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Local and Distant Recurrences - A Comparative Study on Conservative and Radical Surgery for Breast Cancer

M. Ursaru[1], I. Jari[1], D. Negru[1], V. Scripcariu[2]

[1]Discipline of Radiology, University of Medicine and Pharmacy "Gr. T. Popa" Iasi, Romania
[2]Department of Surgery, Regional Institute of Oncology, University of Medicine and Pharmacy "Gr. T. Popa" Iasi, Romania

Rezumat

Recidivele locale și la distanță - aspecte comparative în sânul operat conservator și sânul operat radical pentru neoplasm mamar

Tratamentul cancerului de sân a evoluat mult în ultimii 40 de ani, intervențiile conservatoare urmate de radioterapie fiind opțiuni din ce în ce mai mult preferate de medicii chirurgi şi paciente. Lucrarea de față își propune să semnaleze aspectele comparative privind recidivele locale şi la distanță la pacientele operate radical sau conservator pentru neoplasm mamar. Am efectuat un studiu retrospectiv în perioada 1 ian 2005 - 31 iulie 2013, ce a inclus 477 paciente cu neoplasm mamar în stadiile 0, I şi II, luate în evidență la Institutul Regional de Oncologie Iaşi, din care 248 (52 %) paciente au fost operate radical iar 229 (48 %) paciente au fost operate conservator. S-au efectuat examinări echografice, mamografice, CT şi IRM ce au permis diagnosticarea de recidivă loco-regională şi la distanță. Numărul total de recidive locale şi la distanță a fost mai mare la pacientele operate conservator (86 recidive) față de pacientele operate radical (55 recidive). Recidivele locale sunt mai frecvente la persoanele tinere precum şi la pacientele tratate prin chirurgie conservatoare şi radioterapie față de pacientele cu mastectomii radicale. Cele mai frecvente metastaze sunt localizate la nivel osos, hepatic şi pulmonar.

Cuvinte cheie: mastectomie parțială, mastectomie radicală, ecografie, mamografie, recidive

Abstract

The treatment of breast cancer has evolved over the past 40 years. Followed by radiotherapy, conservative surgical procedures are options increasingly more preferred by surgeons and patients. This paper aims to highlight comparative aspects of local and distant recurrence in patients who had radical or conservative surgery for breast cancer. We performed a retrospective study between January, 2005 - July 2013, that included 477 breast cancer patients from the Regional Institute of Oncology Iasi, who were evaluated by imaging in the Radiology Clinic, Hospital "St. Spiridon", Iasi. We included in the study patients in curable stages 0, I and II; 248 (52 %) patients had radical surgery and 229 (48 %) patients had conservative surgery. We used the ultrasound scan, mammography, CT and MRI, that allowed diagnosis, pretherapeutic staging and diagnosing of the loco-regional and distant recurrences. Local and distant recurrences were higher in patients with conservative surgery (86 recurrences), than in patients who had radical surgery (55 recurrences). Local recurrences are more common in younger individuals and in patients treated with conservative surgery and radiotherapy, than in patients with radical mastectomy. The most common metastases are located in the bone, liver and lung.

Key words: conservative surgery, radical surgery, ultrasound scan, mammography, recurrences

Corresponding author: Manuela Ursaru, MD
Ph.D. Fellow - "Gr. T. Popa" University of Medicine and Pharmacy Iasi
14 Grădinari Street, Bl F1-2, Et 2, Ap 2, Iaşi
E-mail: manuelaumf@yahoo.com

Introduction

Breast cancer is the most common malignancy and the second cause of death by cancer in women (breast cancer represents 24 % of all cancers occurring in women, and breast cancer - specific mortality was 16.4 % of all deaths cancer in women, Commission of the European Communities 2008 European Cancer Observatory 2008).

The treatment for breast cancer has improved over the past 40 years. These changes are due to early diagnosis, better understanding of the natural history of this disease and surgical, medical therapeutic improvements over the years.

Conservative treatment must ensure the same chance of survival to that obtained by radical mastectomy, its aim being to obtain a satisfactory aesthetic result and a small risk of local recurrence. The therapeutic measures of conservative treatment for breast cancer are conservative surgery, radiotherapy and adjuvant therapy (chemotherapy, hormone therapy and molecular targeted therapy) - only in selected cases.

Conservative surgical treatment is indicated in patients with curable stages 0, I and II. This is a frequent alternative (for surgeons and patients) in the radical treatment of breast cancer.

