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Male breast cancer: experience in a University Hospital in Chile

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Abstract

Introduction: Male breast cancer (MBC) is a rare malignancy, accounting for less than 1% of all breast cancers (BC). Evidence guiding its management is largely extrapolated from female BC, although MBC has distinct clinicopathological features that warrant dedicated description in local settings.

Methods: A descriptive retrospective observational study was conducted of men with BC treated surgically at the Hospital Clínico UC CHRISTUS. Clinical presentation, histopathology, treatment patterns, germline testing and follow-up outcomes were described.

Results: Sixteen patients treated between 2008 and 2025 were included. Median age at presentation was 74 years (range 50–84), and all patients presented with a palpable breast mass. Most tumours were invasive (87.5%) and predominantly invasive ductal carcinoma (81.2%). Hormone receptor (HR) positivity was observed in 15 cases, and HER2 amplification was identified in only one patient. Median tumour size was 19 mm (range 5–42). Mastectomy was performed in 93.8% of patients, and sentinel lymph node biopsy in 62.5%; 25.0% had pathologically positive axillary nodes. Neoadjuvant therapy was administered in 31.2% of patients, most commonly chemotherapy. Adjuvant endocrine therapy was the most frequently used systemic treatment (75.0%), followed by chemotherapy (37.5%) and radiotherapy (31.2%). Germline testing was performed in 6 of 16 patients, identifying two breast cancer gene 2 pathogenic variants. During follow-up, three patients died, one due to BC progression and two from non-oncologic causes.

Discussion: This series represents the largest published Chilean cohort of MBC to date. Findings are consistent with a predominantly invasive ductal, HR-positive profile and with contemporary treatment patterns in which mastectomy, axillary staging and adjuvant endocrine therapy are commonly used. Because of the limited sample size and low number of events, outcome findings should be interpreted descriptively. Improved access to standardised biomarker evaluation and genetic testing may help refine care in this uncommon disease.

Research

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Introduction

Male breast cancer (MBC) is an uncommon disease within the broader global burden of breast cancer (BC), accounting for 1% to 1.8% of all BC cases diagnosed annually worldwide [1–4]. A man's lifetime risk of developing BC is approximately 1 in 1,000, compared with 1 in 8 for a woman [5]. MBC is usually diagnosed at more advanced stages, with a mean age at presentation close to 67 years [6, 7]. Lower survival has been observed in men compared with women, due to presentation at older ages and delayed diagnoses [3, 8]. However, the global incidence of MBC has shown a gradual increase over recent decades [9]. Among the main risk factors described for MBC are advanced age, germline mutations in the breast cancer gene 1 (BRCA1) and breast cancer gene 2 (BRCA2) genes and prior thoracic irradiation, among others (Table 1) [9, 10].

Table 1. Risk factors for MBC.

Risk factors for BC in men
Advanced age
Family history of BC
Germline mutations in hereditary cancer predisposition genes BRCA2 BRCA1 Others: CHEK2, PALB2, PTEN
Hormonal factors Klinefelter syndrome Altered estrogen/androgen balance Obesity Excessive alcohol consumption Chronic liver disease Exposure to exogenous estrogens (e.g., hormonal therapy for prostate cancer) Testicular disorders (e.g., cryptorchidism, mumps orchitis, orchiectomy)
Environmental exposures Ionizing radiation Organophosphates
Emerging risk factors
Idiopathic gynecomastia
Type 2 diabetes mellitus
Hyperthyroidism
Cholelithiasis
Null paternity (absence of fatherhood)
Use of male hormonal medications 5-alpha reductase inhibitors Anabolic steroids

Published Chilean data on MBC remain limited, underscoring the need for institutional and national reports that better characterise this disease in the local setting. Therefore, generating local evidence may facilitate the development of timelier, more effective and context-adapted strategies, with potential impact on survival and quality of life in affected patients.

The objective of this study was to describe the demographic, clinicopathological, treatment and follow-up characteristics of male patients with BC treated at the Hospital Clínico UC CHRISTUS between 2008 and 2025.

Materials and methods

An observational, descriptive, retrospective study was conducted based on the longitudinal BC registry of the Pontificia Universidad Católica de Chile Cancer Centre. It included all male patients with a confirmed diagnosis of BC who underwent surgical treatment at this university centre in Santiago, Chile, between 2008 and 2025. For the purposes of this study, the term 'men' was used to refer to individuals assigned male sex at birth, regardless of gender identity.

