# Male Breast Cancer: A Retrospective Analysis Of Single Center Results

Erkek Meme Kanserleri: Tek Merkezli Sonuçların Retrospektif Analizi

Hakan BAYSAL<sup>1</sup>, Ayşegül ERGÜN<sup>1</sup>, Begümhan BAYSAL<sup>2</sup>, Zeynep Çağla TARCAN<sup>3</sup>, Mehmet Sait ÖZSOY<sup>1</sup>, Fatih BÜYÜKER<sup>1</sup>, Orhan ALİMOĞLU<sup>1</sup>

## ABSTRACT

**AIM:** Male breast cancers (MBC), constituting less than 1% of all breast carcinomas, are relatively rare. The average age of diagnosis is between 60-70 years and can affect males of all ages. In this study, our aim was to present the clinicopathological characteristics, treatment, and survival outcomes of patients who were treated and followed up for ten years in outpatient clinic, in accordance with the literature.

**MATERIAL AND METHOD:** Medical records of patients diagnosed with MBC, who were followed and treated at our clinic between start of 2014 and 2023 were examined retrospectively using the hospital database. Clinicopathological characteristics, treatments performed, and the overall and disease-free survival rates were analyzed.

**RESULTS:** A total number of 19 patients were included in the study (mean age: 75.9±11.5, range: 57-96). Four patients with distant metastasis and other system malignancies at the time of diagnosis were excluded. The mean follow-up period was 43.8 months. The most common location of the tumor was to be the retroareolar region (63.2%). BRCA2 gene mutation analysis was positive in three patients. Eleven patients (57.9%) were at Stage 3. Eleven patients had invasive ductal carcinoma. Twelve patients belong to the luminal B subtype. Among the 13 patients who underwent axillary dissection 9 (69.2%) had lymph node involvement. Patients who developed distant metastasis had higher overall mortality and cancer-specific mortality. The body mass index (BMI) of deceased patients was lower than that of surviving patients during the follow-up period. Age group above 75 years had lower overall survival (log-rank p=0.0064) and cancer-specific survival (log-rank p=0.011).

**CONCLUSION:** In our study, we found that distant metastasis significantly affected survival. Although male breast cancers are rare, early diagnosis, as in women, positively influences overall and disease-free survival.

Keywords: male breast cancer, survival, metastases, mastectomy

ÖZET GİRİŞ: Tüm meme karsinomlarının %1'den azını oluşturan erkek meme kanserleri (EMK) oldukça nadirdir. Ortalama tanı 60-70 yaş arasında olup, her yaştan erkek hastalıktan etkilenebilir. Bu çalışmada on yıl boyunca tedavi ve takip edilen hastaların klinikopatolojik özelliklerini, tedavi ve sağkalım sonuçlarını literatür bilgisi ışığında sunmayı amaçladık.

**GEREÇ VE YÖNTEM:** Ocak 2014-Ocak 2023 tarihleri arasında kliniğimizce takip ve tedavi edilen EMK'li hastaların retrospektif kayıtları hastane veri tabanından incelendi. Kliniko-patolojik özellikler, yapılan tedaviler, genel ve hastalıksız sağkalım sonuçları analiz edildi.

**BULGULAR:** Çalışmaya 19 hasta dahil edildi (yaş ortalaması: 75.9±11.5, range:57-96). Tanı anında uzak metastaz ve diğer sistem malignitesi olan 4 hasta dışlandı. Ortalama takip süresi 43.8 aydır. Tümör en sık retroareolar bölgeydi (%63.2). 3 hastada BRCA 2 gen mutasyon analizi pozitif bulundu. 11 hasta (%57.9) Evre 3'tü. 11 hasta invazif duktal karsinomlu idi. 12 hasta Luminal B alt grubunu oluşturmaktaydı. Aksiller diseksiyon yapılan 13 hastanın 9' da (%69.2) tutulum mevcuttu. Uzak metastaz gelişenlerde tüm nedenlere bağlı ve kansere bağlı mortalite daha yüksekti. Ölen hastaların batlı'sinden daha düşüktü. 75 yaş ve üstü olan grubun genel sağkalım (log-rank p=0.0064) ve kansere özgü sağkalım (log-rank p=0.011) süresinin belirgin olarak daha kısa olduğu izlenmiştir.

**SONUÇ:** Çalışmamızda sağkalım üzerine etkide uzak metastaz anlamlı bulunmuştur. Erkeklerde meme kanserleri nadir görülmekle beraber kadınlarda olduğu gibi erken teşhis genel ve hastalıksız sağkalımı olumlu yönde etkilemektedir.

