

## SURGICAL TREATMENT FOR LOCALLY ADVANCED BREAST CANCER

MLADEN STANEC, STJEPAN JUZBAŠIĆ, MIROSLAV LESAR, IVAN MILAS,  
DANKO VELEMIR VRDOLJAK, DUBRAVKA KRLEŽA SUPIĆ and MIROSLAV BANOVIĆ

University Hospital for Tumors, Zagreb, Croatia

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### Summary

Surgical treatment for breast cancer has remained the primary modality for locoregional treatment, except in the case of locally advanced breast cancer. The surgical treatment is aimed at removing the tumor, achieving local control of the disease and obtaining enough tissue for pathohistological diagnosis and evaluation of breast cancer hormone receptor status. The assessment of local spread of the disease is of the utmost importance for surgical decision making.

KEY WORDS: *breast cancer, local spread of the disease, surgical treatment*

### KIRURŠKO LIJEČENJE LOKALNO PROŠIRENOG RAKA DOJKE

#### Sažetak

Kirurško liječenje raka dojke bilo je i ostalo osnovna metoda lokoregionalnog liječenja, osim u slučaju lokalno proširenog raka dojke. Cilj kirurškog liječenja je uklanjanje tumora i postizanje lokalne kontrole bolesti, te osiguravanje dovoljno tkiva za postavljanje patohistološke dijagnoze i određivanje hormonskog statusa tumora. Procjena lokalne proširenosti bolesti od najveće je važnosti u odabiru kirurškog postupka.

KLJUČNE RIJEČI: *rak dojke, lokalna proširenost bolesti, kirurško liječenje*

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Breast cancer is a significant epidemiologic problem and, therefore, a subject of great interest to both physicians and patients. Over time, various options were being offered for the treatment and follow-up of the disease, but in the majority of cases, surgical treatment always was and has remained a primary treatment modality. The surgical treatment is primarily aimed at achieving local control of the disease, or removing the tissue for pathohistological diagnosis and other significant prognostic parameters. Methods and views of the surgical treatment for breast cancer were changing during its history, depending upon new biological knowledge of the nature of the disease, and of new technologies.

The year of 1894 is considered the beginning of modern surgery for breast cancer as this is the year when Halsted reported the results of his en block operation for breast cancer involving the removal of the entire breast, evacuation of axillary lymph node content from all three stages and resection of both pectoral muscles (1, 2). The technique, providing superior local control of the disease along with a significant mutilation, for a long time modelled for a successful oncological principle in the management of malignant disease. The Halsted's approach was based upon teaching of the German pathologist Virchow who considered cancer a local disease and regional lymph nodes a natural barrier for its spread.

Almost a 100 years after, with the introduction of the Fisher's theory of biological tumor growth and tumor behavior, it was shown that the same results could be obtained using modified radical mastectomy, a surgical procedure that does not involve resection of the pectoral muscles (3), and therefore representing a substantially less mutilating procedure. Further development of surgical methods for breast cancer showed a tendency towards using conservative surgical procedures. In his study of 1981 comparing radical mastectomy with quadrantectomy and postsurgical irradiation, Veronesi showed no difference in survival rates and local recurrence between the two studied groups (4). The study included patients with primary tumors of less than 2 cm in diameter and clinically negative axillary lymph nodes. In 1985, the results of the NSABP B-06 study (5), comparing the results of radical mastectomy and segmentectomy with and without radiation in patients with breast cancer ranging up to 4 cm in size with clear segmental margins, were published. Like the Milan study, the B-06 study also showed no difference in survival rates of mastectomy patients compared with patients undergoing conservative surgery. Both studies are representative of the beginning of the era of conservative surgery for breast cancer, showing that a particular group of patients with early breast cancer can be treated with conservative surgery achieving equal success rates as with mastectomy. An increase in the number of conservative surgical procedures for breast cancer was afterward reported worldwide and corroborated by numerous studies (6-8).

Although the majority of early breast cancer patients are considered eligible for that type of treatment, there is also a significant number of patients with early breast cancer for whom the conservation treatment is not a recommendable solution. The most significant factor in making decision about the type of surgery is the advancement of the disease. For a surgeon, the case history and physical examination results, followed by the results obtained using clinical diagnostic tests are the key points for preoperative evaluation of local disease spread. The relationship between the tumor size and the breast size is of great significance. A tumor of 3 cm in size in a patient with small breasts is an impediment to

breast conservation surgery since it does not allow either clear biopsy margins or an adequate cosmetic outcome. For the same reason, a 4 cm large tumor in a patient with large breasts can be successfully managed using conservative surgery.

