

# Breast cancer in men

This article focuses on the diagnosis and treatment of men with breast cancer. Risk factors for developing the condition are also examined. Because of the relative rarity of the condition in men, research evidence is scant resulting in difficulties in identifying best practice. Collaborative international research may help to address this problem.

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**B**reast cancer in men is a rare disease and when comparing the incidence to that of women, men account for a very small minority of cases. However, men more commonly delay reporting their symptoms, often because of lack of awareness of this disease, which in turn leads to later diagnosis and potentially poorer outcomes. Issues relating to the gender-specific needs of men with breast cancer, coupled with a dearth of clinical data pertinent to the treatment and support of men with this condition, can lead to potentially challenging interactions with health-care professionals.

## Risk factors

Less than 1% of all cases of breast cancer occur in men and in the UK, in 2004, an estimated 324 cases of breast cancer were diagnosed in men compared with 44,335 in women.<sup>1</sup> As with breast cancer in women, no single cause of breast cancer in men can be identified, although several factors are thought to contribute towards increased risk. Men typically present with disease later than do women, at an average age of around 71 years.<sup>2</sup>

A family history of breast cancer can be important with reports that 20% of men with the disease will have a first-degree relative who has had breast cancer.<sup>3</sup> A genetic cause of male breast cancer has been implicated in 4–40% of cases.<sup>4</sup> Those carrying the mutated BRCA2 gene are thought to be particularly at risk, although some research has suggested that male carriers of BRCA1 may also have an increased risk of developing this disease.

Other factors thought to influence risk in men include exposure to radiation; working in hot conditions, which may lead to subsequent testicular failure; Klinefelter's syndrome; liver damage; and obesity.<sup>6</sup> Additionally, the incidence of breast cancer in men is higher among those from African countries.<sup>7</sup> Since so few men are diagnosed with breast cancer, identification of lifestyle or environmental factors that may contribute towards risk is difficult, although evidence suggests that alcohol and dietary factors could be implicated.<sup>8</sup>

## Diagnosis

Clinical audit data suggest that men generally present with breast cancer at a much later stage than do women.<sup>9</sup> Since node-positive disease is associated with a poorer prognosis and may affect treatment offered, a late diagnosis can have considerable effects on the physical and emotional needs of men with breast cancer. The trend towards late-stage diagnosis may be due to a number of factors including delay in acting on symptoms because of poor awareness on the part of both men and health-care professionals. As a result, men might require extra support if they have feelings of anger, resentment, or guilt. In a study assessing the effects of breast cancer on men, around a quarter of participants reported high levels of emotional distress.<sup>10</sup> Clear, factual, written and verbal information might be beneficial for reducing emotional distress.

## Treatment

The experience and needs of men with breast cancer will depend on their stage of disease at diagnosis. Those presenting with primary disease could have different requirements to those with life-limiting advanced or metastatic cancer. However, most men will receive a combination of treatments. Any form of treatment will result in side-effects that could affect physical functioning, but may also have an effect on psychological and social wellbeing.

Treatment of breast cancer in men is similar to that in women. Surgery is normally first priority unless neoadjuvant chemotherapy is necessary to shrink the tumour before surgery. Mastectomy is normally done, because men do not usually have enough breast tissue to permit breast conservation. Altered body image is associated with symptoms of depression in men treated for breast cancer<sup>11</sup> and further research indicates that men feel both embarrassed and stigmatised by changes to their body caused by treatment.<sup>12</sup>

Reconstruction is not commonly offered, but reports of successful attempts include use of latissimus dorsi, or transverse rectus abdominus flaps. Occasionally, skin closure on the chest wall is impossible without using tissue from a donor site.<sup>13</sup> An axillary dissection might accompany the mastectomy because men often present with clinically palpable nodal disease, and sentinel-node biopsy is a sensitive and specific procedure for staging the axilla in suspected node-negative patients.<sup>14,15</sup> Sentinel-node biopsy greatly reduces the risk of lymphoedema, but all men who have had axillary surgery will require information to ensure awareness of lymphoedema.

