Original Article

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Male Breast Cancer in Portugal: A Descriptive Analysis of a 20-Year Cohort

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ABSTRACT

Objective: Male breast cancer (MBC) is a rare malignancy, representing less than 1% of all breast cancer cases. Despite the rising incidence, MBC research remains limited, with most data extrapolated from female breast cancer (FBC). This study evaluated the clinicopathological features, treatment strategies, and survival outcomes of MBC patients in Portugal over two decades.

Materials and Methods: A retrospective analysis of MBC cases from the Portuguese National Oncology registry (2001-2021) was conducted. Clinicopathological features, therapeutic strategies, and overall survival (OS) were assessed across three disease categories: localized, locally advanced, and metastatic. Hormone receptor status, human epidermal growth factor receptor 2 (HER2) expression, and Ki-67 index were recorded, and survival was estimated using Kaplan-Meier methods.

Results: A total of 620 MBC cases were included with median age at diagnosis 68 years (interquartile range: 60–77). Localized disease accounted for 60.3% of the cases, locally advanced for 24.5%, and metastatic 15.2%. Most tumours were invasive carcinoma of no special type (86%), and hormone receptor-positive (estrogen receptor: 96.6%; progesterone receptor: 85.6%). HER2 -disease was noted in 11.6% of cases and triple-negative in 1.6%. Mastectomy was the primary surgical intervention while tamoxifen was the most widely used adjuvant endocrine therapy-exemestane therapy (A-ET). ET was the most prescribed first-line therapy. Median OS was 86 months for localized, 70 months for locally advanced, and 41 months for metastatic disease.

Conclusion: This study highlights the unique challenges of MBC, including late-stage diagnoses and reliance on FBC-derived protocols. Findings suggest an urgent need for male-specific clinical trials and molecular research to optimise treatment and outcome. In Portugal increased awareness and early detection initiatives will be important to advance MBC care.

Keywords: Breast neoplasm; HER2 protein; hormone receptors; male breast cancer; mastectomy; survival analysis

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Key Points

- Male breast cancer is rare, accounting for less than 1% of all breast cancer cases, with limited research specific to male patients.
- The majority of tumours were hormone receptor-positive, while human epidermal growth factor receptor 2-positive and triple-negative disease was less common, consistent with female breast cancer subtypes.
- Mastectomy was the primary surgical approach, and tamoxifen was the most commonly prescribed adjuvant therapy.
- This study highlights the need for male-specific clinical trials, increased awareness, and early detection to improve outcomes.

Introduction

Male breast cancer (MBC) is a rare condition, accounting for less than 1% of all breast cancer (BC) cases worldwide, including in Portugal (1-4). Despite a rising incidence in recent decades (5), research on MBC remains limited, with most data extrapolated from female breast cancer (FBC) studies (6, 7).

MBC is often diagnosed at a later stage, with larger tumours, lymph node involvement, and distant metastases (7-11). Approximately half

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of cases are localized, with the remainder being regional or distant (12, 13). Histologically, invasive carcinoma of no special type accounts for 90% of MBC cases (7, 8, 13, 14), and most tumours express hormone receptors, predominantly of the luminal subtype (13, 15).

Risk factors for MBC include genetic predispositions, such as BRCA2 mutations, hormonal imbalances, and lifestyle factors. Elevated estrogen levels due to obesity, cirrhosis, or Klinefelter's syndrome significantly increase risk (14-20). Due to a lack of male-specific trials, MBC treatment usually follows FBC protocols (13). Surgery, particularly modified radical mastectomy, is the mainstay for early-stage disease, followed by adjuvant therapies. Tamoxifen is the standard treatment for hormone receptor-positive MBC, whereas aromatase inhibitors require additional gonadotropin-releasing hormone agonists for efficacy (21-25). Systemic therapies for metastatic disease are in line with FBC guidelines (Abreu).

MBC prognosis is influenced by delayed diagnosis, older age, and comorbidities (21). Survival outcomes vary by stage and molecular subtype, with early-stage MBC showing better prognoses than metastatic cases (3, 15).

The aim of this study was to analyse the clinical and pathological characteristics, treatment approaches, and survival outcomes of MBC patients in Portugal over two decades, addressing knowledge gaps and highlighting the need for tailored management strategies.