Anahtar kelimeler: erkek meme kanseri, sağkalım, metastaz, mastektomi

<sup>1</sup>Istanbul Medeniyet University Goztepe Prof. Dr. Suleyman Yalcin City Hospital, Department of General Surgery, Istanbul, Turkiye <sup>2</sup>Istanbul Medeniyet University, Faculty of Medicine, Department of Radiology, Istanbul, Turkiye <sup>3</sup>Memorial Sloan Kettering Cancer Center, Department of Pathology NY, USA

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#### Sorumlu Yazar / Corresponding Author: Hakan BAYSAL

Adres: İstanbul Medeniyet Üniversitesi Göztepe Prof. Dr. Süleyman Yalçın Şehir Hastanesi, Göztepe mahallesi, Kadıköy İstanbul Türkiye,34722 Phone: +90 532 345 2108 E-mail: hakanbaysal\_tr@yahoo.com, ORCID: 0000-0003-3604-6177

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#### Yazar Bilgileri /Author Information:

Ayşegül ERGÜN: e-mail: aysegulergunrc15@gmail.com, ORCID: 0000-0003-4766-3058 Begümhan BAYSAL: e-mail: baysalbegumhan@yahoo.com, ORCID: 0000-0003-0470-1683 Zeynep Çağla TARCAN: e-mail: tarcanz@mskcc.org, ORCID: 0000-0002-5046-7536 Mehmet Sait ÖZSOY: e-mail: saitozsoy@gmail.com, ORCID: 0000-0003-2935-8463 Fatih BÜYÜKER: e-mail:fbuyuker@gmail.com, ORCID: 0000-0003-1288-4299 Orhan ALİMOĞLU: e-mail: orhanalimoglu@gmail.com, ORCID: 0000-0003-2130-2529

## INTRODUCTION

Male breast cancers (MBC), constituting less than 1% of all breast carcinomas, are relatively rare.<sup>1</sup> According to studies, MBC is more common in elderly men and shows similar behavior to postmenopausal female breast cancer (FBC).<sup>2</sup> The most common clinical symptoms of MBC include mass in the breast, nipple retraction, nipple or skin ulceration, and axillary lymphadenopathy. The etiology of MBC is believed to be influenced by advanced age, radiation exposure, family history, obesity, hormonal imbalance, hyperestrogenism, liver cirrhosis, and Klinefelter syndrome.<sup>3</sup> Current clinical knowledge about MBC is vastly derived from single-center retrospective studies. Consequently, approaches to the treatment of MBC are extrapolated from guidelines for managing FBC, and disease management is largely similar to that in postmenopausal women.<sup>4</sup> In our study, we aimed to share our experiences related to MBC and discuss the clinical, pathological, demographic, overall survival (OS), and disease-free survival (DFS) data of patients followed in our clinic in accordance with the literature.

## **MATERIAL AND METHOD**

Between 2014 and 2023, patients who underwent surgery for MBC at our hospital's General Surgery Department were retrospectively analyzed. Approval of the ethics committee was obtained from the institutional review board (IRB) [IRB number: 2022/0096], and all patients were asked to sign informed consent forms. The study was conducted at a single center. Male patients between the ages of 57 and 96 with histopathologically confirmed breast cancer patients were included in the study. Four cases with distant metastasis and other systemic malignancies at the time of diagnosis were excluded from the study.

Clinical information, imaging results, histopathological characteristics, and treatments performed on the patients were obtained from the hospital database. Body mass index (BMI), risk factors, TNM ( primary Tumor, regional lymph node involvement, presence of distant Metastasis) staging system, recurrence, and localizations of the distant metastasis were documented. DFS is defined as the period between surgery and recurrence and/or death. OS is the period from the surgery up to the time of death by any cause. The presence of distant metastasis and mortality rates of the patients were compared. Additionally, analyses for DFS and OS were carried out. Furthermore, DFS and OS analyses were compared between two groups: patients aged 75 and above and patients aged below 75.

Continuous variables were presented with mean±SD (standard deviation) or median (minimum-maximum). Normality was assessed using histograms and the Shapiro-Wilk test. Non-normal distributed variables were compared with the Mann-Whitney-U test. Categorical variables were expressed with number and percentage (n, %) and compared with Pearson chi-square test or Fisher's exact test. Kaplan-Meier survival curves were generated to compare survival times between the <75 aged-group and ≥75 aged-group using a logrank test. Double-sided p-values of less than 0.05 were considered significant. R version 4.0.2 was used (https://www.r-project.org/) for statistical analysis and visualizations.

### RESULTS

The study group consisted of 19 male patients with a mean age of 75.9 (range: 57-96)

## Table 1: Demographics

|                      | [ALL]       | Ν  |
|----------------------|-------------|----|
|                      | N=19        |    |
| Mean age             | 75.9 (11.5) | 19 |
| Age                  |             | 19 |
| < 75                 | 10 (52.6%)  |    |
| ≥ 75                 | 9 (47.4%)   |    |
| Presenting complaint |             | 19 |
| Mass                 | 15 (78.9%)  | 19 |
| Pain                 | 1 (5.26%)   | 19 |
| Exulceration         | 7 (36.8%)   | 19 |
| Bleeding             | 1 (5.26%)   | 19 |
| Family history       | 4 (21.1%)   | 19 |
| BMI                  | 24.6 (4.58) | 19 |
| BMI                  |             | 19 |
| < 25                 | 11 (57.9%)  |    |
| ≥ 25                 | 8 (42.1%)   |    |
| Risk factors:        |             | 19 |
| None                 | 15 (78.9%)  |    |
| BRCA gene mut        | 3 (15.8%)   |    |
| RT exposure          | 1 (5.26%)   |    |
| Side:                |             | 19 |
| Right                | 10 (52.6%)  |    |
| Left                 | 9 (47.4%)   |    |
| Quadrant:            |             | 19 |
| Retroareolar         | 12 (63.2%)  |    |
| Single focus         | 3 (15.8%)   |    |
| Multicentric         | 2 (10.5%)   |    |
| Accessory            | 1 (5.26%)   |    |

