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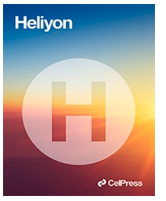

Research article

# Male and female disparities in breast cancer epidemiology: A comparative cross-sectional analysis of a Brazilian cohort (2017–2021)

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ABSTRACT

Male breast cancer (MBC) is a rare condition, accounting for approximately 1 % of all breast cancer cases. Nevertheless, the paucity of MBC-specific research has impeded a thorough understanding of MBC. In this study, we aimed to delineate the epidemiological implications of MBC in Brazil and benchmarked it against female breast cancer (FBC). This retrospective study analyzed data from the DATASUS database (2017–2021), which assessed the incidence of breast cancer in both sexes. All statistical analyses were performed using descriptive statistics and inferential methods, with significance set at a 95 % confidence interval. We identified 4,326 (1.7 %) and 233,793 (94.2 %) patients with MBC and FBC, respectively, in Brazil. Despite the general population concentration in the Southeast, MBC cases were more prevalent in the Northeast ($p < 0.0004$). At breast cancer diagnosis, males were typically older (mean age 59.5 [±10.2] years) than females (mean age 55.7 7 [±9.8] years). MBC was more commonly diagnosed clinically compared with FBC, which was most commonly diagnosed via screening. Surgical diagnostics were twice as likely in males, who also more frequently presented with advanced disease stages (stages III and IV; 72.8 % vs. 59.3 %), leading to a higher rate of mastectomy. Treatment was initiated earlier in males than in females. Although MBC comprises a minority of breast cancer cases, it is more frequently diagnosed at an advanced stage compared with FBC and necessitates

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aggressive treatment. Our study also underscores the potential benefit of prompt initiation of therapy and need for tailored clinical approaches in patients with MBC.

## 1. Introduction

Breast cancer (BC) is a critical global public health issue; it is the most diagnosed cancer among women in Brazil, particularly in the southern, southeastern, central-western, and northeastern regions, with significant implications for the national healthcare system [1,2].

While BC is most prevalent in females, male breast cancer (MBC) accounts for approximately 1 % of all cases and is an often-overlooked public health concern [3]. MBC-specific research is scarce, generally constrained to small institutional cohorts; and coupled with the exclusion of men from BC clinical trials, such constraints result in a substantial knowledge deficit regarding its epidemiology, diagnosis, and treatment [3,4].

Among the predisposing risk factors for male breast cancer, there are some conditions that appear to be significant: (a) breast/chest radiation exposure, (b) estrogen use, diseases associated with hyper-estrogenism (cirrhosis or Klinefelter syndrome), and (c) family health history. Furthermore, there are clear familial tendencies, with a higher incidence among men who have a large number of female relatives with breast cancer and (d) major inheritance susceptibility [5]. Notably, compared with *BRCA1* mutations, *BRCA2* mutations are more closely associated with an increased risk for MBC, and other factors such as radiation exposure and hormonal imbalances contribute to this risk spectrum [6,7]. More recently case-control analyses revealed significant associations of protein-truncating variants not only in BRCA1 and BRCA2 but also in CHEK2, PALB2, and ATM [8].

In terms of diagnosis, staging, and treatment, MBC is typically comparable to female breast cancer (FBC) and most protocols only follow the recommendations for women. Male breasts are smaller, and in theory, any abnormality is liable to be detected early. However, the lack of awareness regarding MBC and the absence of screening protocols lead to delayed reporting [4]. Symptomatically, MBC often presents as a mass under the nipple, and differential diagnosis from prevalent conditions such as gynecomastia is critical [4,9].

There are well-established screening programs for BC, most of which are mammography-based and differ in the age of initiation and periodicity. In Brazil, the Ministry of Health states that BC screening is based on mammography for women aged 50 years and is repeated every 2 years. However, no recommendations are available for MBC [9,10] and screening is not routinely performed in men because of a low disease incidence [11]and given the challenges faced because of smaller breast tissues only high-risk patients could benefit from routine screening [12].

Current guidelines from the American College of Radiology recommend breast ultrasonography for men under 25 years of age with a palpable mass and mammography for those older than 25 years of age, followed by ultrasonography if necessary and core needle biopsy for suspicious findings [10]. Despite these guidelines, the treatment of MBC is often extrapolated from FBC protocols because of the absence of male-specific research, which generally culminates in mastectomy, even in the early stages [13].

This study aimed to fill this gap in sex-specific research by examining the epidemiological profile of MBC in Brazil from 2017 to 2021 and comparing it with that of FBC. Through this comparative ecological analysis, we aimed to illuminate the nuanced differences in BC epidemiology across sexes, proposing considerations for public health policies that may lead to developing targeted treatment guidelines and intervention strategies for MBC and ultimately contributing to a more equitable healthcare landscape.

## 2. Material and methods

### 2.1. Study design

In this ecological observational study, we conducted a retrospective analysis of data from the Information Technology Department of the Unified Health System (DATASUS) database (Cancer Information System; SISCAN). This database is specific to the Brazilian population. From this publicly available resource, we examined data spanning from 2017 to 2021, during which all variables necessary for the analysis were accessible.

### 2.2. Database

The Brazilian public health system, known as the Unified Health System (Sistema Único de Saúde; SUS), provides universal and free healthcare services and includes an extensive health information system, DATASUS. DATASUS is a governmental body tasked with collecting, processing, analyzing, and disseminating public health information nationwide. The data were aggregated from various nationwide sources, such as hospitals, clinics, laboratories, and health units. DATASUS also develops and maintains computerized systems that enable the standardized and integrated registration and management of health data.

Within DATASUS, two databases are particularly relevant: SISCAN and Painel-Oncologia Brazil. SISCAN (available at https://datasus.saude.gov.br/informacoes-de-saude-tabnet/) controls and monitors cervical cancer and breast cancer (BC) in Brazil. In contrast, Painel-Oncologia Brazil is an online platform that consolidates data and information on cancer status in the country. This panel was developed by the National Cancer Institute (INCA) and is designed to provide updated data on incidence, mortality, treatment, and other cancer-related aspects in Brazil. Information from these databases is publicly available and can be freely accessed.

In this study, we extracted data on incidence and mortality from the public database of the INCA platform (https://www.gov.br/inca/pt-br/assuntos/cancer/numeros).

### 2.3. Data extraction process

The data extraction process from the DATASUS database involved several steps to ensure the accuracy and completeness of the information. First, we identified and selected the relevant datasets from SISCAN and Painel-Oncologia Brazil. We then applied specific filters to isolate the records corresponding to patients diagnosed with breast cancer (ICD C50) between 2017 and 2021. During the extraction, we carefully followed standardized procedures to ensure consistency, including cross-referencing data points between different sources within DATASUS to validate their accuracy.

We utilized DATASUS's TABNET tool, which allows for the systematic query and extraction of health data. Queries were designed to retrieve patient demographics, clinical characteristics, and outcomes related to breast cancer. The extracted data were then exported into a secure database for further analysis.

### 2.4. Handling of missing data

Handling missing data is a critical aspect of our study. We employed a systematic approach to address this issue. Initially, cases with missing key epidemiological variables were excluded from the analysis, as indicated in the flowchart (Fig. 1). For the remaining dataset, missing data were handled through multiple imputation techniques when feasible, ensuring that the imputation models were appropriate for the type of data and the patterns of missingness observed.

