

## RESEARCH ARTICLE

# Breast Cancer in Men: a Report from the Department of Radiation Oncology in Kermanshah Province, Iran

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## Abstract

**Background:** Male breast cancer (MBC) is a rare disease that accounts for less than 1% of all cancers in men and less than 1% of all diagnosed breast cancers. In this study, we retrospectively evaluated the clinicopathological features, treatment options and overall survival in Kurdish MBC cases. **Materials and Methods:** Seventeen MBC were referred to Department of Radiation Oncology in Imam Reza Hospital, Kermanshah, Iran, between 2010 and 2016. Immunohistochemical analysis was performed for ER, PR and Her2 biomarkers and FISH for those with Her2 2+. Median follow-up period was 30 months (2-65 months). We excluded from the study patients who did not have follow-up after initial diagnosis. Treatment methods were chemotherapy, radiotherapy, hormonal therapy, target therapy and palliative care. Survival was estimated by the Kaplan Meier method (Prism 5). **Results:** The mean age at diagnosis was  $49.24 \pm 17$  years (range, 24-85 years). Grade II was the most grade in MBC (65%). Fourteen patients (82%) had invasive ductal carcinoma, one (6%) had ductal carcinoma in situ and 2 (12%) had invasive papillary. ER, PR and Her2 were significantly positive in 14/17, 8/17 and 2/17 cases, respectively. The treatment included modified radical mastectomy for most patients. Chemotherapy with TAC and CEF regimens was delivered to 15/17 cases. Tamoxifen therapy was delivered to 14/17 cases. Three stage IV patients received Avestin and two with Her2 3+ were given Trastuzumab (Herceptin). Patients received adjuvant radiotherapy following surgery and chemotherapy. The site of metastasis was the bone in 2 cases, lung in 1 case and liver in 1 case. Zoledronic acid (Zometa) was prescribed for patients with bone metastasis. Five-year overall survival rate was 64%. **Conclusions:** MBC is rare. Thus, we need larger studies are in collaboration with several research centers in the field of breast cancer. ER positive, grade II of invasive ductal carcinoma, stage II and right side happened more with MBC. Overall survival is similar to other studies.

**Keywords:** Male breast cancer - Kurdish Iran - overall survival - ER+ - PR+ - Her2+ - chemotherapy

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## Introduction

Male breast cancer (MBC) is a rare disease that accounts for less than 1% of all cancers in men and less than 1% of all diagnosed breast cancers (Cutuli et al., 2010). The incidence of MBC has remained relatively stable in most countries (La Vecchia et al., 1992). More information on breast cancer in men has been collected from retrospective studies spanning several decades, and treatment recommendations have been extrapolated from results of trials in female patients (Giordano, 2005).

The age frequency distribution in women with breast cancer is bimodal with peaks at 52 and 71 years, whereas in men it is unimodal with a peak at age 71 years (Anderson et al., 2004). It is rare before the age of 30 years, and the average age at diagnosis is approximately 60 years, which is approximately 10 years older than in females with the disease (Ravandi-Kashani and Hayes, 1998). In addition to, prognostic factors such as age,

tumor size, and cancer stage and grade, overexpression of the human epidermal growth factor receptor 2 (HER2)-positive and positivity for estrogen receptor (ER) or progesterone receptor (PR) are heavily studied prognostic (Amirifard et al., 2016). Men tend to be diagnosed at an older age and higher ER and PR expression is notable in men. MBC exhibits more frequent lymph node involvement and more than 40% of individuals having stage 3 or 4 disease (Anders et al., 2009). Obesity has been implicated in the etiology of MBC due to higher circulating ER levels and has fairly consistently been associated with an increased risk of MBC (Ewertz et al., 2001). Local therapy for breast cancer is generally similar in men and women. Most men are treated with modified radical mastectomy with axillary lymph node dissection or sentinel node biopsy (Scott-Conner et al., 1999). In this study, we retrospectively evaluated the clinicopathological features, treatment options and overall survival on Kurdish MBC.

