

Male Breast Cancer: A Public Health Blind Spot in Oncology

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Abstract

Introduction:

Male breast cancer is a rare but clinically significant malignancy, representing 0.6–1% of all breast cancer cases. Its low incidence contributes to delayed diagnosis, advanced disease at presentation, and poorer outcomes compared with female patients. Despite biological similarities to female breast cancer, most clinical guidelines and therapeutic strategies are extrapolated from female-focused studies, creating gaps in evidence-based care for men.

Purpose:

This review aims to synthesize current knowledge on the epidemiology, risk factors, clinical presentation, pathology, treatment, psychosocial impact, and ongoing research gaps in male breast cancer, highlighting the need for sex-specific management strategies.

Materials and Methods:

A comprehensive literature review was conducted, including population-based epidemiologic studies, genetic and molecular analyses, clinical trials, and psychosocial research focused on male breast cancer. Key databases were searched for studies reporting incidence, risk factors, diagnostic approaches, treatment outcomes, and survivorship issues in men.

Results:

Male breast cancer incidence is rising globally, particularly among older men, with BRCA2 mutations, hormonal dysregulation, Klinefelter syndrome, obesity, and radiation exposure identified as significant risk factors. Clinically, men typically present with retroareolar masses, nipple changes, or axillary lymphadenopathy, often leading to delayed diagnosis. Histologically, invasive ductal carcinoma predominates, with high rates of hormone receptor positivity and luminal A subtype predominance. Standard management includes mastectomy or, selectively, breast-conserving surgery, adjuvant radiotherapy, systemic chemotherapy, and endocrine therapy—primarily

tamoxifen. Men face unique psychosocial challenges, including stigma, sexual dysfunction, and body image concerns. Persistent gaps include limited male-specific clinical trials, underrepresentation in guidelines, and inadequate awareness among patients and providers. Emerging approaches focus on molecular profiling, targeted therapies, and male-specific survivorship care.

Keywords:

Male breast cancer, BRCA2, hormone receptor-positive, invasive ductal carcinoma, mastectomy, endocrine therapy, psychosocial impact, epidemiology, genetic predisposition, targeted therapy.**1.**

Introduction

Male breast cancer represents a rare but clinically significant malignancy, accounting for only 0.6-1% of all breast cancer diagnoses worldwide. Its low incidence contributes to limited public and professional awareness, frequently resulting in delayed presentation, more advanced disease at diagnosis, and poorer outcomes compared with female patients. Despite biological similarities between male and female breast tumors, the overwhelming predominance of breast cancer research in women has led to a persistent evidence gap; most diagnostic and therapeutic recommendations for men are derived from studies that exclude or underrepresent male patients. This reliance on extrapolated data poses challenges in optimizing care for this unique patient population, particularly in the context of distinct hormonal profiles, genetic predispositions, and psychosocial experiences (1,2). The aim of this review is to synthesize current knowledge on the epidemiology, risk factors, diagnostic limitations, clinical management, and psychosocial implications of male breast cancer, while identifying persistent gaps that necessitate dedicated research efforts to improve outcomes for affected men.

2. Epidemiology and risk factors

Although male breast cancer remains rare, multiple population-based studies have documented a gradual increase in incidence over recent decades. This rise is most pronounced among older men, with the majority of diagnoses occurring between the ages of 60 and 79 depending on the population studied (2,3). Several hypotheses have been proposed to explain this upward trend. Improved diagnostic imaging, heightened clinical awareness, and greater availability of genetic testing may contribute to earlier identification of cases that previously would have gone unrecognized. At the same time, environmental and lifestyle shifts, including increasing obesity rates and longer life expectancy, may be altering hormonal and metabolic profiles in ways that predispose men to breast carcinogenesis (2,4). The global age-standardized incidence rate of male breast cancer

rose significantly with an average annual percentage increase of approximately 2%. This increase is observed in most regions, and rising fastest in middle Socio-Demographic Index (SDI) countries and east Africa. The incidence and mortality are highest in Eastern Sub-Saharan Africa and Oceania, and lowest in Western Europe and high-income countries (2).

Emerging genomic studies have begun to clarify the molecular architecture of male breast cancer, revealing both areas of overlap and important differences compared with female disease. Tumors in men demonstrate distinct mutation patterns, with higher frequencies of alterations in genes such as BRCA2, PALB2, PIK3CA, and GATA3, and comparatively lower rates of TP53 mutations. These mutations drive carcinogenesis primarily through impaired DNA repair, cell cycle dysregulation, and aberrant signaling (1,5–7).