Materials and Methods

Patient Selection

We retrospectively collected MBC patients from Portugal's national oncological registry, National Oncology Registry (RON), from January 2001 to December 2021. The study included biologically male patients who had been histologically diagnosed with primary BC. Exclusion criteria included patients with incomplete or absent information about receptor expression on immunohistochemistry (IHC) and those with malignancies of skin origin or sarcoma histology on the breast. Initially, patients with incomplete or absent disease staging information, including clinical (c) and/or pathological (p) tumour node metastasis (TNM) staging, were excluded. However, an amendment to the protocol was made to enhance the cohort's representativeness. Patients with unknown tumour size (T) or nodal status (N) were included in the analysis if the TNM stage was known and other relevant clinical or histological data were available. These cases were explicitly categorised as "T unknown" or "N unknown".

This study was approved by the Data Protection and Ethics Committee of IPO-Porto (Opinion EPD 83/2024, date: 19.04.2024), as well as the RON Committee. The need for individual informed consent was waived due to the retrospective nature of the study and the absence of personally sensitive information.

Data Collection

The variables collected included the patient's demographics, clinicopathological characteristics of the disease, treatment modalities, such as surgery, systemic therapy, and survival outcomes. The Eastern Cooperative Oncology group (ECOG) performance status and the Charlson comorbidity index were collected according to medical records. Localised disease was defined as tumour staging c/pT1, c/pT2 without lymph node involvement (c/pN0). Locally advanced disease referred to tumours c/pT3 or c/pT4 and/or involving regional lymph nodes (c/pN1 or higher). Metastatic disease was determined/defined when distant metastases were present at diagnosis. Hormone receptors, human epidermal growth factor receptor 2 (HER2) overexpression, and Ki-67 were defined according to the medical record or the histopathological report. Hormone receptors were considered positive if the percentage of positive cancer cells was >1%. Cases with HER2 IHC "0", "1+", and "2+" with fluorescence *in situ* hybridization (FISH) negative were considered as negative. Cases with HER2 IHC "2+" with FISH positive and "3+" were considered positive. Ki-67 was considered positive if the expression was equal to or greater than 20% and negative if it was less than 20%.

Triple-negative disease was defined as cases where hormone receptors [estrogen receptor (ER) and progesterone receptor (PR)] were negative (<1% staining by IHC) and HER2 was considered negative (IHC 0 or 1+, or IHC 2+ with negative FISH testing).

The primary endpoint was overall survival (OS), defined as the time from first pathologic diagnosis to death from any cause or last follow-up. Survival status was defined according to outpatient records on 31 December 2023. Secondary endpoints included disease relapse, defined as any recurrence post-treatment (local, regional, or distant), and progression-free survival (PFS), measured from diagnosis to disease progression or death.

Statistical Analysis

For continuous variables, the median and respective interquartile range are presented. The underlying normality of data was assessed using the Kolmogorov-Smirnov test with Lilliefors correction. For categorical variables, results are presented as absolute and relative frequencies. Regarding the estimation of OS, the non-parametric Kaplan-Maier estimator was used. Comparisons between survival times for independent groups were performed using the log-rank test. All results with a *p*-value less than 0.05 were considered statistically significant. Data analysis was performed using the software R version 4.2.2.

Results

Patient Characteristics

We investigated 1,439 patients diagnosed with MBC from January 2001 to December 2021. Of these, 819 patients were excluded due to insufficient information regarding the disease's staging and/or IHC classification (Figure 1).

The study included 620 men diagnosed with BC. The patients' characteristics are presented in Tables 1A-1C. The median age at diagnosis was 68 (60–77) years. Median ECOG performance status was 1 (0–1), and the median Charlson comorbidity index was 2 (2–2) across the entire cohort. Geographically, as presented in Figure 2, most cases were located in Lisbon (38.1%), followed by Setubal (12.4%) and Oporto (8.4%). Of all 620 MBC cases, 60.3% of patients were classified as having localized disease, 24.5% locally advanced disease, and 15.2% metastatic disease. Most patients presented with cT1 or cT2 (24.7% and 29.5%, respectively) and had ER/PR-positive disease without HER2 expression (85.3%), while 12.7% had ER/PR/HER2-positive disease. Two patients presented with HER2-overexpressing MBC, and 10 had triple-negative disease. The median OS in the overall population was 70 months [95% confidence interval (CI): 58–87]. Patients with luminal-like disease had a median OS of 68 months (95% CI: 56–87). Those with ER/PR/HER2-positive disease had a