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## Materials and Methods

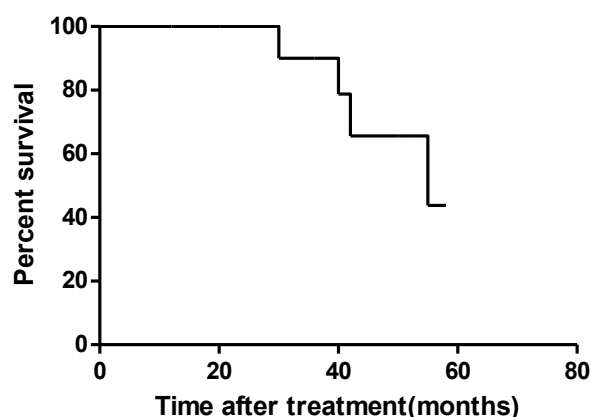
In this study, 17 breast cancer men referred to Department of Radiation Oncology at Imam Reza Hospital, Kermanshah, Iran, from 2010 and 2016. Immunohistochemical analysis was performed using standard procedures to determine ER, PR and Her2 statuses. We used Fluorescence in situ hybridization (FISH) test for patients with Her2 2+. Descriptive of clinical data were expressed in percentage or mean ± SD. Median follow-up period of 30 months (range, 2-65 months). We excluded from the study, patients who had not follow-up after initial diagnosis. Tumor staging was carried out according to the TNM classification. We used treatment methods like chemotherapy, radiotherapy, hormonal therapy, target therapy and palliative care. Survival was estimated by the Kaplan Meier method, and compared with the log rank test (Prism 5 software).

## Results

The mean age at diagnosis was 49.24±17 years (range, 24-85 years). Mean tumor size was 2.25±0.9 cm (range, 1-4 cm). Grade II was the most grade in MBC (65%), following by grade I (14%) and III (21%). Fourteen patients (82%) had invasive ductal carcinoma, one (6%) had ductal carcinoma in situ and 2 (12%) had invasive papillary (Table 1). The most patients were treated with modified radical mastectomy. Chemotherapy regimens were docetaxel, doxorubicin and cyclophosphamide (TAC) and cyclophosphamide, epirubicin, fluorouracil (CEF) regimens that have been delivered to 15 cases (88%). Chemotherapy delivery increased, according particularly to advanced stage and axillary nodal

**Table 1. The baseline characteristics of male breast cancer patients (n=17)**

Variables	n(%)	Mean ±SD	Range
Age,years		49.24 ± 17	24-85
Histopathological types			
Invasive Ductal	14(82)		
Ductal Carcinoma in Situ	01(06)		
Invasive Papillary	02(12)		
Tumor Size, cm		2.25± 0.9	1-4
Tumor Grade (n=14)			
Grade I	02(14)		
Grade II	09(65)		
Grade III	03(21)		
Stage			
I	01(6)		
II	08(54)		
III	03(20)		
IV	03(20)		
Unknown	02		
Vascular Invasion			
Positive	10(58.8)		
Negative	07(41.2)		
Perineural Invasion			
Positive	06(35.3)		
Negative	11(64.7)		
Laterality			
Left	06(35.3)		
Right	11(64.7)		



**Figure 1. The 5-Year Overall Survival for All Male Patients with Breast Cancer**

**Table 2. Immunohistochemical Characteristics**

ER Status		
Positive	14	(82.4%)
Negative	03	(17.6%)
PR Status		
Positive	08	(47.1%)
Negative	09	(52.9%)
Her2 Status		
Positive	02	(11.8%)
Negative	15	(88.2%)

involvement. Hormonal therapy (Tamoxifen) was delivered to 14 cases (82%) due to ER or PR positivity statuses. Three patients in stage IV have been received Avestin and two patients with Her2 3+ have been delivered Trastuzumab (Herceptin). Patients received adjuvant radiotherapy following surgery and chemotherapy. The median delivered doses were 50 Gy to breast, chest wall and regional lymph nodes. Distant metastasis occurred in 4 cases. The site of metastasis was the bone in 2 cases, lung in 1 case and liver in 1 case. Zoledronic acid (Zometa) was prescribed for patients with bone metastasis.

