Discover Oncology

Review

Decoding male breast cancer: epidemiological insights, cutting-edge treatments, and future perspectives

Lei Zhao[1,2] · Huijuan Cheng[1] · Dongqiang He[1,2] · Yalan Zhang[1] · Yahui Chai[4] · Ailin Song[2] · Guodong Sun[1,3]

Received: 8 August 2024 / Accepted: 13 March 2025
Published online: 19 March 2025

Abstract
Breast cancer is predominantly recognized as a condition affecting women, however, male breast cancer (MBC), despite its rarity, represents a significant and serious malignancy in men. Accounting for approximately 1% of all breast cancer cases, MBC is often diagnosed at a later stage compared to female breast cancer, primarily due to a lack of awareness and the absence of screening programs tailored for men. This delayed diagnosis typically results in poorer prognoses and more limited treatment options. Over the past decade, there has been a notable increase in research and awareness surrounding MBC. This surge is largely driven by the recognition of its unique epidemiological and biological characteristics, which are distinct from those of female breast cancer. However, due to its low incidence, many aspects of MBC, including its etiology, clinical presentation, and optimal treatment strategies, remain inadequately understood. This paper aims to provide a comprehensive review of MBC by examining its incidence, mortality rates, and epidemiological characteristics on a global scale. Additionally, it explores the economic burden associated with the disease, identifies key risk factors, and discusses current preventive measures. Finally, the paper will offer insights into future research directions and potential advancements in the diagnosis and treatment of MBC.

Keywords Breast neoplasms · Male · Epidemiology · Risk factors · Disease burden · Treatments

1 Introduction

According to the Global Cancer Observatory (GLOBOCAN) 2020 data, male breast cancer (MBC) remains a rare disease, with an estimated global incidence rate of approximately accounts for approximately 1% of all breast cancer cases. This figure highlights its rarity compared to female breast cancer, which is one of the most commonly diagnosed cancers worldwide [1]. Though significantly lower than that of female breast cancer, it still represents an important health concern due to its late-stage diagnosis and subsequent poorer prognosis. Most male breast cancer patients are diagnosed at an advanced stage due to a lack of early screening and awareness [2]. In recent years, as awareness of male breast cancer has increased, related research has also grown. However, due to its low incidence rate, the etiology, clinical characteristics, and optimal treatment strategies for male breast cancer remain not fully understood.

Lei Zhao and Huijuan Cheng have contributed equally.

✉ Huijuan Cheng, chenghjmph@126.com; ✉ Ailin Song, songail@lzu.edu.cn; ✉ Guodong Sun, sungd2023@lzu.edu.cn | [1]Gansu Province Key Laboratory of Environmental Oncology, The Second Hospital of Lanzhou University, Lanzhou, Gansu, China. [2]Department of General Surgery, The Second Hospital of Lanzhou University, Lanzhou, Gansu, China. [3]Department of Medical Affairs, The First Hospital of Lanzhou University, Lanzhou, Gansu, China. [4]Department of General Surgery, Gansu Provincial Hospital, Lanzhou, Gansu, China.

2 Epidemiology

2.1 Incidence and mortality rates

Reports indicate that the staging of male breast cancer is similar to that of female breast cancer [3]. However, there are significant disparities in incidence and mortality rates. Globally, the incidence of male breast cancer is lower, with GLOBOCAN 2020 reporting an annual rate of 0.5–1.0 per 100,000 [1]. In the United States, the SEER database shows a stable annual incidence of approximately 1.2 per 100,000 from 1975 to 2016 [4]. Mortality rates for male breast cancer have remained relatively unchanged since 1990 to 2021, with the Global Burden of Disease (GBD) 2021,which study reported a rate of 0.34 per 100,000 (95% UI: 0.23–0.41) in 2021, significantly lower than the 14.55 per 100,000 (95% UI: 13.45–15.56) for female breast cancer [5]. This notable disparity highlights the urgent need to raise awareness and implement early detection strategies for male breast cancer, which is often overlooked, as late-stage diagnoses continue to challenge patient outcomes.

2.2 Triad distribution in epidemiology(Epidemiological Characteristics)

2.2.1 Temporal distribution

The incidence rate of male breast cancer increases significantly with age, rising sharply after 60 and peaking between 70 and 80 [6]. This trend may be linked to hormonal changes in older men, particularly fluctuations in estrogen and testosterone levels. Furthermore, older breast tissue may be more susceptible to carcinogenic factors. Bhardwaj PV et al. [7] reported that the average age at initial diagnosis for men is later than that for women (67 years vs. 62 years). Similar findings indicate that men (median age: 71 years) are significantly older than women (median age: 63 years) at the time of diagnosis ($U = 13{,}289.5$, $p = 0.009$). Furthermore, the overall 3-year survival rate is 88.9% for men and 91.1% for women, with a statistically significant difference between the two groups ($p = 0.009$) [8].

Moreover, a study by Ayca Gucalp et al. [9] pointed out that in developed countries, two-thirds of invasive female breast cancers are localized at diagnosis, whereas in men, only half are localized and the other half are regional or distant disease. This disparity may be attributed to multiple factors such as the lack of early screening methods and limited disease awareness. These findings highlight that male breast cancer patients are more likely to be diagnosed at an advanced stage compared to females, underscoring the need for improved awareness and early screening in men.

2.2.2 Geographic distribution

Utilizing the R (version 4.4.1) with the ggplot2 package, an analytical visualization of the Global Burden of Disease Study 2021 [5] (GBD2021 data, https://vizhub.healthdata.org/gbd-results/) was conducted. This analysis highlighted notable geographical disparities in the incidence rates of male breast cancer across continents. The 2021 data delineated that North America, China in Asia, and East Africa exhibited higher incidence rates (Fig. 1A). As shown in Fig. 1B, longitudinal analysis from 1990 to 2021 demonstrated that incidence rates across various regions have plateaued after 2010. Most continents have experienced marginal increments in incidence of male breast cancer; however, Southeast Asia, East Asia, Oceania, Western Europe, and North America recorded the highest rates, exceeding 1.2 per 100,000.

