Risk factors

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There are several factors known to increase the RR for developing breast cancer. These are called the risk factors and can be divided into modifiable (those that can be modified by adopting a healthy diet and lifestyle) and non-modifiable risk factors. The events increasing the oestrogenic exposure of the - breast are said to be risk factors for breast cancer, such as early menarche, late menopause, nulliparity , late first pregnancy and hormone replacement with high oestrogen therapy . These are listed in Table 58.3 . - - - -

Figure 58.27 Mondor’s disease in the lateral aspect of the right breast.

Harris JG Bloom , 1923–1988, radiation oncologist, Royal Marsden Hospital, London, UK. William W Richardson , 1915–2005, pathologist, Middlesex Hospital, London, UK, published a paper with Bloom on the na Breast carcinoma arises from the milk ducts in 90% (ductal carcinoma) or from the lobule in 10% (lobular carcinoma) of patients. The disease may remain confined to the epithelium of the duct or lobule with no breach in the basement membrane; this is called in situ disease . Infiltration of the surrounding tissue through a breach in the basement membrane leads to ‘invasive or infiltrative’ ductal or lobular carcinoma. The tumour may be well di ff erentiated, moderately di ff erentiated or poorly di ff erentiated. The modified Bloom–Richardson scoring system for tumour grade includes the sum of indi - vidual scores for three variables (percentage of tumour cells with tubule formation, nuclear pleomorphism and the size and number of mitoses/HPF), each of which is assigned from 1 /uni00A0 to /uni00A0 3 points according to the deg ree of deviation from normal breast epithelium. A total score of 3–5 defines grade I; 6 or 7 grade II; and 8 or 9 grade III. Invasive carcinoma is usually of no special type (NST), which represents the most common variety of breast cancer. Rare histological variants, usually carrying a better prognosis, include colloid or mucinous carcinoma, whose cells produce abundant mucin; medullary carcinoma, with solid sheets of large cells often associated with a marked lymphocytic reac - tion; and tubular carcinoma. The papillary type of carci - noma (both in situ and invasive) is a rare type of breast cancer accounting for 0.5–1% of all neoplasms. The lesion is char - acterised by papillomas with a fibrovascular core and surface covered by epithelial and myoepithelial cells. It usually carries a better prognosis and rarely spreads to lymph nodes and the bloodstream. The tumour cells may o verexpress oestrogen receptors (ER positive), progesterone receptors (PR positive), human epidermal growth factor receptor 2/neu (HER2/neu positive) and androgen receptors (AR positive). The degree of mitosis can be detected by the Ki-67 mitotic index. Gene array analysis has identified five major subtypes: luminal A, luminal B, basal, HER2/neu receptor enriched and a normal-like group (Table 58.4). In the absence of gene array testing such as prediction analysis of microarray-50 (PAM-50), immune histochemical receptor staining serves as a surrogate marker of molecular subtypes. tural history of breast cancer in 1957.

Remarks Modi /f_i able risk factors Obesity: BMI >30 Increased risk in postmenopausal women: RR = 1.29 Parity Increased risk in nulliparous women or /f_i rst pregnancy after 35 years of age Breastfeeding It is protective for breast cancer and >12 months of breastfeeding by women has a greater protective effect than shorter duration Age at /f_i rst childbirth Early: less risk, <20 years Late: high risk, >35 years Use of HRT Use for >10 years increased risk: RR = 1.2 Tobacco use RR = 1.14 for smoking 25 or more cigarettes/day; RR = 1.07 for smoking for 20 years or more Alcohol consumption RR = 1.05 for light drinking (<1 drink/day); RR = 1.32 for moderate drinking (3 or 4 drinks/day); RR = 1.46 for heavy drinking (>4 drinks/day) Radiation exposure RR = 6 Non-modi /f_i able risk factors Age Increasing age is a risk factor. While the median age at presentation is around 60 years in the West (UK, USA), it is around 48 years in low-/middle-income nations such as India Sex Female sex is a risk factor as only 0.5–1% of all breast cancers occur in males Ethnicity American white, African American (age <45 years), Ashkenazi Jew, Parsi in India Family history of One /f_i rst-degree relative (mother, sister or breast cancer daughter) with breast cancer: RR = 2; two /f_i rst-degree relatives with breast cancer: RR = 3 Genetic 5–10% of all breast cancers are hereditary; predisposition BRCA1 and BRCA2 mutations account for up to 70% of hereditary breast cancers Early menarche (<12 Breast cancer risk increases by around 5% years) for each year earlier menstruation begins: RR = 1.19 for age <11 years Late menopause Breast cancer risk increases by about 3% (>55 years) for each year later menopause begins: RR = 1.12 for menopause at 55 years versus menopause at 45 years High-risk breast Proliferative conditions without atypia: RR lesions = 1.8–2 Complex /f_i broadenoma: RR = 3 Papillomatosis: RR = 3 Proliferative diseases with atypia: atypical ductal and lobular hyperplasia: RR = 4–5 Lobular carcinoma in situ : RR = 8–10 BMI, body mass index; BRCA , breast cancer; HRT, hormone replacement therapy; RR, relative risk. TABLE 58.4 Molecular classi /f_i cation of breast cancer. Classi /f_i cation Hormone HER2/ Others receptor neu Luminal A Positive (either or Negative Ki-67 low both ER/PR) Luminal B Positive (either or Negative Ki-67 high both ER/PR) Basal type (triple Negative Negative Ki-67 usually negative) high HER2/neu Negative Positive Ki-67 high enriched Claudin low Negative Negative Claudin low ER, oestrogen receptor; HER2/neu, human epidermal growth factor receptor 2/neu; PR, progesterone receptor.

Figure 58.28 (a) Diffuse redness (erythema) and skin oedema involving more than one-third of the breast, with an enlarged left breast – features of in /f_l ammatory carcinoma. (b) Peau d’orange refers to the orange peel appearance of the skin of disease. Note that in people with darker skins the erythema takes on a brownish hue.

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