In cases where imputation was not suitable, sensitivity analyses were conducted to assess the potential impact of missing data on the study outcomes. These analyses helped to ensure that the findings were robust and not unduly influenced by missing information. The rationale for each decision regarding missing data was based on maintaining the integrity and validity of the study's results.

### 2.5. Included patients

Data from female and male patients diagnosed with BC (ICD C50) from 2017 to 2021 were included in this study. Data in which not all the epidemiological information was used in the study for both sexes were excluded. The flowchart in Fig. 1 shows the distribution of BC cases in Brazil (2017–2021), including the total number of cases, cases excluded due to incomplete data, and the distribution between male and female patients.

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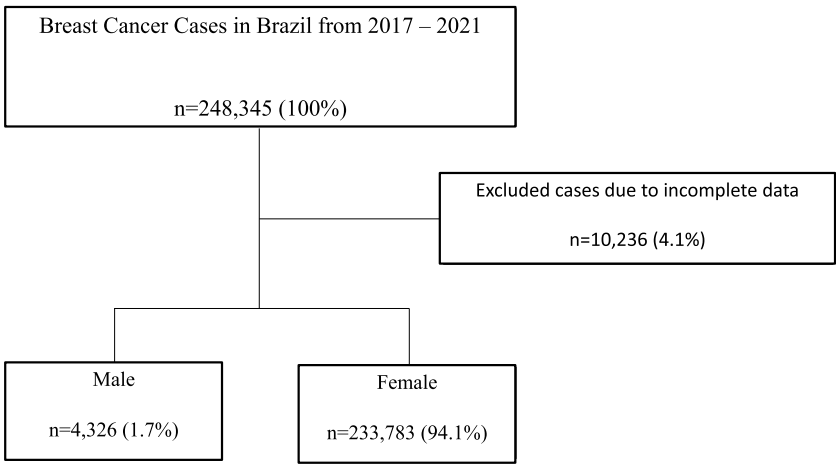


**Fig. 1.** Selected cases for the study.
**Legend:** Flowchart of breast cancer cases in Brazil from 2017 to 2021. The total number of cases included in the analysis was 248,345. Cases with incomplete data (n = 10,236, 4.1 %) were excluded, resulting in 238,109 cases, of which 4,326 (1.7 %) were male and 233,793 (94.2 %) were female.

### 2.7. Database

The Brazilian public health system, known as the Unified Health System (Sistema Único de Saúde; SUS), provides universal and free healthcare services and includes an extensive health information system, DATASUS. DATASUS is a governmental body tasked with collecting, processing, analyzing, and disseminating public health information nationwide. The data were aggregated from various nationwide sources, such as hospitals, clinics, laboratories, and health units. DATASUS also develops and maintains computerized systems that enable the standardized and integrated registration and management of health data.

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In cases where imputation was not suitable, sensitivity analyses were conducted to assess the potential impact of missing data on the study outcomes. These analyses helped to ensure that the findings were robust and not unduly influenced by missing information. The rationale for each decision regarding missing data was based on maintaining the integrity and validity of the study's results.

### 2.10. Included patients

Data from female and male patients diagnosed with BC (ICD C50) from 2017 to 2021 were included in this study. Data in which not all the epidemiological information was used in the study for both sexes were excluded. The flowchart in Fig. 1 shows the distribution of BC cases in Brazil (2017–2021), including the total number of cases, cases excluded owing to incomplete data, and the distribution between male and female patients.

### 2.11. Sociodemographic and clinical characteristics

Sociodemographic characteristics, including the region of diagnosis and age distribution of male and female patients, were descriptively analyzed. Subsequently, diagnostic and treatment processes for BC were assessed in both sexes. This assessment covered various aspects of the disease, such as the histological type, histological grade, and immunohistochemical profiles. The most common diagnostic modalities, imaging findings, types of treatments employed, and surgical interventions undertaken were also evaluated.

### 2.12. Statistical analysis

Data are presented as absolute values and percentages, with comparisons made between MBC (Male Breast Cancer) and FBC (Female Breast Cancer) groups. Statistical analyses were performed using SPSS software, version 29. For all comparisons, significant differences were determined using a 95 % confidence interval (CI). The CI is a range of values that is likely to contain the true effect size, providing an estimate of the uncertainty around the sample mean. The statistical significance threshold was set at $p < 0.05$.

The p-value represents the probability that the observed results occurred by chance. A p-value less than 0.05 indicates strong evidence against the null hypothesis, suggesting that the observed difference is unlikely to have occurred by random chance alone, and is therefore considered statistically significant.

Continuous variables were analyzed for normality, and those following a normal distribution were compared using the independent samples *t*-test. For non-normally distributed variables, the Mann-Whitney *U* test was applied. Categorical variables were compared

using the chi-square test or Fisher's exact test when appropriate. All p-values were two-tailed, and results were considered statistically significant if $p < 0.05$.

### 2.13. Ethics

Given the ecological nature of this study, it was exempt from the requirement for submission to an Ethics Research Committee and need for informed consent. This study relied on publicly available anonymized data, adhering to the ethical standards for secondary data analysis.

## 3. Results

### 3.1. Demographic data

In total, 4,326 (1.7 %) and 233,793 (94.2 %) patients with MBC and FBC, respectively, diagnosed between 2017 and 2021 were included in the study. Fig. 2 depicts the temporal progression of BC cases during the study period. Among these patients, the southeast region had the highest concentration of BC incidences in both sexes, with 1,785 (41.3 %) male and 106,760 (45.1 %) female patients. The states with the highest incidences of MBC were São Paulo and Maranhão, with 1,236 (28.6 %) and 563 (12.0 %) cases, respectively. The states with the highest incidences of FBC were São Paulo and Minas Gerais, with 55,001 (23.5 %) and 26,210 (11.2 %) cases, respectively. Table 1 presents the detailed distribution, and Figs. 3 and 4 show this distribution for the cases among Brazilian provinces.

### 3.2. Clinical and pathological data

On Table 2 we can find clinical and pathological data. The average age of patients with MBC and FBC was 59.5 [±10.2] and 55.7 [±9.8] years, respectively, showing significant differences ($p < 0.001$). MBC patients were predominantly in the 55–69-year age group, were FBC patients were predominantly aged 40–54, indicating significant differences ($p < 0.0001$).

MBC was predominantly diagnosed via physical examination (i.e., clinical complaints) in 2,716 patients (62.8 %), whereas FBC were diagnosed through screening examinations (79,861 patients; 34.1 %) and clinical complaints (73,828 patients; 31.6 %). A comparison of the diagnostic methods revealed that physical examination was more frequently used to diagnose MBC by a factor of 1.308 (95 % CI: 1.264–1.354, $p < 0.05$), and imaging was more frequently used to diagnose FBC by a factor of 0.714 (95 % CI: 0.674–0.757, $p < 0.05$). Imaging results revealed the presence of a nodule in 63.8 % ($n = 2,780$) of MBC patients and 45.1 % ($n = 105,441$) of FBC patients, with the next most common finding being microcalcification.

Core needle biopsy was the most common procedure in both groups. In the MBC), it was performed in 50.2 % ($n = 2,126$) of cases, compared to 68.0 % ($n = 158,979$) in the FBC (difference of 0.099; 95 % CI: 0.084 to 0.1146; $p = 0.02$).