Demographic, clinical, pathological, treatment and outcome data were collected from the institutional registry and entered into a Microsoft Excel database. Continuous variables are presented descriptively as median and range, and categorical variables as counts and percentages. Overall survival was described for the full cohort. Given the small sample size, prolonged accrual period and low number of outcome events, no formal hypothesis testing, subgroup comparisons or multivariable modelling were performed. Survival analyses were included for descriptive purposes only and were not intended to identify prognostic associations. Because of the retrospective design and the prolonged study period, complete clinicopathological data were not available for all 16 patients. Biomarker assessment, particularly HER2 and Ki-67, as well as germline testing, was not uniformly available across all cases. Descriptive analyses were therefore performed according to data availability for each variable. Analyses were conducted in R (version 4.5.0) via RStudio (version 2025.05.0+496).

Data were appropriately anonymised to ensure patient confidentiality, and the study complied with the institution's established ethical standards. The research protocol was reviewed and approved by the Scientific Ethics Committee of the Pontificia Universidad Católica de Chile.

Results

Between 2008 and 2025, 16 men with BC were treated surgically at the Hospital Clínico UC CHRISTUS. Baseline clinicopathological and surgical characteristics are summarised in Table 2. The median age at presentation was 74 years (range 50–84), with most patients in the 70–79 age group (62.5%). All patients presented with a palpable breast mass. Tumours were predominantly invasive (87.5%), most commonly invasive ductal carcinoma (81.2%) and were hormone receptor (HR)-positive in nearly all cases (93.8%). The median tumour size was 19 mm (range 5–42). HER2 assessment on core biopsy was incomplete in a substantial proportion of cases; among those evaluated, most showed IHC 0–2+ and only one patient had HER2 amplification confirmed by fluorescence *in situ* hybridisation (FISH). Pathologic stage was most often early, with pT1 disease in 43.8% and pN0 status in 75.0% of patients. Mastectomy was the most common surgical approach (93.8%), usually combined with sentinel lymph node biopsy (SLNB) (62.5%). Germline testing was performed in 6 of 16 patients, identifying two BRCA2 pathogenic variants.

Note 1: Percentages use the total cohort as the denominator (N = 16) and are rounded to 1 decimal. For variables with missing data, categories are shown as 'Unknown/Not evaluated/Not performed' where applicable. HER2 immunohistochemistry is based on core biopsy results (HER2 core)

Note 2: ER: Estrogen receptor; PR: Progesterone receptor; HER2: Human epidermal growth factor receptor 2; IHC: Immunohistochemistry; FISH: Fluorescence in situ hybridisation; pT: Pathologic primary tumour category; pN: Pathologic nodal category; pTis: Pathologic tumour in situ; BCS: Breast-conserving surgery; SLNB: Sentinel lymph node biopsy; ALND: Axillary lymph node dissection; BRCA1/2: BC susceptibility genes 1 and 2

Table 2. Main clinicopathological characteristics of the MBC cohort (*N* = 16).

Characteristic	*n* (%)
Age	
<70 years	4 (25.0)
70–79 years	10 (62.5)
≥80 years	2 (12.5)
Tumour invasiveness	
Invasive carcinoma	14 (87.5)
In situ carcinoma	1 (6.2)
Microinvasive carcinoma	1 (6.2)
Histologic type	
Invasive ductal carcinoma	13 (81.2)
Papillary carcinoma	2 (12.5)
Neuroendocrine carcinoma	1 (6.2)
Histologic grade	
Grade 1	2 (12.5)
Grade 2	6 (37.5)
Grade 3	6 (37.5)
Unknown	2 (12.5)
Biomarkers	
HR positive	15 (93.8)
HR negative	1 (6.2)
ER <1%	1 (6.2)
ER ≥1%	15 (93.8)
PR <1%	1 (6.2)
PR ≥1%	14 (87.5)
PR not evaluated	1 (6.2)
HER2 IHC on core biopsy	
0	4 (25.0)
1+	3 (18.8)
2+	3 (18.8)
3+	0 (0.0)
Not evaluated	6 (37.5)
FISH HER2	
Positive	1 (6.2)
Negative	3 (18.8)
Not performed	11 (68.8)
Unknown	1 (6.2)
Pathologic staging	
pT category	

