

TENDINȚELE ÎN TRATAMENTUL ACTUAL AL CANCERULUI LA SÂN – 2002-2010

Trends in surgical treatment of breast cancer between 2002-2010

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ABSTRACT

Introduction. These conservative surgery combined with radiotherapy is an effective treatment in many cases of breast cancer.

Materials and methods. The authors reviewed 603 cases of breast cancer (mean age 51.3 years) with an average tumour size of 18 mm (\pm 40.46 mm) treated by conservative surgery combined with radiotherapy.

Results. In 370 cases was performed tumorectomy (61.4%) while cvadrantectomy was performed in 233 cases (38.6%). During the 5 years of follow-up, 87.79% of the patients were disease free; in 12 cases we are not informed of the patients' present status. The percentage of recurrences was variable 1.7-6.7% for a time schedule between 15.6-65.4 months. The time between surgery and recurrences was about 8.6-36 month, with a media of 29 month. Local recurrences after conservative treatment were 9.2% at 5 years and 17.1% at 10 years. Recurrences were 6% in T1, 10% in T2 and 13% for T3 (87).

Discussions. The presence of lymph node invasion increases the risk of relapse. More than 30% patients under 35 years present a risk of local recurrence risk in the first 10 years.

Conclusions. There was a significant decrease in the number and proportion of mastectomies performed, an increase in the number of BCS procedures performed and an increase in the number of women undergoing breast RT due to a slight trend in smaller tumors diagnosis at presentation and the multidisciplinary clinical aboard of the disease.

Key words: breast cancer, conservative surgery, tumor margins, breast recurrence

INTRODUCTION

The oncological surgery is defined by the use of plastic surgery techniques in the conservative treatment which correlates tumor excision with the plastic remodeling gesture in order to defeat mammary gland morphology and to improve the aesthetic results (1). Regardless the histological aspect, the risk of this therapeutic method is given by a high incidence of relapse tumor in accordance with risk clinical and therapeutic factors (2). If the volume ratio tumor-breast volume favors large tumorectomies oncological surgery allows conservative treatment in retroareolar tumors and in some tumors larger than 3 cm in diameter, without significant augmentation of local recurrence or equivalences in terms of long distance survivals. Surgical treatment should be individualized for each case, the choice of conservative techniques being accomplished after a rigorous multidisciplinary

selection that requires clinical examination, anamnesis, imaging and histological appropriate examinations. Differences in the applying of this treatment in different regions of the globe is secondary to multiple factors such as the screening practice, the technical performance levels of the operators, the impact on patient therapeutic alternatives, personal options, possibility of adjuvant treatment. The present study describes our own results obtained using conservative therapeutic strategy.

MATERIALS AND METHODS

The current study is performed in accordance with the Romanian medical laws, all living patients having authorized the review of their medical records. There were retrospectively reviewed the data of 605 patients with breast cancer stages I, II and III (8 cases) treated with breast-conserving surgery (BCS) followed by radiotherapy (RT) in

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603 cases in the fourth Clinic of Obstetrics and Gynecology from Iasi during 2002-2010. RT was administered to the breast and/or regional lymphatic's as clinically indicated and described elsewhere to a total median dose to the tumor bed of 64 Gy. Systemic therapy was administered in accordance with standard clinical practice during this time interval. In 2 cases, RT was interrupted before reaching the required dosage because of side effects (pulmonary fibrosis). Practiced surgical technique consisted of partial mastectomy with preservation of intraoperative resection margins (free edges lower than 5 mm) and axillary node surgery followed by external radiotherapy. Time interval between surgery and radiotherapy onset was 10 ± 7.7 weeks (average values between 1 and 45 weeks). All patient data were entered into a computerized database. Local or regional relapses were defined as clinically and histological documented relapse in the ipsilateral breast or regional nodes. Distant metastasis was defined as clinical evidence of distant disease based on clinical and/or radiographic findings. All events were calculated from the time of initial diagnosis to the time of the event.

The model included the terms for treatment type, TNM staging, and age group at diagnosis. Patients were eligible for breast surgery if the tumor was less than 3 cm diameter, but breast volume and expected cosmetic outcome were taken into account. After surgical resection a separate evaluation of pathological responses were classified. Exception made a number of 14 cases with clinically negative axilla that have not undergone axillary clearance.

Survival, distant metastasis, and local relapse-free times were calculated using standard life-table methods. In 301 cases the follow-up of the patients was performed for a maximum period of 5 years (mean 37 months), every 3 months in the first 3 years and every 6 months in the last 2 years, by clinical examination supplemented by mammography/ultrasound and chest radiograph. In order to determine the vital status of the patients diagnosed with breast cancer two years before the completion of the study 486 letters were sent to the addresses mentioned in the case report forms, asking the patients to return to medical control for reassessment of the current statuses. There were received answers in 246 cases and 259 patients were submitted to regular controls until the end of the study.