In terms of MBC mortality, the highest rates are predominantly found in Africa, followed by South America, with the lowest rates observed in Asia, Europe, and North America (Fig. 2A). Longitudinally, Sub-Saharan Africa reports the highest mortality rates, while other regions have shown relative stability (Fig. 2B).

The aforementioned analysis results are consistent with previous studies, that the incidence rate of male breast cancer shows significant variation across different regions and countries. It is notably higher in North America and East Asia, while being considerably lower in Europe [10]. This variation can be attributed to differences in genetic predisposition, environmental exposures, lifestyle factors, and the availability of medical resources. This pattern is significantly correlated with levels of socioeconomic development and the allocation of healthcare resources. Additionally, limited access to medical resources and lower levels of public awareness in these regions may lead to underdiagnosis [11].

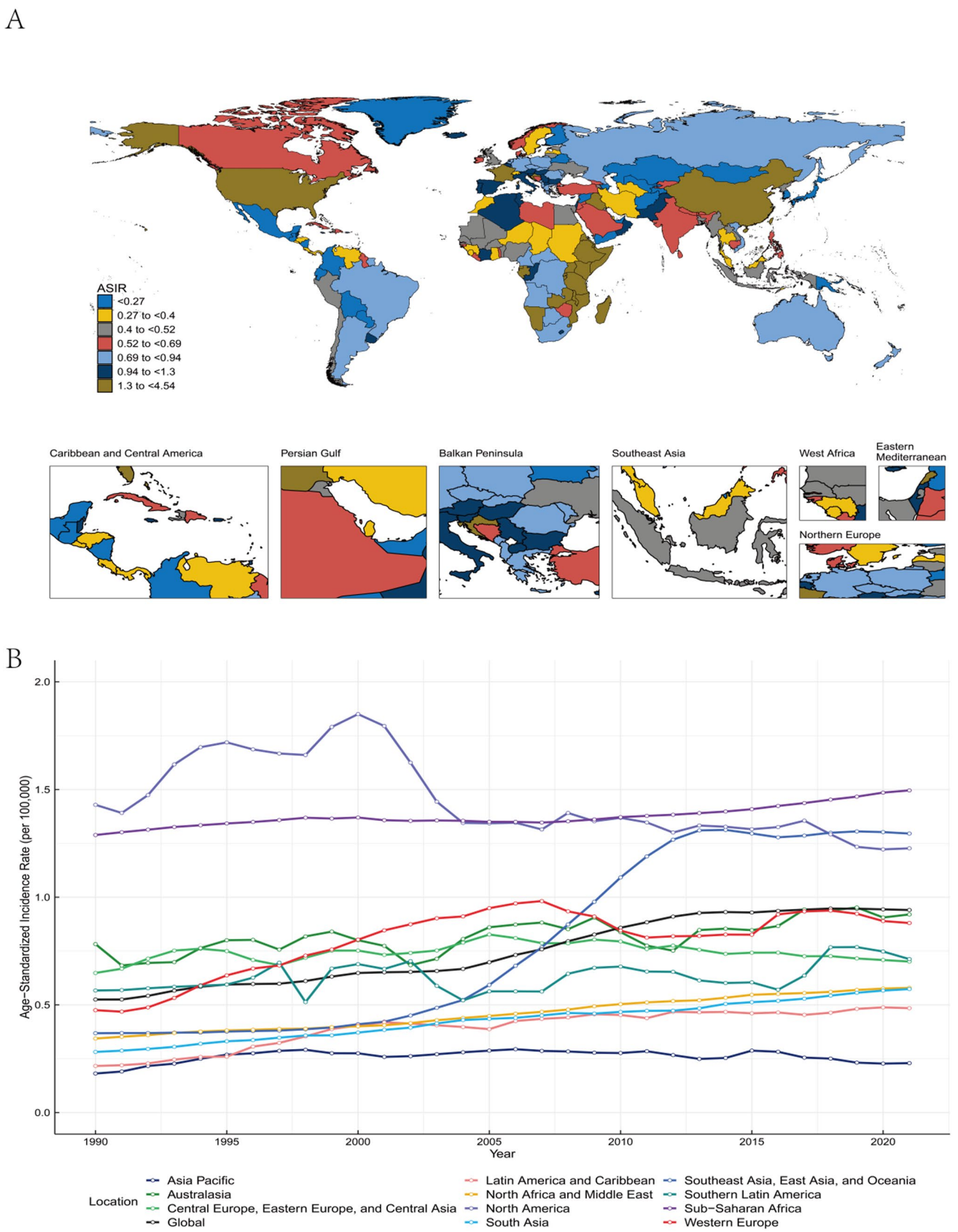

Fig. 1 **A** Global map of ASIR of male breast cancer in 2021. **B** Trends in ASIR of Male Breast Cancer Across Regions from 1990 to 2021.(ASIR, Age-Standardized Incidence Rate)