In addition, other findings revealed by physical examination and playing a role in the preoperative evaluation of local disease spread are as follows: tumor mobility, or its potential fixation to the underlying fascia or skin, nipple involvement in the case of Paget's disease, changes to the skin in the form of *peau d'orange* indicating a more extensive and aggressive form of inflammatory breast carcinoma, as well as examination results of the contralateral breast including axillae and supraclavicular fossae with possibly palpable lymph nodes. After complete clinical analysis and taking into consideration all findings, the surgeon can make decision about the type of surgery to achieve the best possible local control of the disease, and also spare the patient from unnecessary surgical treatments.

Although today there are many diagnostic methods and various surgical techniques for breast cancer, many problems related to choosing the right option for each particular patient remain unsolved. The patient-tailored choice of surgical treatment for breast cancer should however take into consideration a wide range of physical, emotional, psychological factors and rehabilitative necessities of each particular patient (9, 10).

## **SURGICAL MANAGEMENT OF PRECANCEROSES AND NON-INVASIVE BREAST CANCER**

Lobular carcinoma *in situ* (LCIS) is nowadays considered as a marker of increased risk. In choosing optimum treatment several important factors should be taken into consideration: LCIS, generally a disease of premenopausal women and often accidentally detected on biopsy for some other indications, may be a multicentric and bilateral tumor. It is most frequently approached by clinical observation, and if an appropriate biopsy has been performed, LCIS should be continuously and regularly monitored, taking into consideration mirror biopsy of the

contralateral breast, too. Some studies report the role of tamoxifen in reducing the risk of developing invasive breast cancer (11).

With the development of diagnostics and introduction of the program for early cancer detection, ductal carcinoma *in situ* (DCIS) has become a therapeutic problem with increasing frequency, accounting for 25% of all breast cancer diagnoses in the developed world. There is no uniform treatment approach to DCIS: the most frequently used surgical procedure is a wide excision, while for tumors that exceed 4 cm in size and multicentric DCISs, ablation of the breast without dissection of the axilla is indicated. The Van Nuys prognostic index is a decisive factor in making a definitive decision about the surgical procedure.

#### **SURGICAL PROCEDURE FOR STAGE I AND II INVASIVE BREAST CANCER**

The most frequent treatment methods for stage I and II breast cancer include breast conservation surgery, modified radical mastectomy, skin or mamilla preservation mastectomy, and breast reconstruction. Following the Fisher's biological theory according to which biological factors are responsible for breast cancer metastasizing, breast conservation techniques have been suggested as the treatment of choice when deciding among available surgical procedures. Indications for conservation surgery for breast cancer include: lesions less than 4 cm in size, mammography and ultrasound results without signs of multicentricity and multifocality, appropriate breast volume and patient consent to breast conservation surgery. If any of these criteria is not met, modified radical mastectomy should be chosen.

#### **SURGICAL PROCEDURE FOR STAGE III AND IV LOCALLY ADVANCED BREAST CANCER**

Locally advanced breast cancer patients include patients with stage IIIb, IIIa, IIIb and IV of the disease. In this group of patients for whom surgery is not the primary treatment option, treatment should start with neoadjuvant system

therapy, with surgery playing a role in removal of the tumor mass, or obtaining material for pathohistological analysis and determining the hormonal status. The most frequently used method is a modified radical mastectomy, or breast conservation techniques if indicated. The term locally advanced breast cancer comprises a heterogeneous group of breast tumors ranging from relatively slow growing, large primary tumors to small breast tumors with widespread metastases to axillary lymph nodes. The biological difference of locally advanced tumors rather impedes both the comparison of results obtained using various treatment options and creation of a unique recommendation that would include all the patients. Despite efforts for early detection of breast cancer, 10-20% will present with locally advanced disease at diagnosis. Despite different tumor types and different prognosis, the achievement of local control and longer survival by preventing the development of distant metastases are common problems encountered in the treatment of this group of patients (12).

#### **SELECTION OF PATIENTS FOR BREAST CONSERVING SURGERY**

Breast conserving surgery is an appropriate treatment method in almost 75%-80% of stage I and II breast cancer patients. Factors influencing the selection of patients for this treatment modality can be divided in three major groups: patient factor, clinical factors and pathohistological factors. The question of special clinical significance that encumbers the procedure, is how often and how many tumor cells are going to be found outside the clinically evident tumor focus. The frequency of these distant foci plays a significant role in therapy selection. Standard intraoperative guidance for the confirmation of clear margins at the time of tumor extirpation includes: preoperative radiological needle-marking of the tumor, marking of biopsy margins for pathohistological orientation, good communication between the surgeon, radiologist and pathologist, and radiological verification of the extirpated material. Histological analysis of tumor bed margins can also provide a significant advantage. A statistically significant difference in the development of local recurrences is observed following conserva-

tion procedures in patients with positive margins (13). Most frequently positive are the anterior margins of the tumor bed, which in case the tumor is less than 1 cm from the skin, indicates an elliptic excision of the skin above the tumor. The impact of the type of anesthesia was also observed in relation to histologically positive tumor bed margins, with negative margins identified in 76% of patients operated under general anesthesia compared to 56% of patients undergoing surgery under local anesthesia (14).

