of MBC was 3.6% compared to 96.4% for FBC which was highly significant ($P < 0.04$) figure 1. The median age was 56 years for males and 49 years for females. As regarding to the stage of the tumor, no differences were seen between MBC and FBC, 82.4% stage I & II for MBC versus 77.4% for FBC and 17.3% stage III & IV for MBC versus 22.6% for FBC. No significant differences between MBC and FBC as regarding the type of pathology, ductal carcinoma in situ (DCIS) was found in 5.9% versus 1.3%, IDC was found in 94.1% versus 96.7%, and invasive lobular carcinoma (ILC) was found in 2% of FBC. In MBC 88.2% were ER positive versus 75% in FBC ($P < 0.04$) while 70.6% of MBC were PR positive versus 71.1% in FBC ($P = NS$). As regarding to HER2/neu status 23.5% were positive in MBC versus 66.7% positive in FBC ($P < 0.04$).

Adjuvant treatment of both groups was presented in Table 2. Figure 2. Adjuvant radiotherapy was administrated to 52.9% of MBC and to 69.8% of FBC which was significantly different. There was a great percentage of female received chemotherapy compared to males (88.0% versus 29.4%, $P < 0.04$). As regarding the hormonal treatment, most of male patients received hormonal treatment (82.4% versus 71.9%) which was significantly different. All male patients received tamoxifen while female patients received tamoxifen and/or aromatase inhibitor (AI).

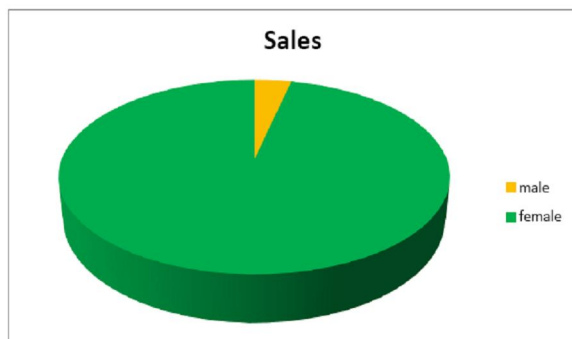
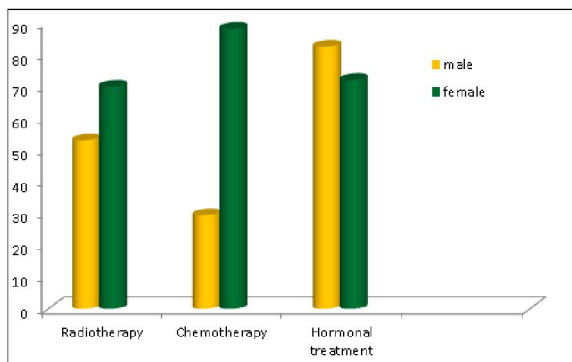
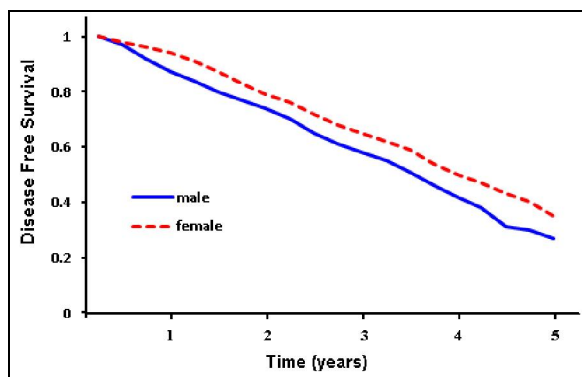
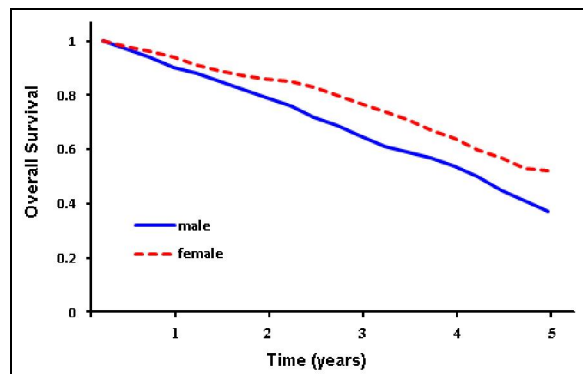
There were no significant differences between MBC and FBC as regarding DFS. The median DFS was 3.9 years for FBC versus 3.4 years for MBC figure 3. In term of OS, the MBC had poor OS when compared to FBC figure 4.