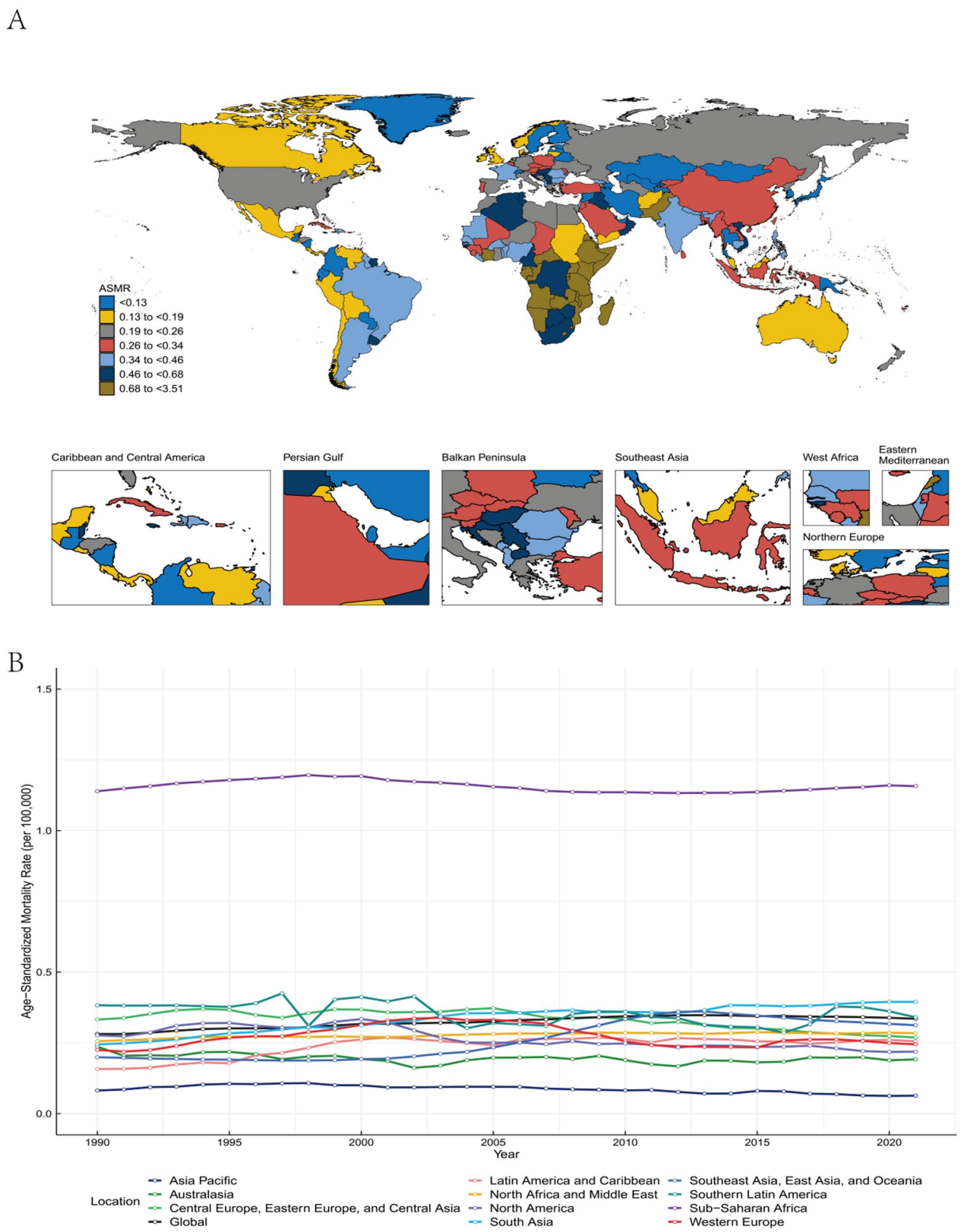

Fig. 2 **A** Global map of ASMR of male breast cancer in 2021. **B** Trends in ASMR of Male Breast Cancer Across Regions from 1990 to 2021. (ASMR, Age-Standardized Mortality Rate)

2.2.3 Population distribution

The incidence rate of male breast cancer shows significant variation across racial and ethnic groups. Research has consistently indicated that the incidence is higher among Black men compared to White men [2]. Early data from 2004 reported that male breast cancer incidence rates were slightly higher among Black men than White men, with an incidence of 1.8 per 100,000 in Black men and 1.1 per 100,000 in White men [12]. This disparity was further supported by 2020 SEER data, which showed that in 2016, Black men had an incidence rate of 3.02 per 100,000, compared to 1.05 per 100,000 among White men [13]. This difference may be attributed to genetic factors, socioeconomic status, and health behaviors. Understanding the racial and ethnic disparities in male breast cancer could offer clinical and etiological insights for different populations, thus more research is needed to fully explore these factors and provide up-to-date data.

3 Burden of male breast cancer

According to the Global Burden of Disease (GBD) study, the age-standardized Disability-Adjusted Life Year (DALY) rates of MBC have increased in several regions, particularly in some developing countries in Southeast Asia, East Asia, and Oceania (Fig. 3).

(According to Institute for Health Metrics and Evaluation (IHME), DALY consists of two components: YLL (Years of Life Lost) = Number of deaths × Remaining years of life expectancy, and YLD (Years Lived with Disability) = Number of cases × Disability weight × Duration of the disease. In regions with high mortality rates, YLL contributes more to the overall DALY. As shown in the figure, Sub-Saharan Africa has consistently had higher mortality rates compared to other regions from 1990 to 2021, resulting in higher YLL values and a significantly elevated DALY rate.)

Despite the relatively low number of MBC cases, the treatment and management of MBC impose a significant economic burden on healthcare systems. The expenses include surgery, chemotherapy, radiation therapy, targeted therapies, and often extensive follow-up care. According to recent studies, the average treatment cost for MBC in the United States ranges from $50,000 to $100,000, with advanced-stage treatment costs potentially reaching $200,000 [14, 15]. These figures highlight the significant financial impact on both patients and healthcare systems, exacerbated by the often delayed diagnosis and the necessity for intensive treatment regimens.

Male breast cancer not only imposes a significant economic burden but also profoundly affects patients' quality of life and mental health. Studies have shown that men with breast cancer often experience high levels of psychological distress, including anxiety and depression, due to the stigma associated with a disease predominantly seen in women