Invasive carcinoma was the predominant histological type in both groups. It accounted for 89.2 % ($n = 3,850$) of cases in the MBC, whereas in the FBC, it was present in 73.0 % ($n = 170,668$) of cases (difference of −0.239; 95 % CI: -0.248 to 0.229; $p < 0.001$).

The most common histological grade found in both sexes was grade 2, with 2,163 (50.0 %) MBC patients and 112,220 (48.0 %) FBC patients ($p < 0.001$). The luminal subtype was the most common subtype found in MBC (3,720 patients; 86.0 %) and FBC (140,276 patients; 60.0 %) patients. Additionally, there was a significant difference ($p < 0.001$) in the proportions of cases between MBC and FBC. The triple-negative BC subtype was the second most common subtype, with 363 (8.4 %) MBC patients and 51,434 (22.0 %) FBC patients; there was also a significantly different ($p < 0.001$).

The distribution of clinical staging revealed notable differences between the MBC and FBC groups. Stage III was the most common

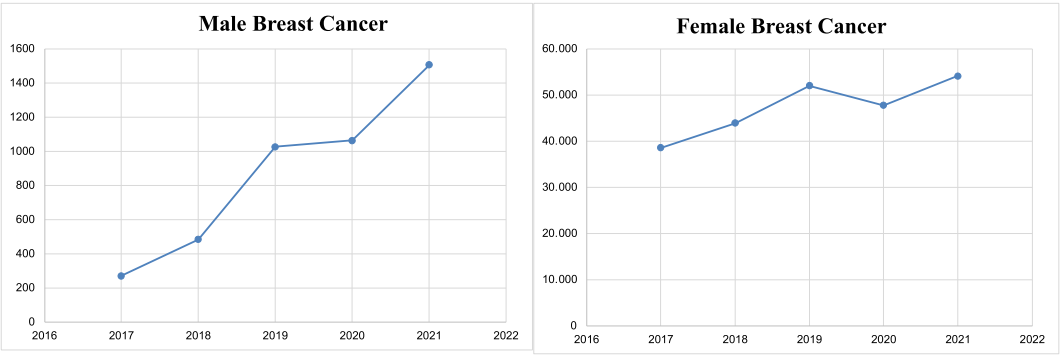


**Fig. 2.** Comparison of breast cancer number of cases evolution from 2017 to 2021.
**Legend:** Trends in breast cancer cases in Brazil from 2017 to 2021, stratified by gender. The left panel displays the annual number of male breast cancer cases, showing a consistent increase over the years. The right panel shows the number of female breast cancer cases, which also demonstrates variability with an overall upward trend.

**Table 1**
Demographic distribution of breast cancer patients in Brazil.

| Demographic Distribution | Males (n = 4,326) | | Females (n = 233,793) | | 95 % CI | p-value |
|---|---|---|---|---|---|---|
| | N | % | n | % | | |
| **Regions** | | | | | | |
| North | 180 | 4.2 | 9,375 | 4.0 | −0.001 (−0.007 to 0.004) | 0.42 |
| Northeast | 1,591 | 36.8 | 56,754 | 24.0 | −0.125 (−0.139 to −0.110) | 0.004 |
| Southeast | 1,785 | 41.3 | 106,760 | 45.1 | 0.044 (0.029–0,059) | 0.004 |
| South | 580 | 13.4 | 48,001 | 20.3 | 0.071 (0.060–0,081) | 0,003 |
| Central-West | 190 | 4.4 | 12,903 | 5.5 | 0.011 (0.004–0.017) | 0.003 |
| **Federative Units (States)** | | | | | | |
| Rondônia | 65 | 1.5 | 2,015 | 0.9 | −0.006 (−0.010 to −0.003) | 0.003 |
| Acre | 4 | 0.1 | 408 | 0.2 | 0.000 (−0.000 to 0.001) | 0.19 |
| Amazonas | 71 | 1.6 | 2,382 | 1.0 | −0.015 (−0.019 to −0.011) | 0.002 |
| Roraima | 5 | 0.1 | 430 | 0.2 | 0.000 (−0.000 to 0.001) | 0.23 |
| Pará | 31 | 0.7 | 3,815 | 1.6 | 0.009 (0.006–0.011) | 0.002 |
| Amapá | 4 | 0.1 | 325 | 0.1 | 0.000 (−0.001 to 0.001) | 0.21 |
| Maranhão | 563 | 13.0 | 5,181 | 2.2 | −0.108 (−0.118 to −0.098) | 0.002 |
| Piauí | 32 | 0.7 | 2,928 | 1.3 | 0.005 (0.002–0.007) | 0.003 |
| Ceará | 189 | 4,4 | 10,223 | 4.4 | 0.000 (−0.006 to 0.006) | 0.87 |
| Rio Grande do Norte | 429 | 9.9 | 5,390 | 2.3 | −0.076 (−0.085 to −0.067) | 0.002 |
| Paraíba | 29 | 0.7 | 4,628 | 2.0 | 0.013 (0.010–0.015) | 0.002 |
| Pernambuco | 151 | 3.5 | 11,377 | 4.9 | 0.013 (0.007–0.018) | 0.03 |
| Alagoas | 35 | 0.8 | 2,844 | 1.2 | 0.004 (0.000–0.006) | 0.041 |
| Sergipe | 22 | 0.5 | 1,961 | 0.8 | 0.003 (0.000–0.005) | 0.037 |
| Bahia | 141 | 3.3 | 12,222 | 5.2 | −0.024 (−0.029 to −0.019) | 0.004 |
| Minas Gerais | 243 | 5.6 | 26,210 | 11.2 | 0.056 (0.048–0.062) | 0.002 |
| Espírito Santo | 97 | 2.2 | 5,176 | 2.2 | −0.000 (−0.005 to 0.003) | 0.12 |
| Rio de Janeiro | 209 | 4.8 | 20,373 | 8.7 | 0.038 (0.032–0.045) | 0.002 |
| São Paulo | 1,236 | 28.6 | 55,001 | 23.5 | −0.050 (−0.064 to −0.037) | 0.002 |
| Paraná | 215 | 5.0 | 16,488 | 7.1 | 0.020 (0.014–0.027) | 0.009 |
| Santa Catarina | 100 | 2.3 | 11,529 | 4.9 | 0.026 (0.021–0.030) | 0.003 |
| Rio Grande do Sul | 265 | 6.1 | 19,984 | 8.5 | 0.024 (0.016–0.031) | 0.003 |
| Mato Grosso do Sul | 30 | 0.7 | 2,121 | 0.9 | 0.002 (−0.000 to 0.004) | 0.062 |
| Mato Grosso | 51 | 1.2 | 2,202 | 0.9 | −0.002 (−0.006 to 0.000) | 0.071 |
| Tocantins | 8 | 0.2 | 730 | 0.3 | 0.001 (−0.000 to 0.002) | 0,059 |
| Goiás | 70 | 1.6 | 4,987 | 2.1 | 0.005 (0.001–0.009) | 0.002 |
| Distrito Federal | 31 | 0.7 | 2,863 | 1.2 | −0.006 (−0.010 to −0.003) | 0.001 |

Legend: Demographic distribution of breast cancer patients in Brazil, stratified by gender. The table presents the distribution of male (n = 4,326) and female (n = 233,793) breast cancer patients across different regions and federative units (states) of Brazil from 2017 to 2021. The data includes the percentage of cases within each region/state, along with the 95 % confidence intervals and corresponding p-values obtained from Fisher's Test.

stage at diagnosis in both groups, with 58.9 % (n = 2,548) of cases in the MBC group and 52.8 % (n = 123,442) in the FBC group (difference of −0.118; 95 % CI: -0.133 to −0.103; p = 0.03). Additionally, Stage IV was diagnosed in 13.9 % (n = 601) of MBC cases, which is significantly higher than the 6.5 % (n = 15,199) observed in the FBC group (difference of −0.080; 95 % CI: -0.091 to −0.070; p < 0.001). These findings indicate that male breast cancer tends to be diagnosed at more advanced stages compared to female breast cancer.