Materials and Methods

We performed a retrospective study between January 2005 - July 2013, that included 477 breast cancer patients from the Regional Oncological Institute Iasi, who were evaluated and staged by imaging methods, in the Radiology Department at St. Spiridon Hospital, Iasi Romania.

We included in this study patients in curable stages 0, I and II; 248 (52 %) patients had radical surgical procedures and 229 (48 %) patients had conservative surgical procedures. We used the ultrasound scan, mammography, CT and MRI techniques, that diagnosed the loco-regional and distant recurrences. The statistical processing consisted in performing the chi-square test, considering a p value < 0.05 significant. We used MedCalc software version 6.

Out of 477 patients, 9 patients (1.88 %) had bilateral cancer:

- Synchronous 5 patients (one patient had bilateral, radical breast surgery, a patient had bilateral conservative breast surgery, 3 patients had one breast radical surgery procedure and conservative surgery procedure to the other breast);
- Metachronous 4 patients (one patient - radical surgery bilaterally, one patient operated conservatively bilaterally, two patients with radical surgery in one breast and conservative of the other breast).

The age distribution of our patients is shown in (*Fig. 1*). Most cases have been aged 40-70 years, with a peak incidence between 50-60 years old. The youngest patient was 21 years old and has been operated conservatively, and the oldest was 86 years old and was operated radically.

The (*Fig. 2*) shows the location of the primary tumor, the right breast being equally affected as the controlateral, without any preferential localization of neoplasia to the right or left.

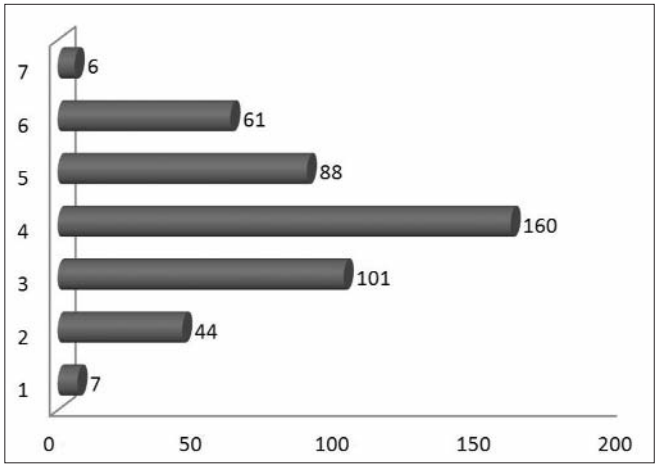

Figure 1. *Distribution by age decade.*
Legend: 1. Decade 21-30 years, 2. Decade 31- 40 years, 3. Decade 41- 50 years, 4.Decade 51- 60 years, 5.Decade 61-70 years, 6. Decade 71- 80 years, 7. Decade 81- 90 years

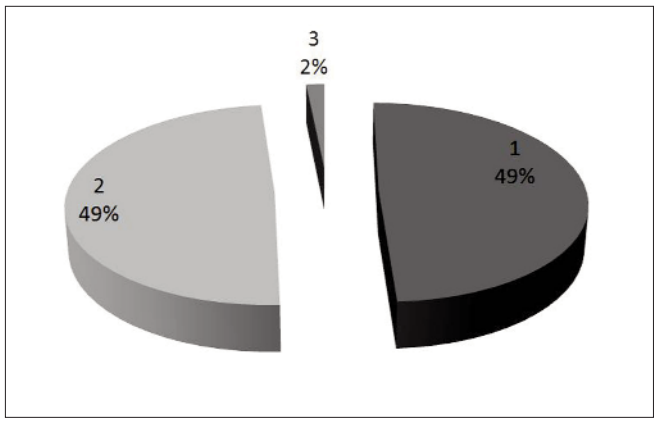

Figure 2. *Location of primary tumor.*
Legend: 1. Right breast cancer, 2. Left breast cancer, 3. Bilateral breast cancer

The types of conservative surgical procedures are shown in *Table 1*. The most common procedures were quadrantectomy with axillary lymphadenectomy (180 cases) and biquadrantectomy + axillary lymphadenectomy (37 cases).

In case of surgery with axillary lymphadenectomy and excision of a quadrant, the distribution on quadrants was as follows: upper outer quadrant 132 cases (73.33 %), supero - internal quadrant 27 cases (15 %), infero-external quadrant 11 cases (6.11%), central quadrant 9 cases (5%) and infero - internal quadrant 1 case (0.55 %).

