In the UK, the incidence of breast cancer in both sexes is increasing. In 2012, there were 53,696 new cases of breast cancer: 50,750 in women and 340 in men (ratio of 158:1). The incidence increases with age and presents later in men (median age 67) than women (median age 65). In general, men are diagnosed with more advanced-stage disease, with increasing tumour size and frequency of axillary node involvement. This is particularly true in countries like the UK, where routine screening mammography is offered to women. 

Overall survival rates in male breast cancer (MBC) tend to be lower than for females, partly due to the comorbidities associated with older age at diagnosis. When adjusted for age and stage the survival rates are comparable, with five-year survival rates of 96, 84, 52 and 24% for stages I–IV respectively.

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk factors</th>
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<tr>
<td>Genetic</td>
<td>Family history in first-degree relative</td>
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<tr>
<td></td>
<td>Klinefelter’s syndrome</td>
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<td></td>
<td>BRCA-2 (+1)</td>
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<tr>
<td>Endocrine</td>
<td>Testicular abnormalities – orchitis/congenital</td>
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<td></td>
<td>inguinal hernia, undescended testes</td>
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<td></td>
<td>Obesity</td>
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<td>Cirrhosis</td>
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<td>Environmental/exposure</td>
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<td>High temperature (occupational)</td>
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<td>Volatile organic compounds</td>
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<td>Finasteride</td>
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<td>Socio-demographic</td>
<td>Ashkenazi Jewish</td>
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<td></td>
<td>Black men</td>
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<td></td>
<td>Sedentary lifestyle</td>
</tr>
</tbody>
</table>

Table 1. Risk factors for male breast cancer

**RISK FACTORS**

Age, race and previous radiation exposure are well-described risk factors for the development of MBC (Table 1). Black men have a slightly higher incidence compared with white men at all ages and also tend to have poorer prognostic factors, such as advanced stage at presentation and an increased frequency of high-grade tumours.

Genetic predisposition plays an important role and genetic counselling should be offered to men diagnosed with breast cancer. Family history of breast or ovarian cancer is reported in 15-20% of cases. The risk of a man developing breast cancer when his mother and sister are affected is 10 times higher than in the general population.

The most clearly associated genetic mutation is in BRCA-2. In a population-based series,

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4–16% of cases of MBC were reported to carry a BRCA-2 mutation, mutation carriers having a lifetime risk of developing breast cancer of approximately 7%. This tends to present younger and is associated with poorer prognosis. BRCA-2 male carriers are also at increased risk of developing prostate and pancreatic cancer.

An imbalance in the oestrogen/testosterone ratio is thought to increase the risk of developing breast cancer. Testicular abnormalities resulting in lowered testosterone levels are consistently associated with MBC. 7% of men diagnosed with breast cancer are found to have Klinefelter’s syndrome (XXY karyotype), and men with Klinefelter’s have a 50-fold increased risk of developing MBC.

Case-control studies report that obesity and liver cirrhosis are associated with male breast cancer, secondary to increased circulating oestrogens. Published data from the NIH American Association of Retired Persons Diet and Health Study Cohort found that men with a body mass index (BMI) of 30 or above had an 80% increased risk of developing breast cancer compared with those with a BMI less than 25. The study also found an association with increased alcohol intake and smoking.

Breast abnormalities, including breast trauma and nipple discharge, have been reported to increase risk of MBC. Gynaecomastia is common in the general population and does not seem to be associated with increased risk. A prospective cohort study of 446 patients with gynaecomastia over a 30-year period found no occurrences of MBC.

PATHOLOGY
Invasive ductal carcinoma accounts for the majority of MBC. In contrast to female breast cancer (FBC), lobular carcinoma is extremely rare, as males lack terminal lobules required for lactation. MBC is more likely to express hormone receptors compared with FBC, with 90% expressing oestrogen receptors and 81% expressing progesterone receptors. In contrast, HER-2 amplification appears to be less common in men.

SCREENING
Men considered to be in the ‘increased risk’ category should be offered screening. This group includes those with a strong family history of breast cancer (FBC and MBC), a known genetic predisposition, such as BRCA-1 or 2 mutations, and importantly a personal history of breast cancer. Men with a diagnosis of breast cancer have a 93-fold increased risk of developing it in the contralateral breast.

These men should also be educated to perform monthly breast self-examination and have a twice-yearly clinical breast examination. If baseline gynaecomastia is present, annual mammography is recommended.