### *3.3. Treatment characteristics*

In Table 2 we can find the treatment characteristics of MBC and FBC. Surgical treatment was performed in 3,417 (79.0 %) MBC and 210,412 (90.0 %) FBC patients, with no significant differences observed. Mastectomy with sentinel lymph node biopsy was the most prevalent treatment in MBC patients, accounting for 1,808 (41.8 %) patients. The primary treatment for FBC patients was conservative breast surgery with sentinel lymph node biopsy, totaling 110,584 (47.3 %) patients, and a significant difference was noted between the type of surgery and sex (P < 0.001).

Chemotherapy was administered to 2,530 (58.5 %) MBC patients and 177,215 (75.8 %) FBC patients, with significant differences between the two groups (p < 0.001). Radiation therapy was administered to 1,899 (43.9 %) MBC patients and 193,580 (82.8 %) FBC patients, and the between-sex difference was significant (p < 0.001).

Regarding treatment initiation, 1,370 (31.7 %) MBC patients began treatment within 30 days, whereas 57,292 (24.5 %) FBC patients started treatment within the same timeframe. However, 1,197 (27.7 %) MBC and 62,347 (26.7 %) FBC patients delayed treatment initiation for more than 4 months. There was a significant difference in the time to treatment initiation between MBC and FBC patients, with a greater prevalence of treatment commencement within the first 30 days for MBC patients and within 30–120 days for FBC patients, beyond which there was no difference in the proportions. Table 3 lists the distribution details.

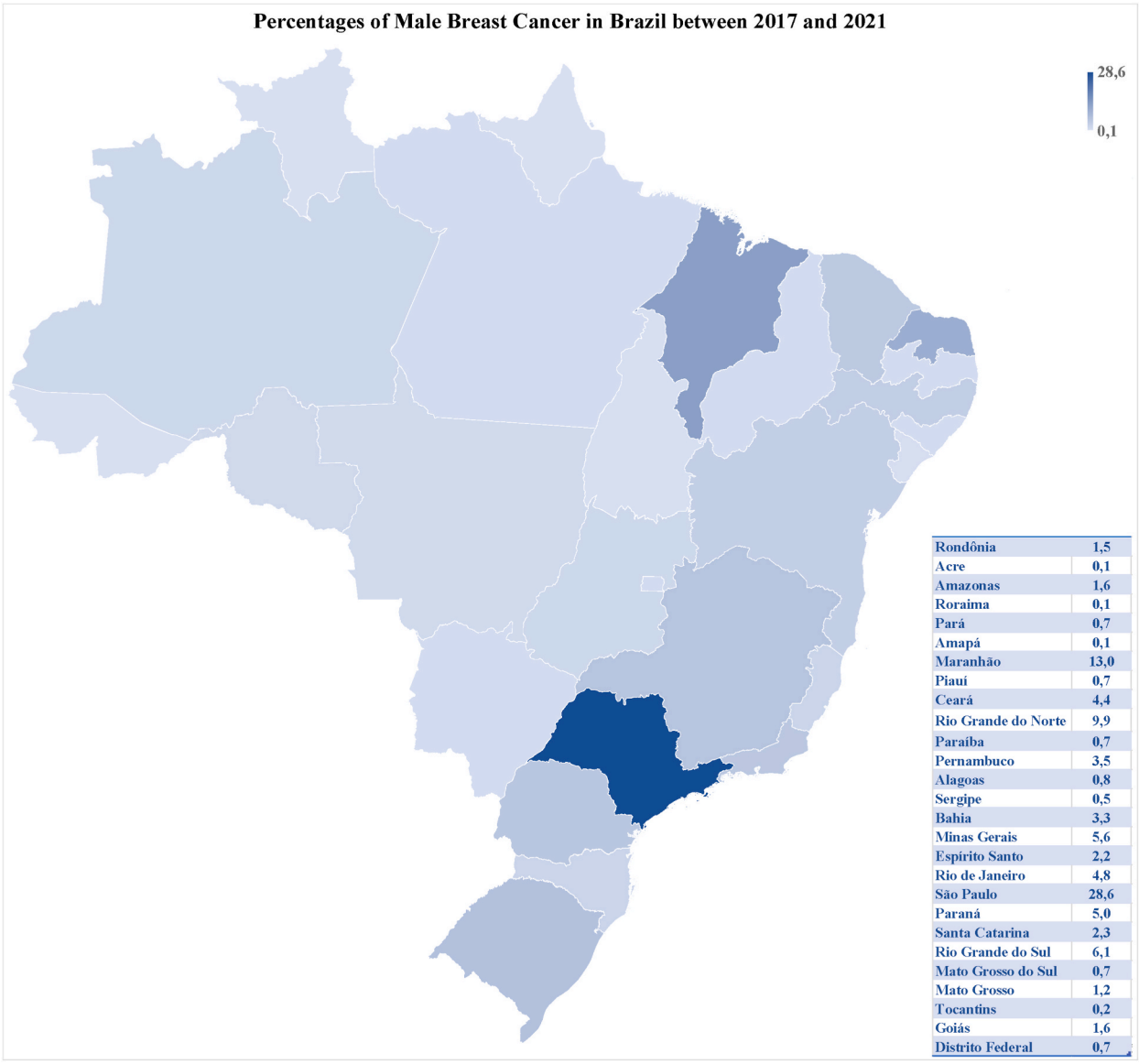


**Fig. 3.** Percentages of male breast cancer cases from 2017 to 2021.
**Legend:** Geographic distribution of male breast cancer cases as a percentage of all breast cancer cases in Brazil between 2017 and 2021. The map highlights the varying prevalence of male breast cancer across different states, with higher percentages observed in states such as São Paulo (28.6 %) and Rio de Janeiro (10.4 %), while lower percentages are seen in regions like Roraima (0.1 %) and Amapá (0.1 %).

### *3.4. Mortality*

In Brazil, BC mortality rates exhibited significant sex disparities during the study period from 2017 to 2021. In Table 3 we have the comparative analyses of mortality between MBC and FBC.

The average mortality rate for FBC was 16.54 %, whereas that for MBC was notably lower at 0.21 %. A decrease in BC mortality was observed in 2020 and 2021, which can be attributed to the impact of the coronavirus disease pandemic on healthcare and healthcare-seeking behaviors. Table 3 provides a detailed comparison of BC mortality rates, showing the absolute number of cases in MBC and FBC. The statistics revealed that every year from 2017 to 2021, mortality rates for FBC were higher than those for MBC ($p < 0.001$). In Fig. 5, we can observe the comparison of mortality rates between MBC and FBC in the period from 2017 to 2021.

## 4. Discussion

Our study found that MBC represented a small percentage of BC cases in Brazil, with a higher incidence in the northeast region.

