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Breast-Conserving Surgery in Breast Cancer

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Rezumat

Chirurgia conservatoare în cancerul mamar

Tratamentul cancerului mamar se bazează la ora actuală pe o nouă opțiune chirurgicală și anume chirurgia conservatoare a sânului aplicată cel puțin pentru stadiile I și II, evident cu intenție de radicalitate. În Clinica de Chirurgie CF Craiova am început practicarea protocolului conservator de tratament al cancerului mamar în stadiile I și II în urma cu 16 ani și am realizat până în prezent un număr de 303 operații conservatoare dintr-un total de 673 cazuri de cancer mamar. Am înregistrat 12 recidive locale (3,96%) și 2 decese ca urmare a evoluției neoplaziei. Protocolul include rezecția tumorii primare împreună cu suficient țesut sănătos din jur, pentru a asigura margini negative piesei de rezecție, la care se asociază obligatoriu radioterapia postoperatorie pe sân. Chimioterapia și hormonoterapia au fost indicate de medicul oncolog, în funcție de o serie de parametrii postoperatori: mărimea tumorii, invazia ganglionilor axilari, vârsta pacientei, etc. Scopul acestei lucrări este de a aduce în prim plan rezultatele și experiența noastră modestă, dar mai ales de a atrage atenția asupra rezultatelor obținute prin urmărirea pe termen lung a pacientelor operate conservator în două protocoale operatorii prospective, de care lumea chirurgicală nu poate să nu țină cont și care au demonstrat aplicabilitatea largă a tratamentului chirurgical conservator. Concluzia studiului este că indicația chirurgiei conservatoare în stadiile I și II are o largă aplicabilitate, cu rezultate similare mamectomiilor radicale, singurul factor important fiind obținerea unui rezultat cosmetic satisfăcător, condiționat în principal de raportul tumoră/sân.

Cuvinte cheie: chirurgie conservatoare, cancer mamar, dimensiune tumoră

Abstract

The breast cancer treatment is based nowadays on new surgical options: breast-conserving surgery, which applies at least for the first and second stage cancer, with radical intention. We have been practicing breast-conserving surgery for the last 16 years and we have performed 303 breast-conserving operations from a total of 673. We recorded 12 local recurrences (3,96%) and 2 deaths due to cancer progression. Our protocol includes removal of the primary tumor with enough surrounding tissue to ensure negative margins of the resecable specimen, associated with axillary limph-node dissection and postoperative breast irradiation. Our oncologist indicated chemoterapy on different postoperative conditions: tumor size, axillary limph node involvement, patient's age, etc. The purpose of this paper is to emphasize our modest experience, nevertheless to draw the attention on important results, obtained by long-term monitoring of the patients who underwent breast-conserving surgery, in a two prospective protocols, and demonstrate the importance and applicability of breast conserving therapy. The conclusion of this study is that breast-conserving surgery followed by breast irradiation is reliable, as the results are similar with radical mastectomies; the main objective is to obtain a good cosmetic result, which depends on tumor size / breast size.

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Key words: conservative surgery, breast cancer, tumor size.

Introduction

Breast cancer represents a very important public health issue, having both high incidence and high prevalence worldwide; at the present day, 20-25% of all malignant pathology in women is represented by breast cancer and not to mention that 15-20% of all cancer related deaths are caused by breast cancer. (1,2)

From a therapeutic point of view, surgical intervention continue to be the centre of breast cancer therapy, although important progress has been made when it comes to the role of chemotherapy in treating breast cancer. Although, at the moment, there is a tendency when it comes to the surgical approach in treating breast cancer, to switch from an older model of "the more the better", to a newer one that advocates for a more conservative approach with good effectiveness. Therefore, although we can see a decrease in the number of mutilating interventions in Romania, there is still a hesitation when it comes to treating breast cancer using conservative surgical approaches.

The latest studies, mostly prospective studies, have clearly showed, using a significant number of patients that even as early as 20 years old, using conservative surgery (lumpectomy + quadrantectomy + lymphadenectomy + breast postoperative radiotherapy) used in stages I and II of breast cancer has similar effects, when it comes to overall life expectancy and cancer free interval, to those of radical mastectomies.

The only real counter-argument, brought against conservative techniques, is the high number of local recurrences, but associating postoperative radiotherapy has shown to significantly reduce their numbers, so in conclusion we can say the only opponent of the use of conservative surgery in breast cancer is the "conservative view" of some surgeons. (3)

We can strongly say that, at the present day, it is unacceptable that patients diagnosed with breast cancer stages I and II, do not have conservative surgery mentioned amongst the therapeutic approaches. (4)

Material and Method

We used as a method for our study, retrospective analyses of all clinical notes and oncologic reports from all patients that have undergone a conservative surgical procedure following a diagnosis of breast cancer. We used as a setting, patients treated in Surgical Department IV (CF Hospital) Craiova.