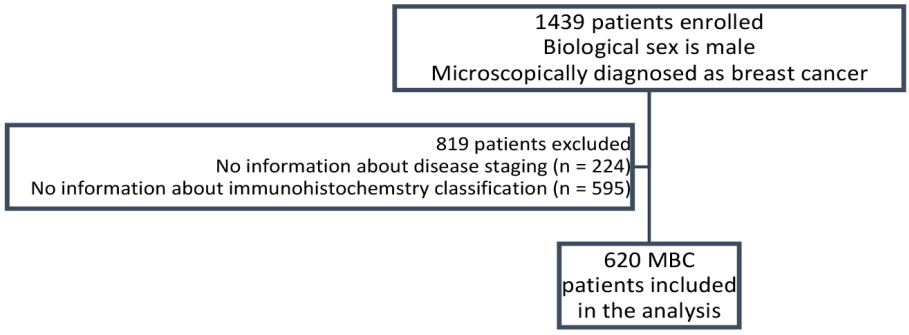

Figure 1. Flowchart outlining the patient selection criteria for MBC incidence across Portugal

MBC: Male breast cancer

Table 1A. Clinical and pathological characteristics of the study population

Variable	Overall population (*n* = 620)
Median age (IQR)	68.0 (60.0–77.0)
ECOG performance status	
0	200 (32.3%)
1	62 (10.0%)
2	18 (2.9%)
3	10 (1.6%)
4	7 (1.1%)
Unknown	323 (52.1%)
Charlson comorbidity index (median, IQR)	2.0 (2.0–2.0)
Tumor topography	
Central portion (subareolar)	236 (38.1%)
Unspecified breast	189 (30.5%)
Overlapping regions	102 (16.5%)
Upper outer quadrant	43 (6.9%)
Other regions	48 (7.7%)
Unknown	2 (0.3%)
Histology	
Non-special type carcinoma	533 (86.0%)
Lobular carcinoma	26 (4.2%)
Other histologies	41 (6.6%)
Unknown	20 (3.2%)
Receptor Status	
ER positive/negative	599 (96.6%)/21 (3.4%)
PR positive/negative/unknown	531 (85.6%)/53 (8.6%)/36 (5.8%)
HER2 positive/negative/unknown	72 (11.6%)/463 (74.7%)/85 (13.7%)
Ki67	
≥ 20%	437 (70.5%)
Unknown	183 (29.5%)
Grade	
1	73 (11.8%)
2	367 (59.2%)
3	132 (21.3%)
Unknown	48 (7.7%)
T Stage	
T0/is	11 (1.8%)
T1	153 (24.7%)
T2	83 (13.4%)
T3	36 (5.8%)
T4	30 (4.8%)
Unknown	207 (33.4%)
N stage	
N0	175 (28.2%)
N1	167 (26.9%)
N2	45 (7.3%)
N3	8 (1.3%)
Unknown	225 (36.3%)
Stage at diagnosis	
Stage I	222 (35.8%)
Stage II	152 (24.5%)
Stage III	152 (24.5%)
Stage IV	94 (15.2%)
Overall survival (median, 95% CI, months)	70 (58-87)

CI: Confidence interval; ER: Oestrogen receptor; HER-2: Human epidermal growth factor receptor 2 disease; IQR: Interquartile range; N: Nodal; PR: Progesterone receptor; T: Tumour; ECOG: Eastern cooperative oncology group; IQR: Interquartile range

Table 1B. Disease stage and treatment modalities

Variable	Localized (*n* = 374)	Locally advanced (*n* = 152)
Surgery performed		
Mastectomy[a]	360 (96.3%)	136 (89.5%)
Breast-conserving surgery	14 (3.7%)	-
Unknown	-	16 (10.5%)
Surgical radicality		
R0	22 (5.9%)	4 (2.6%)
Unknown	352 (94.1%)	148 (97.4%)
Adjuvant endocrine therapy		
Tamoxifen	213 (57.0%)	83 (54.6%)
Anastrozole	11 (2.9%)	2 (1.3%)
ET+GnRHa	14 (3.7%)	4 (2.6%)
Letrozole	6 (1.6%)	-
Switch ai to tamoxifen (or vice versa)	5 (1.3%)	4 (2.6%)
Unknown	125 (33.4%)	59 (38.8%)
Disease recurrence	12 (3.2%)	12 (7.9%)
Overall survival (median, 95% CI, months)	86 (62-106)	70 (53-94)

a: The specific type of mastectomy (modified radical, nipple-sparing, skin sparing or radical mastectomy) was not consistently reported in the dataset
ET: Endocrine therapy; CI: Confidence interval; ET+GnRHa: Endocrine therapy combined with gonadotropin-releasing hormone agonist; R0: Complete resection