Table 1. *Types of conservative surgery*

Types of conservative surgery	Nr. of cases (%)
Quadrantectomy + axillary lymphadenectomy	180 cases (78.60 %)
Biquadrantectomy + axillary lymphadenectomy	37 cases (16.15%)
3 quadrants + axillary lymphadenectomy	1 case (0.43 %)
Tumorectomy without axillary lymphadenectomy	11 cases (4.80 %)

In case of biquadrantectomy with axillary lymphadenectomy, the quadrant distribution was as follows: upper biquadrantectomy 21 cases (56.75 %), external biquadrantectomy 8 cases (21.62 %), internal biquadrantectomy 3 cases (8.10 %) lower biquadrantectomy 2 cases (5.40 %), central quadrant and upper outer quadrant 2 cases (5.40 %), central quadrant and infero - internal quadrant 1 case (2.70 %).

Distribution of cases according to pathology (*Table 2*) shows that the most frequently encountered histological type was invasive ductal carcinoma (IDC) - 75 % of cases, and carcinoma in situ (ductal / lobular) in 4 % of cases.

Results

The study consists in a surveillance of the radiology imaging procedures, during the period January 2005 - July 2013 performed for 477 patients, diagnosed with breast cancer in stages 0, I and II, patients treated by radical or conservative surgical procedures. The imaging surveillance was done after a predetermined protocol, both for patients undergoing surgery within 0-5 years and for patients at more than 5 years after surgery.

Patients in the range of 0-5 years after surgery were submitted to:

- mammary ultrasound scan (including the axillary region, in the case of radical mastectomy) and abdominal- pelvic echography, quarterly in the first 3 years after surgery and every six months over the next two years;
- Mammography (unilateral / bilateral), every year;
- chest radiographiess - every year;
- CT/IRM/scintigraphy - for suspected secondary lesions.

In patients with more than 5 years after surgery, every year breast and abdominal- pelvic echography, mammography, chest X-rays were performed, and in the case of a suspected secondary lesion, scintigraphy / CT / MRI were performed. Most local recurrences were diagnosed in the first 5 years after surgery: 22 cases (9.60%) patients with conservative surgery and 7 cases (2.82 %) patients with radical surgery. The difference is highly statistically significant, $p = 0.0037$. 5 years after surgery the number of local recurrences significantly decreased, but remained higher in patients with conservative surgery: 6 cases (2.62 %) patients with conservative surgery and 1 case (0.40 %) patients with radical surgery. The difference is not statistically significant, $p = 0.1$.

The local recurrence was removed 13 years after surgery in a patient with conservative surgery.

Cutaneous recurrences (lymphatic permeation) were diagnosed in the first 5 years after surgery: in 2 cases (0.87 %) - patients with conservative surgery and in 3 cases (1.20 %) -patients with radical surgery.

Nodal recurrences were more frequent in patients with conservative surgery (most commonly axillary): in 8 cases (3.49 %) in the first 5 years after surgery and in 2 cases (0.87 %) after 5 years of surgery. In patients with radical surgery, nodal recurrences were found relatively rarely: in 2 cases (0.80 %) in the first 5 years after surgery (axillary location) and in 3 cases (1.20 %) after 5 years (supraclavicular location).

Bone metastases were more frequent in the first 5 years after surgery: in 16 cases (6.45 %) - patients with radical surgery and in 11 cases (4.80 %) - patients with conservative surgery. After 5 years of surgery, their number decreased: in 1 case (0.40 %) patients with radical surgery and in 5 cases (2.18 %) patients with conservative surgery. The most early bone metastases were diagnosed in the first year after surgery, and the latest 8-9 years after surgical treatment.

Lung metastases were more frequently diagnosed in the first 5 years after surgery: in 8 cases (3.22 %) with radical surgery and in 8 cases (3.49 %) conservative surgery. Lung metastases after 5 years of surgical treatment have decreased as frequency: in 3 cases (1.20 %) for radical surgery, and in 1 case (0.43 %) for conservative surgery.

Liver metastases were more frequent in patients with conservative surgery: in 10 cases (4.36 %) for the first 5 years after surgery and in 2 cases (0.87 %) after 5 years postoperatively. In patients with radical surgery, liver metastases were found only in the first 5 years after surgery in 7 cases (2.82 %).