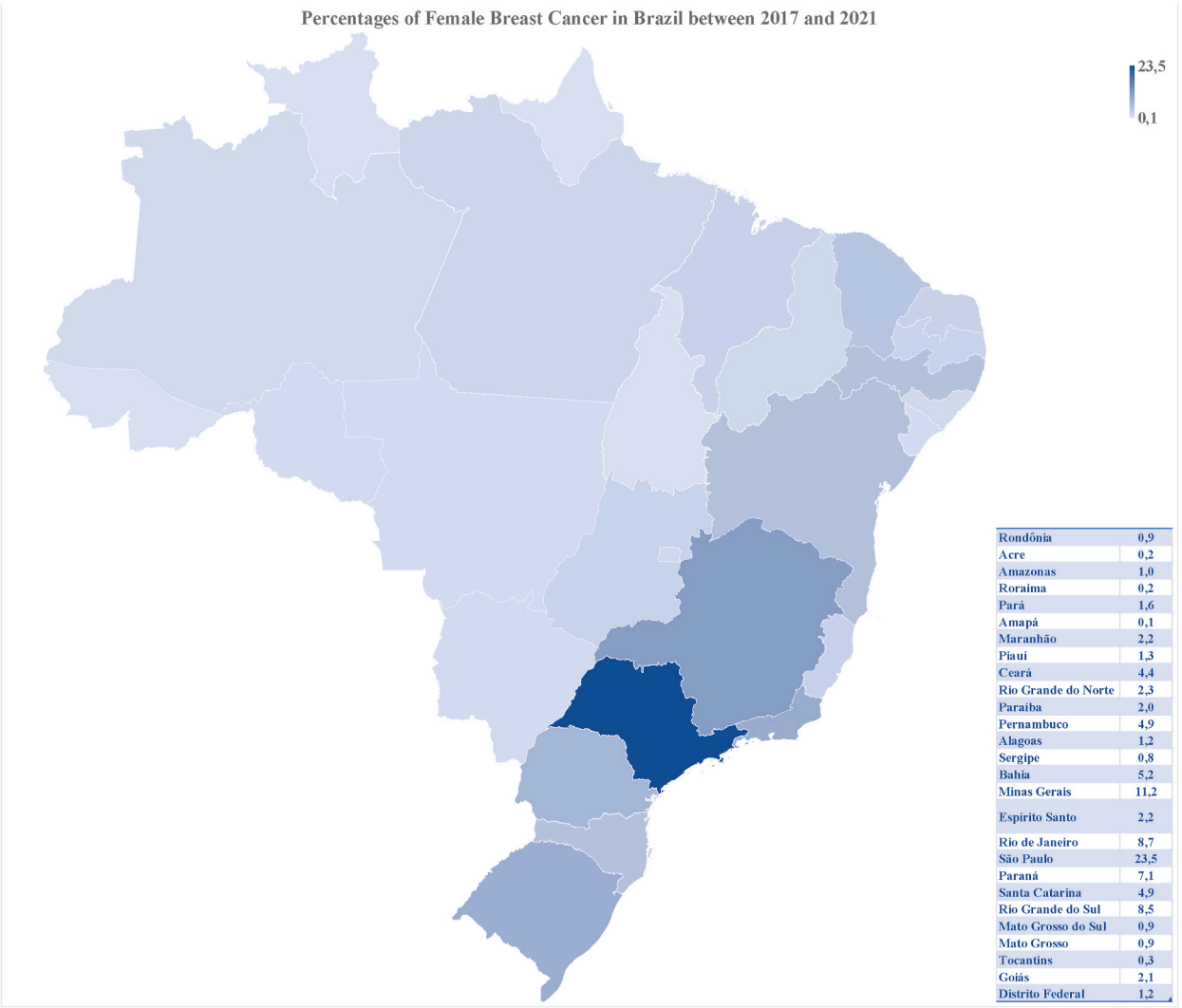


**Fig. 4.** Percentages of female breast cancer cases from 2017 to 2021.
**Legend:** Geographic distribution of female breast cancer cases as a percentage of all breast cancer cases in Brazil between 2017 and 2021. The map shows the distribution of female breast cancer prevalence across Brazilian states, with the highest percentages found in São Paulo (23.5 %) and Rio de Janeiro (11.2 %), while lower percentages are observed in states like Roraima (0.2 %) and Acre (0.2 %).

Similar to previous findings, our results corroborated the prevalence of MBC, which constitutes approximately 1–2% of all BC cases and mirrors global trends [3,14–16]. This modest prevalence may be attributable to the historical under-recognition and marginalization of the disease in males. The death of data exemplifies this substantial underestimation, an issue endemic to retrospective analyses yet pronounced in this study owing to the previously limited scope of related research [17–19].

Regionally, the northeast region exhibited a surprisingly high incidence of MBC, rivalling that of the southeast region despite its significantly larger population [15]. Notably, states such as Maranhão and Rio Grande do Norte reported a greater proportion of MBC patients than FBC patients. Such disparities may reflect underlying socioeconomic inequities and differential healthcare access, exacerbating disease outcomes [20]. Furthermore, the male population's engagement in preventive health measures remained low, contributing to the observed suboptimal disease management [15,21].

Globally, both MBC and FBC incidences have increased; however, their epidemiological features are not entirely understood. The global number of MBC incidence increased from 8.5 thousand in 1990 to 23.1 thousand in 2017, with the age-standardized incidence rate increasing from 0.46/100,000 to 0.61/100,000. This trend is in line with the findings in Brazil, where MBC is less common. However, the global increase in FBC cases, from 870.2 thousand to 1937.6 thousand during the same period, was much more pronounced than that of MBC. This global trend mirrors the higher prevalence of FBC observed in this study, despite regional differences within Brazil. Global data emphasize the need for tailored prevention strategies for both FBC and MBC, aligning with the implications of our study [3,14,19].

At the time of diagnosis, MBC patients were typically older and more frequently diagnosed clinically than FBC patients which is