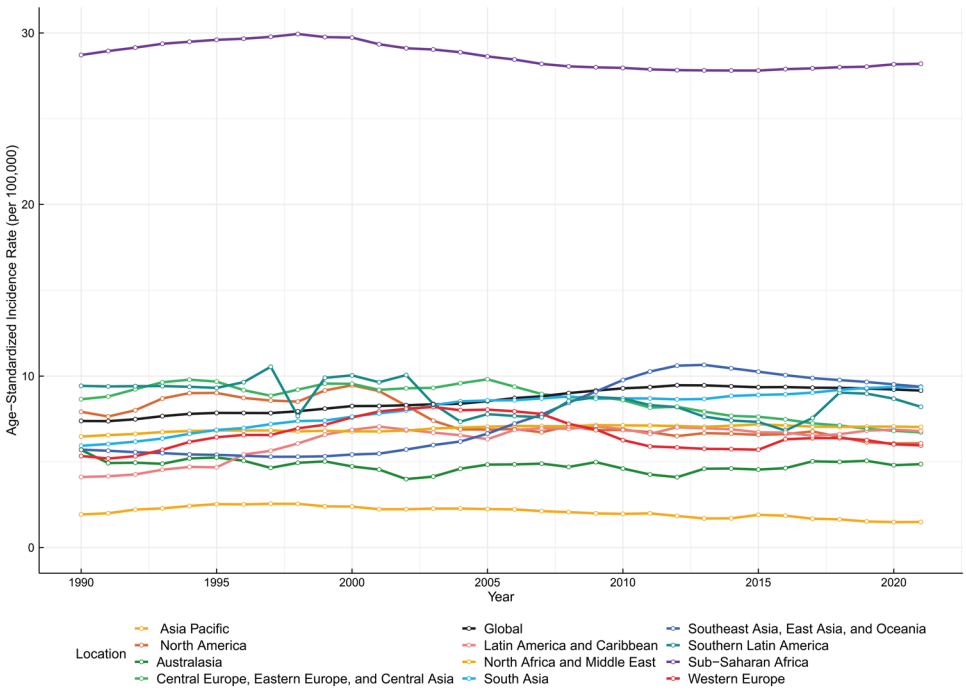

Fig. 3 Trends in ASDR of Male Breast Cancer Across Regions from 1990 to 2021.(ASDR, Age-Standardized Disability-Adjusted Life Year Rate)

[10]. Additionally, sexual dysfunction, a common side effect of breast cancer therapies, is frequently under-reported but significantly impacts patients' intimate relationships and overall well-being. Mancino et al. found that during treatment for MBC, 41.7% (15 of 36) of patients reported a significant change in sexual activity, while 47.2% (17 of 36) noted a change after surgery [16]. Similar researches indicates that changes in sexual interest also occur during treatment for breast cancer in men, significantly affecting their quality of life [17, 18]. The psychosocial burden is further compounded by the physical side effects of treatment, such as fatigue, pain, and reduced physical function, which can persist long after treatment completion. Addressing the dual burden of economic and psychosocial impacts requires a multifaceted approach, including increased awareness, early detection, and tailored support services for men with breast cancer.

4 Risk factors

Male breast cancer shares some risk factors with female breast cancer, but also has unique characteristics specific to men. These risk factors contribute to the likelihood of developing MBC and highlight the importance of awareness and early detection.

4.1 Advancing age

Like many cancers, the incidence of male breast cancer increases with age, typically peaking in the seventh decade of life. Men in the USA who are diagnosed with breast cancer tend to be 5–10 years older than their female counterparts [19, 20]. In a recent large retrospective study conducted by Cardoso et al., only 10% of male breast cancer patients were 50 years old or younger at the time of diagnosis, with the median age at diagnosis being 68 years [21].

4.2 Genetic factors

Germline pathogenic variants (PVs) in *BRCA2* are significant risk factors for male breast cancer, while the association with *BRCA1* PVs is less clear and not as strongly established. A large-scale study involving 1,939 U.S. families and 97 MBC patients found that *BRCA2* PV carriers have higher cumulative risks of MBC at all ages compared to non-carriers, whereas the risk associated with *BRCA1* PVs is lower. Notably, *BRCA2* PVs confer greater relative and cumulative risks. By age 70, the estimated cumulative risk of MBC is 6.8% (95% CI 3.2%–12%) for male *BRCA2* PV carriers, significantly higher than 1.2% (95% CI 0.22%–2.8%) for male *BRCA1* PV carriers [22]. Another study also demonstrated that men carrying *BRCA2* PVs have an 80-fold increased risk of developing breast cancer compared to the general male population [23]. Furthermore, the lifetime risk for men with *BRCA2* PVs ranges from 5 to 10%, while for those with *BRCA1* PVs, the risk is approximately 1% to 5% [24, 25]. These findings underscore the stronger association and higher penetrance of *BRCA2* PVs in MBC compared to *BRCA1* PVs, whose penetrance remains less well established and requires further research. This highlights the importance of continued studies to fully elucidate the role of *BRCA1* PVs in MBC risk, which may have implications for genetic counseling and screening strategies.

Beyond BRCA genes, other hereditary cancer syndromes, such as Li-Fraumeni syndrome and Cowden syndrome, also elevate the risk of MBC. Li-Fraumeni syndrome, caused by mutations in the TP53 gene, predisposes individuals to a variety of cancers, including breast cancer [26]. Similarly, Cowden syndrome, associated with mutations in the PTEN gene, increases the risk of breast cancer among other malignancies [27, 28].

4.3 Hormone levels

Elevated estrogen levels are closely linked to the development of male breast cancer [19]. Various conditions can lead to increased estrogen levels in men, thereby heightening the risk of MBC. Testicular dysfunction, for instance, can result in lower testosterone and higher estrogen levels, creating an imbalance that promotes breast tissue growth [29]. Similarly, liver disease impairs the liver's ability to metabolize estrogen, leading to elevated levels in the bloodstream. Obesity also contributes to higher estrogen levels as adipose tissue can convert androgens into estrogens through aromatization [30]. Moreover, prolonged use of androgen deprivation therapy, particularly as part of endocrine treatment for prostate cancer, significantly increases the risk of developing MBC. Men undergoing such treatments are exposed to elevated estrogen levels over an extended period, which can stimulate the growth of breast tissue and potentially lead to cancer development [31, 32].

4.4 Family history

Men with a family history of breast cancer are at significantly increased risk of developing the disease themselves. Studies have shown that men with a first-degree relative who has had breast cancer have approximately twice the risk of developing male breast cancer [2].

4.5 Other factors

In addition to the aforementioned risks, several other factors contribute to the likelihood of developing male breast cancer. These include radiation exposure, Klinefelter syndrome, certain occupational exposures, and prolonged alcohol consumption [33]. Men who have undergone radiation therapy to the chest area, particularly for conditions such as lymphoma, have an increased risk of developing breast cancer [34]. Alcohol consumption can lead to elevated estrogen levels in the body, which is associated with the development of breast cancer. Studies have shown that even moderate alcohol intake can increase the risk of breast cancer due to its effect on estrogen levels and its potential to cause DNA damage [35]. Klinefelter syndrome, a chromosomal disorder characterized by the presence of an extra X chromosome (XXY), is particularly significant. Men with Klinefelter syndrome have a markedly increased risk of breast cancer, estimated to be 20–50 times higher than that of the general male population [36].

