The role of surgery in hereditary breast cancer prevention

Breast cancer prevention methods in high-risk women include strict screening, preventive chemotherapy and surgery.

The usual surveillance for high-risk women consists in a physical examination, a yearly mammogram starting at 25 –the effectiveness of magnetic resonance in younger women is being speculated with– and transvaginal echography to discard the possibility of ovarian cancer. The high density in these women's breasts and the difficulty in diagnosing ovarian cancer early make it usual to find tumors in the ovaries and breast in an undesirable stage. Up to now, periodic determination of tumoral markers has not been considered.

Preventive chemotherapy in breast cancer is a proven fact. Treatment with tamoxifen on surgically treated patients during 5 years reduces contralateral breast cancer risk by 40%¹. The benefits of using it in high-risk patients that have not developed cancer has already been proven in the USA, where it has been administered to these patients since 1998². In the European Community trials undertaken had not had these results, but for the first time in 2002 a British publication reports they obtained the same results as the American³.

Traditionally, women eligible for preventive breast cancer surgery are those with benign lesions considered high-risk, which include:

- 1) Lobular neoplasia (lobular carcinoma *in situ*).
- 2) Ductal hyperplasia or atypical lobular hyperplasia.
- 3) Multiple papillomatosis.
- 4) Some types of proliferative fibrocystic mastopathy, difficult to follow-up, especially, in cases with a family history of breast cancer and cancerophobia.
- 5) Primary breast *phylloide* tumor and relapses.

For years it has been known that *BRCA1* and *BRCA2* mutations significantly increase the risk of developing breast cancer. *BRCA1* is located on chromosome 17 and is associated with 45% of hereditary breast cancer and with 85% of breast and ovarian cancer syndromes. Its mutation affects 0.0006% of the population (one in every 1,600) and is the cause of breast cancer in 5% of women under 40, in 2% of women between 40 and 49, and in 1% of those aged between 50 and 70. There is an 85% risk of developing contralateral breast cancer in *BRCA1* mutation carriers among women aged 70⁴. Specific mutations of this ge-

ne have been found in certain groups, among them Ashkenazi and Sephardic Jews and some Eskimo tribes. It must be pointed out that the behaviour of breast cancer in women with this type of gene mutation is more favorable than other type of hereditary cancer. *BRCA2*, less studied so far, is located on chromosome 17 and causes 40% of hereditary breast cancer. Other genes implied in hereditary breast cancer are p53 and the ataxia-telangiectasia gene.

There is no agreement on the type of surgery that should be used to treat high-risk women. It seems paradoxical, when a universal consensus has been reached about the validity of conservative breast surgery in invasive cancer, that bilateral mastectomy is advocated when a cancer has not appeared and may never appear. Less aggressive interventions, like skin-sparing mastectomy or subcutaneous mastectomy, that preserve all the skin and do not remove all breast tissue, are not criticized for being less safe.

Bilateral prophylactic mastectomy is being tested on *BRCA1* and *BRCA2* mutation carriers to prove that it does reduce the risk of breast cancer. A recent analysis done at Rotterdam University on a group of 139 patients, out of which 76 underwent bilateral mastectomy and 63 were placed under surveillance, concludes that after 3 years this intervention reduces the incidence of breast cancer⁵.

Breast reconstruction after a mastectomy is not a minor problem. To recuperate breast volume the patient's own tissues or an implant can be used. The advantage of using the patient's own tissues is better tolerance; the inconveniences, a more complex surgical intervention, more scars and worse aesthetic results. Implants are easier to use, but are sometimes not well tolerated –periprosthetic capsules may be formed– they can be rejected and are usually prone to a greater number of surgical infections. The areola-nipple complex also poses problems for reconstruction surgery, which are solved by means of complicated technical devices. The final result is often unsatisfactory for both the patient and the surgeon. There is no agreement either on the timing of reconstruction surgery. Some advocate performing it just after mastectomy, others prefer a differed intervention.

Skin-sparing mastectomy is a less radical mastectomy with regards to its capacity to eliminate the totality of glandular tissue⁶. The skin removed is limited to the

areola-nipple complex and to a variable in size spindle of skin, which includes the projection surface of the tumor. This technique allows creating mammary volume with the patient's own skin to cover the implant. It has a more aesthetic result.

Subcutaneous or subdermic mastectomy or adenomastectomy, consists in the exeresis of the glandular tissue totally or partially, preserving the breast cutaneous cover, including the areola and the nipple, eliminating the skin or not, depending on aesthetic reasons. Liberating the mammary parenchyma from the thin adipose layer which separates it from the skin, makes it difficult to remove it completely keeping the skin viable. On the other hand, the nipple has to be considered mammary tissue and to avoid necrosis, a small amount of gland has to be left under it. Therefore, even when done with the best oncological intention, it must be accepted that subcutaneous mastectomy leaves 10% of the mammary parenchyma, which is susceptible of malignancy. Breast volume is usually obtained by using implants. Recently endoscope-assisted procedures have been introduced with apparently better aesthetic results⁷.

Subcutaneous mastectomy as breast cancer prevention in high-risk patients has been widely studied. Pennisi and Capozzi⁸, analysed 1,500 patients in 1989 and showed that after 10 years, only 6 (0,4%) out of 1,007 patients screened (454 were lost for screening, less than -30% loss), developed breast cancer. In a more recent retrospective study conducted by the Mayo Clinic⁹, to prove the results of prophylactic mastectomy in women with a family history of breast cancer, 7 out of 573 patients who underwent bilateral subcutaneous mastectomies presented breast cancer after 14 years screening (0.81% frequency).

This operation, followed by axillary lymphadenectomy has recently been compared with radical mastectomy for extensive intraductal breast cancer, which does not allow conservative procedures. A comparative study of 133 subcutaneous mastectomies and axillary lymphadenectomy with 910 radical mastectomies was undertaken at Gunma University, Japan in 2001. Local relapses were more frequent in the group treated with subcutaneous mastectomy (much younger patients), but survival rates were higher among these than among the mastectomized ones¹⁰.

Because surgery is not a safe prevention method; because it is a complex procedure and often does not give satisfactory results; because there is no agreement on which procedure is more satisfactory and because it has been recently proven that tamoxifen prevention is more effective in *BRAC1 BRAC2* mutation carriers, where risk reduction is close to 84% if associated with oophorectomy¹¹, it will be difficult to accept surgery as a preventive method for hereditary breast cancer, in spite of being a logical procedure.

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