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EDITORIAL

Breast-Conserving Treatment for Breast Cancer: Rational, Current Reality & Limitations

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ABSTRACT

Recently published 20-years follow-up scientific data confirm that there is no difference in survival after breast conservation therapy or total mastectomy in women with stage I or II breast cancer. However, breast conservation treatment is associated with an increased risk of both positive margins and local recurrence. Current estimates suggest that 10 to 20% of women after breast-conserving treatment is at high-risk of local failures. This is a characteristic example of limitations and lack of generalizability of randomized controlled trials, although they provide the best available evidence for treatment decision-making.

Most of the 20th century the Halsted radical mastectomy and during the last decades the modified total mastectomy, were the standardized operation for cancer of the breast in all stages, early or late. However, with advances in the understanding of breast cancer spread mechanisms a new concept towards a less radical surgery[1] has been developed with breast-conserving treatment increasingly to replacing mastectomy.

The rational of a less extensive surgical approach has been based on both histological data indicated that small solid tumors can be completely removed by limited surgery and clinical results suggested that this approach might result in a lower side-effects profile than extensive surgery without increasing risk of cancer death. This creative thoughtful concept represents an important advance towards a lower morbidity and better quality of life of patients with breast cancer[1] and other solid tumors including gastric cancer.[2,3]

However, long-term survival data from randomized controlled trials (RCTs), that provide the best scientific evidence for a decision-making, are essential before the incorporation of a new treatment into routine clinical practice. A trend towards a less extensive surgery has already been started for the most common solid tumors such the prostate cancer, gynecologic cancer or gastrointestinal tract cancer and the effect of such limited surgery or minimally invasive approach on patient's outcomes is now evaluating in ongoing RCTs.

For breast cancer however, there are now accumulating evidence-based data that allow us to drawn conclusions about the effectiveness of breast conservation therapy. Survival data from RCTs after a follow-up of 5 or 10 years[4-10] have showed that there is no significant difference in overall survival or breast-cancer specific survival after breast-conserving surgery and mastectomy. The lack of long-term follow-up data was an argument against breast-conserving surgery because of the long natural history of breast cancer.

Now, the recently published 20-years results by Fisher et al.[11] and Veronesi et al.[12] confirm that mastectomy is not superior to breast conservation treatment with respect to long-term survival. In an accompanying editorial Dr. Morrow points out that it is time to declare the case against breast-conserving therapy closed, to expand the eligibility criteria and to increase the currently low rate of breast-conserving surgery that is performed in approximately 42% of women with stage I or II breast cancer.[13] Indeed, as breast conservation therapy is a woman's friendly and preferable procedure leading to a better quality of life than total mastectomy, a wider clinical use of breast conservation treatment is expected in the next years.

The key question from the increasing replacement of mastectomy by breast conservation procedures such lumpectomy, quadrantectomy or local/wide excision is whether this trend is parallel associated with an increased risk of close or positive margins and local recurrence in ipsilateral breast. Indeed, the analysis of scientific data available [14: details in positive margins in this issue of GBC] let no doubt that breast-conserving surgery is associated with higher rates of close or positive margins

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than mastectomy. The magnitude of this risk varies from 10% in the National Surgical Adjuvant Breast and Bowel Project (NSABP, B-06) trial[5,11] to 48% in the European Organization for Research and Treatment of Cancer (EORTC) trial.[9] The risk of local recurrence among women with close or positive margins is high and ranges between 9% and 20% with the surgical re-excision to remain a standard procedure.[14] Clear surgical margins continuous to be the principal goal of breast-conserving treatment despite the availability of current adjuvant treatment.

Local recurrence represents currently the major disadvantage of breast-conserving treatment. It occurs in 8.8% to 20% after breast-conserving surgery despite the use of adjuvant irradiation therapy in reports with long-term follow-up.[5,8-11] Postoperative adjuvant whole breast irradiation after breast-conserving surgery has been established effective in reducing local recurrence[2,5-9] and improving survival,[15] but it is unable to fully eliminate the risk of local failure. Particularly late recurrence is challenging occurring at a rate of approximately 1% per year after the tenth year of treatment.[16] Additional boost to the primary tumor bed, chemotherapy, and tamoxifen contribute to the reduction of local failure but in some patients they rather delay time to recurrence than fully eliminate late recurrence.[16,17] The underlying mechanisms of this late tumor formation are unclear but either it is a true recurrence or a new primary tumor[9] must take into account for primary treatment decision-making.

Efforts have been focused on the identification of risk factors and use of more effective treatment for risk-reduction local recurrence. Of multiple clinical, pathologic and treatment-related risk factors reported, young age, close or positive margins, extensive intraductal component (EIC) and the non-use of adjuvant systemic chemotherapy in node-negative patients or tamoxifen[9,16,17] are consistently associated with increased risk of local failure in most series.[12,14-17] Although with careful patient selection and appropriate multidisciplinary treatment local failures can be reduced, in some women with stage I or II breast cancer but at risk of local failure - if they undergo in breast-conservation treatment, total mastectomy may be indicated after patient consultation about the risk and benefits of each one of these treatment options. It should be noted however, that even after mastectomy some local failures can be occurred in the chest wall reflecting biologically aggressive disease. Promises for the identification of these patients provide current reports with new biologic markers such as particularly Gene-expression profiling[18,19] and Cyclin E levels[20,21] that may lead to a new tailored treatment and improved outcome.

Randomized controlled trials (RCTs) are the “gold standard” for treatment decision-making. They represent the best evidence-based available method necessary to assess the possible clinical risks of a new treatment before its incorporation into routine clinical practice.

However, RCTs are limited by the lack of generalizability to the individual patients.[22] Another pitfall for some patients enrolled in RCTs is an increased risk of morbidity and mortality. A characteristic example of limitations and pitfalls of RCTs is the critical analysis of the results of breast-conserving therapy available for breast cancer. Thousands of women have been enrolled in these trials that compared breast-conserving surgery with or without adjuvant irradiation, chemotherapy or tamoxifen and total mastectomy. Several hundreds of these women were affected by an inappropriate patient selection and treatment. The rate of positive margins after breast conserving surgery reached an unacceptable rate of 48% in the EORTC trial.[9] In the NSABP B-06 trial the incidence of local recurrence after lumpectomy among women without postoperative adjuvant irradiation was high (39%)[11] resulting in reduced survival as demonstrates a recent meta-analysis.[15]

The lack of generalizability of RCTS to individual patients is reflected by the fact that although for most women with stage I or II breast cancer breast conservation treatment is the treatment of choice, some others may benefit from total mastectomy rather than breast conservation. Current research efforts are focused on the pretreatment identification of these women.

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