5 Clinical characteristics and diagnosis

5.1 Clinical presentation

Male breast cancer presents with clinical symptoms similar to those observed in female breast cancer. Common signs include a palpable breast lump, nipple discharge, nipple retraction, and skin changes over the breast, such as dimpling or redness. Due to the relatively smaller amount of breast tissue in men, these lumps are often more easily detectable [37, 38].

5.2 Diagnostic methods

The diagnosis of MBC relies primarily on imaging studies and histopathological examination. Common imaging techniques include mammography, ultrasound, and magnetic resonance imaging (MRI). Mammography and ultrasound are typically used for the initial evaluation, while MRI provides a more detailed assessment when necessary. Histopathological confirmation is typically achieved through core needle biopsy or, in some cases, surgical excisional biopsy, allowing for the examination of tissue samples to identify cancerous cells [10, 36].

5.3 Immunohistochemical and molecular characteristics

The immunohistochemical and molecular characteristics of MBC bear some resemblance to those of female breast cancer. Most male breast cancers are estrogen receptor-positive (ER+), progesterone receptor-positive (PR+), and have a lower rate of human epidermal growth factor receptor 2 (HER2) positivity. Additionally, *BRCA2* PVs mutations are more common in male breast cancer patients compared to *BRCA1* PVs, which are relatively rare [39].

6 Current treatment options

6.1 Surgical treatment

Surgical intervention remains the cornerstone of male breast cancer treatment, with mastectomy and modified radical mastectomy being the most common approaches. Breast-conserving surgery may also be a viable option [40]. Leone et al. [41]. analyzed 6,919 male breast cancer patients from the SEER database from 1988 to 2017, revealing an overall

mastectomy rate of 81.6%. Giordano's [42] study noted that while breast-conserving surgery utilization is low, its safety in male breast cancer is comparable to that in females. Current research shows no significant difference in overall survival (OS) between breast-conserving surgery and mastectomy, with similar 5-year and 10-year OS rates [43]. Sauder et al. [44]. also found no significant differences in disease-free survival (DFS), cancer-specific survival, or OS between the two surgical options, though adherence to post-operative radiotherapy was lower in patients undergoing breast-conserving surgery. This highlights the importance of shared decision-making between physicians and patients.

For early-stage male breast cancer, breast-conserving surgery may be a viable option. Evolving evidence, as highlighted in the NCCN guidelines [40], suggests that when surgically feasible, breast-conserving surgery can offer outcomes equivalent to mastectomy. Thus, surgical decisions for male breast cancer should be guided by criteria similar to those used in female breast cancer, with an emphasis on individualized treatment plans. Given the limited breast tissue in men, early-stage tumors frequently involve the nipple-areola complex, making an R0 resection margin the standard surgical principle.

In terms of axillary lymph node management, male breast cancer follows the same guidelines as female breast cancer. Clinically node-negative patients typically undergo sentinel lymph node biopsy, while axillary lymph node dissection is recommended for node-positive patients to ensure comprehensive treatment of the disease [40].

6.2 Radiation therapy

In male breast cancer, radiation therapy is commonly used as part of the multidisciplinary approach due to the limited amount of breast tissue, which may cause small tumors to be close to the skin and chest wall, increasing the risk of recurrence if not adequately treated. It is primarily used as an adjuvant treatment following surgery, particularly after breast-conserving surgery or in patients with positive axillary lymph nodes. Radiation therapy can reduce the risk of local recurrence and improve patient outcomes [34].

6.3 Chemotherapy

Chemotherapy also plays a significant role in the treatment of male breast cancer, especially for high-risk or advanced-stage patients. Common chemotherapy regimens include combinations based on anthracyclines and taxanes [36]. Recent years, neoadjuvant chemotherapy has been recommended for male breast cancer patients, drawing on protocols used in female breast cancer treatment due to the limited specific research on male breast cancer. Schiza et al. compared 487 male breast cancer patients with 82,401 female breast cancer patients (stages I-III) undergoing neoadjuvant chemotherapy and found no significant differences in pathological complete response rates between genders [45].According to the 2023 Male Breast Cancer Guidelines, neoadjuvant chemotherapy can be considered for male breast cancer patients similar to female patients.

6.4 Endocrine therapy

Given that most male breast cancers are hormone-receptor positive (HR +) [46], endocrine therapy is one of the mainstays of treatment. Common endocrine therapy drugs include tamoxifen and gonadotropin-releasing hormone agonist (GnRH-a) concurrent with an aromatase inhibitor [47]. The American Society of Clinical Oncology (ASCO) Guidelines for MBC recommend that hormone receptor-positive male breast cancer patients eligible for adjuvant endocrine therapy but with contraindications to tamoxifen may be treated with aromatase inhibitors combined with GnRH-a [47]. Tamoxifen is the standard treatment for male breast cancer, significantly prolonging disease-free survival and overall survival [10, 48].Notably, the results of the MALE phase II clinical trial suggest that combining tamoxifen or aromatase inhibitors with GnRH-a can further suppress estradiol levels, potentially impacting sexual function and overall quality of life [18]. Therefore, the potential adverse effects of GnRH-a should be carefully considered when selecting treatment options.

In addition, therapies targeting androgen receptors have emerged as potential treatment options for male breast cancer. A recent case report demonstrated that male breast cancer patients undergoing anti-androgen therapy with bicalutamide and goserelin were able to maintain tumor progression-free status on imaging for up to four months [49]. These findings suggest potential clinical applications for bicalutamide and goserelin, though they remain under investigation and are primarily used for advanced or metastatic disease. Given that most evidence comes from small-sample studies and there is a lack of consensus on androgen receptor positivity rates in male breast cancer, further research is required to establish the efficacy of targeting androgen receptors.

6.5 Targeted therapy

Although the incidence of HER2-positive male breast cancer is relatively low, targeted therapies such as trastuzumab remain crucial for those with HER2-positive tumors. Studies have shown that combining trastuzumab with chemotherapy significantly improves survival rates and disease-free survival in HER2-positive male breast cancer patients. While PARP inhibitors in male breast cancer is still limited, preliminary evidence suggests it could become an important treatment option for this subgroup of patients [50]. Recent developments in PARP inhibitors, such as olaparib, have shown promise in treating male breast cancer patients with BRCA mutations [51]. Other targeted therapies, such as PI3K/AKT/mTOR pathway inhibitors, have also shown potential in some clinical trials. The development and application of these treatments are expected to provide more options and improve the prognosis for male breast cancer patients [52].