Table 1C. Survival outcomes and metastatic treatment

Variable	Metastatic (*n* = 94)
Metastatic sites	
Bone	36 (38.3%)
Lung/pleura	25 (26.6%)
Liver	11 (11.7%)
Skin	7 (7.4%)
Unknown	15 (16.0%)
Systemic treatment (first-line)	32 (34.0%)
Fulvestrant	8 (25%)
Letrozole	2 (6.3%)
Exemestane	1 (3.1%)
Ribociclib + letrozole	5 (15.6%)
Palbociclib + letrozole	2 (6.3%)
Taxane + double blockade	6 (18.8%)
Taxane monotherapy	4 (12.5%)
Taxane - anthracycline sequence	2 (6.3%)
Taxane - platinum combination	2 (6.3%)
Systemic treatment (second-line)	12 (12.9%)
Fulvestrant	5 (41.7%)
Letrozole	1 (8.3%)
Capecitabine	3 (25.0%)
Everolimus + fulvestrant	1 (8.3%)
Sacituzumab-govitecan	1 (8.3%)
Vinorelbine	1 (8.3%)
Overall survival (median, 95% CI, months)	41 (25–65)

CI: Confidence interval

median OS of 80 months (95% CI: 45-NA). For patients with triple-negative disease, three death events occurred, and the median OS was 119 months (95% CI: NA; NA). Regarding the two patients with HER2-overexpressing disease, one died one month after diagnosis, and the other was alive at the end of follow-up. Kaplan-Meier survival curves for each stage and each subtype are presented in Figure 3 and Figure 4.

Localized Disease

The median age for patients with localised disease was 67 (60–76) years. Regarding IHC subtypes, 85.6% were classified as luminal-like disease, 12.6% as luminal-like with HER2-positive, 0.3% as HER2-overexpression and 0.8% as triple negative disease. Most patients with localized disease underwent mastectomy (96.3%) while a smaller proportion underwent breast-conserving surgery (3.7%). Tamoxifen was the most commonly prescribed adjuvant endocrine therapy (A-ET), used in 57.0%, as summarized in Table 1B. Anastrozole was the second most prescribed ET, used in 2.9% of the patients. The combination of ET with gonadotrophin-releasing hormone analogue (GnRHa) was used in 3.7% of the cases, while letrozole alone was used in 1.6%. Adjuvant therapy data was missing in 33.4% of the patients. Disease relapse was experienced in 12 patients. The median OS was 86 months (95% CI: 62–106).

Locally Advanced Disease

The median age for patients with locally advanced disease was 71 (61–78) years. As in localized disease, locally advanced tumours were predominantly luminal-like (84.9%) subtypes. Luminal-like HER2-positive disease was present in 11.2% of cases, while HER2 overexpression and triple-negative subtypes accounted for 0.7% and 2.0%, respectively. Most patients with locally advanced disease underwent mastectomy (89.5%), as presented in Table 1B. However, the type of surgery was not documented in 10.5% (n=16). Regarding A-ET, tamoxifen was the most commonly used adjuvant treatment, similarly to localised disease, prescribed to 54.6% of patients. A combination of ET with a GnRH analogue was used in 2.6% of patients, as well as a switch in therapy between aromatase inhibitors and tamoxifen (or vice versa). Adjuvant treatment data was missing in 38.8% of the cases. Data regarding neoadjuvant/adjuvant chemotherapy was missing in all cases. Disease relapse was experienced in 12 patients. Concerning survival, patients with locally advanced disease had a median OS of 70 months (95% CI: 53–94).