The mean follow-up for OS was 43.84±38.6 months. Nine of our patients were aged 75 and above (47.4%). Tumors were in the right breast in 10 patients (52.6%) and in the left breast in 9 patients (47.4%). The tumor was most commonly found in the retroareolar region (n=12/19, 63.2%). The most common presenting complaint was a palpable mass in the breast (n=15/19, 78.9%). Family history was present in 4 patients (47.4%). BRCA gene mutation analysis was positive for 3 patients (15.8%). Radiation exposure (radiotherapy) was detected in one patient, and 8 patients (42%) had a body mass index (BMI) above 25. According to TNM staging, 1 patient (5.3%) had stage I disease, 7 patients (36.8%) had stage II, and 11 patients (57.9%) had stage III disease

Table 2: Tumor, radiological axilla, pathology and stage findings of the patients

mastectomy and breast conserving surgery (BCS) were performed in 11 (57.9%), 5 (26.3%), 2 (10.5%) and 1 (5.26%) patients, respectively

|                           | [ALL]                  | Ν  |
|---------------------------|------------------------|----|
|                           | N=19                   |    |
| T:                        |                        | 19 |
| T1                        | 5 (26.3%)              |    |
| T2<br>T3                  | 8 (42.1%)<br>3 (15.8%) |    |
| 13<br>T4                  | 3 (15.8%)              |    |
| N:                        | 5 (15.676)             | 19 |
| None                      | 9 (47.4%)              |    |
| USG ,MRI, PET Suspicious  | 10 (52.6%)             |    |
| USG:                      |                        | 19 |
| No suspicion              | 8 (42.1%)              |    |
| Suspicion present<br>MRI: | 11 (57.9%)             | 8  |
| No suspicion              | 6 (75.0%)              | 8  |
| Suspicion present         | 2 (25.0%)              |    |
| PET CT:                   | _ (                    | 13 |
| No suspicion              | 9 (69.2%)              |    |
| Suspicion present         | 4 (30.8%)              |    |
| Pathology:                |                        | 19 |
| 2 Galerieg):              |                        |    |
| İnvasive Ductal ca        | 11 (57.9%)             |    |
| Papillary ca              | 2 (10.5%)              |    |
| İnvasive Ductal ca+DCIS   | 2 (10.5%)              |    |
|                           |                        |    |
| Other                     | 4 (21.1%)              | 10 |
| Molecular_type:           |                        | 19 |
| Luminal A                 | 6 (31.6%)              |    |
| Luminal B                 | 12 (63.2%)             |    |
| Her2+                     | 1 (5.26%)              |    |
| Hormone ER+               | 19 (100%)              | 19 |
| Hormone PR+               | 19 (100%)              | 19 |
| Grade:                    |                        | 19 |
| 1                         | 1 (5.26%)              |    |
| 2                         | 14 (73.7%)             |    |
| 3                         | 4 (21.1%)              |    |
| Ki 67:                    |                        | 19 |
| < 14                      | 10 (52.6%)             |    |
| ≥ 14                      | 9 (47.4%)              |    |
| STAGE 1                   | 1 (5.3%)               |    |
| STAGE 2                   | 7(36.8%)               |    |
| STAGE 3                   | 11(57.9%)              |    |

Radiological imaging methods including ultrasonography (USG), magnetic resonance imaging (MRI), and positron emission tomography-computed tomography (PET-CT) revealed 10 patients (52.6%) with suspected axillary nodal involvement. Regarding the pathology results of our patients showed invasive ductal carcinoma (n=11, 57.9%), combination of invasive ductal carcinoma and ductal carcinoma in situ (n=2, 10.5%), papillary carcinoma (n=2, 10.5%), and the remaining cases had other types of carcinomas.

The Luminal B subtype was found in 63.2% of the patients (n=12), whereas 31.6% (n=6) had the Luminal A subtype, and 5.26% (n=1) had HER 2 (+) according to the molecular subtypes. Tumor grade was determined as Grade 2 in 14 cases (n=2, 73.7%), Grade 3 in 3 cases, and Grade 1 in 1 case. Ki-67  $\geq$ 14 was detected in 9 patients (47.4%).