PRESENTATION AND INVESTIGATIONS
MBC most commonly presents with a painless, retro-areolar swelling with a slight left-sided predominance. The principle differential diagnosis is gynaecomastia, which is found in 30% of the normal population. The patient may also present with changes in the nipple areolar complex, such as nipple retraction (Figure 1), ulceration, rash and nipple discharge, which may be serous or blood-stained.

Mammography is helpful in differentiating MBC from benign conditions with 92% sensitivity and 90% specificity. Appearances are of an irregular lesion with spiculated edges. Micro-calciﬁcation is less commonly seen in male breast cancer. Ultrasonography can also be useful and provide information regarding nodal involvement.

Diagnosis and staging follows the same pathway as FBC, with ultrasound-guided biopsy to confirm diagnosis and determine hormone receptor status, followed by assessment of nodal involvement with node dissection or sentinel node sampling. Axillary nodal spread is present in approximately 50% of men at initial diagnosis and is important in predicting risk of local relapse and metastases. If axillary nodes are positive, a bone scan and CT chest, abdomen and pelvis is required for full staging. The routine use of Magnetic Resonance Imaging (MRI) is currently not advocated.

MANAGEMENT
MBC remains understudied and treatment recommendations are generally extrapolated from larger trials in women. The lack of larger, prospective studies means that important questions around the optimal management of MBC remain unanswered.
LOCALISED DISEASE

**Surgery**

The most common procedure performed is a modified radical mastectomy (Figure 2). Breast-conserving surgery is considered less in men with early stage disease because of the lack of breast tissue and the central location of most tumours. Nodal dissection with either sentinel node sampling or axillary node clearance at the time of surgery reduces the risk of recurrence and metastases. Sentinel lymph node sampling has been examined in numerous small series and seems to be feasible and accurate in MBC.

**Radiotherapy**

Few trials have assessed the benefit of post-mastectomy radiotherapy for male breast cancer, but it is commonly offered to men due to the higher rate of nipple and skin involvement. In some observational studies, post-mastectomy radiotherapy has been shown to reduce local recurrence in men; however, these were underpowered to detect survival benefit.

Radiotherapy should be offered as standard care in cases considered to be at high risk of local relapse, including T3 or T4 tumours or N2 or N3 disease. In addition, a retro-areolar location of tumour and muscle invasion should be considered as further indications for loco-regional radiation treatment.

**Endocrine therapy**

Endocrine therapy has an important role in male breast cancer due to the high rates of hormone receptor positivity. The gold standard is tamoxifen, retrospective data on tamoxifen in the adjuvant setting having demonstrated a survival benefit in men. The role of aromatase inhibitors is less clear and there is insufficient evidence for the use of adjuvant aromatase inhibitors in MBC. In one study of anastrozole in healthy male volunteers, men did not appear to have as complete oestrogen suppression as seen in women.

Chemotherapy-related decisions are extrapolated from FBC trials, many of which have not allowed the inclusion of male patients. The limited data on adjuvant chemotherapy in MBC suggests a comparable benefit in men to women. One of the larger studies of 135 cases of MBC treated with adjuvant hormones or hormones and chemotherapy found a non-statistically significant lower risk of death at 14-year follow-up with the addition of chemotherapy (hazard ratio 0.78).

**METASTATIC DISEASE**

In general, the approach to metastatic breast cancer is similar in men and women. Hormone therapy is offered first line in metastatic disease, with an 80% response rate with tamoxifen. The role of aromatase inhibitors is not established, but some small series have demonstrated radiological response in patients treated with anastrozole, letrozole and exemestane. In HER-2 positive disease, trastuzumab should be offered.

Rapidly progressive or hormone refractory disease should be treated with palliative chemotherapy. The data on chemotherapy for MBC come from studies with very limited sample size. There are no data to support the optimal choice of chemotherapy drugs in metastatic MBC and treatment recommendations are extrapolated from FBC.

**PSYCHOLOGICAL BURDEN**

Breast cancer is primarily considered a female disease and the oncology service has been developed to best meet women’s needs. However, it is imperative that the psychological effects of MBC diagnosis are recognised. This includes anxiety, embarrassment and emasculation, which may prevent men from presenting earlier and impact on treatment compliance. There is also a need for gender-specific information to help counter the understandable fear and uncertainty associated with diagnosis.

**CONCLUSION**

In contrast to breast cancer in females, MBC is rare. Late presentation is an ongoing issue, which is in part due to lack of doctor and patient awareness of the risk of disease in men. In order to improve identification and evidence-based management of MBC, education of patients and doctors is essential and greater efforts need to be made for international research collaboration to develop the evidence base.

**Declarations of interests:** none declared.

**REFERENCES**