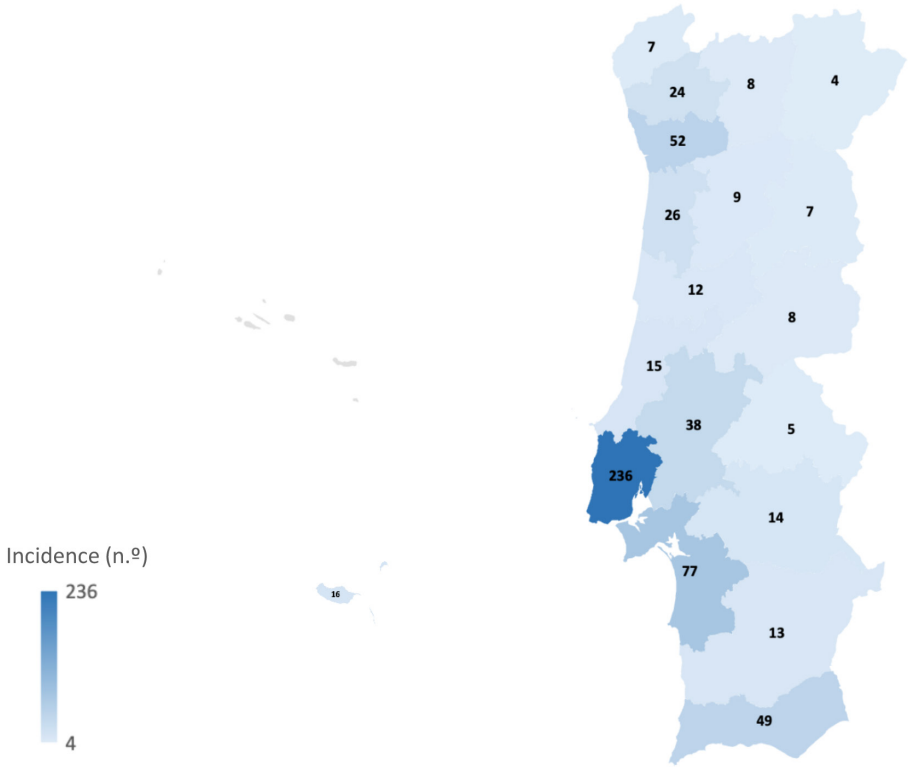

Figure 2. Map illustrating the incidence (n.º) of MBC across districts in Portugal between January 2001 to December 2021

MBC: Male breast cancer

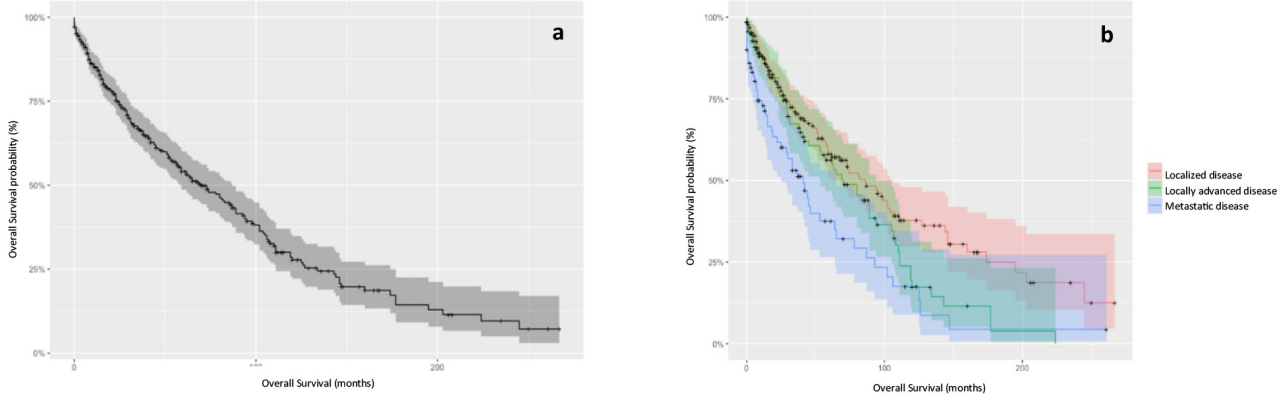

Figure 3. Kaplan-Meier curves for overall survival for MBC patients. (a) Depicts the total population. (b) Depicts patients with localized, locally advanced and metastatic disease