Hereditary predisposition represents one of the most clearly defined contributors, with BRCA2 mutations being the most frequent and conferring the strongest known genetic risk. Men carrying a pathogenic BRCA2 variant face a 20- to 44-fold increase in the risk of male breast cancer compared with non-carriers. BRCA1 mutations, though a major driver of breast cancer in women, are linked to a more moderate yet clinically meaningful risk increase, estimated at about 4.3-fold (1,6,8). Among men who carry BRCA mutations, the estimated lifetime risk of developing breast cancer is about 6.8% for BRCA2 carriers compared to roughly 1.2% for those with a BRCA1 mutation and around 0.1% for the general male population (1,6). Additional susceptibility genes—including PALB2, CHEK2, and ATM—have been implicated through familial clustering and next-generation sequencing studies, though penetrance estimates in men remain less precise due to limited male-specific data. For PALB2 mutations population-based studies estimate a 7- to 17-fold increased risk, while CHEK2 mutations confer a 3- to 10-fold increased risk, and ATM 1.8- to 5-fold (5,9–11). As genetic testing becomes increasingly accessible, identifying male mutation carriers has significant implications for early detection strategies, risk counseling, and treatment selection, particularly given the distinct molecular signatures associated with BRCA-related tumors.

Hormonal dysregulation plays a central role in the pathophysiology of male breast cancer, and conditions that elevate estrogen levels relative to testosterone substantially increase risk. An increased estrogen-to-testosterone ratio heightens the risk by driving estrogen-receptor–mediated proliferation and survival of breast epithelial cells, and the accompanying loss of androgen-mediated growth restraint further supports carcinogenic progression (1,12,13). Klinefelter syndrome (47,XXY) is the most striking example, conferring an estimated 20- to 50-fold increase in male breast cancer incidence due to testicular dysgenesis, hypogonadism, and high estrogen-to-androgen ratio (14). Outside of

chromosomal disorders, several endocrine and metabolic conditions modify hormonal balance in ways that facilitate carcinogenesis. Obesity increases aromatase activity in adipose tissue, enhancing peripheral conversion of androgens to estrogens (12,15). Liver diseases such as cirrhosis impair hepatic metabolism of sex hormones, leading to elevated circulating estrogen levels (12,16). Testicular disorders, including orchitis, cryptorchidism, or prior orchiectomy, may likewise disrupt normal androgen production, further contributing to estrogen dominance (17–19). Together, these conditions emphasize how crucial balanced endocrine function is to male breast cancer risk, underscoring the need to consider hormone-related comorbidities when evaluating an individual's vulnerability.

Beyond genetic and endocrine determinants, numerous lifestyle and environmental exposures have been implicated in modifying the risk. Obesity stands out as a major modifiable risk factor, both because of its impact on estrogen production and its association with metabolic inflammation (19,20). Alcohol consumption may promote carcinogenesis through mechanisms involving hepatic dysfunction, oxidative stress, and altered estrogen metabolism (21,22). Radiation exposure, particularly therapeutic chest irradiation for childhood or adolescent malignancies, has long been recognized as a significant risk factor for both male and female breast cancer, with risk persisting for decades after exposure (1,18). Occupational hazards such as exposure to high temperatures, electromagnetic fields, and polycyclic aromatic hydrocarbons have been suggested as possible risk factors, although less rigorously studied in men, have drawn attention as potential contributors. These exposures may act through endocrine disruption or direct genotoxic effect, but no definitive causal relationship has been established (18,23,24).

3. Clinical presentation and diagnostic delays

Male breast cancer typically presents with a constellation of signs that should prompt immediate clinical evaluation, yet these symptoms are often subtle and easily overlooked. The most common presenting feature is a firm, painless retroareolar mass, reflecting the concentration of ductal tissue directly behind the nipple, which may be accompanied by nipple retraction, ulceration, spontaneous or bloody nipple discharge. Additional findings can include palpable axillary lymphadenopathy, reflecting early regional spread due to the limited volume of male breast tissue—even small tumors may infiltrate underlying structures early in the disease course (25–27). These symptoms are often overlooked or misattributed to gynecomastia or other benign conditions, leading to delays in diagnosis. Studies consistently show that men experience a longer interval between

symptom onset and diagnosis than women, with mean delays of 6–10 months still reported in contemporary cohorts. This delay is clinically significant, as more than 40% of men present with stage III or IV disease, and nodal involvement is observed in up to 42% of cases at diagnosis, contributing to poorer outcomes compared with women (1,27,28).