**Table 2**
Comparison between male and female patients with breast cancer.

| | Male (n = 4,326) | | Female (n = 233,793) | | 95 % CI | p-value |
|---|---|---|---|---|---|---|
| | N | % | n | % | | |
| **Age** | | | | | | |
| Average (years) [standard deviation] | 59.5 [10.3] | | 55.7 [9.8] | | | <0.001 |
| **Age Groups** | | | | | | |
| Below 40 years | 519 | 12.1 | 27,587 | 11.8 | 1.022 (0.932–1.121) | 0.37 |
| Between 40 and 54 years | 826 | 19.1 | 84,165 | 36.0 | 0.420 (0.389–0.453) | 0.002 |
| Between 55 and 69 years | 1,787 | 41.3 | 83,932 | 35.9 | −0.055 (−0.070 to −0.040) | 0.0001 |
| Above 70 years | 1,194 | 27.6 | 38,109 | 16.3 | −0.111 (−0.124 to −0.098) | 0.001 |
| **Diagnostic Method** | | | | | | |
| Clinical Complaint | 2,716 | 62.8 | 73,828 | 31.6 | −0.312 (−0.326 to −0.297) | <0.001 |
| Screening | – | – | 79,861 | 34.1 | | |
| Imaging (other) | 1,619 | 37.2 | 80,104 | 34.3 | −0.031 (−0.046 to −0.017) | |
| **Imaging Findings** | | | | | | |
| Nodule | 2,780 | 63.8 | 105,441 | 45.1 | 0.044 (0.030–0.059) | 0.003 |
| Microcalcifications | 458 | 10.6 | 55,643 | 23.8 | 0.256 (0.246–0.265) | 0.002 |
| Focal Asymmetry | 122 | 2.8 | 40,212 | 17.2 | 0.233 (0.227–0.238) | 0.003 |
| Architectural Distortion | 966 | 22.8 | 32,497 | 13.9 | −0.011 (−0.024 to 0.000) | 0.051 |
| **Biopsy Type** | | | | | | |
| Core Needle | 2,126 | 50.2 | 158,979 | 68.0 | 0.099 (0.084–0.1146) | 0.02 |
| Incisional | 147 | 3.4 | 7,481 | 3.2 | −0.005 (−0.011 to −0.000) | 0.04 |
| Excisional | 537 | 12.4 | 24,080 | 10.3 | −0.036 (−0.046 to −0.026) | <0.001 |
| Intraoperative | 1,470 | 34.0 | 43,253 | 18.5 | −0.485 (−0.499 to −0.471) | <0.001 |
| **Histological Type** | | | | | | |
| Invasive Carcinoma | 3,858 | 89.2 | 170,668 | 73.0 | −0.239 (−0.248 to 0.229) | <0.001 |
| Lobular Carcinoma | 177 | 4.1 | 34,601 | 14.8 | 0.090 (0.084–0.096) | <0.001 |
| Ductal Carcinoma in situ | 44 | 1.0 | 21,042 | 9.0 | 0.069 (0.066–0.072) | <0.001 |
| Others | 247 | 5.7 | 7,482 | 3.2 | 0.793 (0.785–0.800) | <0.001 |
| **Histological Grade** | | | | | | |
| G1 | 1,042 | 24.1 | 112,220 | 48.0 | 0.186 (0.173–0.198) | <0.001 |
| G2 | 2,163 | 50.0 | 81,827 | 35.0 | −0.188 (−0.202 to −0.173) | <0.001 |
| G3 | 1,121 | 25.9 | 39,746 | 17.0 | −0.107 (−0.120 to −0.094) | <0.001 |
| **Subtypes** | | | | | | |
| Luminal | 3,720 | 86.0 | 140,276 | 60.0 | −0.260 (−0.274 to −0.243) | <0.001 |
| TNBC | 363 | 8.4 | 51,434 | 22.0 | 0.136 (0.123–0.148) | <0.001 |
| HER-2+ | 243 | 5.6 | 42,083 | 18.0 | 0.123 (0.111–0.132) | <0.001 |
| **Clinical Staging** | | | | | | |
| 0 | 44 | 1.0 | 16,365 | 7.0 | 0.052 (0.048–0.054) | <0.001 |
| I | 294 | 6.8 | 28,756 | 12.3 | 0.041 (0.033–0.048) | <0.001 |
| II | 839 | 19.4 | 50,031 | 21.4 | 0.003 (−0.015 to 0.008) | 0.073 |
| III | 2,548 | 58.9 | 123,442 | 52.8 | −0.118 (−0.133 to −0.103) | 0.03 |
| IV | 601 | 13.9 | 15,199 | 6.5 | −0.080 (−0.091 to −0.070) | <0.001 |
| **Treatment** | | | | | | |
| **Surgical** | 3,417 | 79.0 | 210,413 | 90.0 | 0.011 (−0.000 to 0.024) | 0.329 |
| BCS + SLNB | 324 | 7.5 | 110,584 | 47.3 | 0.345 (0.337–0.353) | <0.001 |
| BCS + ALND | 809 | 18.5 | 31,562 | 13.5 | −0.066 (−0.078 to −0.055) | <0.001 |
| Mastectomy + SLNB | 1,808 | 41.8 | 43,251 | 18.5 | −0.252 (−0.267 to −0.238) | <0.001 |
| Mastectomy + ALND | 432 | 10.0 | 39,043 | 16.7 | 0.048 (0.039–0.057) | <0.001 |
| BCS | 44 | 1.0 | 9,351 | 4.0 | 0.025 (0.021–0.028) | <0,001 |
| **Chemotherapy** | 2,530 | 58.5 | 177,215 | 75.8 | 0.089 (0.075–0.104) | <0.001 |
| **Radiotherapy** | 1,899 | 43.9 | 193,580 | 82.8 | 0.297 (0.282–0.312) | <0.001 |
| **Time to Start of Treatment** | | | | | | |
| Up to 30 days | 1,370 | 31.7 | 57,292 | 24.5 | −0.072 (−0.086 to −0.056) | <0.001 |
| 31–60 days | 782 | 18.1 | 49,514 | 21.2 | 0.031 (0.019–0.042) | <0.001 |
| 61–90 days | 568 | 13.1 | 38,075 | 16.3 | 0.032 (0.021–0.041) | <0.001 |
| 91–120 days | 409 | 9.4 | 26,565 | 11.4 | 0.019 (0.009–0.027) | <0.001 |
| More than 121 days | 1,197 | 27.7 | 62,347 | 26.7 | −0.010 (−0.023 to 0.003) | 0.72 |

Legend: Comparison between male and female breast cancer patients in Brazil. The table summarizes the demographic, diagnostic, histological, and treatment characteristics of male (n = 4,326) and female (n = 233,793) breast cancer patients from 2017 to 2021. Key differences in age distribution, diagnostic methods, imaging findings, biopsy types, histological types and grades, clinical staging, and treatment approaches are presented, along with 95 % confidence intervals and p-values indicating the statistical significance of these differences. BCS + SLNB, breast-conserving + sentinel lymph node biopsy; ALND, axillary lymph node dissection; TNBC, triple-negative breast cancer. CI, confidence interval. Fisher's Test.

most commonly diagnosed via screening. Patients with MBC often present with more advanced disease stages and undergo mastectomies at a higher rate, the lack awareness and screening programs for high-risk patients in Brazil and in the world is the main cause [12,22].

Additionally, treatment for MBC tended to begin sooner than that for FBC, highlighting the differences in management.

**Table 3**
Comparison of the evolution of breast cancer case mortality rates from 2017 to 2021.

| Year | Male (n = 4,326) | | Female (n = 233,793) | | 95 % CI | p value |
|---|---|---|---|---|---|---|
| | N | % | n | % | | |
| 2017 | 203 | 0,20 | 16,724 | 15.83 | 0.0164 (−0.1561 to −0.1505) | <0.001 |
| 2018 | 189 | 0.19 | 17,572 | 16.50 | 0.0155 (−0.1600 to −0.1543) | <0.001 |
| 2019 | 227 | 0.22 | 16,068 | 15.53 | 0.0177 (−0.1498 to −0.1443) | <0.001 |
| 2020 | 207 | 0.20 | 17,285 | 14.47 | 0.0148 (−0.1403 to −0.1349) | <0.001 |
| 2021 | 220 | 0,21 | 16,139 | 16.63 | 0.0155 (−0.1710 to −0.1654) | <0.001 |
| Average | 209 | 0.21 | 16,757 | 16.54 | 0.0163 (−0.1741 to −0.1524 | <0.001 |

Legend: Comparison of the evolution of breast cancer mortality rates from 2017 to 2021 in Brazil. The table presents the annual mortality rates for male (n = 4,326) and female (n = 233,793) breast cancer patients, along with the 95 % confidence intervals and p-values from Fisher's Test. The data highlights a consistent trend in mortality rates over the five-year period, with statistically significant differences observed between male and female patients. CI, confidence interval. Fisher's Test