Patients we looked at were hospitalized and treated between 1995 and 2010. In all cases the intervention was performed using the surgical protocol developed by "Istituto Clinici di Perfezionamento" of Milan, Italy. The surgical intervention is performed with the intent of being a radical intervention and is used for managing malignancies in stages I or II (T_1 N_0,1 M_0 or T_2(< 3 cm) N_0,1 M_0) (segmentectomy + lymphadenectomy + breast radiotherapy, postoperative if N+ and adding chemo and hormonotherapy, if N- the suggestion is monitoring and regular follow-ups).

The exact use of the protocol was done only in the first 3 years. After that, encouraged by both literature data and our own personal results (lack of local recurrences), we extended the use of conservative interventions to malignant tumours above 3cm and up to 5cm in dimensions, as we showed in *Table 1*.

The tumour size was determined by using a combination of data obtained from the mammography, ultrasound and clinical examination.

With regards to malignancies in stage T_{4b}, in the 7 cases

Table 1. *The size of the primary tumor for which conservative surgeries were performed*

Year	T< 2 cm	T between 2-3 cm	T between 3-5 cm	T 4b
1995	8	4	-	-
1996	7	5	-	-
1997	9	6	1	-
1998	11	5	3	-
1999	7	7	6	-
2000	12	7	2	-
2001	10	5	3	-
2002	11	7	3	2
2003	7	6	4	-
2004	6	4	3	-
2005	7	5	6	-
2006	5	7	4	1
2007	6	5	7	1
2008	10	6	13	2
2009	7	9	12	1
2010	3	5	8	-
TOTAL	126 (41,58%)	94 (31,03%)	76 (25,08%)	7 (2,31%)

mentioned, there were tumours of 2 cm in size, in 4 of the cases and 4cm size in remaining 3 cases, which were infiltrating the above dermal layers. For these cases pre-operative chemotherapy was used.

The monitoring period ranged between 1 and 16 years. In a number of 86 cases the monitoring failed (patients opted to receive oncologic treatment in a different clinic or patients failed to attend follow-up appointments). We managed to monitor a number of 210 patients for periods ranging from 10 to 16 years. On top of the 86 cases, for which there is a lack of data, we had two deaths, due to the rapid progression of the malignant process, and also 5 patients died due to other causes, unrelated to the diagnosis of breast cancer.

The demographic details are shown in *Fig. 1*, and the age distribution is shown in *Fig. 2*. As you can observe there was one incidence peak around the 40-50 years interval and another one around the 60-70 years interval.

In the first 3 years of the study there is a huge prevalence of stages I and II of malignancy. Starting from 1998 we began practicing conservative breast surgery for cancers diagnosed in stage III of evolution, and also for cancers up to 5 cm in size combined with axillary adenopathy (29 cases with adenopathic blocks – N_2) and 7 cases of stage T_{4b}, in all of the above cases adding the pre-operative chemotherapy, distribution of the stages is presented in *Table 2*.

10 patients (3.30%) diagnosed in stage 0 (carcinoma in situ) of the disease have received conservative intervention, following a more aggressive attitude towards sclerocystic mastosis, allowing us, as a consequence, to identify a more relevant number of patients in incipient stages of the disease.

As far as the distribution of the sites of malignancy we encountered: upper outer quadrant in 160 cases (52.8%), upper inner quadrant in 49 cases (16.18%), lower outer quadrant in 47 cases (15.51%), lower inner quadrant in 26 cases (8.58%) and central/areolar quadrant in 21 cases (6.93%).

We give a brief description of histopathological types of carcinomas that we encountered in *Table 3*. In 17 cases we diagnosed areas of in situ carcinoma associated with invasive carcinoma, and in 8 of the cases with in situ carcinoma the extemporaneus histopathological examination, using paraffin inclusion techniques, has revealed areas of invasive carcinoma.

During axillar lymphadenectomy, we removed and examined histopathologically, between 5 and 18 axillary lymph nodes, located on the same side as the malignant process; between 1995 and 1998 it was routine practice to surgically remove lymphatic stations I and II, which later extended to removing the III rd station as well.