Continued

Table 2. Main clinicopathological characteristics of the MBC cohort (*N* = 16). *Continued*

pTis	2 (12.5)
pT1 (overall)	7 (43.8)
pT1a	1 (6.2)
pT1b	2 (12.5)
pT1c	3 (18.8)
pT1 (unspecified)	1 (6.2)
pT2	4 (25.0)
pT4b	3 (18.8)
pN category	
pN0	12 (75.0)
pN1mi	1 (6.2)
pN1	1 (6.2)
pN2	2 (12.5)
Surgery	
Mastectomy	15 (93.8)
BCS	1 (6.2)
Axillary surgery	
SLNB	10 (62.5)
Axillary lymph node dissection (ALND)	5 (31.2)
None	1 (6.2)
Genetic testing (BRCA1/2)	
BRCA2 pathogenic variant	2 (12.5)
BRCA negative	4 (25.0)
BRCA not tested	10 (62.5)

Treatment patterns are summarised in Figure 1. Neoadjuvant therapy was administered in 5 of 16 patients (31.2%), most commonly chemotherapy. Adjuvant endocrine therapy was the most frequently used systemic treatment (75.0%), followed by adjuvant chemotherapy (37.5%) and radiotherapy (31.2%). Core-biopsy Ki-67 was ≥20% in 8 of 16 patients, but was not evaluated in 8 cases.

Survival outcomes are shown in Figure 2. During follow-up, three patients died: one due to BC progression and two from non-oncologic causes.

Discussion

Literature review

Clinical, diagnostic and pathological characteristics of MBC

The most common clinical presentation of MBC is a palpable, non-tender retroareolar mass. Other signs include nipple retraction, skin ulceration and axillary lymphadenopathy [5, 9, 10]. Rare nipple-centred presentations such as Paget disease of the breast may also occur in men, although they were not represented in our cohort [11]. Initial evaluation is based on mammography and breast ultrasound, while confirmation is obtained by core needle biopsy [5]. Due to delays in detection, men are more likely to present with axillary lymph node metastases at

the time of diagnosis [2, 5, 12]. Limited awareness of this disease in males contributes to diagnostic delays; it is estimated that up to 40% of men are diagnosed at advanced stages (III–IV) [9].

Histologically, invasive ductal carcinoma is the most common type, followed by less frequent variants such as tubular and lobular carcinoma [12]. MBC follows the same molecular classification used in women [13, 14]. However, there is a clear predominance of HR-driven subtypes, with 95% of tumours classified as luminal and only a minority as HER2-positive or triple-negative [9]. Accordingly, compared with women, male tumours show higher expression of estrogen (ER), progesterone (PR) and androgen (AR) receptors, while approximately 10% are HER2-positive [5].