Modified radical mastectomy (MRM), simple mastectomy, salvage

Table 3.: Treatments applied to patients, recurrence and mortality data

|   | [ALL]      | Ν  |  |  |
|---|------------|----|--|--|
|   | N=19       |    |  |  |
| Axillary dissection                                   | 13 (68.4%) | 19 |  |  |
| Pathological involvement<br>after axillary dissection |            | 16 |  |  |
| Surgery:  |            | 19 |  |  |
| Mastectomy  | 5 (26.3%)  |    |  |  |
| BCS   | 1 (5.26%)  |    |  |  |
| Salvage. Mastectomy                                   | 2 (10.5%)  |    |  |  |
| MRM   | 11 (57.9%) |    |  |  |
| Axilla method:  |            | 19 |  |  |
| AD  | 10 (52.6%) |    |  |  |
| SLNB+AD   | 3 (15.8%)  |    |  |  |
| SLNB  | 3 (15.8%)  |    |  |  |
| No AD   | 3 (15.8%)  |    |  |  |
| CT:   |            | 19 |  |  |
| None  | 11 (57.9%) |    |  |  |
| Adjuvant  | 7 (36.8%)  |    |  |  |
| NAC   | 1 (5.26%)  |    |  |  |
| RT  | 13 (68.4%) | 19 |  |  |
| HT  | 17 (89.5%) | 19 |  |  |
| Regional recurrence                                   | 3 (15.8%)  | 19 |  |  |
| Local recurrence                                      | 1 (5.26%)  | 19 |  |  |
| Distant met   | 3 (15.8%)  | 19 |  |  |
| Mortality   | 7 (36.8%)  | 19 |  |  |
| Mortality_disease                                     | 4 (21.1%)  | 19 |  |  |

Axillary lymph node dissection (ALND) was performed in a total of 13 patients (68.4%) including three patients with a positive sentinel lymph node (SLN). In 9 patients (69.2%) who underwent ALND, metastatic involvement was present. Axillary lymph node dissection was not performed in 3 patients, no other intervention was performed in a total of 3 patients with negative SLN biopsy results.

total of 3 patients with negative SLN biopsy results. In our study, among a total of 19 patients, 13 (68.4%) received radiotherapy, 17 (89.5%) received hormone therapy (HT), 1 (5.1%) received neoadjuvant chemotherapy (NAC) and 7 (36.8%) patients received adjuvant chemotherapy. Mortality took place in 7 (36.8%) patients as the 3 (15.8%) were due to breast carcinoma, 2 (10.5%) due to cerebrovascular disease, 1 (5.26%) due to myocardial infarction (MI), and 1 (5.26%) due to Covid-19.

Locoregional recurrence was detected in 3 of our patients, occurring at 12th, 84th, and 96th months. We performed a reoperation on the first patient, who developed recurrence in the axillary region, but unfortunately, they passed away due to MI at 41st month. The second patient is still alive, while the third patient, who had local and regional recurrence at 96 months, passed away at 103 months due to distant metastases. One (5.26%) out of 3 (15.8%) patients with distant metastasis developed a lung metastasis while the remaining 2 (10.5%) patients developed synchronous visceral organ and bone metastases. We lost all three of these patients at 12th, 17th, and 103rd months, respectively.

The relationship between disease-related mortality and clinical and pathological variables was analyzed in table 4.