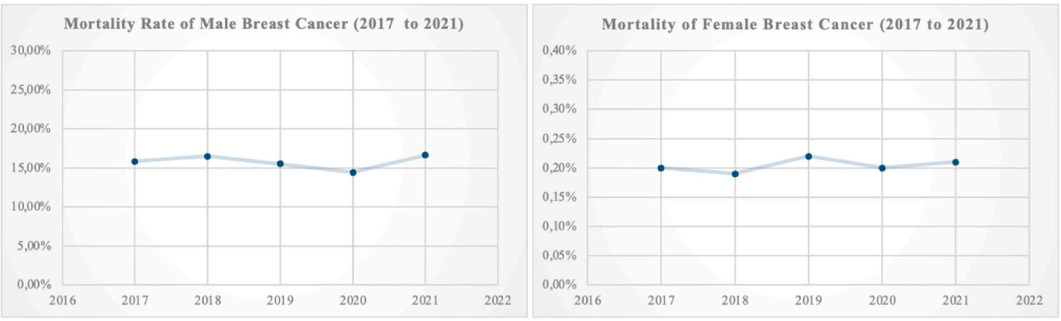


**Fig. 5.** Comparison of the evolution of breast cancer case mortality rates from 2017 to 2021.
**Legend:** Mortality rates of breast cancer in Brazil from 2017 to 2021, stratified by gender. The left panel illustrates the mortality rate of male breast cancer, which fluctuated slightly over the years, with a slight increase in 2021. The right panel shows the mortality rate of female breast cancer, which remained relatively stable over the observed period.

The age predilection for MBC in our cohort aligns with previous findings, which indicate a higher prevalence of MBC in older demographic groups; our data indicated that males aged 55–69 years are disproportionately affected [16]. This age-related disparity may be attributed to the asymptomatic progression of MBC and ensuing delay in diagnosis in males. A contributing factor may be the interplay between MBC and estrogen, considering that most MBC patients are estrogen receptor-positive [21]. This hormonal association becomes increasingly relevant in males after 50 years of age, potentially influencing the disease dynamics [23]. Diagnostic differences were also observed; while FBC diagnosis peaks in the 40–54-year age bracket, coinciding with the onset of routine screening, such practices are markedly less prevalent in males [24]. This disparity explains our finding that while physical examination predominates in MBC diagnosis, imaging is more prevalent in FBC diagnosis. Such trends underscore the need for increased clinical vigilance and possibly the introduction of tailored screening approaches for at-risk male populations [25].

Hung et al. observed in their national survey conducted in Taiwan of 578 male and 100,915 female breast cancers that the standardized incidence rate (SIR) for a second nonbreast primary cancer was higher compared to female patients (HR 3.01).

In our study of MBC, the least frequent histological type was lobular histology, which accounted for 4.1 % of all tumors (vs. 14.8 % in FBC), and the most frequent immunohistochemical subtype was luminal, whereas basal-like and HER2+ BC were less represented, in agreement with the findings of Johansson et al. [25]; a Surveillance, Epidemiology, and End Results [SEER] database analysis published in 2012; and other studies [16,26].

Our study further reinforces the notion that MBC is commonly diagnosed at a more advanced stage than FBC, underscoring the global pattern of neglect [18,26]. This late presentation correlates with a diminished survival rate in males, which is reported to be approximately 5 years lower than that in women [18]. These findings advocate a paradigm shift toward more proactive and sex-inclusive diagnostic practices.

Proportionally, stage I diagnoses are more frequent in FBC patients, whereas stage IV diagnoses predominate in MBC patients, reflecting sex disparities in healthcare accessibility, screening adherence, and differences in health-seeking behaviors [21]. Treatment in MBC patients frequently commences with chemotherapy because of the advanced stage and lymph node involvement upon diagnosis [19]. However, our study suggested that surgery is more commonly the initial intervention for MBC patients, which is in line with the scarcity of breast-conserving strategies used in MBC treatment protocols [27].

MBC is often diagnosed at an advanced stage for several reasons. First, there is a general lack of awareness of MBC among the public and, sometimes, within the medical community. This lack of awareness can delay seeking medical advice regarding the symptoms. Second, there is no established screening program for MBC, such as that for FBC, leading to missed early detection opportunities. As a result, MBC tends to be diagnosed when symptoms are more advanced, eventually affecting survival rates. Early-stage BC generally has

a better prognosis than cancer diagnosed at a later stage; therefore, delayed diagnosis can lead to poorer outcomes in male patients [12].

The prevalence of radical surgeries such as mastectomy in MBC patients, compared with more conservative approaches, is reflective of the broader clinical narrative that favors aggressive treatment of MBC [27]. Conversely, the underutilization of radiation therapy in MBC patients, despite its increased proportional use in our study, remains a concern, highlighting potential gaps in multidisciplinary care approaches [26,27].

Although there are no specific guidelines, the traditional surgical approach for managing early-stage male breast cancer historically has been mastectomy. In the largest real-world study of male breast cancer, more than two thirds underwent a mastectomy; however, it was also noted that those who underwent mastectomy had worse outcomes than those undergoing breast conservation therapy which was attributed to an overrepresentation of patients with larger tumors and positive lymph nodes [31, 32].

Socioeconomic status and access to healthcare in Brazil likely influenced the disparities in BC diagnosis and treatment observed in this study. In Brazil, regions with lower socioeconomic status often face challenges in accessing healthcare, including the limited availability of advanced medical facilities and cancer screening programs. This can lead to a delayed diagnosis, particularly in MBC patients for whom screening is less common. Additionally, disparities in healthcare quality and availability of treatment options can affect patient outcomes. These factors may have contributed to the higher incidence of advanced disease at diagnosis and variations in treatment approaches between MBC and FBC patients observed in our study [28].

Based on these findings, public health policies in Brazil should focus on increasing awareness of MBC to encourage early detection. This could involve educational campaigns and training of healthcare professionals. Clinical practice should incorporate additional sex-inclusive screening and diagnostic protocols. Considering the rapid initiation of MBC treatment, psychological support should be integrated into the care process. Policies should address the disparities in healthcare access to ensure equitable treatment for both MBC and FBC patients, particularly in regions with lower socioeconomic status.

In this analysis, we observed that gender disparities in breast cancer presented unique characteristics within the Brazilian cohort, which may not be entirely comparable to international data. This will not only allow us to identify the specific features of the Brazilian cohort but also provide a better understanding of how regional factors might influence the epidemiology of breast cancer among men and women.

Ecological studies, including our study, have certain limitations, most notably a lack of individual information related to risk factors in previous years that was not available in population censuses or other public databases. Thus, we could not associate them with the population based In addition, geographic comparisons should not be used to make inferences at individual levels. However, the results of this study can lead to new investigations in which the observation unit is the individual. Unfortunately, based on the diagnosis of Death Certificate Only, around 13.6 % of colon-rectal cancer were not considered when estimating net survival. This drawback should recognize and addressed since it may cause bias for survival rate estimates, especially in cities where the number of patients is extremely low. The advanced stage of MBC at diagnosis hints at a lack of screening for males, a subject not fully addressed in our study. While early treatment initiation in MBC appears beneficial, we cannot claim causality owing to the observational nature of our analysis. The study did not delve into treatment specifics or assess the impact of systematic screening for MBC. Additionally, the reasons behind regional disparities in MBC prevalence remained unexplored. These factors underscore the necessity for more detailed, prospective research to refine our understanding of MBC and enhance gender-specific clinical approaches.