Delayed diagnosis remains one of the most significant challenges in the management of male breast cancer, driven largely by persistent misconceptions and limited public awareness. Men often do not perceive themselves to be at risk for breast malignancy and healthcare providers may also inadvertently contribute to under-recognition; the rarity of the disease can lead to low clinical suspicion, particularly in younger men or those without clear risk factors. Additionally, sociocultural stigma and embarrassment surrounding breast symptoms in men may deter timely medical consultation. Collectively, these factors create diagnostic inertia, allowing tumors to progress unchecked and emphasizing the need for targeted education for both clinicians and the general public, as early-stage disease is associated with substantially better survival (7,27,29–31).

Once male breast cancer is suspected, a structured diagnostic workup analogous to that used in female breast cancer is essential. Ultrasound is often the preliminary imaging modality due to its accessibility and effectiveness in characterizing palpable masses and assessing axillary lymph nodes, especially in younger men (<25 years) due to lower pretest probability of malignancy and to avoid unnecessary radiation. Mammography remains the cornerstone for initial evaluation in men aged ≥ 25 years, distinguishing malignant from benign retroareolar lesions with high sensitivity and specificity (32–35). Breast MRI may be employed selectively, particularly in cases with indeterminate findings or strong genetic predisposition, but it is not recommended for routine initial evaluation due to limited incremental diagnostic yield in most cases (35,36). Definitive diagnosis, however, relies on tissue sampling, with core needle biopsy, preferably ultrasound-guided, serving as the gold standard. This technique provides high sensitivity and specificity for malignancy and enables histopathologic subtyping which are central to therapeutic planning (37). Timely and accurate diagnosis along this pathway decreases the number of men who present with advanced-stage disease and leads to better overall clinical outcomes (1,32,37).

4. Pathology and tumor biology

The histologic profile of male breast cancer is notably distinct from that of female breast cancer, reflecting underlying anatomic and developmental differences in breast tissue. Invasive ductal carcinoma (IDC) accounts for approximately 85-90% of all cases, a markedly higher proportion than

seen in women, while invasive lobular carcinoma (ILC) is exceedingly rare in men, comprising only 1-2% cases. This contrasts with female breast cancer, where ILC represents about 12% of invasive tumors (1,27,38,39). This predominance is largely attributable to the absence or rudimentary development of functional lobular structures in the male breast, as the hormonally driven maturation of lobules does not occur without estrogenic stimulation during puberty. Consequently, the male breast consists almost exclusively of ductal structures, making ductal rather than lobular neoplasia the predominant pattern of malignant transformation (1,27). Other histologic subtypes, including papillary, medullary, mucinous, and Paget disease of the breast, do occur but represent a small minority of cases in comparison to IDC and ILC (7).

The hormonal receptor profile of male breast cancer is characterized by a high prevalence of estrogen receptor (ER) and progesterone receptor (PR) positivity, a low frequency of HER2 overexpression, and predominance of the luminal A molecular subtype. This profile has important implications for tumor biology, prognosis, and systemic treatment strategies. High rates of ER and PR expression (up to 99% and 81%, respectively), together with the predominance of the luminal A subtype, are associated with lower proliferative activity (low Ki-67), lower histologic grade, and improved overall and disease-free survival compared with HER2-positive or triple-negative disease. HER2-positive breast cancer tests positive for a protein called human epidermal growth factor receptor 2 (HER2) which promotes the growth of cancer cells and its overexpression is less common in men than in women—it is observed in only 8–13% of male breast cancers. Triple-negative breast cancer (TNBC) in men is extremely rare, accounting for less than 1% of all cases. It is defined by the absence of ER, PR and HER2 expression. Both HER2-positive and triple-negative subtypes are associated with more aggressive tumor behavior and worse clinical outcomes. Molecular profiling consistently demonstrates that most male breast cancers fall within the luminal A subtype, which is generally associated with favorable differentiation, lower proliferation indices, and good prognostic outcomes (1,5,40–42).