6.6 Adjuvant therapy

Currently, there are limited reports on adjuvant therapy for male breast cancer, and treatment plans are often based on those for female breast cancer. Chemotherapy regimens for male breast cancer typically include docetaxel plus cyclophosphamide or doxorubicin plus cyclophosphamide, with or without the addition of paclitaxel [53]. In stage II and III male breast cancer, anthracycline and taxane combinations can reduce recurrence and improve overall survival (OS) [54]. For HER2-positive male breast cancer patients, targeted therapies such as trastuzumab and pertuzumab are used [47]. Given the frequency of BRCA mutations in male breast cancer, PARP inhibitors like olaparib have shown promising results in treating BRCA-mutated male breast cancer. Studies have shown that the pathological complete response rate for male breast cancer patients receiving neoadjuvant chemotherapy is similar to that of female breast cancer patients. However, due to the differing pathological characteristics between male and female breast cancer, treatment efficacy may vary [51].

7 Preventive measures

Due to the rarity of male breast cancer, specific preventive measures tailored to it are limited. However, the following general measures may help reduce the risk:

7.1 Genetic counseling and testing

For men with a family history of breast cancer or known BRCA gene mutations, genetic counseling and testing can aid in early detection and prevention. Genetic counseling helps individuals understand their risk and develop personalized screening and prevention plans. This proactive approach can be crucial for those at high risk, allowing for timely interventions and monitoring [55].

7.2 Healthy lifestyle

Maintaining a healthy weight, limiting alcohol consumption, reducing occupational exposures can potentially lower the risk of male breast cancer. Adopting a healthy lifestyle not only helps in reducing the risk of breast cancer but also lowers the risk of other chronic diseases. Regular physical activity and a balanced diet are fundamental components of a healthy lifestyle that contribute to overall well-being.

7.3 Regular check-ups

Regular medical check-ups and self-examinations are vital for the early detection of breast abnormalities, enabling prompt diagnosis and treatment. Although routine screening for male breast cancer is not widespread, it is necessary

for high-risk individuals, such as those with BRCA mutations, to undergo regular check-ups and imaging studies. Early detection through vigilant monitoring can significantly improve treatment outcomes and survival rates [7].

8 Future outlook

The future of male breast cancer diagnosis and treatment appears promising, driven by ongoing research and advancements in medical science. Genomic and molecular biology studies are anticipated to uncover more pathogenic mechanisms, which will provide novel therapeutic targets. Genomic research has already identified several specific mutations and molecular characteristics in male breast cancer, presenting new opportunities for targeted therapy. For example, BRCA2 mutations are relatively common in male breast cancer, and PARP inhibitors show significant potential in treating this subset of patients [7, 36, 50]. Additionally, as public awareness of male breast cancer increases, early screening and intervention measures are likely to become more widespread and effectively implemented. As the field progresses, it is expected that a deeper understanding of the molecular and genetic underpinnings of male breast cancer will lead to more personalized and effective treatment strategies. Continued advancements in genomic studies and the development of new targeted therapies will be pivotal in improving the prognosis and quality of life for male breast cancer patients.

9 Conclusion

Male breast cancer is a rare disease with distinct biological characteristics and risk factors. Compared to female breast cancer, it often presents at an older age, in more advanced stages, and with a higher likelihood of hormone receptor positivity. Due to its low incidence, limited research, and lack of awareness, identifying causal factors for MBC is challenging. Educating both patients and healthcare workers about the existence of breast cancer in men and its known risk factors, such as BRCA2 mutations, family history, and conditions that alter androgen/estrogen balance like Klinefelter syndrome, is the first critical step.

Patients undergoing hormonal therapy for prostate cancer or other conditions should be aware of the risk of male breast cancer, and any breast symptoms in these patients should be thoroughly evaluated. Similarly, in cases of hyperestrogenism from liver failure or other causes, healthcare providers should consider the possibility of cancer, not merely attributing symptoms to gynecomastia. Further research is necessary to aid clinicians in better serving and counseling men at increased risk for this disease.

Despite being relatively rare, male breast cancer shows a rising incidence and remains under-researched. Most current clinical practices are extrapolated from female data. However, available evidence suggests that male breast cancer has unique molecular and clinicopathological characteristics that may warrant different clinical approaches. New treatments, such as PARP inhibitors and anti-androgen therapies, are being tested in female and may also be successful in male. There is a promising trend of including male patients in clinical trials to build a robust evidence base for future treatments.

10 Study limitations

The data in this review were primarily extracted from the GBD2021 database and various published studies. Variations in data quality and completeness, as well as discrepancies between reported and actual data, may lead to estimation inaccuracies. Additionally, publication bias and heterogeneity in sample characteristics, study design, and reporting standards across studies can limit the overall conclusions drawn.

Acknowledgements We would like to thank the following institutions for providing publicly available data and resources used in this research: Institute for Health Metrics and Evaluation (IHME) for the GBD Results Tool. Cancer Trends Progress Report (CTPR) for the Financial Burden of Cancer Care data. National Cancer Institute (NCI) for information on Cowden Syndrome, Male Breast Cancer Treatment (PDQ®), and Genetic Testing for Hereditary Cancer Syndromes. National Institutes of Health (NIH) for confirming risk factors for male breast cancer. Mayo Clinic for resources on hormone therapy for prostate cancer and diagnosis and treatment of male breast cancer. Special thanks to all the researchers and institutions involved in the data collection and analysis.

Author contributions Lei Zhao conceptualized and designed the study. Lei Zhao and Huijuan Cheng drafted the manuscript. Dongqiang He and Yahui Chai was responsible for downloading and cleaning the data, as well as running all codes and generating plots using statistical

software. Ailin Song conducted the data analysis and interpretation. Yalan Zhang and Guodong Sun critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

Funding This research was supported by the Cuiying Technology Innovation Project of Lanzhou University Second Hospital (CY2023-MS-B16), the Gansu Province Natural Science Foundation Project (22JR5RA916), the Lanzhou University First Hospital In-House Fund (ldyyyn2020-46).