In case of removed axillary lymph nodes, the examination revealed invaded lymph nodes in 145 from 210 cases we studied. From 145 cases, in 68 cases the axillary lymph nodes were invaded as this was associated with tumour size below 2 cm (30% of all tumours under 2 cm in size have been associated with lymph node metastasis); in 8 cases of in situ carcinoma, micro metastases were found in the lymphatic station I. From 145 cases with axillary invasion, 29 cases showed an isolated invasion of lymphatic station II, with no invasion of the lymphatic station I; in 1998, when we started

Table 2. *Evolution stages for which we performed breast-conservative surgery*

Stage	0	I	II	III
No of cases	10	109	148	36
%	3,30	35,97	48,84	11,89

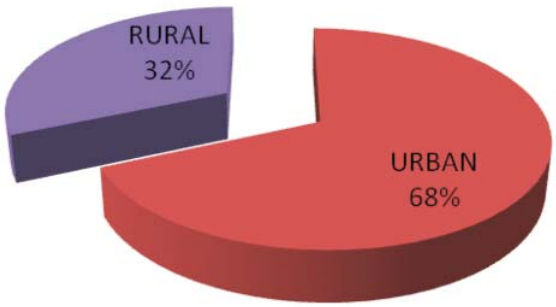

Figure 1. *Cases repartition according to demographic data, appartenance to rural / urban environment*

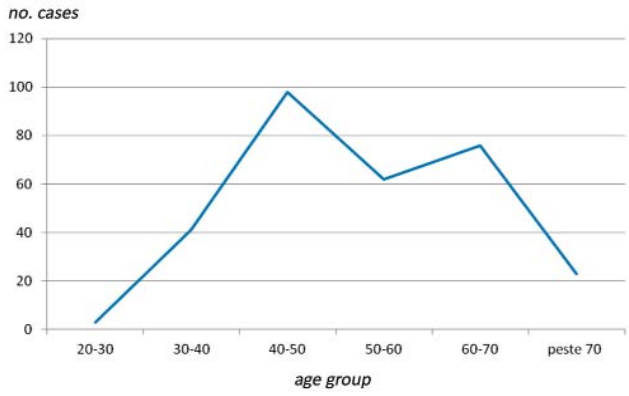

Figure 2. *Age group repartition*

Table 3. *Histopathological types of mammary carcinomas encountered*

Hispathologic type	Number of cases	%
Ductal in situ	12	3,96%
Lobular in situ	3	0,99%
Ductal invasive	183	60,39%
Lobular invasive	50	16,5%
Medullary	10	3,30%
Colloide	8	2,64%
Papillary	7	2,31%
Tubular	7	2,31%
Mixt (Ductal + Lobular)	3	0,99%
Trabecular	6	1,98%
Muciparous	4	1,32%
Cribriform	4	1,32%
Comedocarcinoma	4	1,32%
Paget disease	1	0,33%
Angiosarcoma	1	0,33%

to perform lymphadenectomy on lymphatic station III as well, we recorded 12 cases with metastases situated at the top of the axillary region.

Between 2001 and 2002, we practiced conservative surgery for type N2 adenopathies as well, after first administering neo adjuvant chemotherapy.

We also performed lymphadenectomy in 9 cases that have undergone conservative surgery in another surgical department (only segmentectomy has been performed), and in 5 of these cases we discovered that axillary region was invaded by the malignant process.

In combination with the surgical treatment of the primary tumour and lymphadenectomy, we suggested, in collaboration with the Oncology Department that all patients undergo radiotherapy, following a standard protocol; chemotherapy and hormonotherapy have been suggested by the oncologist in cases with axillary invasion or in the absence of other histopathogical markers associated with a negative prognosis (peritumoural intravascular or lymphatic invasion, moderate or poorly differentiation factor).

Thus, the complete therapeutic protocol comprised of postoperative radiotherapy aimed at the mammary gland, with a dose of 5000 cGy, adding an extra dose of 1000 cGy it aimed strictly at the tumour bead.

The chemotherapy protocols are comprised of:

- CMF: Cyclophosphamid (600 mg/m^2) in day 1 + Methrotexat (40 mg/m^2) in days 1 and 8 + 5-Fluorouracil (600 mg/m^2) in days 1 and 8 of the protocol; 6 therapeutic sessions were performed with a 3 week pause.
- FEC: 5-Fluorouracil (600 mg/m^2) in day 1 + Epirubicin (60 mg/m^2) in day 1 + Cyclophosphamid (600 mg/m^2) in day 1; we administered 6 therapeutic sessions with a 3 week pause.

Depending on the therapeutic response, Navelbine, Gemcitabine and Xeloda can be used as well.

For HER2 positive patients, we performed chemotherapy in association with Herceptin (Trastuzumab) administration. For patients with positive estrogens and progesterone receptors, they must continue with hormonotherapy after the chemotherapy has been administered following the protocol:

- pre-menopause patients can benefit by: surgical ophorectomy, ovarian irradiation, chemical castration (Goserelin acetat; Triptorelin, Buserelin, Leuprolin) and Tamoxifen;
- post-menopause patients can benefit by: Tamoxifen, Aromatase Inhibitors (Anastrazol, Letrozol, Exemestane) and progestatives.