Despite this favorable biology, tailored endocrine therapy strategies remain underutilized in clinical practice, partly due to the extrapolation of treatment guidelines from trials conducted largely in women (7). Although current datasets remain limited by small sample sizes, the available evidence underscores that male breast cancer cannot simply be viewed as a biological mirror of female breast cancer. Expanding genomic profiling in male cohorts is critical for advancing precision oncology, guiding therapeutic stratification, and identifying novel molecular targets.

5. Treatment approaches

Surgery remains the cornerstone of treatment for male breast cancer, with mastectomy historically constituting the standard operative approach. Because male breast tissue is limited and tumors tend to arise in close proximity to the nipple–areolar complex, total mastectomy has traditionally been favored to achieve clear margins. However, breast-conserving surgery (BCS), while less commonly performed, has been demonstrated to be both feasible and oncologically safe in carefully selected cases, particularly when tumors are small and located peripherally (43–46). Axillary staging is an essential component of surgical management, given the high likelihood of nodal involvement at diagnosis. Sentinel lymph node biopsy (SLNB) is now widely accepted as the preferred staging technique and has largely replaced routine axillary lymph node dissection (ALND) in clinically nodal-negative disease. ALND remains reserved for patients with confirmed nodal metastases or when SLNB is not technically feasible (47–50). Because surgical decision-making in men has historically mirrored practice in women, emerging evidence supports the need for individualized consideration of tumor location, breast size, and patient preference in operative planning.

Radiation therapy plays an important adjunctive role in the multidisciplinary management of male breast cancer and is typically recommended following surgery for patients with locally advanced disease, positive margins, or nodal involvement. The American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology recommend postmastectomy radiation therapy (PMRT) for men with node-positive disease, residual nodal disease after neoadjuvant (presurgical) systemic therapy, or select node-negative patients with high-risk features (51–53). Systemic chemotherapy is administered according to principles similar to those used in female breast cancer, with treatment tailored to stage, tumor grade, and molecular characteristics. Anthracycline- and taxane-based regimens remain the backbone of cytotoxic therapy for high-risk or node-positive disease. Although evidence guiding systemic therapy in men derives almost entirely from trials conducted in women, retrospective analyses suggest comparable benefits (1,47,53–55). The challenge lies in appropriately extrapolating female-derived data while recognizing male-specific biological nuances.

Endocrine therapy constitutes a critical component of treatment for male breast cancer, given the overwhelmingly high prevalence of hormone receptor–positive disease. Tamoxifen is the preferred first-line agent and has demonstrated clear survival benefits, making it the standard of care across stages. It is usually prescribed for 5-10 years and poor patient adherence is associated with

increased risk of recurrence and mortality. Barriers to adherence are largely driven by tamoxifen-associated adverse effects, including hot flashes, mood disturbances, weight gain, reduced libido, erectile dysfunction, and an increased risk of thromboembolic events. These toxicities are common and may be sufficiently severe to prompt early treatment discontinuation, with real-world discontinuation rates reported as high as 20–50% in some series. The risk of venous thromboembolism is particularly noteworthy, with most events occurring within the first 18 months of therapy (1,7,56,57). If tamoxifen is contraindicated or not tolerated, the recommended alternative endocrine strategy is the combination of a gonadotropin-releasing hormone (GnRH) analog with an aromatase inhibitor. Aromatase inhibitor monotherapy is ineffective in men because it does not achieve adequate suppression of estradiol levels and should therefore be avoided. When aromatase inhibitors are used, they must be combined with GnRH agonists to suppress testicular function and achieve a clinically meaningful reduction in circulating estrogen levels (1,7,58).

Despite the strong biological rationale for endocrine therapy, adherence remains a persistent challenge among male patients. Better counseling, toxicity management, and patient-centered adherence strategies are essential to optimizing outcomes.

6. Psychosocial impact and social care

Psychosocial distress, including embarrassment, stigma, and perceived threats to masculinity, significantly affects men diagnosed with breast cancer, largely driven by societal perceptions of the disease as predominantly female (59,60). Although male-specific data are limited, the mean prevalence of clinically significant depression among breast cancer patients is approximately 21.2%, with a comparable burden of anxiety; pooled estimates indicate an anxiety prevalence of 17.9% among longer-term survivors (61–63). Notably, the five-year risk of late-onset depression among breast cancer survivors is estimated at 13.3%, exceeding that observed in survivors of prostate or colorectal cancer (64).