Breast tumours in men can often involve the chest wall or skin, because of differences in their anatomy, and consequently radiotherapy after mastectomy is more commonly done on men compared with women.<sup>6</sup> However, evidence suggests that gender is not a prognostic factor in patients undergoing mastectomy for early-stage breast cancer. Men should receive adjuvant radiotherapy according to guidelines similar to those developed for women.<sup>16</sup> Radiotherapy close to the chest wall might result in additional long-term pulmonary or cardiovascular complications in men, particularly as they tend to be older than are women when they present with breast cancer, and therefore will be more likely to suffer from pre-existing cardiovascular or pulmonary complaints.<sup>6</sup>

Systemic treatment such as chemotherapy and hormone therapy may be appropriate. Chemotherapy will usually be offered to patients at higher risk, for example, those with affected lymph nodes. Hormone therapy will be offered to those with hormone-receptor positive disease (around 90% of men with breast cancer), most commonly tamoxifen.<sup>17</sup> Because of the small numbers of men diagnosed with breast cancer, research studies looking at the efficacy of treatment in this cohort of patients are few. Although breast cancer in a man is assumed to respond similarly to treatment for breast cancer in women, little convincing evidence supports this hypothesis. Women are treated adjuvantly with anthracyclines, and most recently taxanes, but the benefit that men may receive from these drugs can be extrapolated only from studies on women, although men now commonly receive anthracyclines as part of their chemotherapy treatment.<sup>18</sup>

This uncertainty about efficacy may cause the availability of newer treatments to be delayed for male patients. For example, NICE guidance for treatment of breast cancer is for women only, meaning that primary-care trusts are not under obligation to provide the same drugs to male patients. In postmenopausal women, aromatase inhibitors have either replaced tamoxifen or have been added to the treatment schedule to form a new gold standard of adjuvant hormonal treatment.<sup>19</sup> Strong evidence from the ATAC<sup>20</sup> and BIG 1-98<sup>21</sup> trials suggests that they reduce risk of recurrence compared with tamoxifen.

Preliminary evidence suggests that aromatase inhibitors effectively reduce oestrogen production in male patients with evidence from case studies of disease response to letrozole and anastrozole.<sup>22,23</sup> Gonadotrophin-releasing hormone analogues have been proposed for use with aromatase inhibitors to block two routes of oestrogen production for men with advanced breast cancer.<sup>24</sup> Newer treatments are commonly used in patients with advanced and metastatic disease before they are used as adjuvant treatment, but this process might move faster for women than for men because of the number of patients needed to confirm efficacy.

Hormonal therapies in men can cause hot flushes, mood disturbances, and sexual dysfunction. In one study male patients had a 20.8% discontinuation rate related to side-effects of tamoxifen treatment.<sup>24,25</sup> Men with advanced breast cancer can be offered an orchidectomy as a treatment for those with hormone-receptor positive cancer, although it is becoming much less frequent because of other hormonal methods of tumour control.

Other than case studies, little research has been done on the use of trastuzumab in men with breast cancer. However, data suggest that cancers of the male breast are much less likely to overexpress the HER2 protein than are breast cancers in women.<sup>26</sup> For those found to be HER2 positive, trastuzumab should be considered, in view of the survival advantage that has been shown for women using this drug.<sup>6</sup>

Research findings from studies of women are often extrapolated for men,<sup>27</sup> but the validity of this approach, could take many years to establish for each intervention. Men will need to have this situation explained carefully to them when consenting for treatment, or if a particular treatment is not being offered to them. Health-care professionals may be able to reassure their patients that, when matched stage-for-stage, no significant differences are seen in survival rates between men and women.<sup>9</sup> Men will have physical needs during treatment for controlling or managing any symptoms. Access to comprehensive patient-specific information and support is available from the cancer charity Breast Cancer Care in the form of written text and a web chat forum.<sup>28</sup>

## Conclusion

Although breast cancer is rare in men, the incidence is increasing.<sup>1</sup> Men may be disadvantaged by delays in diagnosis due to lack of awareness that men are also susceptible to breast cancer and a paucity of evidence supporting optimum treatment, because of the small numbers of men available for clinical trials. Even though the number of male breast-cancer patients worldwide is small, collectively they may lend themselves to collaborative working through international trials. For men who have a significant family history of breast cancer or a known BRCA1 or BRCA2 mutation, information about screening options should be

available. More health-care professionals are becoming aware of the risk of breast cancer in men, and men should be given information relating to breast awareness and the same speedy referral for diagnosis and treatment as women.

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