Table 1. Demographic and pathologic data

| | Males | Female | P value |
|---------------------------------|----------|-----------|---------|
| Incidence (total no=477) | 17(3.6) | 460(96.4) | <0.04 |
| Median age | 56 | 49 | |
| Stage no (%) | | | |
| I & II | 14(82.4) | 356(77.4) | NS |
| III & IV | 3(17.6) | 104(22.6) | |
| Pathology no (%) | | | |
| DCIS | 1(5.9) | 6(1.3) | NS |
| IDC | 16(94.1) | 445(96.7) | |
| ILC | 0 | 9(2.0) | |
| ER status no (%) | | | |
| Positive | 15(88.2) | 345(75) | <0.04 |
| Negative | 2(11.8) | 115(25) | |
| PR status no (%) | | | |
| Positive | 12(70.6) | 327(71.1) | NS |
| Negative | 5(29.4) | 133(28.9) | |
| HER2/neu status no (%) | | | |
| Positive | 4(23.5) | 307(66.7) | <0.04 |
| Negative | 7(41.2) | 96(20.9) | |
| Not analyzed | 6(35.3) | 57(12.4) | |

Table 2. Adjuvant treatment of male breast cancer and female breast cancer patients

| | Male n=17 (%) | Female n=460 (%) | P value |
|------------------|---------------|------------------|---------|
| Radiotherapy | 9(52.9) | 321(69.8) | <0.04 |
| Chemotherapy | 5(29.4) | 405(88.0) | <0.04 |
| Hormonal therapy | 14(82.4) | 331(71.9) | <0.04 |

**Figure 1. Incidence of male breast cancer and female breast cancer****Figure 2. Adjuvant treatment of male breast cancer and female breast cancer patients****Figure 3. 5-years disease free survival of male breast cancer and female breast cancer****Figure 4. Overall survival in male breast cancer and female breast cancer**

4. Discussion

Male breast cancer is a rare disease compared to female breast cancer. It accounts less than 1% of all cases of breast cancer and less than 1% of all cancers in men. In the recent decade, the frequency of male breast cancer has increased especially in United State, United Kingdom, and Canada, which support our results (3.6% MBC versus 96.4% FBC) [1]. the median age of male with breast cancer is 67 years at diagnosis while the median age of female with breast cancer is 5-10 years less [1, 12, 16]. The median age in our study was 56 which lower than that in the other studies. This study revealed that there were significant differences between MBC and FBC as regarding ER status (88.2% versus 75%). Most of the previous studies revealed that MBC had higher expression of ER/PR than FBC [19]. Our results were consistent with the previous studies as regarding the significant differences of HER2/neu status between MBC and FBC (23.5% versus 66.7%) [20, 21]. In our study there were no significant differences as regarding stage of tumor, this finding was different from several previous studies that revealed more advanced stage [17, 22, 23]. As regarding the treatment, we found significant differences in patients received local radiotherapy which came in contrast with that reported by Nahleh et al [24]. On the other hand, Scott-Connor reported that MBC were more likely to receive local radiotherapy after mastectomy but less likely after lumpectomy [25]. In accordance with other reports, our study revealed significant differences between MBC and FBC as regarding adjuvant chemotherapy (29.4% versus 88.0%) [24-26]. Most of patients with MBC

received hormonal treatment (82.4 versus 71.6, $P < 0.04$). All MBC received tamoxifen while FBC received tamoxifen and/or AI. This finding supports the uncertain efficacy effect of AI in MBC [27, 28]. In terms of DFS there were no significant differences between MBC and FBC as regarding DFS, The median DFS was 3.9 years for FBC versus 3.4 years for MBC. However there were differences between MBC and FBC in terms of OS. Swedish study reported that there were significant differences between MBC and FBC as regarding DFS, poor DFS for MBC [23]. Our findings were consistent with the previous studies [22, 25, 29]. It was thought that FBC has better prognosis than MBC, this may be due to the different tumor biological profile in males which is responsible for the poor prognosis of MBC [1,2]. Donegan et al reported that, poor survival in MBC patients was contributed to the high rate of post-treatment mortality from comorbid disease; male patients were more likely to die of second primary cancers and other causes than the female patients [30]. Recent studies showed improved survival rates for both MBC and FBC, but progress for males has lagged behind that for females this may be due to the application of chemotherapy treatment [31]. Pich A attributed the slower increase of survival rates in MBC to a limited benefit from hormonal treatment [32].

Limitation of this study was the small sample size of male patients, no data about the cause of deaths of patients to analyze the poor OS of MBC.

Conclusion

MBC outcome was poor when compared to FBC that may be due to the differences in the biology of MBC. More studies are needed to further understand the differences between MBC and FBC.

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