Sexual dysfunction, peripheral neuropathy, musculoskeletal symptoms, and fatigue represent the most frequently reported long-term sequelae among men treated for breast cancer. Body image concerns are also prominent, particularly after mastectomy, which alters chest contour and can negatively influence self-perception, sexual identity, and confidence. Men tend to disclose these issues less readily than women, and sexual health problems, including diminished libido, erectile dysfunction, and dyspareunia, are often insufficiently recognized and managed in clinical practice (65,66).

Routine mental health screening is advised for all cancer survivors, including men with breast cancer. Effective psychosocial care for this population relies on intentional, gender-sensitive communication that normalizes the male breast cancer experience and directly addresses concerns related to body image, sexual function, endocrine therapy–associated side effects, and emotional resilience. Incorporating partners and family members into survivorship planning and follow-up care further strengthens support and improves long-term well-being (63,67).

7. Gaps in research and guidelines

A persistent obstacle to evidence-based management of male breast cancer is the marked underrepresentation of men in clinical trials. Most studies either exclude male participants or include too few to permit robust sex-specific analyses, resulting in treatment recommendations that are largely extrapolated from female populations. This reliance on female-derived evidence is problematic, given meaningful differences in hormonal levels, genetic risk profiles, and psychosocial experiences, and it contributes to the continued absence of male-specific guidelines and ongoing clinical uncertainty (7,68).

Gaps in provider awareness further exacerbate disparities. Deficits in provider awareness contribute substantially to delayed diagnosis in male breast cancer. Clinical suspicion is often low, presenting symptoms are frequently under-recognized, and diagnostic and management decisions are commonly extrapolated from female-focused protocols. As a result, clinicians may misattribute key warning signs, such as a retroareolar mass, nipple discharge, or skin changes, to benign conditions like gynecomastia. This pattern of misclassification leads to postponed evaluation and a higher likelihood of men presenting with more advanced disease (1,68).

Recent collaborative efforts, such as the Male Breast Cancer Pooling Project, the International Male Breast Cancer Program, and expanding national and international registries, are beginning to generate much-needed male-specific data on epidemiology, treatment response, and outcomes (19,38). Strengthening male participation in clinical trials, developing sex-tailored survivorship models, and incorporating male-focused content into professional education are critical steps toward closing these gaps and improving care for this historically overlooked population.

8. Future directions

Future directions in male breast cancer increasingly emphasize personalized oncology, driven by comprehensive molecular profiling and targeted therapeutic approaches. Next-generation

sequencing and multigene testing reveal actionable alterations in more than 70% of cases, including BRCA2, PIK3CA, GATA3, and a range of DNA-repair and cell-cycle regulators, informing the use of CDK4/6 inhibitors, PI3K inhibitors, PARP inhibitors, and emerging antibody–drug conjugates (5,69,70).

Parallel efforts aim to establish male-specific diagnostic pathways, incorporating risk-adapted imaging strategies and tailored genetic screening, particularly for BRCA2 and other high-penetrance mutations (68).

At the same time, expanding male participation in clinical trials has become a priority. Current studies are evaluating endocrine therapies, targeted agents, and optimal surgical and radiotherapy approaches. Active areas of investigation include the efficacy and tolerability of tamoxifen, aromatase inhibitors with or without GnRH analogues, androgen-receptor–directed therapies, and PARP inhibitors, as well as comparative outcomes of breast-conserving surgery versus mastectomy and the role of adjuvant radiotherapy (1,7,69,70).

9. Conclusion

Improving awareness, representation in research, and support infrastructure is essential. Male breast cancer, while accounting for only a small fraction of overall breast cancer cases, represents a biologically distinct and clinically under-recognized malignancy. Its rarity contributes to delayed diagnosis, limited public and professional awareness, and the absence of male-specific clinical guidelines, resulting in management strategies that are often extrapolated from female breast cancer protocols. Beyond these clinical challenges, male patients face unique psychosocial burdens, including stigma, threats to masculinity, and underdeveloped support networks, which further complicate timely care and adherence to therapy. Addressing these gaps requires a multipronged approach: enhancing education for both healthcare providers and the public, expanding male inclusion in clinical trials and registries, and implementing precision oncology strategies tailored to male biology. Collectively, these efforts are essential to improve early detection, optimize treatment, and enhance quality of life for men affected by this historically neglected disease.

Disclosure

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