ER was significantly positive in 14 (82.4%), PR was positive in 8 (47.1%) and Her2 was positive in 2 (11.8%) cases. Her2 status of three patients was Her2 2+, so we sent them for Fish test. The results of the test were negative for all (Table 2). Four patients (23%) died and 2 were excluded. Five-year overall survival rate was 64% (Figure 1).

## Discussion

AIIn the past decade's according to Surveillance, Epidemiology, and End Results (SEER), a rise in the incidence of MBC from 1 to 1.2 per 100000 men have been reported from 1970 to 2004 (Speirs and Shaaban, 2008 ). A study showed the mean age at diagnosis for men with breast cancer is 67 years, which is approximately 5-10 years older than the average age at diagnosis for women, (Yoney et al ., 2009) but in this study, the mean age at diagnosis was lower (49 years). Data from more than 2,000 male patients in the SEER cancer registry show that 93.7% of MBCs are ductal or unclassified carcinomas, 2.6% are papillary, 1.8% are mucinous, and only 1.5% are lobular (Giordano et al., 2004). Also, another study expressed

majority of men's cancers are invasive ductal carcinomas. Papillary carcinomas are comparatively more common, and lobular carcinomas are rare in men (Nahleh et al., 2007). Ductal carcinoma in situ comprises approximately 10% of breast cancers in men (Hittmair et al., 1998). Similar to the above studies 14/17(82%), 1/17(6%) and 2/17(21%) had invasive ductal carcinoma, ductal carcinoma in situ and invasive papillary in pathological records, respectively. Tumor size and lymph node involvement are two clear prognostic factors for MBCs (Giordano et al., 2004). Men with tumors measuring 2–5 cm have a 40% higher risk of death than men with tumors <2 cm in maximum diameter. Similarly, men with lymph node involvement have a 50% higher risk of death than those without lymph node involvement (Giordano et al., 2004). Mean tumor size was  $2.25 \pm 0.9$  cm (range, 1-4 cm) in our study. The majority of these tumors are low grade like our study (Hittmair et al., 1998). In contrast, a very small study of 41 MBCs, found that 73% were grade 3. HER2 overexpression rates range from 2% to 42% in other studies (Kornegoor et al., 2012; Shaaban et al., 2012) and other study HER2-positive was 45% (Willsher et al., 1997). In this study, HER2 overexpression was 11.8%. Local therapy for breast cancer is generally similar in men and women. Most men are treated with modified radical mastectomy with axillary lymph node dissection or sentinel node biopsy (Scott-Conner et al., 1999).

Chemotherapy should be used in the absence or doubt about endocrine-responsiveness. Frequently used chemotherapy regimens were CMF, FEC and EC (Tunon de Lara et al., 2008). Chemotherapy with Docetaxel, doxorubicin and cyclophosphamide (TAC) and cyclophosphamide, epirubicin, fluorouracil (CEF) regimens have been delivered to most our cases. Adjuvant hormonal therapy clearly has a role in male breast cancer patients with hormone receptor-positive tumors (Ribeiro and Swindell 1992). Tamoxifen has proven to lead to an increase in survival rates in women with hormone-responsive disease and to date is generally considered the standard adjuvant treatment for hormone-dependent MBC (Fogh et al., 2011). In the National Cancer Institute's SEER database between 1973 and 2005, 92% of the 5494 MBCs, but only 78% of the 838 805 female breast cancers were ER-positive (Anderson., 2010). Hormonal therapy (Tamoxifen) was delivered to 14 cases (82%) due to ER or PR positivity statuses. Overall survival rates are lower for men, but this is due to an older age at diagnosis and more advanced disease at presentation (Giordano et al., 2004). 5 and 10 years overall survival rate of MBCs are around 60% (50-80), 40% (50-60) in elderly (Xia Q et al., 2011). Five-years overall survival rate was 64% in our patients.

In conclusion, MBC is rare. So, we need larger studies are in collaboration with several research centers in the field of breast cancer. ER positive, grade II of invasive ductal carcinoma, stage II and right side happened more with MBC. Overall survival is similar to other studies.

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