MBC: Male breast cancer

Metastatic Disease

The median age at diagnosis for metastatic disease was 68 (58-78) years. The most frequent sites of metastases were bone (38.3%), lung/pleura (26.6%), and liver (11.7%), as detailed in Table 1C. Regarding IHC subtypes, 88.3% of the patients had luminal-like disease, 6.4% had luminal-like with HER2 co-expression and 4.3% triple negative-like. The information about systemic treatment was available in 32 (34%) of metastatic disease patients. Of those, 11 received ET as a first-line treatment, eight fulvestrant, two letrozole and one exemestane. Seven patients were treated with cyclin-dependent kinase 4/6 inhibitors (iCDK4/6) in combination with endocrine therapy: five patients with the combination of ribociclib and letrozole and two with palbociclib and letrozole. The remaining patients received chemotherapy as first-line treatment. Disease progression on first-line therapy was reported in twelve patients; of those, six received second-line ET. The median duration of first-line treatment for metastatic disease was 5 (3.3–6.7) months. Due to small numbers and incomplete/absent data, median PFS calculation was not performed. In addition, one patient with ER/PR-positive disease was treated with PARP inhibitors, with a presumed BRCA pathogenic variant, though no direct confirmation was available in the database. The median OS for metastatic disease was 41 months (95% CI: 25–65).

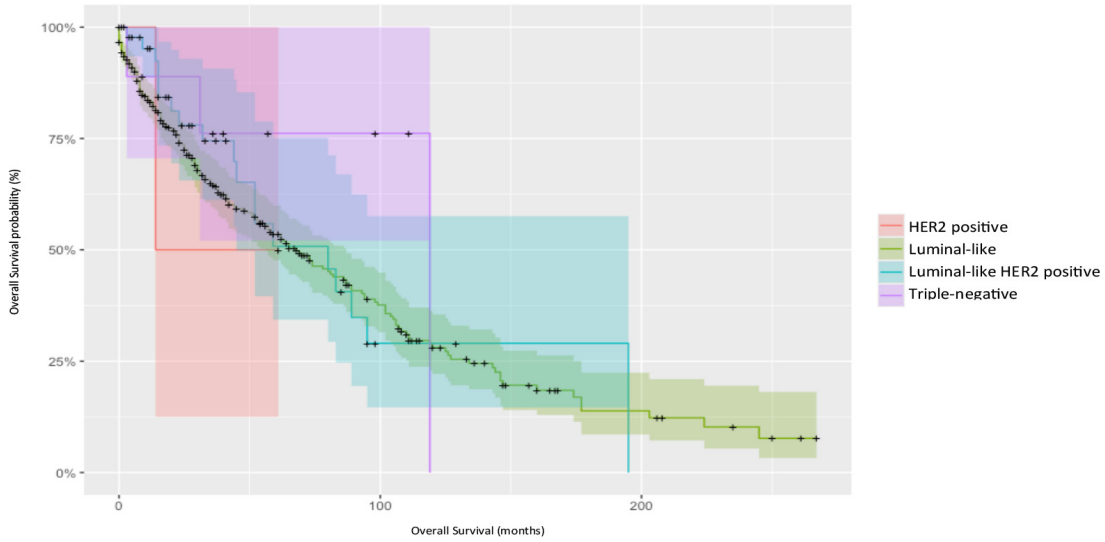

Figure 4. Kaplan-Meier curves for overall survival for MBC patients, stratified by IHC subtypes

HER2: Human epidermal growth factor receptor 2 disease; IHC: Immunohistochemistry; MBC: Male breast cancer

Discussion and Conclusion

This study comprehensively analysed MBC patients in Portugal over two decades, highlighting this rare malignancy's clinical and pathological characteristics, treatment modalities, and survival outcomes. Our findings corroborate established MBC trends while providing valuable insights into specific characteristics observed within this study population. MBC was predominantly diagnosed in older men, with a median age of 68 years. Our findings are consistent with previous literature and earlier Portuguese studies, which reported median ages ranging from 63 to 68 years (2, 3, 15, 26, 27). These results underscore the consistent pattern of older age at diagnosis in MBC compared to FBC. Furthermore, within our cohort a significant proportion of patients presented with localised or locally advanced disease, while 15.2% were diagnosed with metastatic disease. The proportion of patients with metastatic disease in this study markedly exceeds international reports (3.8%) and national averages (7.2%) (13, 15). The higher prevalence of advanced-stage disease may reflect delays in recognition and diagnosis, underscoring the pressing need for heightened awareness among both patients and healthcare providers.