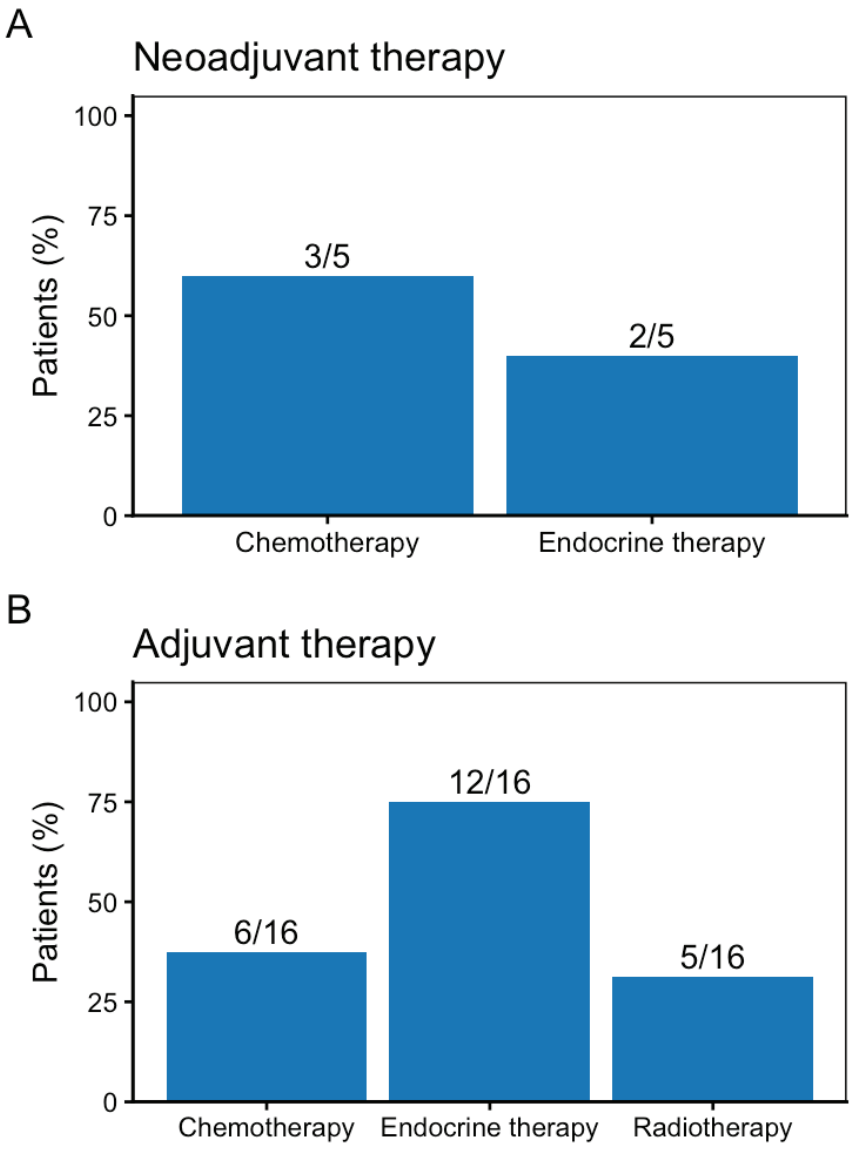

Figure 1. Neoadjuvant therapy and adjuvant treatment distribution (*n* = 16; neoadjuvant subset *n* = 5).

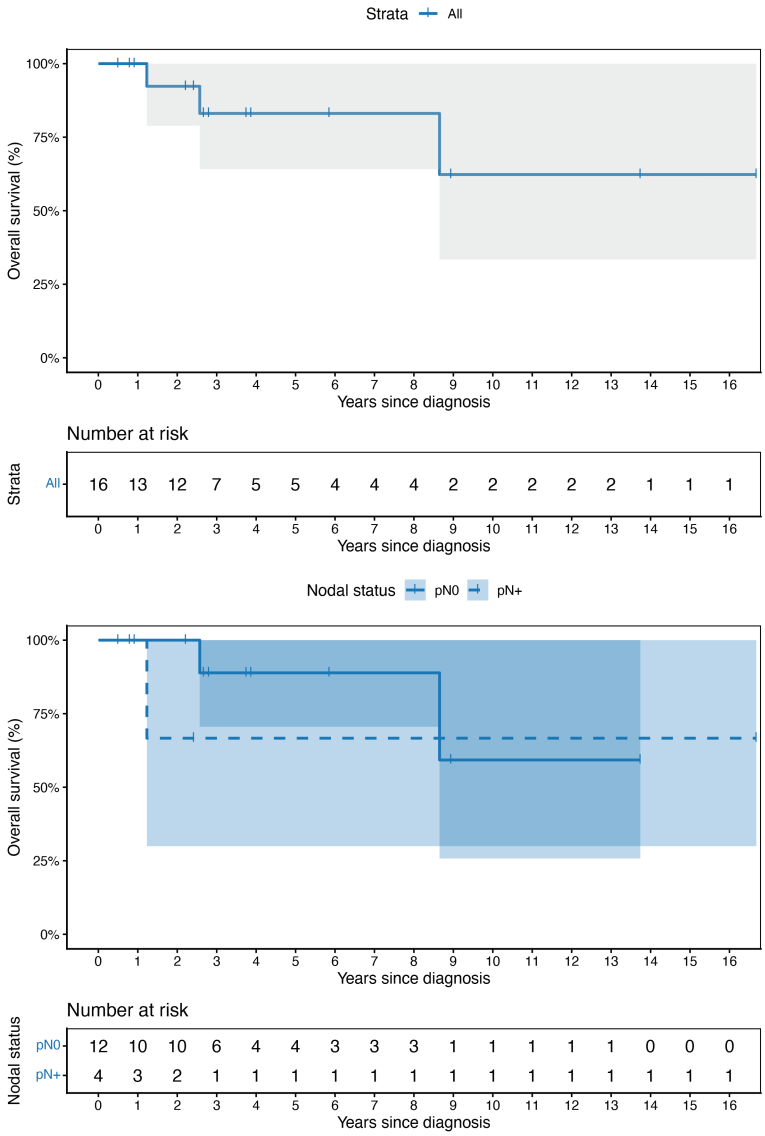

Figure 2. Descriptive overall survival in the full cohort of MBC patients (*n* = 16).