Pleural, mediastinal and brain metastasis were diagnosed in relatively equal figures, in a small number of patients (from 0.45 to 1 %). In patients with radical procedures, these metastases were found only in the first 5 years after surgery and in patients with conservative surgery they were found in the same number in the first 5 years after surgery and after 5 years postoperatively.

Distribution of the number of cases of local and distant recurrence for radical interventions (248 patients) is shown in *Fig. 3*, and conservative interventions (229 patients) in *Fig. 4*.

Table 2. *Histopathological types*

Histopathological types	Radical breast surgery	Conservative breast surgery
IDC	186 patients - 75 %	174 patients - 75.98%
Invasive lobular carcinoma	21 patients - 8.46 %	11 patients - 4.80 %
IDC+other histopathological types	18 patients - 7.25 %	19 patients - 8.29 %
CD / lobular carcinoma in situ	10 patients - 4 %	9 patients - 3.93 %
Mucinous carcinoma	8 patients - 3.22 %	2 patients - 0.87%
Medullary carcinoma	3 patients - 1.20 %	2 patients - 0.87 %
Papillary carcinoma	2 patients - 0.80%	7 patients - 3.05 %
Tubular carcinoma	-	2 patients - 0.87 %
Melanoma	-	1 patient - 0.43
Neuroendocrine tumor	-	1 patient - 0.43

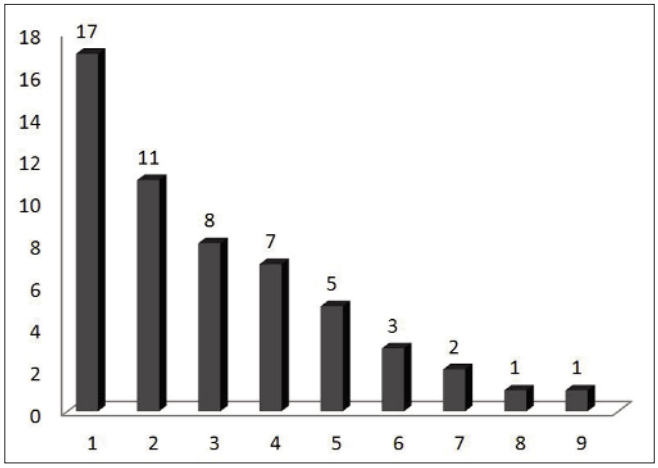

Figure 3. *Distribution of local or distant recurrences in patients with radical surgery*

Legend: 1. Bone metastases, 2. Lung metastases, 3. Local recurrence, 4. Liver metastases, 5. Node recurrences (axillary and supraclavicular), 6. Skin metastases, 7. Pleural metastases, 8. Cerebral metastases, 9. Mediastinal metastases

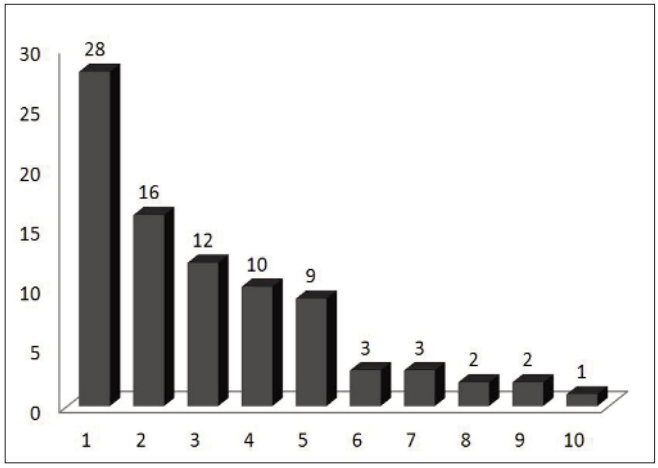

Figure 4. *Distribution of local or distant recurrence in patients with conservative surgery*

Legend: 1. Local recurrence, 2. Bone metastases, 3. Liver metastases, 4. Node recurrences (axillary and supraclavicular), 5. Lung metastases, 6. Pleural metastases, 7. Cerebral metastases, 8. Skin metastases, 9. Mediastinal metastases, 10. Peritoneal metastases

Discussions

Conservative treatment for breast cancer has become an option increasingly frequent in recent years, as a preoperative staging of breast neoplasia, according to a fixed protocol of clinical imaging. Numerous scientific papers, with retrospective and prospective studies have shown that conservative surgical procedures in breast cancer patients (with good pretherapeutic staging protocol), may be followed by similar results in terms of survival, as radical mastectomy (1). All studies conducted so far, have shown a clear difference in local recurrences, which are more common after conservative surgery than after radical mastectomy (2,3).