Moreover, it is crucial to acknowledge and discuss the limitations inherent to this study. One of the main limitations is the presence of confounding factors that could influence the results. Previous studies have highlighted significant regional disparities, both in access to healthcare services and in the quality of care provided, which could directly impact health outcomes. These disparities, combined with varying levels of awareness and access to early diagnosis, should be carefully considered when extrapolating our results to other populations or international contexts. Therefore, any attempt to generalize our findings must take into account these regional variations and the potential biases introduced by them.

## 5. Conclusion

This study highlights significant disparities in breast cancer epidemiology and treatment between male breast cancer (MBC) and female breast cancer (FBC) patients in Brazil. The key findings include a lower incidence but more advanced stage at diagnosis in MBC, differences in treatment approaches, and quicker initiation of treatment in MBC patients. These results underscore the need for increased awareness, the development of sex-inclusive screening protocols, and equitable access to healthcare services across genders.

From a public health policy perspective, these findings advocate for the integration of MBC-specific considerations into existing breast cancer screening and treatment guidelines. This could involve tailored awareness campaigns that emphasize the importance of early detection in men and ensuring that healthcare providers are equipped to recognize and treat MBC effectively. Moreover, policy efforts should aim at reducing the disparities in access to timely and appropriate care, which is critical for improving outcomes in both men and women.

Future research should delve deeper into understanding the biological underpinnings of the disparities observed between MBC and FBC. This includes exploring potential genetic, hormonal, and environmental factors that may contribute to these differences. Additionally, research should focus on developing and evaluating targeted public health interventions that address these disparities, with the ultimate goal of improving breast cancer outcomes for all patients in Brazil, regardless of gender.

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## Data availability

The data is available as open resources on the platform https://datasus.saude.gov.br/.

## CRediT authorship contribution statement

**Marcelo Antonini:** Writing – original draft, Methodology, Conceptualization. **André Mattar:** Writing – review & editing, Conceptualization. **Gabriel Duque Pannain:** Writing – original draft, Methodology. **Steffi Ferreira Buttenbender:** Writing – original draft, Methodology. **Denise Joffily Pereira da Costa Pinheiro:** Writing – review & editing. **Marina Diógenes Teixeira:** Writing – review & editing. **Andressa Gonçalves Amorim:** Writing – review & editing. **Odair Ferraro:** Writing – review & editing, Supervision. **Reginaldo Guedes Coelho Lopes:** Writing – review & editing, Supervision. **Luiz Henrique Gebrim:** Writing – review & editing, Supervision.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## References

[1] F. Lima, Estimativa 2023 : incidência de câncer no Brasil, 2023.
[2] H. Sung, et al., Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, CA A Cancer J. Clin. 71 (3) (2021) 209–249.
[3] R.L. Siegel, K.D. Miller, A. Jemal, Cancer statistics, CA A Cancer J. Clin. 68 (1) (2018) 7–30, 2018.
[4] S.H. Giordano, Breast cancer in men, N. Engl. J. Med. 379 (14) (2018) 1385–1386.
[5] S. Ionescu, et al., An update on the general features of breast cancer in male patients-A literature review, Diagnostics 12 (7) (2022).
[6] A. Antoniou, et al., Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case Series unselected for family history: a combined analysis of 22 studies, Am. J. Hum. Genet. 72 (5) (2003) 1117–1130.
[7] L.A. Brinton, et al., Prospective evaluation of risk factors for male breast cancer, J. Natl. Cancer Inst. 100 (20) (2008) 1477–1481.
[8] M. Rolfes, et al., Prevalence of cancer predisposition germline variants in male breast cancer patients: results of the German consortium for hereditary breast and ovarian cancer, Cancers 14 (13) (2022) 3292.
[9] T.D. Ellington, et al., Breast cancer survival among males by race, ethnicity, age, geographic region, and stage - United States, 2007-2016, MMWR Morb. Mortal. Wkly. Rep. 69 (41) (2020) 1481–1484.
[10] M.B. Mainiero, et al., ACR appropriateness criteria evaluation of the symptomatic male breast, J. Am. Coll. Radiol. 12 (7) (2015) 678–682.
[11] S.H. Giordano, Breast cancer in men, N. Engl. J. Med. 378 (24) (2018) 2311–2320.
[12] R.W. Woods, et al., Image-based screening for men at high risk for breast cancer: benefits and drawbacks, Clin. Imag. 60 (1) (2020) 84–89.
[13] A. Gucalp, et al., Male breast cancer: a disease distinct from female breast cancer, Breast Cancer Res. Treat. 173 (1) (2019) 37–48.
[14] M.J. Hassett, et al., Management of male breast cancer: ASCO guideline, J. Clin. Oncol. 38 (16) (2020) 1849–1863.
[15] B.d.R. Perreira, in: I.M.O. de Jesus, M.M.F. Martins (Eds.), PERFIL SOCIODEMOGRÁFICO DA MORTALIDADE DA POPULAÇÃO IDOSA NO NORDESTE BRASILEIRO, 2020.
[16] A. Ahmad, Breast cancer statistics: recent trends, Adv. Exp. Med. Biol. 1152 (2019) 1–7.
[17] J.M. Greif, et al., Gender differences in breast cancer: analysis of 13,000 breast cancers in men from the National Cancer Data Base, Ann. Surg Oncol. 19 (10) (2012) 3199–3204.
[18] F. Wang, et al., Overall mortality after diagnosis of breast cancer in men vs women, JAMA Oncol. 5 (11) (2019) 1589–1596.
[19] J.P. Leone, et al., Locoregional treatment and overall survival of men with T1a,b,cN0M0 breast cancer: a population-based study, Eur. J. Cancer 71 (2017) 7–14.
[20] F. Cardoso, et al., Characterization of male breast cancer: results of the EORTC 10085/TBCRC/BIG/NABCG international male breast cancer program, Ann. Oncol. 29 (2) (2018) 405–417.
[21] S. Konduri, et al., Epidemiology of male breast cancer, Breast 54 (2020) 8–14.
[22] J. White, et al., Male breast carcinoma: increased awareness needed, Breast Cancer Res. 13 (5) (2011) 219.
[23] F.A.B. Campos, et al., Genetic landscape of male breast cancer, Cancers 13 (14) (2021).
[24] F. Accomasso, et al., Clinical, pathological, and prognostic features of male breast cancer: a multicenter study, Curr. Oncol. 30 (11) (2023) 9860–9871.
[25] I. Johansson, et al., Molecular profiling of male breast cancer - lost in translation? Int. J. Biochem. Cell Biol. 53 (2014) 526–535.
[26] D. Tural, et al., Male breast cancers behave differently in elderly patients, Jpn. J. Clin. Oncol. 43 (1) (2013) 22–27.
[27] B. Sousa, E. Moser, F. Cardoso, An update on male breast cancer and future directions for research and treatment, Eur. J. Pharmacol. 717 (1–3) (2013) 71–83.
[28] R.A. Leon-Ferre, et al., A contemporary review of male breast cancer: current evidence and unanswered questions, Cancer Metastasis Rev. 37 (4) (2018) 599–614.