Table 4. : Comparison of the group with and without disease-related mortality

|   | no                       | present                 | p.overall   | Ν        |
|---|--------------------------|-------------------------|-------------|----------|
| Age, median (%25-%75)                                       | N=15<br>73.0 [70.5;81.0] | N=4<br>79.0 [72.8;85.8] | 0.515       | 19       |
| Age:  |                          |                         | 0.303       | 19       |
| < 75  | 9 (90.0%)                | 1 (10.0%)               |             |          |
| ≥ 75<br>Mass:   | 6 (66.7%)                | 3 (33.3%)               | 0.530       | 19       |
| absent  | 4 (100%)                 | 0 (0.00%)               |             |          |
| present<br>Exulceration:                                    | 11 (73.3%)               | 4 (26.7%)               | 0.603       | 19       |
| no  | 10 (83.3%)               | 2 (16.7%)               | 0.002       |          |
| Family History:   | 5 (71.4%)                | 2 (28.6%)               | 1.000       | 19       |
| none  | 12 (80.0%)               | 3 (20.0%)               | 1.000       | 19       |
| present   | 3 (75.0%)                | 1 (25.0%)               |             | 10       |
| BMI, median (%25-%75)<br>BMI:                               | 25.7 [22.6;27.6]         | 20.5 [18.8;22.0]        | 0.021 0.103 | 19<br>19 |
| < 25  | 7 (63.6%)                | 4 (36.4%)               |             |          |
| ≥25<br>Risk Factor_   | 8 (100%)                 | 0 (0.00%)               | 0.178       | 19       |
| None  | 13 (86.7%)               | 2 (13.3%)               | 0.1,0       |          |
| BRCA gene mutation  | 2 (66.7%)                | 1 (33.3%)               |             |          |
| RT exposure<br>Rf_BRCA mut:                                 | 0 (0.00%)                | 1 (100%)                | 0.530       | 19       |
| no  | 13 (81.2%)               | 3 (18.8%)               |             |          |
| yes<br>RT exposure:   | 2 (66.7%)                | 1 (33.3%)               | 0.211       | 19       |
| no  | 15 (83.3%)               | 3 (16.7%)               | 0.211       | 19       |
| yes   | 0 (0.00%)                | 1 (100%)                | 0.007       |          |
| Laterality<br>right   | 6 (60.0%)                | 4 (40.0%)               | 0.087       | 19       |
| left  | 9 (100%)                 | 0 (0.00%)               |             |          |
| Quadrant  | 0.(75.06/)               | 3 (25.0%)               | 0.486       | 19       |
| Retroareolar<br>Single focus                                | 9 (75.0%)<br>3 (100%)    | 3 (25.0%)<br>0 (0.00%)  |             |          |
| Multicentric  | 2 (100%)                 | 0 (0.00%)               |             |          |
| Accessory<br>Retroareolar Multicentric                      | 1 (100%)<br>0 (0.00%)    | 0 (0.00%)<br>1 (100%)   |             |          |
| T:  | 0 (0.0078)               | 1 (100%)                | 0.546       | 19       |
| TI  | 5 (100%)                 | 0 (0.00%)               |             |          |
| T2<br>T3  | 6 (75.0%)<br>2 (66.7%)   | 2 (25.0%)<br>1 (33.3%)  |             |          |
| T4  | 2 (66.7%)                | 1 (33.3%)               |             |          |
| N Radiological Suspicion                                    | a (aa aa))               | 1 (11 14)               | 0.582       | 19       |
| No<br>USG ,MRI, PET   | 8 (88.9%)<br>7 (70.0%)   | 1 (11.1%)<br>3 (30.0%)  |             |          |
| Patology  |                          |                         | 0.603       | 19       |
| Învasive Ductal ca<br>Papillary ca                          | 9 (81.8%)<br>2 (100%)    | 2 (18.2%)<br>0 (0.00%)  |             |          |
| İnvasive Ductal ca+DCIS                                     | 2 (100%)                 | 0 (0.00%)               |             |          |
| Other   | 2 (50.0%)                | 2 (50.0%)               |             | 10       |
| Molecular Subtype:<br>Luminal A                             | 6 (100%)                 | 0 (0.00%)               | 0.404       | 19       |
| Luminal B   | 8 (66.7%)                | 4 (33.3%)               |             |          |
| Her2+<br>Grade:   | 1 (100%)                 | 0 (0.00%)               | 1.000       | 19       |
| 1   | 1 (100%)                 | 0 (0.00%)               | 1.000       |          |
| 2   | 11 (78.6%)               | 3 (21.4%)               |             |          |
| 3<br>ki67:  | 3 (75.0%)                | 1 (25.0%)               | 0.087       | 19       |
| <14   | 6 (60.0%)                | 4 (40.0%)               |             |          |
| ≥ 14<br>Pathological involvement after axillary dissection: | 9 (100%)                 | 0 (0.00%)               | 0.585       | 16       |
| Yes   | 6 (85.7%)                | 1 (14.3%)               | 0.565       | 10       |
| No  | 6 (66.7%)                | 3 (33.3%)               |             |          |
| Surgery:<br>Mastectomy                                      | 5 (100%)                 | 0 (0.00%)               | 0.503       | 19       |
| BCS   | 1 (100%)                 | 0 (0.00%)               |             |          |
| Salvage. Mastectomy<br>MRM                                  | 2 (100%)                 | 0 (0.00%)<br>4 (36.4%)  |             |          |
| Axilla method:  | 7 (63.6%)                | 4 (30.4%)               | 0.338       | 19       |
| AD  | 6 (60.0%)                | 4 (40.0%)               |             |          |
| SLNB+AD<br>SLNB   | 3 (100%)<br>3 (100%)     | 0 (0.00%)<br>0 (0.00%)  |             |          |
| No AD   | 3 (100%)                 | 0 (0.00%)               |             |          |
| СТ  |                          |                         | 0.404       | 19       |
| None<br>Adjuvant  | 9 (81.8%)<br>6 (85.7%)   | 2 (18.2%)<br>1 (14.3%)  |             |          |
| NAC   | 0 (0.00%)                | 1 (100%)                |             |          |
| RT<br>No  | 5 (83.3%)                | 1 (16.7%)               | 1.000       | 19       |
| No<br>Yes   | 5 (83.3%)<br>10 (76.9%)  | 3 (23.1%)               |             |          |
| HT  |                          |                         | 0.386       | 19       |
| No<br>Yes   | 1 (50.0%)<br>14 (82.4%)  | 1 (50.0%)<br>3 (17.6%)  |             |          |
| res<br>Regional recurrence:                                 | 14 (02.4%)               | 5 (17.0%)               | 0.530       | 19       |
| No  | 13 (81.2%)               | 3 (18.8%)               |             |          |
| Yes<br>Local Recurrence:                                    | 2 (66.7%)                | 1 (33.3%)               | 0.211       | 19       |
| No  | 15 (83.3%)               | 3 (16.7%)               |             | .,       |
| Yes<br>Distant Mate   | 0 (0.00%)                | 1 (100%)                | 0.004       | 10       |
| Distant_Met:<br>No  | 15 (93.8%)               | 1 (6.2%)                | 0.004       | 19       |
| Yes   | 0 (0.00%)                | 3 (100%)                |             |          |
|   |                          |                         |             |          |

While all patients with distant metastases were lost (100%), cancer-related mortality was observed in 1 (6.2%) of 16 patients without distant metastases (p=0.004). The BMI of the deceased patients was lower than the BMI of the patients who were alive during the follow-up period (p=0.021).

