

Male breast cancer in Tripoli, Libya

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ABSTRACT

الأهداف: دراسة صفات المرضى الذكور المصابين بسرطان الثدي ومعدل الحياة والانتكاس لهذا المرض.

الطريقة: أجريت دراسة استيعادية غير عشوائية شملت المرضى الذكور المؤكد إصابتهم بسرطان الثدي عن طريق الخزعة. تم تسجيل 1568 مريض ما بين الفترة يناير 1990 إلى يونيو 2008 قسم الأورام - مركز طرابلس الطبي - طرابلس - ليبيا. وكان 22 من المرضى ذكور (1.4%)

النتائج: كان متوسط العمر لدى المرضى الذكور 61 عام. وجدت أمراض مستعصية لدى 65% حالة، وكان 93.3% من الحالات لديهم غدد ليمفاوية إيجابية. استئصال الثدي واستئصال الإبط من الأدوية الجراحية المفضلة لدى 65%، كما وجد سرطان القناة الباضعة لدى 85%. ويخضوص حالة الهرمون المستقبلي، كانت نسبة الاستروجين وبروجستيون إيجابية لدى 70%. تلقى 71% علاج كيميائي يحتوي على عقار الانتراسيكلين، ومن خلال المتابعة حصل انتكاس في 47% من الحالات. كان أكثر المناطق انتكاسا هي العظام 37.5%. كانت نسبة معدل البقاء العامة في الأولى، والثانية، والخامسة هي 82.4% و 76.5% و 57% على التوالي. اثنان من المرضى إخوان، تطور في أحدهم الورم النقوي المتعدد خلال المتابعة.

خاتمة: مقارنة مع المرضى الإناث المصابين بسرطان الثدي، المرضى الذكور أكبر عمر ولديهم أمراض مستعصية، كما أن أمراض الهرمون لديهم إيجابية.

Objectives: To study the epidemiology, characteristics, and survival of male breast cancer patients.

Methods: This non-randomized retrospective study includes male patients with breast cancer confirmed by biopsy. A total of 1568 breast cancer patients were registered in the Oncology Department, Tripoli Medical Center, Tripoli, Libya between January 1990 to June 2008. Twenty-two patients were male (1.4%).

Results: The mean age of male breast cancer patients was 61 years. They tend to have advanced local disease, as 65% of them were tumor (T)3 and T4, and 93.3% have positive lymph nodes. The preferred

surgical treatment was mastectomy and axillary clearance in 65%, and 85% had invasive duct carcinoma. Regarding hormone receptor status, 70% were estrogen and progesterone positive. A total of 71% received chemotherapy as anthracycline based. During follow up, the overall recurrence rate was 47%. The bone was the most common site of relapse (37.5%). Overall survival rate was 82.4% at first, 76.5% at second, and 57% at fifth year. Two patients were brothers, and one of them developed multiple myeloma during follow up.

Conclusion: In comparison to female patients with breast cancer, male patients are older, and have more advanced and more hormone positive disease.

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Breast cancer is globally the most common malignancy for females with more than one million new patients per year.¹ Male breast cancer is a very rare disease with an incidence of approximately 0.5-1% of the incidence of female breast cancer.¹ Male breast cancer has a peak incidence at 71 years of age.^{2,3} It behaves just like breast cancer in postmenopausal women.^{2,4} Male breast cancer is more frequently seen in families with an autosomal dominant mutation in the breast cancer type 2 susceptibility protein (BRCA2) gene, and occasional mutation in BRCA1.² Male breast cancer patients tend to have advanced local disease, and more positive hormone status, and low tumor grade.² Men diagnosed with breast cancer are at high risk of contralateral breast cancer, and increased risk of second primary cancer such as malignant melanoma, stomach, prostate, colon, and pancreatic tumor.^{5,6} Our aim is

to study the epidemiology of male breast cancer and survival among male patients with breast cancer.

Methods. This retrospective study reviewed the records of 1568 patients who were treated from January 1990 to June 2008 for histologically proven breast carcinoma registered in the Oncology Department, Tripoli Medical Center, Tripoli, Libya. Twenty-two patients were male (1.4%). This study was approved by the hospital ethics committee of Tripoli Medical Center, Tripoli, Libya. The clinical data including age, family history, surgery, pathological feature (tumor size, lymph node status, tumor grade, estrogen and progesterone receptor status), date and site of first recurrence, date of last follow up or death were collected from their file. The site of recurrence was detected by computerized axial tomography scan of the chest and abdomen, magnetic resonance imaging for brain and spine metastases, and isotope scan for bone metastases. All patients were treated with chemotherapy, endocrine therapy such as tamoxifen 20 mg/day for those who had positive or unknown receptor status, and locoregional radiotherapy to the chest wall and axilla if they have advanced local disease, or more than 3 positive lymph nodes. Disease free survival was calculated from the date of diagnosis until the first recurrence. Median overall survival was calculated from the date of diagnosis until death or last follow up. All male patients (22 patients) diagnosed with breast cancer and registered in the Oncology Department were included, and out of these, 2 patients have no follow up and were excluded in the calculation of disease free survival or overall survival.

The results were analyzed statistically using the Statistical Package for Social Sciences version 11 computer package (SPSS Inc., Chicago, IL., USA). The Fisher exact test was used for comparison of frequency, and a *p*-value <0.05 was considered significant. The Kaplan-Meier curve was used for survival analysis.