In terms of histopathological characteristics, invasive carcinoma of no special type accounted for the majority of cases, in line with prior Portuguese and global studies (3, 7, 8, 14, 15). Hormone receptor positivity was highly prevalent, with ER positive and PR positive-disease exceeding 90% across all stages. This aligns with findings by Abreu et al. (15) and André et al. (3), who reported ER-positivity rates of 91–95% and PR-positivity rates of 75–89%. HER2-positivity was observed in approximately 11.6% of cases, corresponding to rates of 6.8–8.1% reported in earlier studies (28). Triple-negative-like disease was rare, at 1.6%, matching the previously reported range of 0.3–3.2%, further emphasising the differences between MBC and FBC (3, 13).

Concerning treatment patterns, surgical intervention remained central to MBC management, with mastectomy being the most commonly employed approach. This strategy is consistent with established treatment guidelines and findings from previous global and Portuguese studies, which highlight the anatomical constraints of the male breast that limit the feasibility of breast-conserving surgery (15, 21, 22). A-ET, particularly tamoxifen, was widely used and reflects the predominance of hormone receptor-positive tumours (13, 15). These findings underscore the continued reliance on extrapolated FBC protocols due to the scarcity of male-specific evidence.

The median OS in our cohort was 70 months, markedly lower than the global median OS of 10.4 years reported by Cardoso et al. (13). According to the methodology of our study, localized disease was defined as c/pT1 or c/pT2 and c/pN0; locally advanced disease as c/pT3 or c/pT4 and/or c/pN1 or higher, and metastatic disease as the presence of distant metastases at diagnosis. These methodological differences in disease classification at presentation may partly explain the observed disparity in survival outcomes. Specifically, the median OS for localized disease was 86 months (95% CI: 62–106), while patients with locally advanced disease had a median OS of 70 months (95% CI: 53–94). The median OS for metastatic disease was notably lower, at 41 months (95% CI: 25–65). While direct comparison with global literature is limited, Cardoso et al. (13) reported a median OS of 10.4 years (95% CI: 8.8–11.8) for early-stage disease (N0M0), 8.4 years (95% CI: 7.1–9.4) for N-positive, M0 disease, and 2.6 years (95% CI: 2.0–3.7) for M1 disease (13).

Notable variations in survival outcomes were observed across subtypes. For instance, luminal-like disease demonstrated a median OS of 68 months, which is significantly lower than the 10.5 years reported by Abreu et al. (15). Paradoxically, triple-negative-like disease exhibited an unexpectedly high median OS of 119 months, contrasting with the poor prognosis typically associated with this subtype, as evidenced in earlier studies (1.3 years) (15). These findings may be attributed to the small sample size of triple-negative cases and the limited number of deaths (three) recorded. Of the two patients with HER2-overexpressing disease, one succumbed 14 months after diagnosis. However, the small sample sizes of these subtypes constrain the robustness of our analysis and limit comparisons with existing literature.

Notably, factors such as tumour size greater than 2 cm and nodal involvement, which have been highlighted as significant prognostic factors in previous Portuguese studies by Abreu et al. (15, 28-30) were

not observed to have a similar impact on survival outcomes in our cohort.

Over the past two decades, advances in systemic therapy have redefined BC treatment and may hold significant potential for MBC. CDK4/6 inhibitors have become the standard of care for hormone receptor-positive disease, improving survival and disease control. Novel HER2-targeted therapies, such as antibody-drug conjugates and tyrosine kinase inhibitors, have expanded options for HER2-positive patients, while immune checkpoint inhibitors have enhanced outcomes in triple-negative BC. Despite these advances in FBC, their impact on MBC remains unclear, highlighting once again the need for further research.