In the study we have performed, local recurrences are 3,5 times more frequent after conservative interventions than after radical (slightly elevated compared to the figures in the literature).

Local recurrences are easily diagnosed by ultrasound scan in the case of radical surgery. In the case of conservative surgery, due to fibrous scarring the diagnosis of local recurrence might be difficult. In our study in this case the ultrasound scan has been used (*Fig. 5*), along with mammography (*Fig. 6*), and sometimes breast MRI (4-7) or core biopsy.

Local radiation therapy after conservative surgery lowers the risk of local recurrence (8). In our study only two patients with conservative surgery did not receive radiotherapy (patients' choice).

Axillary lymph node dissection is an important prognostic and therapeutic factor. There are several theories regarding the level and the number of nodes to be excised. The standard number of 10-14 lymph dissection involves excision of axillary lymph nodes in stations I and II Berg.

For early breast tumors (less than 2 cm in greatest diameter), with no palpable lymph nodes in the armpit, the technique of sentinel lymph node biopsy has been introduced (9,10). In our study, this technique has been used in only 5 patients out of 477. In the study group 13 (5.24 %) local recurrences or lymph nodes (axillary and supraclavicular) were diagnosed after radical intervention, compared to 38 (16.5 %) after conservative interventions, the difference being highly statistically significant, $p = 0.0001$.

Risk factors for local or distant recurrence developments are: multicentric tumors, microscopic invasion in skin/nipple,

Figure 5. *Local recurrence – ultrasound appearance*

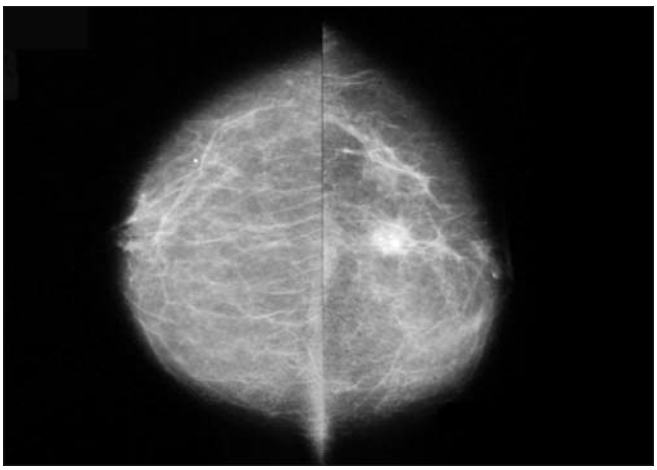

Figure 6. *Local recurrence - mammographic appearance*

positive resection margins, extensive intraductal composition, tumor emboli in lymphatic vessels, reduced degree of cell differentiation, at least 4 lymph nodes locally invaded, age 35, hormone receptor negative (ER, PR), HER -2/neu protein overexpression (11,12).

Correlation of local or distant recurrences (141 recurrences in patients with radical and conservative surgery) with hormone receptor status (RH) and Her -2/neu protein is shown in *Table 3*.

Conclusions

The imaging surveillance of patients with conservative or radical surgery for breast cancer has as first goal the diagnosis of early local recurrence, in order to improve the general survival rate. The clinical examination and imaging studies (ultrasound, breast ultrasound, abdomen and pelvis, mammography, chest radiography, CT / MRI / scintigraphy) performed after preset protocols, have to be done routinely for an unlimited period, for both situations: in the first 5 years of surgery and after 5 years of surgery.

Local recurrences are more frequent in patients treated with conservative surgery and radiotherapy than in patients with radical mastectomy. Local recurrence risk is higher in the first 5 years after surgery and then lowers, but last longer in the case of hormone-sensitive tumors. Metastases occur with approximately the same frequency in patients with conservative and radical surgery, and the most frequent sites are the bone, liver and lung.

Table 3. *Correlation of recurrences with hormone receptor status (RH) and protein –Her -2/neu*

Status RH and protein Her-2/neu	Local or distant recurrences
RH pozitive and protein Her-2/neu negative	76 cases (53.90%)
RH positive and protein Her-2/neu positive	30 cases (21.27%)
RH negative and protein Her-2/neu negative	26 cases (18.43%)
RH negative and protein Her-2/neu positive	9 cases (6.38%)

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