The data were analyzed with the SPSS software no.10, all statistical testes being two-tailed and differences considered to be statistically significant if $p \leq 0.05$.

RESULTS

At the time of initial diagnosis the women ranged in age from 21 to 85 years, with a median age of 51.3 years. In 109 cases (18.08%) breast cancer diagnosis was made by screening mammography or clinical routine control gynecological examination. The tumors were located in the superolateral quadrant of the breast in most cases (61.2%). The time interval between the time of diagnosis and the precise diagnosis was 9 weeks (1-14 weeks in extreme values).

Primary breast cancer diagnosis was performed in 561 cases (92.7%). In 5 patients the tumor was diagnosed as a second primary breast neoplasia (0.8%). In 15 cases the disease was bilateral, synchronous, and bilateral in 22 cases, but asynchronous. One patient presented history of intraductal carcinoma diagnosed 2 years before, neoplasia located in another quadrant of the same breast and treated by simple excision.

Histological, the tumors were of invasive ductal type in 123 cases, lobular in 11 cases and mucinous in one case (Table 1). The average size of the resected tumors was 18 mm (± 40.46 mm) with values between 2 and 60 mm.

TABLE 1. Distribution of histological types of breast cancer in resected specimens

Histology	Number	Percentage
infiltrating carcinoma	2	0.3%
invasive intraductal cancer	510	84.6%
medular carcinoma	6	1%
mucoïd carcinoma	12	2%
tubular carcinoma	12	2%
medular atypic carcinoma	14	2.3%
mixt carcinoma (CDI + CLI)	26	4.3%
CLI	12	2%
infiltrating comedocarcinom	9	2%

Histologic examination of specimens revealed positive margins in 490 cases (82.9%) (Table 2)

TABLE 2. Distribution of patients according to the marginal status

Surgical borders	Percentage
Positif borders	27%
Negativ borders	73%
Positif borders	29%
Negativ borders	71%

Axillary clearance was done in 589 cases (97.5%) in most patients presenting level I and level II axillary dissection. Mean number of nodes dissected were 12 ± 5.5 (range 1-35), number that correlates significantly with the tumor stage.

TABLE 3. Clinico-hystologic characteristics of patients

Variable	Positive margins	Negative margins	P value
Type of lesion			
Palpable	33%	67%	.087
nonpalpable	26%	74%	
Histologic type			
Ductal	25%	75%	.003
lobular	32%	68%	
Tumor grading			
I	21%	79%	.040
II	29%	71%	
III	36%	64%	
Tumor diameter			
T1a/b	25%	75%	.026
T2	30%	70%	
T3	35%	65%	
Multicentricity			
Present	35%	65%	.000
Absent	22%	78%	
Oestrogenic receptors			
Present	25%	75%	.000
Absent	32%	68%	
Extensive intraductal component			
positif	33%	67%	.026
negativ	27%	73%	
Lymphonodular status			
Present	34%	66%	.017
Absent	27%	73%	

TABLE 4. Distribution after immediate postoperative complication

Postoperative complication	Number	Percentage
none	417	68.93
pain	115	19.01
pain and arm lymphedema	24	3.97
pain and local edema	33	5.45
pain, lymphedema, tumefaction of the arm	16	2.64
Total	605	100

19% patients developed osseous distant metastasis, followed by pleuropulmonary metastasis in 25.81% of cases and hepatic dissemination in 19.35% cases.

Regarding the 5 years survival rate there were obtained information in only 301 cases. 21 patients died by diffuse metastasis without local recurrence, 3 cases being stadialized in the II stage in the moment of the initial diagnosis, 12 in the second stage and 6 in the first stage. With one exception, all deceased patients had more than 50 years before initiating cancer surgery. The actual survival rate was 91%.

DISCUSSION

The main goal of BCS is to convert in conservative surgery involves the complete tumor excision with safety margins, the main breast conservation advantage, with cosmetic outcome that increases

the quality of life and prolong disease-free interval. Conservative treatment requires application of radiotherapy in order to reduce local tumor recurrence risk and, according to this risk, the need for a strict control in breast surgery. Selection of cases for conservative treatment requires appropriate quantification of individual clinical, histological and therapeutic factors (3).