Prognosis and management of MBC

Nodal involvement and metastatic disease are the main adverse prognostic factors in MBC [13]. Although 5-year survival rates may be comparable to those of women after adjusting for stage, men's diagnosis at more advanced stages adversely affects mortality [13]. Prognosis depends on multiple factors, including demographic characteristics, tumour biology, stage at diagnosis and treatment received. Beyond tumour-related factors, population-based evidence suggests that survival in MBC is also shaped by social and healthcare-access variables.

Restrepo *et al* [15] reported that race, insurance status, income, education and facility type were associated with mortality risk in men with BC, underscoring that outcome disparities may reflect not only stage and biology, but also structural differences in access to care.

Treatment of MBC is largely based on strategies extrapolated from studies in women, due to the scarcity of male-specific research [1, 5, 16]. Management is complex and requires a multidisciplinary approach involving multiple medical specialties [1].

Surgery is usually the cornerstone of treatment for localised disease. In most cases, mastectomy is performed with or without axillary evaluation; only about 20% of cases are managed with breast-conserving surgery (BCS). Given the high proportion of HR-positive tumours, most patients receive concomitant endocrine therapy [17]. In patients with early-stage disease and no clinical evidence of axillary lymph node involvement, SLNB is recommended for axillary staging [12, 16, 18].

The use of adjuvant radiotherapy after surgery follows the same principles as in women and is particularly recommended in cases of locally advanced cancer or positive surgical margins [18–20]. A statistically significant reduction in the risk of death has been observed among patients who receive radiotherapy [21].

Systemic chemotherapy in men follows the same regimens used in women [16, 22], for both localised and advanced disease [1]. Neoadjuvant or adjuvant chemotherapy should be considered in patients at high risk of recurrence or mortality, as well as HER2-targeted therapies when indicated [22]. Different regimens have been used, including anthracyclines and taxanes, as well as cyclophosphamide, methotrexate and 5-FU [1, 23].