(p=0.021). In this study, the 5-year probability of OS and cancer-specific survival (CSS) was found to be 55.7% and 74.2%, respectively. Also, the 5-year probability of DFS was 93.8%. Figure 1 shows Kaplan Meier survival curves for OS, CSS and DFS by age group. Age group according to 75 years was significant for OS (log-rank p=0.0064) and CSS (log-rank p=0.011), but not for DFS (log-rank p=0.32)

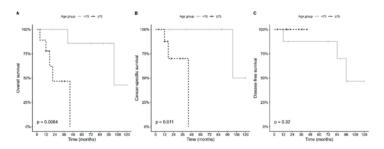


Figure 1: Kaplan Meier survival curves for overall survival (A), cancer-specific survival (B) and disease-free survival (C) according to age group (<75 and ≥75 years)

#### DISCUSSION

Male breast cancer is usually diagnosed between the ages of 60 and 70, with an average age of diagnosis being 67. Diagnostic age was observed to be 5 to 10 years older than that in female population. The incidence increases in accordance with age, peaking at 50 years (1.7/100,000) and reaching a plateau at 80 years and older (8.3/100,000).5 In our study, we identified an average age of diagnosis that is higher than the literature (75.9). Differences in average age at diagnosis may be due to age distribution of our study population. According to the literature and the World Health Organization, the age range of 75-90 is classified as senile age.<sup>6</sup>

In our study, 10 patients were (52.6%) below and 9 cases (47.4%) were above the age of 75 years of age, making a total of 19 cases. Family history studies suggest that 15-20% of men who received a diagnosis of MBC have a first-degree relative who was also diagnosed with breast cancer.7 We identified positive family history in 4 pa-tients (21.1%). Both BRCA2 and less commonly BRCA1 mutations are identified risk factors for MBC. In population studies that do not select for family history, BRCA2 mutations were detected in 4-33% while BRCA1 mutations seen only in 0-6% of the population. The average BRCA2 mutation rate calculated from the collected data is 10%.8 In our study, we detected BRCA2 gene mutations in 3 patients (15.8%). Apart from BRCA, there are 11 other gene mutations responsible for MBC. Other factors related to MBC include conditions that alter the estrogen/androgen ratio, obesity, and radiation exposure. Obesity with a BMI above 30 increases the risk by up to 80%. Physical activity appears to be a protective factor.9 Another risk factor is associated with exposure to therapeutic ionizing radiation and radiotherapy in childhood.10 In our study, one patient had a history of radiotherapy. In our patients, contrary to the commonly observed tumor side in the literature, we found a higher number of tumors on the right side, although there was no statistical significance. Patients (75%) most commonly present with a painless mass in the retroareolar region. Early signs of nipple involvement such as retraction, discharge, or ulceration are present in most of the patients. In our series, 15 cases (78.9%) presented with a complaint of a mass, and retroareolar involvement was present in 13 cases (68.4%).

Mammography, digital breast tomosynthesis, and ultrasound imaging are the main methods of imaging. In a young patient, if the USG findings are suspicious, a mammogram should be performed. The American College of Radiology suggests performing USG for males under 25 years old with a palpable mass and mammography for males over 25 years old. It should be noted that there is no evidence supporting the necessity of screening in asymptomatic males.11 When required, additional imaging techniques such as computed tomography (CT), magnetic resonance imaging, and PET-CT may be employed to complement the investigation and assist in treatment planning.<sup>12</sup>

In the histology of MBC, 85-95% of cases show invasive ductal carcinoma. Ductal carcinoma in situ (DCIS) is diagnosed in 5-10% of MBC cases.<sup>13</sup> In the largest multicenter study, out of 1483 cases, 85% were reported as invasive ductal carcinoma, 5.9% as mixed type (invasive and lobular), 3% as papillary carcinoma, 1.9% as mucinous carcinoma, and 1.4% as lobular carcinoma. Approximately 50% of the forementioned invasive cancers were histological grade 2.14 In our study, we identified 11 cases (57.9%) of invasive ductal carcinoma, 2 cases (10.5%) of invasive ductal carcinoma and others. We classified a total of 14 cases (73.7%) as nuclear grade 2. In the IMBCP study, they reported that 99.3% of cases were ER-positive, 81.9% were PR-positive,

96.7% were AR-positive, and 87% were HER2-positive. They found high Ki-67 levels in 25% of cases. According to their study, 42% were classified as Luminal A, 49% as Luminal B, 9% as HER2-positive, and 0.3% as triple-negative. In our study, we found that 31.6% were Luminal A, 63.2% were Luminal B, and 5.26% were HER2-positive. We did not have any triple-negative cases. In 9 cases, our Ki-67 proliferation index was found to be  $\geq$  14.

Male breast cancer is often an advanced stage at the time of diagnosis. Recent studies have shown that T4 disease accounts for 20-25% of cases. The probability of presenting at pT3-T4 stage significantly increases with age, reaching the highest percentage of 42% in patients over 70 years old. Axillary lymph node involvement is found in about 50% of MBC cases and is significantly associated with the pathological tumor size.<sup>15</sup>,<sup>16</sup> In our study, we classified 11 patients (57.9%) as Stage III.