Recurrence rate in our study was 2.86%, the tumor inflammatory characters requiring mastectomy before chemotherapy. The literature emphasizes that the incidence of tumor recurrence depends on possible risk factors such as tumor histology, tumor volume, the patient characteristics, presence or absence of intraductal extension (CIE), axillary node status, resection margins (4,5). Although adequate margins of excision are rigorous elements, there are practitioners who believe that the edges can be considered “free” when there is peritumoral normal tissue (without units), obtained originally or secondary to the reexcision (6,7). Histologic evaluation of resection margins status represents the best indicator of conservative surgery outcome. Excision of tumor tissue ensures the removal of malign peritumoral glandular tissue and fat, together with the suprajacent great pectoral fascia and cutaneous tissue. Tumors over 1.5 cm diameter are excised through partial mastectomy, a generic term that combines lumpectomy, quadrantectomy, tylectomy. In tumors equal to or less than 1.5 cm diameter are proposed axillary clearance and tumorectomy. The presence of positive margins requires complete excision in safe tissue and/or complete mastectomy. Veronesi believes that the free edge limit is 2 mm (4), while Ryoo increases the limit up to 5 mm (1, 2). Multiple studies reveals major difficulties in obtaining free margins in infiltrating lobular carcinomas that determine architectural distortion through surgery, making compulsory the surgeon experience in order to limit the resection margins (6, 8). Axillary lymph histological examination represents an important prognostic factor especially in terms of number of affected nodes. Actually it is considered to be sufficient the removal of at least 6 axillary nodes (9).

The current trend in BCS is to eliminate axillary dissection. In cases of carcinoma in situ lymphonodular invasion is absent making axillary dissection unnecessary. In T1a tumors frequency of lymph node dissemination is between 3-9%, a percentage questions the usefulness of this method. Thus, it was to imagine an alternative to axillary dissection represented by sentinel lymphadenectomy. Diagnosis of breast cancer mammography is a specific category in sentinel lymphadenectomy. The Consensus of Saint Galen

considered the standard method of lymphatic staging in cases of tumors fewer than 3 cm without ipsilateral axillary invasion (5,7,8).

Conservative treatment indications are constantly expanding, increasingly more patients with advanced tumors benefit from this treatment option because of the many protocols of neoadjuvant chemotherapy occurred in recent years. Integration of plastic surgery techniques in the conservative interventions during the treatment of breast cancer is a new approach that allows more extensive resections.

From our perspective we believe that there are three major reasons that currently require the development of conservative therapy in breast cancer: surgical and radiological evidence of treatment failure, aggressive educational and informational increase in patients and the widespread use of mammography, which may reveal a tumor a preclinical phase, more rational vision impairment cancer based on clinical records that may explain the biological characteristics of breast cancer development.

Conservative procedures (partial mastectomy, lumpectomy, mastectomy subcutaneous mastectomy with nipple preservation, tumorectomy, wide local excision) keep free as much breast tissue, providing satisfactory cosmetic results, in terms of good local control and a low risk of recurrence.

The limitations of the current study derives from socio-cultural factors (late response of patients to letters, which resulted in a loss of the initial number of cases considered, the complete refusal of mastectomy, the use of complementary therapies, lack of health education), economic factors (patient uninsured medical, difficult way of selection of cases due to incomplete case report forms, lack of seasonality of breast tumor), technical factors (diagnostic evaluation and therapeutic approach must be multidisciplinary breast cancer, patients between specialties find passage sometimes difficult, which determine random intervals between therapeutic moments, vary from case to case, depending on therapist availability).

CONCLUSION

Conservative treatment in breast cancer involves complete lifting of the tumor, axillary dissection, radiotherapy and individualized systemic therapy. The main advantage of the wider local incision is the possibility of removing the tumor with a safety margin of up to 2cm in the normal adjacent breast tissue.

The only way in order to obtain clinical efficacy of the treatment is ongoing monitoring to identify local or systemic recurrence. The occurrence of relapses does not increase the risk of dissemination and therefore requires meticulous surgical excision in order to minimize the risk of local recurrence. Survival rate observed in the current study within a 5-year average is similar to that cited in the literature, the results being favorable to the segmental resection of the mammary gland. Emergence of multimodal therapy and multidisciplinary treatment is conditioned by a combination of systemic radiotherapy and surgery, and it is applied usually after local treatment in full agreement with pathological and clinical criteria.

The major concept of conservative therapy consists in elimination of the primary tumor with free histological margins and axillar dissection followed by postoperative radiotherapy. Individualized conservative treatment is a demonstrated principle checked by patients participating in therapeutic decision because it has an important influence on body image, quality of life, marital and sexual satisfaction.

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Conflict of interest

The authors have no conflicts of interest.

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