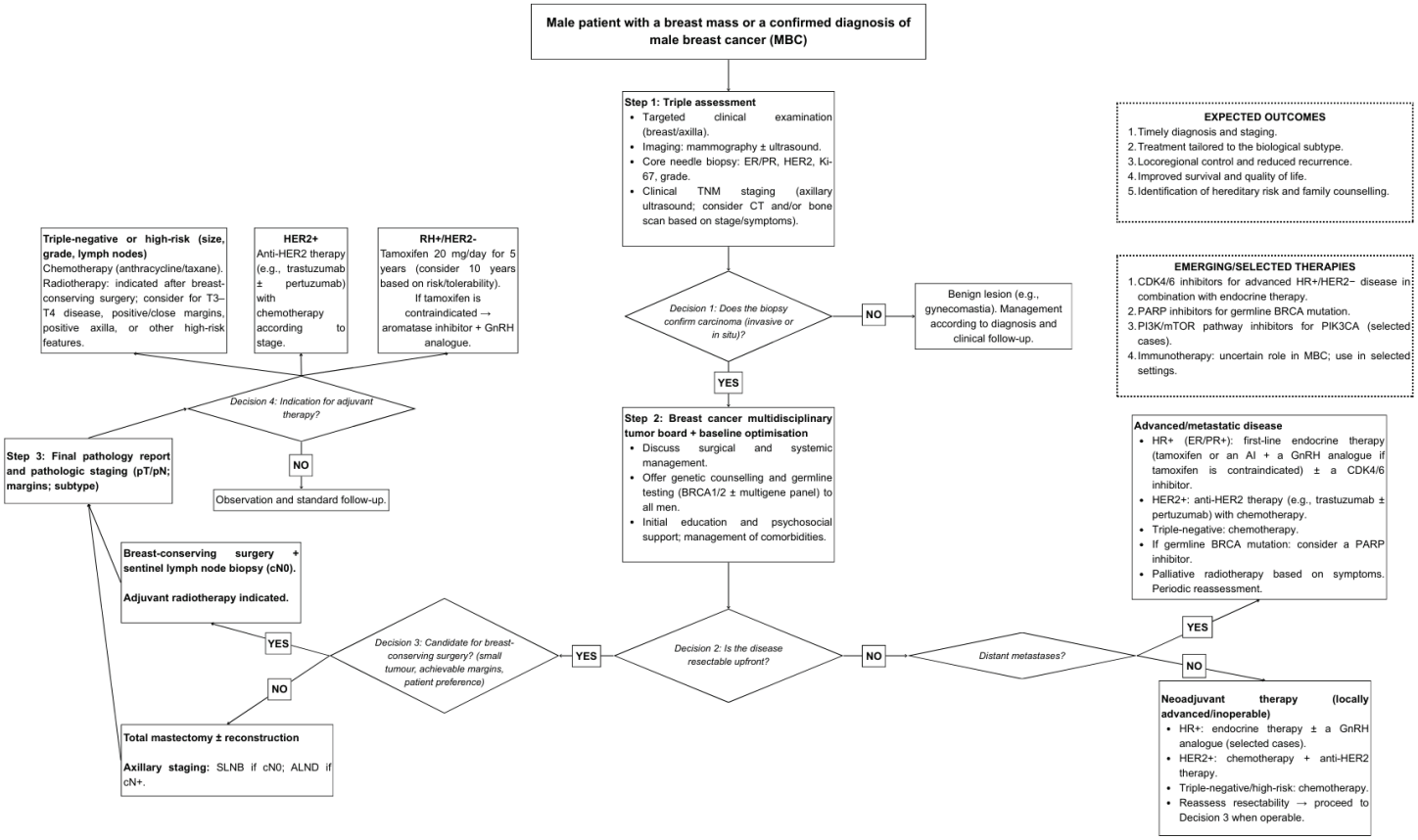

Figure 3. Institutional management algorithm for MBC. Abbreviations: ER/PR: estrogen/progesterone receptors; HR: hormone receptors; SLNB: sentinel lymph node biopsy; AI: aromatase inhibitor; GnRH: gonadotropin-releasing hormone; CT: computed tomography.

In the setting of advanced or metastatic disease, standard chemotherapy regimens are used, along with targeted therapies such as HER2 inhibitors, PIK3CA-targeted agents, immune checkpoint inhibitors (PD-L1) and specific treatments in patients with germline BRCA mutations [18]. However, there are no randomised clinical trials specifically in men evaluating these therapies [19].

Because HR positivity (estrogen and progesterone) is particularly relevant to therapeutic decision-making in men [18], endocrine therapy plays a key role. The most commonly used hormonal agent is tamoxifen, due to its effectiveness in cases with HR–positive disease [17, 18, 24]. Men with hormone-dependent tumours are candidates for adjuvant endocrine therapy with tamoxifen for 5 years at a dose of 20 mg daily, which may be extended to 10 years depending on recurrence risk and treatment-related toxicity [23]. If tamoxifen is contraindicated, a combination of gonadotropin-releasing hormone (GnRH) analogs plus aromatase inhibitors may be considered [5, 17, 18].

The efficacy of aromatase inhibitors in men is not fully established and may be lower than in women [5], because men, unlike postmenopausal women, continue to produce estrogens directly in the testes. Therefore, GnRH agonists/antagonists are added; otherwise, treatment would be suboptimal [25].

Multiple treatments can be added to endocrine therapy and chemotherapy [1, 23]. Some have been studied in men, while others have been extrapolated from therapies used in women. Among these newer therapies are monoclonal antibodies, including anti-HER2 agents (trastuzumab, pertuzumab, neratinib), which are used in HER2-positive patients, although most recommendations are extrapolated from studies in women [1, 23]. Regarding immunotherapy, the role of immune checkpoint inhibitors, such as anti–PD-L1 agents, is uncertain, because no specific evidence is available; their use has mainly been explored in studies combining them with other therapies such as PARP inhibitors or CDK4/6 inhibitors [1, 23]. The use of CDK4/6 inhibitors, such as palbociclib, ribociclib and abemaciclib, has been approved in men with advanced HR-positive and HER2–negative BC in combination with endocrine therapy [23].