Of patient characteristics that play a role in the selection of surgical procedure, pregnancy is considered an absolute contraindication, as pregnancy is a contraindication to postoperative radiation for its potential teratogenous and cancerogenous effects on the fetus (15). There are only few published reports about the effect of prior radiation therapy for other malignomas and breast conservation surgery (16). Women with collagen-vascular diseases are also not eligible for conservation treatment as they tolerate irradiation poorly (17). As relative contraindications reported are a large tumor in a small breast as well as the breast size itself since women with big breasts can have an increased postirradiation retraction, resulting in a bad cosmetic outcome (18).

The effect of age on the selection of surgical procedure for breast cancer is controversial. Some authors report that patients aged 35-40 years run a significantly greater risk for developing local recurrence after breast conservation surgery compared to older age groups (19, 20).

The significance of family history and genetic risk factors in relation to the selection of patients for breast conserving surgery remains vague. Some studies report a significant increase in risk for developing local recurrence in patients treated with breast conservation therapy and a family history of breast cancer (21, 22), while others do not find such a relationship (23, 24). The relationship between genetic malformations (BRCA 1 or BRCA 2) and the development of local recurrence in patients receiving conservation surgery (25) not confirmed in some studies, has on the other hand been found in others (26). Today, the positive family history and confirmed genetic malformations, related to the development of breast cancer, are not considered to be contraindications for breast conserving surgery.

Some clinical factors may play a role in the treatment selection for their undesirable effect on local recurrence after breast conserving surgery. Both patients with palpable and impalpable tumors are considered to be at equal risk of developing local recurrence, as well as it is considered that the tumor size has no influence to its development (27- 29). However, in practice, an acceptable cosmetic outcome is hardly achievable, following the principle of clear margins, in the majority of patients with tumors larger than 4-5 cm in diameter. Patients with bilateral breast carcinoma can be successfully treated with conservation surgery, without any significant increase in risk of local recurrence (30).

Generally accepted is the role of preoperative mammography in the determination of the disease spread. Patients with mammographically detected microcalcifications often show multifocality in the pathohistological preparation, and therefore run an increased risk of developing local recurrence after conservation surgery. The same applies to patients in whom more than 50% of an extensive intraductal component have been found (31, 32).

The role of magnetic resonance in the evaluation of the extensiveness of breast cancer remains to be fully confirmed.

Among pathohistological factors influencing the selection of surgical treatment for breast cancer, the most important by all means are histologically clean margins of the tumor bed after breast conserving surgery. Literature references suggest a significant increase in the development of local recurrence in patients with no clean excision margins, or with margins less than 1 cm (33-35). Attention should be also paid to the significance of adjuvant system therapy and radiotherapy in the reduction of local recurrence, even in patients in whom clean margins have not been obtained (34, 36).

Tumor histology has no significant effect on the development of local recurrence after conservation surgery and postoperative radiation therapy. The significance of the extensive intraductal component has already been pointed out.

There is no statistically significant difference in the development of local recurrence after breast conserving surgery between patients with invasive lobular carcinoma and those with inva-



sive ductal carcinoma. Tumors with mixed, ductal and lobular elements also show similar forms of behavior (37-39).

The role of DCIS in the development of local recurrences after conserving surgery and postoperative radiation therapy is not quite clear. Results of some multicentric studies show that the combination of a high nuclear grade and comedo component relates to an increased risk of local recurrence (40).

## CONCLUSION

In their selection of surgical treatment for breast cancer, surgeons combine information obtained using preoperative, intraoperative and postoperative techniques, clinical diagnostic methods and pathohistological analysis with the aim of assessing the disease spread within the breast and to the regional lymph nodes, or distant organs. Using all these modalities, the most optimum locoregional treatment can be chosen and the patient spared from unnecessary surgical interventions.

The majority of patients with early invasive breast cancer are considered eligible for breast conserving surgery. In some, postoperative radiation therapy is absolutely contraindicated for teratogenous or toxic effects (pregnancy, sclerodermia). On the other hand, breast conserving surgery does not always produce an expected cosmetic outcome (patients with a large tumor in a small breast). Breast cancer patients undergoing conservation surgery require careful control, either by physical examination or mammographic imaging, for possible early detection of local recurrence of the disease.

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*Author's address: Mladen Stanec, M.D., Ph.D., Department of Surgical Oncology, University Hospital for Tumors, Ilica 197, 10 000 Zagreb, Croatia*