Data availability No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate Not applicable. This study uses publicly available data from the GBD2021 and various published sources, which do not require ethics approval. All data were de-identified and anonymized prior to analysis.

Competing interests The authors declare no competing interests.

References

1. Sung H, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71:209–49. https://doi.org/10.3322/caac.21660.
2. Korde LA, et al. Multidisciplinary meeting on male breast cancer: summary and research recommendations. J Clin Oncol. 2010;28:2114–22. https://doi.org/10.1200/JCO.2009.25.5729.
3. Fox S, Speirs V, Shaaban AM. Male breast cancer: an update. Virchows Arch. 2022;480:85–93. https://doi.org/10.1007/s00428-021-03190-7.
4. Anderson WF, Jatoi I, Tse J, Rosenberg PS. Male breast cancer: a population-based comparison with female breast cancer. J Clin Oncol. 2010;28:232–9. https://doi.org/10.1200/JCO.2009.23.8162.
5. Evaluation, I. f. H. M. a. *GBD Results Tool*, <https://vizhub.healthdata.org/gbd-results/> (2024).
6. Gomez-Raposo C, Zambrana Tevar F, Sereno Moyano M, Lopez Gomez M, Casado E. Male breast cancer. Cancer Treat Rev. 2010;36:451–7. https://doi.org/10.1016/j.ctrv.2010.02.002.
7. Bhardwaj PV, Gupta S, Elyash A, Teplinsky E. Male breast cancer: a review on diagnosis, treatment, and survivorship. Curr Oncol Rep. 2024;26:34–45. https://doi.org/10.1007/s11912-023-01489-z.
8. Varzaru VB, et al. Observational study of men and women with breast cancer in terms of overall survival. Cancers (Basel). 2024. https://doi.org/10.3390/cancers16173049.
9. Gucalp A, et al. Male breast cancer: a disease distinct from female breast cancer. Breast Cancer Res Treat. 2019;173:37–48. https://doi.org/10.1007/s10549-018-4921-9.
10. Ruddy KJ, Winer EP. Male breast cancer: risk factors, biology, diagnosis, treatment, and survivorship. Ann Oncol. 2013;24:1434–43. https://doi.org/10.1093/annonc/mdt025.
11. Ottini L, et al. Male breast cancer. Crit Rev Oncol Hematol. 2010;73:141–55. https://doi.org/10.1016/j.critrevonc.2009.04.003.
12. Anderson WF, Althuis MD, Brinton LA, Devesa SS. Is male breast cancer similar or different than female breast cancer? Breast Cancer Res Treat. 2004;83:77–86. https://doi.org/10.1023/B:BREA.0000010701.08825.2d.
13. Institute, N. C. *SEER Cancer Statistics Review (CSR) 1975–2016*, <https://seer.cancer.gov/archive/csr/1975_2016/index.html> (2020).
14. Bluethmann SM, Mariotto AB, Rowland JH. Anticipating the "Silver Tsunami": prevalence trajectories and comorbidity burden among older cancer survivors in the United States. Cancer Epidemiol Biomarkers Prev. 2016;25:1029–36. https://doi.org/10.1158/1055-9965.EPI-16-0133.
15. Report, C. T. P. *Financial Burden of Cancer Care*, <https://progressreport.cancer.gov/after/economic_burden> (2023).
16. Mancino M, et al. Male breast cancer and sexual aspects research and analysis (MASARA study): preliminary results. J Med Imag Int Radiol. 2024. https://doi.org/10.1007/s44326-024-00031-0.
17. Avila J, Herrick B, Attai DJ, Leone JP. Treatments for breast cancer in men: late effects and impact on quality of life. Breast Cancer Res Treat. 2023;201:489–98. https://doi.org/10.1007/s10549-023-07027-6.
18. Reinisch M, et al. Efficacy of endocrine therapy for the treatment of breast cancer in men: results from the MALE Phase 2 randomized clinical trial. JAMA Oncol. 2021;7:565–72. https://doi.org/10.1001/jamaoncol.2020.7442.
19. Giordano SH, Cohen DS, Buzdar AU, Perkins G, Hortobagyi GN. Breast carcinoma in men: a population-based study. Cancer. 2004;101:51–7. https://doi.org/10.1002/cncr.20312.
20. Bielcikova Z, et al. Treatment and prognosis of male breast cancer: a multicentric, retrospective study over 11 years in the Czech republic. Oncologist. 2024;29:e750–62. https://doi.org/10.1093/oncolo/oyae031.
21. Cardoso F, et al. Characterization of male breast cancer: results of the EORTC 10085/TBCRC/BIG/NABCG international male breast cancer program. Ann Oncol. 2018;29:405–17. https://doi.org/10.1093/annonc/mdx651.
22. Tai YC, Domchek S, Parmigiani G, Chen S. Breast cancer risk among male BRCA1 and BRCA2 mutation carriers. J Natl Cancer Inst. 2007;99:1811–4. https://doi.org/10.1093/jnci/djm203.