Other agents include PARP inhibitors, such as olaparib and talazoparib, which affect DNA damage repair mechanisms. Their use may be intended for patients with BRCA1 and BRCA2 mutations [1, 23]. PI3K/mTOR inhibitors may be useful in patients with mutations in the PIK3CA gene (alpelisib) and everolimus could be used in selected cases, although there are insufficient data to confirm this [23]. Some androgen-targeting therapies, such as enzalutamide and abiraterone, are being investigated as experimental treatments due to the high overexpression of AR in MBC [23].

Genetic testing, follow-up and recommendations

Given the high proportion of men with BC who carry an identifiable hereditary risk factor, genetic counseling and germline testing are recommended for all patients to detect BRCA2 and BRCA1 mutations. Mutations in other genes such as CHEK2, PALB2 and PTEN are less common but also appear to confer an increased risk of MBC [1, 5].

Men with BC often experience a lack of disease-specific educational information, which may lead to feelings of isolation and distress compared with the resources available for women [16]. It is essential to educate patients about signs of recurrence and oncologic surveillance [19].

Follow-up should be conducted by a physician experienced in BC, including clinical evaluation and imaging studies [19]. Follow-up recommendations extrapolated from evidence in women include: annual ipsilateral mammography in patients treated with BCS, when technically feasible, regardless of genetic predisposition [1, 19]; and contralateral mammography may be offered to patients with a history of BC and predisposing mutations [1, 19]. Healthy lifestyle counseling, including weight management, regular physical activity and limiting alcohol consumption, is also recommended [2].

Interpretation of our institutional findings

This study reports the institutional experience in the management of MBC at the Hospital Clínico UC CHRISTUS, including 16 cases diagnosed between 2008 and 2025. To our knowledge, this is the largest single-centre Chilean series published to date [7, 24]. Because MBC

is rare and national data are scarce, we aimed to describe clinical presentation, tumour biology, treatment and outcomes in a tertiary-care setting.

Our findings mirror international and regional reports, with a predominance of invasive ductal carcinoma, frequent HR positivity and a palpable mass as the most common presentation. The limited size and retrospective design of most Latin American studies further support the value of institutional case series that document real-world practice and follow-up in the region.

Patients were diagnosed at an advanced age (median 74 years), consistent with the usual age distribution reported for MBC [1, 2]. Most tumours were managed at relatively early pathologic stages, with a predominance of lower T categories and node-negative disease, a pattern that has been increasingly observed as awareness and access to care improve [2].

Pathologically, invasive ductal carcinoma remained the dominant subtype, consistent with prior reports [16]. HR positivity was nearly universal in our cohort, in keeping with the predominantly luminal biology described in MBC [5, 25]. Adjuvant endocrine therapy was the most frequently used systemic treatment, reflecting contemporary treatment paradigms for HR-positive disease rather than demonstrating treatment effectiveness within this series.

HER2 overexpression was uncommon; however, complete biomarker data were not available for all patients. In particular, HER2 assessment on core biopsy was not evaluated in 6 of 16 cases, Ki-67 was not evaluated in 8 of 16 and germline testing was performed in only 6 of 16 patients. This incomplete clinicopathological characterisation limits more refined biological classification and warrants cautious interpretation of biomarker-related observations.

Recent Chilean institutional reports provide an emerging local benchmark for the clinicopathological profile and real-world management of MBC. A 10-year retrospective series from Santiago described predominantly luminal disease with very high HR positivity, low HER2 positivity and mastectomy-based surgery with frequent axillary staging followed by adjuvant endocrine therapy in most cases [26]. Similarly, regional experiences from the public health system in the Aconcagua Valley and the Hospital Regional de Talca have reported small cohorts with a predominance of ductal histology and HR-positive tumours, while also documenting that a subset of patients still present with locally advanced or metastatic disease at diagnosis [27]. Together with earlier national overviews emphasising the scarcity of Chilean data and the consequent reliance on evidence extrapolated from female BC, these studies support the need for multicentre registries and improved access to standardised biomarker and genetic testing to refine risk stratification and optimise management in Chile [6].

Surgical management was dominated by mastectomy, while BCS was rare, consistent with reports indicating limited use of conservative approaches in men [2]. SLNB was commonly performed, reflecting the adoption of less invasive axillary staging strategies in appropriately selected patients [6]. The institutional management pathway applied to these patients is summarised in the institutional treatment flowchart (Figure 3).

