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Mini-Review **Open Access**

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Contralateral risk reducing mastectomy in Non-BRCA-Mutated patients

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Abstract: The use of contralateral risk reducing mastectomy (CRRM) is indicated in women affected by breast cancer, who are at high risk of developing a contralateral breast cancer, particularly women with genetic mutation of BRCA1, BRCA2 and P53. However we should consider that the genes described above account for only 20-30% of the excess familiar risk. What is contralaterally indicated when genetic assessment results negative for mutation in a young patient with unilateral breast cancer? Is it ethically correct to remove a contralateral "healthy" breast? CRRM rates continue to rise all over the world although CRRM seems not to improve overall survival in women with unilateral sporadic breast cancer. The decision to pursue CRRM as part of treatment in women who have a low-to-moderate risk of developing a secondary cancer in the contralateral breast should consider both breast cancer individual-features and patients preferences, but should be not supported by the surgeon and avoided as first approach with the exception of women highly worried about cancer. Prospective studies are needed to identify cohorts of patients most likely to benefit from CRRM.

Keywords: Breast Cancer, contralateral risk reducing mastectomy, Non-mutated patients

1 Introduction

Breast cancer represent the second leading cause of cancer-related deaths in the United States [1] and the UK [2]. Although it regards predominantly older women, approximately 12% of new breast cancer cases occur in women younger than 45 years [3]. Younger age is usually related with more aggressive and less responsive tumours and consequently with lower survival rates, higher recurrence rates, and negative prognostic variables [4-6]. Therapeutic interventions include chemotherapy, hormone-therapies and surgery with or without radiotherapy. Systemic treatments impact on fertility prompting early menopause and ovarian decline [7]. Higher depression rates with effect on family life are also reported in these patients [8]. Refer to surgery could be cause of a negative body image that influence post-operative quality of life. Breast surgery includes breast conserving surgery (BCS) followed by radiation-therapy (RT) for early breast cancer or unilateral mastectomy (UM). BCS with RT and UM survival rates are equivalent [9], but preserving the breast, considering an oncoplastic technique could achieve better satisfaction levels and improve post-operative quality of life. Recently, however, numerous papers revealed a consistent growth in the use of both UM and contralateral risk reducing mastectomy (CRRM) [10,11]. CRRM consist in a so-called conservative mastectomy, the Nipple Areola Complex-Sparing Mastectomy that preserve the native breast skin and the nipple-areola complex, resulting in improved aesthetic results with local recurrence rates comparable to the traditional modified radical mastectomy [12]. The use of UM and CRRM is indicated in women affected by breast cancer, who are at high risk of developing a contralateral

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breast cancer (CBC), particularly women with genetic mutation of BRCA1, BRCA2 and P53. However, we should consider that the genes described above account for only 20–30% of the excess familial risk [13,14]. Consequently, the genetic etiology for the majority of families with an increased familial breast cancer risk remains unknown. Young age at diagnosis is a feature of hereditary disease and it is currently suggested that all women diagnosed with breast cancer younger than 37 should be referred for genetic assessment. But what is indicated in the contralateral breast when genetic assessment results are negative for mutation in a young patient with unilateral breast cancer? Is it ethically correct to remove a contralateral "healthy" breast?

2 Literature search

We reviewed PubMed database using the keywords "contralateral breast cancer", "contralateral prophylactic mastectomy" and "contralateral risk reducing mastectomy". We included only articles in English focused on contralateral mastectomy in women who presented a low-to-moderate risk of developing a secondary cancer in the contralateral breast. We considered as low-to-moderate risk patients, all women with a unilateral breast cancer in young age without a genetic mutation of BRCA1, BRCA2, P53 and without an evidence of strong familiarity for breast cancer. All papers reporting BRCA gene mutation carriers and other high-risk women have been excluded.

3 Results

Between January 1, 2005 and March 1, 2016 more than 300 papers were retrieved. Only 10% of retrieved papers addressed the impact of contralateral risk reducing mastectomy on overall survival [16-31]. Contralateral risk reducing mastectomy is estimated to reduce the risk of developing a contralateral breast cancer by approximately 94% [15]. Some studies showed a disease free survival (DSF) benefit associated with CRRM, but not an overall survival benefit [25,29].

4 Discussion

As a preventive measure, CRRM in women with low-to-moderate risk of developing a secondary cancer in contralateral breast remains controversial and potential benefits and disadvantages need to be discussed. The risk of mortality from contralateral disease must always be weighed against risk of mortality from primary tumour metastases, without an overall survival benefit. Different studies in fact showed as patients prognosis is strongly related to the features of their first breast cancer [32-34]. Moreover, mastectomy does not remove all breast tissue and therefore cannot eliminate risk of breast cancer at all, even if this surgery is shown to be effective in reducing risk. Presently, we are participating in a serious paradox: "a lesser surgical procedure is always more used in patients with an invasive breast cancer thanks to the screening program that allows an early detection of small cancer while mastectomy is offered in healthy breast for cancer prevention [32]". In addition, there is no demonstrated survival benefit [35] and CRRM may cause significant physical morbidity: complication including infection, nipple areola complex necrosis, bleeding with a re- operation rate up to 16% of patients [36]. Chronic pain and unsatisfactory aesthetic results are also been reported respectively up to 50% and 84% of the CRRM affecting irreparably post-operative quality of life [37,38]. Women should be thoroughly informed about achievable outcomes in breast reconstructive surgery when considering undergoing risk reducing procedures. On the other side, CRRM in non affected breast have potential benefits connected with the reduction of both risk of cancer and anxiety patient. Given the potential complications and no demonstration of survival benefits, CRRM could be safely omitted in patients with low-to-moderate breast cancer risk.

5 Conclusion

CRRM rates continue to rise all over the world although CRRM seems not to improve overall survival in women with unilateral sporadic breast cancer. The decision to pursue CRRM as part of treatment in women who have a low-to-moderate risk of developing a secondary cancer in the contralateral breast should consider both breast cancer individual-features and patients preferences, but should not be supported by the surgeon and avoided as first line approach with the exception of women highly worried about cancer. Prospective studies are needed to identify cohorts of patients most likely to benefit from CRRM.

Conflict of interest statement: Authors state no conflict of interest

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