Due to lack of sufficient studies, there is an inadequate clinical understanding concerning treatment options, regimens, and durations for localized and metastatic disease in MBC, which are generally extrapolated from recommendations and guidelines for FBC. A combination of surgery, radiotherapy, and systemic therapies are the treatment modalities for MBC.17 In early-stage MBC cases, surgery plays a fundamental role. Preferred surgical approach for early-stage MBC is modified radical mastectomy (MRM) which is performed in approximately 70% of patients (14). Breast-conserving surgery (BCS) is performed in the range of 10-24%. In our study, MRM was performed in 11 patients (57.9%), simple mastectomy in 5 patients, salvage mastectomy in 2 patients, and BCS in 1 patient. In a study, no significant difference was found in OS, DFS and disease-specific survival between BCS and mastectomy.18,19 ALND has become a standard procedure in MBC. Although studies on sentinel lymph node biopsy (SLNB) have shown similar accuracy rates to FBC, it is still underutilized.20 However, there aren't any randomized controlled studies focusing on the optimal surgical approach for the axilla in men. The use of SLNB alone is increasing in clinically No MBC, while ALND is decreasing (12). In our study, ALND was performed in 10 cases (52.6%), ALND after positive SLNB in 3 cases (15.8%), and no further axillary surgery after negative SLNB in 3 cases (15.8%). Nodal involvement was detected in a total of 9 cases (69.2%) after ALND. Hormonotherapy is the gold standard treatment for hormone re-ceptor-positive MBC. Since over 90% of MBCs are hormone re-

ceptor-positive MBC. Since over 90% of MBCs are hormone receptor-positive, Tamoxifen has been the most used anti-estrogen treatment in both men as in women. There is no prospective study specifically evaluating the effect of Tamoxifen in MBC. However, studies in early-stage MBC have shown that adjuvant Tamoxifen improves OS in node-positive disease.<sup>21</sup>,<sup>22</sup> Adjuvant chemotherapy is recommended for patients who are considered as high-risk typically due to their young age, high tumor grade, and/or axillary nodal involvement. Adjuvant chemotherapy regimens with cyclophosphamide, methotrexate, anthracycline-based, anthracycline-taxane-based, and 5-Fluorouracil improved OS in stage II and III disease.<sup>22</sup> There is no strong evidence for the use of radiotherapy following mastectomy. Recommendations for FBC regarding the prevention of disease recurrence and reduction of mortality are generally applicable to MBC.<sup>23</sup> In our study, hormone therapy was administered to 17 patients (89.5%), radiotherapy to 13 patients (69.4%), adjuvant chemotherapy to 7 patients (36.8%), and neoadjuvant chemotherapy to 1 patient.

Comparing the overall prognosis of male and FBC patients is controversial. Generally, the prognosis for MBC is worse. In a study, after adjusting for clinical characteristics, age, race/ethnicity, access to care, and treatment factors; the death rates at 3 and 5 years were higher in men.<sup>24</sup> Conversely, another study found that the relative 5-year survival of men was worse compared to women, but after adjusting for age, diagnosis year, stage, and treatment, they found that men had longer survival than women.<sup>25</sup> The 5 and 10-year survival rates for MBC have been reported as 89% and 72%, respectively.<sup>26</sup>

In our study, during an average follow-up period of 43.8 months, we identified one case of local recurrence, three cases of regional recurrence, and three cases of distant metastasis. Seven patients, three of whom were disease-related, succumbed to the disease. When investigating the impact of clinical-pathological characteristics on survival, we found that patients who developed distant metastasis had significantly lower OS (p: 0.004). The BMI of the deceased patients was lower than that of the surviving patients during the follow-up period (p=0.021).

## CONCLUSION

We observed high mortality in patients who developed distant metastasis in our study. Age group above 75 years had lower OS and CSS. We found a lower median BMI in relation to disease-related mortality. Similar to female breast cancer, male breast cancers, which continue to have increasing incidence rates, have different pathogenic factors compared to women. Regardless of a positive oncologic family history, genetic testing should be recommended for a male patient diagnosed with breast cancer. Evidence regarding somatic-level epigenetic changes may improve mortality and morbidity in specific subsets of male breast cancers with future targeted therapies.

## REFERENCES

1.Zheng G, Leone JP. Male Breast Cancer: An Updated Review of Epidemiology, Clinicopathology, and Treatment. J Oncol. 2022;2022:1734049. doi:10.1155/2022/1734049

2.Garreffa E, Arora D. Breast cancer in the elderly, in men and during pregnancy. Surgery. 2022;40:139–46.

3.Brinton LA, Carreon JD, Gierach GL, McGlynn KA, Gridley G. Etiologic factors for male breast cancer in the U.S. Veterans Affairs medical care system database. Breast Cancer Res Treat. 2010;119(1):185-192. doi:10.1007/s10549-009-0379-0

4.Giordano SH. Breast Cancer in Men. N Engl J Med. 2018;378(24):2311-2320. doi:10.1056/NEJMra1707939

5.Agrawal A, Ayantunde AA, Rampaul R, Robertson JF. Male breast cancer: a review of clinical management. Breast Cancer Res Treat. 2007;103(1):11-21. doi:10.1007/s10549-006-9356-z

6.Dyussenbayev, A. Age Periods Of Human Life. Advances in Social Sciences Research Journal, 2017; 4(6): 258-63. Dol:10.14738/ass-rj.46.2924.

