6 Management Strategies for Women at an Inherited High Risk of Breast Cancer

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6.1 Introduction

Many women acknowledge the fact of having some relative with breast cancer which can cause anxiety and fear. The risk of getting breast cancer gets higher with every case of breast cancer in close relatives (first/second degree) and that of early onset. A family history of breast cancer in any relative is prevalent and does not automatically infer an increased risk. Breast cancer occurring early, bilateral, in men and in first-degree relatives is much less common. An inherited predisposition for breast cancer will occur in about 10–15%, and about half a genetic predisposition is found to cause the disease. Autosomal dominant pattern of inheritance in specific genes is associated with an increased risk. Mutations in the two high penetrant tumor suppressor genes BRCA1 and BRCA2 account for 30% of inherited breast/ovarian cancers. Screening for these mutations can be done. Other mutated genes causing breast cancer are Tumor protein 53 (TP53), Phosphatase and tensin homologue (PTEN), Ataxia-telangiectasia (mutated) gene (ATM), E-Cadherin, Checkpoint kinase2 (Chek2), and cyclin-dependent kinase inhibitor 2A (CDKN2A). Information regarding predisposition of prostate and/or pancreatic should be included.

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Before referring the patient to a familial cancer clinic, a clinical estimation in an asymptomatic individual can be made, for instance, based on an algorithm named Familial Risk Assessment-Breast and Ovarian Cancer (FRA-BOC) produced by Cancer Australia [1].

6.2 Familial Cancer Clinics: Oncogenetic Counselling

The goal is to assemble family history, establish risk and counsel regarding management, and offer follow-up according to the risk profile. The counsellor takes a thorough family history regarding relatives, type of malignancy, and age of onset. Diagnosis needs verification through cancer registries. The relatives' permission is mandatory to review charts. Deceased siblings can be analyzed using paraffin blocks. The dilemma arises when few family members exist or are unavailable for further case history or testing. Patients qualifying for surveillance enter control programs that include imaging often with breast MRI and mutation carriers are offered risk-reducing surgical options [2].

6.3 Risk Assessment Instruments

Several risk instruments exist that take different clinical parameters into account. The Gail model [3] uses the woman's information in eight

M. Rezai et al. (eds.), *Breast Cancer Essentials*, https://doi.org/10.1007/978-3-030-73147-2_6

questions related to medical condition, reproduction, and family history of cancer to assess risk. The Tyrer-Cuzick breast cancer risk assessment model originated from the chemoprevention trial IBIS [4]. The model is not validated. The Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA) will predict lifetime risk to develop cancer and the probability of being a mutation carrier [5].

6.4 Surgical Consideration and Techniques Used

To date, removal of target organs is the only preventive method available. This will be offered to known mutational carriers and in individuals with a proven breast/ovarian cancer syndrome despite no known mutation. Several considerations should be made. A multidisciplinary and multiprofessional team will provide service and advice to families and individuals at high risk. Most women who undergo risk-reducing mastectomies are convinced about their decision. Risk-reducing oophorectomies are performed later as ovarian cancer occurs more frequently after age 40.

The efficacy of the procedure has been demonstrated in both mutation carriers and in women at increased risk with a reduction rate of 95% [6]. Women considering this option should however be informed that a total ablation of the breast gland cannot be achieved. A statistical model to calculate survival benefit from risk-reducing procedures in asymptomatic mutation carriers showed an absolute benefit of risk-reducing oophorectomy and mastectomy at age 40 with a survival gain of 24% and 11% in BRCA1 and BRCA2 mutation carriers. When performed earlier, the gain was minimal, and surveillance with MRI of the breasts seemed a reasonable option [7]. A clinical retrospective study in mutation carriers with long follow-up time (median 14.3 years) found a survival rate at 20 years after contralateral risk-reducing mastectomy of 88% (CI 83–93%) versus 66% (CI 59–73%). The authors conclude that with a long life expectancy, longer periods after diagnosis are necessary to account for [8].

6.4.1 Women with Inherited Risk and Breast Cancer

There are currently recommendations as to whom should be considered for genetic testing. Unequivocally individuals with family members of known mutation in BRCA1/2, PALB2, TP53, ATM, CHEK2 genes. As a rule of thumb, one first-degree affected member below the age of 40, two first-degree relatives below the age of 50, and three first-degree relatives below the age of 60 are also candidates for genetic testing. Also women below the age of 40 with breast cancer and those with triple-negative breast cancer below 60 years should also be considered for genetic testing. Bilateral cancer and male breast cancer also merit genetic testing. This may affect the primary treatment especially in triple-negative cases [9]. Whether to conserve the breast or not is debatable. Breast irradiation will definitely affect the outcome if reconstruction will be done at a later stage. Risk-reducing measures for the contralateral unaffected breast should also be available. Trials with targeted chemotherapies such as the PARP inhibitors are ongoing [10].

The surgical procedures for bilateral risk-reducing mastectomy often include restoration of a breast mould by either implants or by autologous means. Depending on the volume of the breasts, patients' expectations, and feasibility, different incisions are used for mastectomies. Conserving the skin envelope facilitates using permanent implants. On the other hand, in ptotic breasts, redundant skin may have to be excised or performance of the mastectomy through Wise pattern incisions. Nipple-areola-sparing techniques have become standard to improve cosmesis and are performed via periareolar or sub-mammary incisions [11]. Acellular dermal matrix/dermal sling methods (subcutaneous tissue as a flap after removal of glandular tissue) have become an adjunct to achieve volume and ptosis. However, both methods are associated with some complications. Especially ADM giving red skin features and increased seroma formation [12].

6.4.2 Contralateral Risk-Reducing Mastectomy in High-Risk Women with a Previous Breast Cancer History

BRCA1/2 gene mutation carriers diagnosed with breast cancer still carry an increased lifetime risk to develop a contralateral breast malignancy. The primary treatment whether surgical and oncologic targets the index lesion and is preventive for systemic spread. It will also protect the remaining breast. As local relapses often occur within 2 years of primary treatment, many breast surgeons prefer to wait for the risk-reducing procedure to overcome this risk.

The bilateral procedure in asymptomatic women challenges the cosmetic outcome somewhat differently than when a contralateral risk-reducing mastectomy is done. Studies of both groups found an overall high satisfaction and retained health-related quality of life [13–15]. Lack of sensation, sexual impairment, and discomfort in social situations occur in both groups [15]. Women with breast cancer having had radiation therapy to the breast face revision surgeries in the reconstructed, irradiated breast in about 40% [16, 17]. However, very few women regret their decision of ablative surgery.

Tips and Tricks

Asymptomatic women and women with increased risk and breast cancer are managed by a multidisciplinary team where surveillance or risk-reducing options are alternatives. The removal of all breast glandular tissue is paramount. Mastectomy incisions and type and mode of breast reconstruction should be tailor-made to patients' expectations and bodily contour.

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