23. Ferzoco RM, Ruddy KJ. The epidemiology of male breast cancer. Curr Oncol Rep. 2016;18:1. https://doi.org/10.1007/s11912-015-0487-4.
24. Kuchenbaecker KB, et al. Risks of breast, ovarian, and contralateral breast cancer for BRCA1 and BRCA2 mutation carriers. JAMA. 2017;317:2402–16. https://doi.org/10.1001/jama.2017.7112.
25. Evans DG, et al. Risk of breast cancer in male BRCA2 carriers. J Med Genet. 2010;47:710–1. https://doi.org/10.1136/jmg.2009.075176.
26. Grill S, et al. TP53 germline mutations in the context of families with hereditary breast and ovarian cancer: a clinical challenge. Arch Gynecol Obstet. 2021;303:1557–67. https://doi.org/10.1007/s00404-020-05883-x.
27. Arango-Ibanez JP, Parra-Lara LG, Zambrano AR, Rodriguez-Rojas LX. Li-Fraumeni syndrome presenting with de novo TP53 mutation, severe phenotype and advanced paternal age: a case report. Hered Cancer Clin Pract. 2024;22:1. https://doi.org/10.1186/s13053-023-00272-2.
28. Institute, N. C. *Cowden Syndrome*, <https://www.cancer.gov/types/breast/patient/male-breast-treatment-pdq> (2023).
29. NIH. *Study confirms risk factors for male breast cancer*, <https://www.cancer.gov/news-events/press-releases/2014/breastcancermalepoolingstudy> (2014).
30. Kurylowicz A. Estrogens in adipose tissue physiology and obesity-related dysfunction. Biomedicines. 2023. https://doi.org/10.3390/biomedicines11030690.
31. Clinic, M. *Hormone therapy for prostate cancer*, <https://www.mayoclinic.org/tests-procedures/hormone-therapy-for-prostate-cancer/about/pac-20384728> (2023).
32. Rozenberg S, Di Pietrantonio V, Vandromme J, Gilles C. Menopausal hormone therapy and breast cancer risk. Best Pract Res Clin Endocrinol Metab. 2021;35: 101577. https://doi.org/10.1016/j.beem.2021.101577.
33. Brinton LA, et al. Prospective evaluation of risk factors for male breast cancer. J Natl Cancer Inst. 2008;100:1477–81. https://doi.org/10.1093/jnci/djn329.
34. Madden NA, et al. Radiotherapy and male breast cancer: a population-based registry analysis. Am J Clin Oncol. 2016;39:458–62. https://doi.org/10.1097/COC.0000000000000078.
35. Visvanathan K, et al. Alcohol dehydrogenase genetic polymorphisms, low-to-moderate alcohol consumption, and risk of breast cancer. Alcohol Clin Exp Res. 2007;31:467–76. https://doi.org/10.1111/j.1530-0277.2006.00334.x.
36. Abdelwahab Yousef AJ. Male breast cancer: epidemiology and risk factors. Semin Oncol. 2017;44:267–72. https://doi.org/10.1053/j.seminoncol.2017.11.002.
37. Staff, M. C. *Male breast cancer - Diagnosis and treatment*, <https://www.mayoclinic.org/diseases-conditions/male-breast-cancer/diagnosis-treatment> (2024).
38. Accomasso F, et al. Clinical, pathological, and prognostic features of male breast cancer: a multicenter study. Curr Oncol. 2023;30:9860–71. https://doi.org/10.3390/curroncol30110716.
39. Chamseddine RS, et al. Penetrance of male breast cancer susceptibility genes: a systematic review. Breast Cancer Res Treat. 2022;191:31–8. https://doi.org/10.1007/s10549-021-06413-2.
40. Network, N. C. C. *NCCN Guidelines Version 5.2024(Breast Cancer)*, <https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1419> (2024).
41. Leone JP, et al. Survival in male breast cancer over the past 3 decades. J Natl Cancer Inst. 2023;115:421–8. https://doi.org/10.1093/jnci/djac241.
42. Giordano SH. Breast cancer in men. N Engl J Med. 2018;378:2311–20. https://doi.org/10.1056/NEJMra1707939.
43. Lin AP, Huang TW, Tam KW. Treatment of male breast cancer: meta-analysis of real-world evidence. Br J Surg. 2021;108:1034–42. https://doi.org/10.1093/bjs/znab279.
44. Sauder CAM, Bateni SB, Davidson AJ, Nishijima DK. Breast conserving surgery compared with mastectomy in male breast cancer: a brief systematic review. Clin Breast Cancer. 2020;20:e309–14. https://doi.org/10.1016/j.clbc.2019.12.004.
45. Schiza A, Fredriksson I, Sund M, Valachis A. Treatment utilization and effectiveness of neoadjuvant chemotherapy comparing men and women diagnosed with breast cancer: a Swedish retrospective cohort study. Breast Cancer Res Treat. 2024;203:235–43. https://doi.org/10.1007/s10549-023-07129-1.
46. Masci G, et al. Clinicopathological and immunohistochemical characteristics in male breast cancer: a retrospective case series. Oncologist. 2015;20:586–92. https://doi.org/10.1634/theoncologist.2014-0243.
47. Hassett MJ, et al. Management of male breast cancer: ASCO guideline. J Clin Oncol. 2020;38:1849–63. https://doi.org/10.1200/JCO.19.03120.
48. Burstein HJ, et al. Adjuvant endocrine therapy for women with hormone receptor-positive breast cancer: American society of clinical oncology clinical practice guideline update on ovarian suppression. J Clin Oncol. 2016;34:1689–701. https://doi.org/10.1200/JCO.2015.65.9573.
49. Wang XH, et al. Case report: response to immunotherapy and anti-androgen therapy in male occult triple-negative breast cancer. Front Oncol. 2022;12: 840453. https://doi.org/10.3389/fonc.2022.840453.
50. Turk AA, Wisinski KB. PARP inhibitors in breast cancer: bringing synthetic lethality to the bedside. Cancer. 2018;124:2498–506. https://doi.org/10.1002/cncr.31307.
51. Robson M, Im SA, Senkus E, Xu B, Domchek SM, Masuda N, Delaloge S, Li W, Tung N, Armstrong A. Olaparib for metastatic breast cancer in patients with a germline BRCA mutation. N Engl J Med. 2017. https://doi.org/10.1056/NEJMx170012.
52. Fuso P, et al. PI3K inhibitors in advanced breast cancer: the past, the present new challenges and future perspectives. Cancers (Basel). 2022. https://doi.org/10.3390/cancers14092161.
53. Board PATE. *Male Breast Cancer Treatment (PDQ®): Health Professional Version*, <https://www.cancer.gov/types/breast/patient/male-breast-treatment-pdq> (2024).
54. Zheng G, Leone JP. Male breast cancer: an updated review of epidemiology, clinicopathology, and treatment. J Oncol. 2022;2022:1734049. https://doi.org/10.1155/2022/1734049.
55. Institute, N. C. *Genetic Testing for Hereditary Cancer Syndromes*, <https://www.cancer.gov/about-cancer/causes-prevention/genetics/genetic-testing-fact-sheet> (2023).