Study Limitations

This study has several limitations that warrant consideration. The retrospective design restricts the ability to establish causal relationships and depends on the completeness of medical records, which may introduce reporting biases. A substantial proportion of patients (819 out of 1439) were excluded due to insufficient information on disease staging (n = 224) or IHC classification (n = 595), potentially leading to selection bias and limiting the generalizability of the findings. Despite this, an analysis of the excluded cohort revealed that their basic demographic and clinical characteristics, such as mean age at diagnosis (67.5 years, standard deviation 12.2), tumour topography (predominantly central region of the breast, 38.1%), and morphology (86% carcinoma SOE), were comparable to those of the included cohort. This suggests that the potential impact of selection bias may be mitigated. A substantial number of included cases (33.4% for tumour size and 36.3% for nodal status) had staging information classified as "unknown". To improve representativeness, these patients were included in the analysis if their TNM stage was known and relevant clinical or histological data were available. This approach reduced the loss of valuable information but highlights the challenge of data collection during the study period. Moreover, these findings underscore the importance of improving national cancer registries to enhance data collection on staging and disease characteristics. Strengthening cancer registries will support more accurate epidemiological studies and inform clinical decision-making in MBC. Another limitation of our study was that while mastectomy was the predominant surgical approach, the specific type of procedure (simple, modified radical, or radical) was not consistently reported in the dataset. This lack of detail prevents a more granular analysis of surgical outcomes. Moreover, the study did not include molecular subtyping, such as genetic profiling or analysis of genomic alterations, which constrains its capacity to explore the molecular landscape and heterogeneity of MBC. Key factors such as BRCA mutation status, androgen receptor expression, and other emerging biomarkers were not assessed, limiting insights into the genetic and epigenetic underpinnings of MBC. While trends associated with age, ECOG score, and Charlson index were identified, none achieved statistical significance, possibly due to the sample size or cohort heterogeneity, highlighting the need for further research with larger datasets. In addition, systemic therapy data for metastatic patients were incomplete, with detailed information available for only 26.6% of cases, potentially skewing the analysis of treatment efficacy. Moreover, the absence of comprehensive data on relapse management for localized and locally advanced cases hinders a complete understanding of long-term treatment outcomes. These limitations emphasize the critical need for better policies. National Registries must have the capacity to use data very effectively in order to support public health policy proposals and inform political decisions. Prospective, male-specific studies like EORTC 10085/TBCRC/BIG/NABCG International MBC Program that is ongoing, are eagerly awaited to better understand and manage MBC. This study emphasised the unique characteristics and challenges associated with managing MBC. Despite its rarity, MBC presents a complex interplay of late-stage diagnosis, hormonal receptor expression, and comorbidities that influence outcomes. While current treatment strategies rely heavily on FBC cancer protocols, this study highlights the need for dedicated male-specific research to optimise treatment and improve survival outcomes. Efforts should focus on early detection programs and male-specific clinical trials to address these unique challenges. While routine screening for MBC is not widely recommended due to its low incidence, high-risk individuals "particularly BRCA mutation carriers" require targeted surveillance strategies. According to National Comprehensive Cancer Network and European Society for Medical Oncology guidelines, men with BRCA1 or BRCA2 mutations should undergo annual clinical breast exams from age 35 years and perform regular breast self-examinations (31-33). Mammography is not routinely advised but may be considered in cases of gynecomastia or palpable abnormalities (31-33). Given the challenges in early detection and the limited MBC-specific evidence, further research is needed to refine screening protocols and improve outcomes in high-risk male populations. In parallel, a deeper understanding of the molecular landscape of MBC is essential to identify targeted treatment opportunities. Future studies should explore the role of personalized treatment approaches, paving the way for tailored therapeutic strategies and improved patient care.

To conclude, we advocate for action to support potential initiatives like using advanced technologies such as artificial intelligence to improve national clinical data management. Aligned with European Union publications (EU health data centre and a common data strategy for public health, 2021), we urge the need to endorse policy options on how to set up health data centres with a common strategy for health data, as a way to achieve a public health datafication multi-level process. This would also create a central coordination and support structure together with advanced digital public health functions, having the potential to alter public health significantly, including for MBC.

Ethics

Ethics Committee Approval: This study was approved by the Data Protection and Ethics Committee of IPO-Porto (Opinion EPD 83/2024, date: 19.04.2024), as well as the RON Committee.

Informed Consent: The need for individual informed consent was waived due to the retrospective nature of the study and the absence of personally sensitive information.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.A.M., S.D.O.; Concept: M.A.M., S.D.O.; Design: M.A.M., T.D.G., S.D.O.; Data Collection or Processing: M.A.M., T.D.D., T.D.G.; Analysis or Interpretation: M.A.M., T.D.D., T.D.G., R.Q.F.; Literature Search: M.A.M., R.Q.F., I.T.F., D.C.S., L.F., S.D.O., R.E., F.R.V.; Writing: M.A.M., T.D.D., T.D.G., R.Q.F., I.T.F., D.C.S., L.F., S.D.O., R.E., F.R.V.

Conflict of Interest: No conflict of interest was declared by the authors.

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