7.46.2924. 7.Ferzoco RM, Ruddy KJ. The Epidemiology of Male Breast Cancer. Curr Oncol Rep. 2016;18(1):1. doi:10.1007/s11912-015-0487-4

8.Ding YC, Steele L, Kuan CJ, Greilac S, Neuhausen SL. Mutations in BRCA2 and PALB2 in male breast cancer cases from the United States. Breast Cancer Res Treat. 2011;126(3):771-778. doi:10.1007/s10549-010-1195-2

9.Brinton LA, Richesson DA, Gierach GL, Lacey JV Jr, Park Y, Hollenbeck AR, et al. Prospective evaluation of risk factors for male breast cancer. J Natl Cancer Inst. 2008;100(20):1477-1481. doi:10.1093/ jnci/djn329

10. Johansen Taber KA, Morisy LR, Osbahr AJ 3rd, Dickinson BD. Male breast cancer: risk factors, diagnosis, and management (Review). Oncol Rep. 2010;24(5):1115-1120. doi:10.3892/or\_00000962 11.Expert Panel on Breast Imaging:; Niell BL, Lourenco AP, Moy L, Baron P, Didwania AD, et al. ACR Appropriateness Criteria®

Evaluation of the Symptomatic Male Breast. J Am Coll Radiol. 2018;15(11S):S313-S320. doi:10.1016/j.jacr.2018.09.017

12.Ionescu S, Nicolescu AC, Marincas M, Madge OL, Simion L. An Update on the General Features of Breast Cancer in Male Patients-A Literature Review. Diagnostics (Basel). 2022;12(7):1554. doi:10.3390/diagnostics12071554

13.Korde LÁ, Zujewski JA, Kamin L, Giordano S, Domchek S, Anderson WF, et al. Multidisciplinary meeting on male breast cancer: summary and research recommendations. J Clin Oncol. 2010;20;28(12):2114-22. doi:10.1200/JCO.2009.25.5729 14.Doebar SC, Slaets L, Cardoso F, Giordano SH, Bartlett JM, Tryfonidis K, et al. Male breast cancer precursor lesions: analysis of the

14.Doebar SC, Slaets L, Cardoso F, Giordano SH, Bartlett JM, Tryfonidis K, et al. Male breast cancer precursor lesions: analysis of the EORTC 10085/TBCRC/BIG/NABCG International Male Breast Cancer Program. Mod Pathol. 2017;30(4):509-18. doi:10.1038/modpathol.2016.229

15.Cutuli B. Strategies in treating male breast cancer. Expert Opin Pharmacother. 2007;8(2):193-202. doi:10.1517/14656566.8.2.193

16.Sarmiento S, McColl M, Musavi L, Gani F, Canner JK, Jacobs L, et al. Male breast cancer: a closer look at patient and tumor characteristics and factors that affect survival using the National Cancer Database. Breast Cancer Res Treat. 2020;180(2):471-79. doi:10.1007/ s10549-020-05556-y

17.Pensabene M, Von Arx C, De Laurentiis M. Male Breast Cancer: From Molecular Genetics to Clinical Management. Cancers (Basel). 2022;14(8):2006. doi:10.3390/cancers14082006

18.Sauder CAM, Bateni SB, Davidson AJ, Nishijima DK. Breast Conserving Surgery Compared With Mastectomy in Male Breast Cancer: A Brief Systematic Review. Clin Breast Cancer. 2020;20(3):e309-14. doi:10.1016/j.clbc.2019.12.004

19.De La Cruz LM, Thiruchelvam PTR, Shivani J, Trina J, Blankenship SA, Fisher CS. Saving the Male Breast: A Systematic Literature Review of Breast-Conservation Surgery for Male Breast Cancer. Ann Surg Oncol. 2019;26(12):3939-44. doi:10.1245/s10434-019-07588-1

20.Flynn LW, Park J, Patil SM, Cody HS 3rd, Port ER. Sentinel lymph node biopsy is successful and accurate in male breast carcinoma. J Am Coll Surg. 2008;206(4):616-21. doi:10.1016/j.jamcollsurg.2007.11.005

21. Grenader T, Goldberg A, Shavit L. Second cancers in patients with male breast cancer: a literature review. J Cancer Surviv. 2008;2(2):73-8. doi:10.1007/s11764-008-0042-5

22.Yadav S, Karam D, Bin Riaz I, Xie H, Durani U, Duma N, et al. Male breast cancer in the United States: Treatment patterns and prognostic factors in the 21st century. Cancer. 2020;1;126(1):26-36. doi:10.1002/cncr.32472

23.Strnad V, Ott OJ, Hildebrandt G, Kauer-Dorner D, Knauerhase H, Major T, et al. 5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial. Lancet (London, England). 2016;387:229–38. doi:10.1016/S0140-6736(15)00471-7

24.Wang F, Shu X, Meszoely I, Pal T, Mayer IA, Yu Z, et al. Overall Mortality After Diagnosis of Breast Cancer in Men vs Women. JAMA Oncol. 2019;1;5(11):1589-96. doi:10.1001/jamaoncol.2019.2803

25.Miao H, Verkooijen HM, Chia KS, Bouchardy C, Pukkala E, Larønningen S, et al. Incidence and outcome of male breast cancer: an international population-based study. J Clin Oncol. 2011;20;29(33):4381-6. doi:10.1200/JCO.2011.36.8902

26.Adams SJ, Kanthan R. Paget's disease of the male breast in the 21st century: A systematic review. Breast. 2016;29:14-23. doi:10.1016/j.breast.2016.06.015