During follow-up, three deaths were observed, one attributable to BC progression. These findings should be interpreted cautiously, given the small sample size, prolonged accrual period and low number of outcome events, which preclude robust prognostic or treatment-effect inference. In addition, survival in MBC is likely influenced not only by tumour biology and inherited susceptibility, but also by sociodemographic and healthcare-system factors that were not captured in our institutional registry [15].

Strengths and limitations

This study has several strengths. It provides institutional data on surgically treated MBC from a tertiary-care university hospital in Chile, in a field where national evidence remains scarce. To our knowledge, this represents the largest published single-centre Chilean series to date. Despite the rarity of the disease and the limited number of cases, the cohort offers a comprehensive descriptive overview of clinical presentation, tumour biology, surgical management, systemic therapy, germline testing and follow-up. Given the rarity of this condition in men, descriptive institutional reports such as this remain valuable for strengthening the limited evidence base and documenting real-world patterns of care. In addition, the study places its findings in the context of recent Chilean reports, contributing local evidence on an uncommon disease that remains underrepresented in the regional literature.

Several limitations merit consideration. The retrospective single-centre design, small sample size, prolonged study period and low number of outcome events limit the strength of any outcome interpretation. Survival findings should therefore be understood as descriptive only and not as evidence of prognostic associations or treatment effectiveness. In addition, complete clinicopathological data were not available for all 16 patients. Biomarker assessment was not uniform across the study period, particularly for HER2 and Ki-67, and germline testing was performed in only a minority of patients. This heterogeneity in data completeness reduces the granularity of biological characterisation, limits subgroup and biomarker-related interpretation and restricts broader conclusions regarding hereditary predisposition.

The study has other important constraints. Its external generalisability is inherently limited, as this was a single-centre study conducted at a tertiary university hospital in Santiago; patterns of referral, diagnostic work-up, biomarker availability and treatment access may differ in other Chilean institutions and healthcare settings. In addition, the prolonged inclusion period from 2008 to 2025 likely introduced temporal heterogeneity in diagnostic practices, pathological evaluation, access to germline testing and treatment strategies, which may reduce comparability across cases managed in different years. Because the study was retrospective and based on an institutional registry, the dataset is also subject to information bias, including incomplete capture, inconsistent documentation and variable availability of clinically relevant variables across the study period.

Interpretation of overall survival also requires caution in this elderly cohort, whose median age at presentation was 74 years, because only one of the three recorded deaths was attributable to BC progression, whereas the other two were due to non-oncologic causes. Overall survival in this series should therefore not be interpreted as a direct surrogate of BC-specific prognosis. Finally, the study design did not allow formal hypothesis testing, subgroup comparisons or multivariable modelling; accordingly, no robust inferences can be made regarding prognostic factors or treatment effects.

In summary, this series describes a predominantly luminal clinicopathological profile, frequent early-stage presentation and contemporary treatment patterns in a Chilean tertiary-care setting. Because of the limited sample size, low number of events and incomplete biomarker and germline data in some patients, these findings should be interpreted as descriptive. Larger multicentre collaborations with more standardised biological characterisation are needed to strengthen the evidence base for this uncommon but clinically important disease.

Conclusion

This series describes MBC in a high-complexity university centre in Chile, showing a predominance of ductal histology, HR positivity and frequent use of mastectomy and adjuvant endocrine therapy. Although few deaths were observed during follow-up, outcome findings should be interpreted cautiously given the small sample size, prolonged accrual period and low number of events. Larger multicentre studies with more standardised biomarker and genetic assessment are needed to better characterise MBC in the Chilean setting.

Conflicts of interest

None.

Funding

None.

Ethical responsibilities

No experimental interventions involving humans or animals were performed. This study was based on retrospectively collected and anonymised clinical data.

Author contributions

Catalina Vargas, Álvaro Torres, Martín Urra and Renata Soto contributed equally to the study design, data analysis, interpretation of results and manuscript writing. Maite Azócar conducted the literature review. Drs. Mauricio Camus, Francisco Domínguez, César Sánchez and Francisco Acevedo provided clinical and academic guidance and supervised the work. Catalina Vargas served as the corresponding author and led the final preparation of the manuscript.

Data confidentiality

The authors declare that this article contains no patient-identifiable data.

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