Results. The mean age of male breast cancer patients was 61 years, and 20% had a family history of breast carcinoma. Of these, 65% of patients had large tumor sizes of T3 and T4 disease (T1 [10%], T2 [5%], T3 [30%], and T4 [35%]), and 20% had undetermined tumor size. These patients have known lymph node status (75%), 93.3% had node positive status, and only 6.67% was node negative. At diagnosis, 15% had distant metastases, 66.6% had bone metastases, and 33.3% had brain metastases. The stages of breast cancer patients were as follows: stage I (0%), stage II (30%), stage III (35%), and stage IV (15%), and 20% had undetermined stage. Surgical treatments carried out were mastectomy and axillary clearance in 75%, lumpectomy and axillary clearance in 20%, and biopsy only in 5%. Almost 85%

of the patients had invasive duct carcinoma, 15% of patients had other different histopathology, 50% had known receptor status, 70% with positive receptor status, and 30% with negative receptor status. A total of 70% of the patients received chemotherapy as follows: 71% received anthracycline based chemotherapy CAF (cyclophosphamide, adriamycin, and 5-fluorouracil), 21.4% received CMF (cyclophosphamide, methotrexate, and 5-fluorouracil), and 7.6% received anthracycline and taxanes. Some patients (45%) received radiotherapy as adjuvant locoregional treatment to the chest wall and axilla, and 65% received tamoxifen in those with positive receptor status, or unknown receptor status. Out of these patients, 47% had recurrence (37.5% in the first year, 37.5% in the second year, 12.5% in the third year, and 12.5% in the fifth year). Recurrences occurred in 37.5% in the bone only, 12.5% in the lungs, 12.5% had visceral and bone, and 37.5% had local metastases. The overall survival rate in the first year was 82.4%, 76.5% in the second year, and 57% in the fifth year. Two male brothers were diagnosed at the same period, one of them was diagnosed at 60 years of age with stage III disease in October 2003, and died with liver, bone, and lung metastases in June 2004. The second patient, 75 years of age had breast cancer with bone metastases at diagnosis in December 2003. He received chemotherapy as CAF, palliative radiotherapy to lumbar metastases, and tamoxifen. Later, he developed stage II multiple myeloma and lived until January 2008. There was another 70-year-old patient who had stage II breast carcinoma, and later developed prostate carcinoma and died after 10 months due to ischemic heart disease.

Discussion. Breast cancer among men is relatively rare, with an age-standardized incidence rate of approximately 1 per 10,000 person-years in most countries, and approximately 1% of the incidence rate among women.⁷ Similar to that of breast cancer in women, an increased risk of breast cancer in men has been associated with family history of breast cancer.^{6,8,9} Breast cancer in men is characteristic of the BRCA 2 phenotype, occasionally, a mutation is seen in the BRCA1 gene.⁴ In the general population, these genes are rare with a frequency of less than 0.5%, and accounts for fewer than 5-10% of breast cancer.^{10,11} It is important for clinicians to identify high risk families not only at initial diagnosis, but to update the family history periodically. Additional known risk factors include hormonal abnormalities such as Klinefelter's syndrome, gynecomastia, testicular disease, liver cirrhosis, and treatment with exogenous estrogens.^{12,13} In our study of male breast cancer patients, stage III and stage IV represents 50%, which is similar to our female patients with stage III and stage IV cancer (43%, *p*>0.05).¹⁴ In

another study, 42% of male patients are in stage III, and stage IV.² The explanation for this is very likely the breast size, and the low public awareness of male breast cancer in combination with likely psychological factors. As in females, the common histopathology in males was invasive duct carcinoma in 85%. In our study, hormone receptors were positive in 70% of the male patients, in one series the hormone receptors status were positive in 75-92%, which is similar to postmenopausal women.³ In our postmenopausal female patients with breast cancer, 53.8% have positive hormone receptor status, ($p>0.2$) which is not significantly different from male patients.¹⁴ A total of 93% among male patients had positive lymph nodes. In contrast to our female patients, only 60% had positive lymph node ($p=0.02$). In one study of male breast cancer including 308 patients, 56% had a positive axillary nodes ($p=0.003$),¹ which significantly differ from our patients, and this indicates more advanced stage of disease in our patients.

The most common treatment carried out for male patients was radical mastectomy and axillary clearance with, or without radiotherapy.¹⁵ Mastectomy was carried out in 75% of our patients, and radiotherapy, treated to a dose of 25 fraction as 2Gy/fraction over 5 weeks. Tamoxifen should be considered as the optimal adjuvant treatment option for male patients with endocrine responsive disease, as well as aromatase inhibitor can be used with LHRH analogues as in postmenopausal women, but the experience is limited.¹⁶

In our study, the most common site of distant metastases was bone either on diagnosis, or at recurrence (54.5%). In those patients who have regular updated follow up, second malignancy occurred in 12.5%, prostate carcinoma in one patient, and the other patient developed multiple myeloma. Another study shows that men diagnosed with a first primary breast cancer have a 16% increased risk of developing a new primary cancer in comparison to men in the general population.⁵ Men belonging to BRCA families are at risk for several cancers, and seem to adhere to genetic testing and surveillance.¹⁷

The overall survival rate in male patients at the first, second, and fifth year is less than the overall survival rate in our female patients (at first [95%], second [87.4%], and fifth years [78.6%]) ($p=0.045$). This was expected as most of our male patients were diagnosed at advanced stages.¹⁴

Complete information regarding tumor size and lymph node status was not available in the histopathology reports in the period between 1990 to 1996, and hormone receptor and human epidermal growth factor receptor 2 (Her2) status were not studied before 2003 as it was not available, and this limited our studies.

The results of our study conclude that male breast cancer patients have old age and advanced stage of disease. Further studies should include a larger number of patients, and this probably requires collaboration with other centers in the area. The association of breast cancer with other malignancies must be considered in other future studies.

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