For patients who have been identified as having metastases we recommend molecular therapies aimed at the vascular growth factor (VEGH) - Avastin (Bevacizumab) associated with Paclitaxel. For patients with bone metastases we recommend bisphosphonates treatment (Clondronat, Bondronat, Acidum Zolendronicum).

Results

Between 1995 and 2010 in Surgical Department IV (CF Hospital) of Craiova, there was a total number of 303 breast conservative surgical interventions for stages I, II and III of breast cancer, from 673 cases of breast cancer; there was the possibility to follow a total number of 210 patients for periods ranging between 1 and 16 years.

Starting from 2000, we also started practicing extemporaneus histopathological examination using the margins of the remaining cavity after segmentectomy; as a consequence, we identified 11 cases that, although they seemed suitable for conservative treatment, we were able to identify malignant cells remaining in the margins of the surgically removed piece and in the remaining cavity also, which led us to the conversion of the segmentectomy in a Madden type mastectomy.

During the immediate post-operative evolution there were no records of fatalities. Following the patients for a longer period of time we recorded 7 deaths, 2 caused by the direct evolution of the malignancy and 5 deaths not related to the malignancy.

The post-intervention evolution was complicated by the following:

- post-operative oedema of the breast in 23 cases (7,6%); the complication was noticed at intervals ranging from 1 to 10 months after the intervention.
- arm swelling in 7 cases (2,3%); the onset was acute in 1 case (3 weeks post-surgery), in all the other cases the interval ranged up to 9 months after intervention;
- false recurrences in 9 cases (2,9%):
  - in 5 cases we discovered imprecisely delimitated tumours, 3 located at the site of the post-segmentectomy scar and 2 at the site of the axillary scar;
  - nipple sanguinolent discharge in 2 cases;
  - mastalgia associated with breast post-surgical oedema in 2 cases.

In these 4 last cases mastectomy was carried out at patients' request:

- true recurrences in the breast already affected occurred in 12 cases (3,96%), in all of these cases, patients failed to respect the suggested protocol (they didn't receive radiotherapy).

In one case, 2 years after the conservative breast intervention, a cervical neoplasm was diagnosed, for which she received appropriate treatment. There was no evidence of any recurrence of the breast cancer.

In one case we noticed the development of a supraclavicular adenopathy post-operative, but which was spontaneously resolved. At that time, the patient was undergoing chemo and hormonotherapy.

Discussions

Breast conservative surgery was first developed over 40 years ago, as an alternative to more mutilating procedures, like Halsted procedure and even supra-radical mastectomies, which were often followed by severe functional impairment and stigma not to mention, sometimes disappointing long-term results. The lack of any lengthy prospective studies did

not allow the popularisation and establishment of any clear indication criteria for the use of conservative techniques in treating breast cancer.

In the last few years a lot of papers have been published, especially prospective studies, that demonstrate based on significant numbers, followed for more than 20 years, that patients undergoing breast conservative surgery (removal of tumour within safety margins, the association of axillary limphadenectomy and radiotherapy), can benefit by similar results when it comes to overall survival rate then the ones having radical procedures. On top of that we add the cosmetic benefits, a reduction of post-operative complications especially those directly linked to surgical act, not to mention a better compliance from patients, as they get to keep their breast and their femininity (3,5,6,7).

Although some authors report data similar to those reported for mastectomies, when it comes to overall survival rate in case of conservative interventions, there are still preconceptions when it comes to the surgical intervention of the initial tumour and that of the axillary region, and related also to other therapeutic interventions associated with surgical act (8,9).

Problems relating to surgical removal of primary tumour

When it comes to the surgical removal of the primary tumour there are a few problems arising, related to the different terminology used to identify different types of interventions performed, and relating to the width of the surgical excision and the control over the remaining cavity in order to insure a good control over the local expansion of the malignancy. (8,10)

The authors that mainly use conservative breast surgery for stages I and II of breast cancer, use various terms to define the extent of the mammary resection: tylectomy, lumpectomy, segmentectomy, quadrantectomy, segmental mastectomy. None of these terms is complete consent, just by their definition, lumpectomy and tylectomy imply both the surgical removal of the tumour and of a certain width of healthy tissue, without actually mentioning the exact extent of the resection. Segmental mastectomy is not anatomically justified (the breast does not have a segmental structure, unlike other organs), and the term quadrantectomy is considered, by some authors, to be a bit exaggerated, as it involves both the removal of the primary tumour and 2 cm of the surrounding healthy tissue, with poor results from a cosmetic point of view.

We prefer the term conservative mastectomy with radical intent for stage I and II breast malignancies, and palliative conservatory mastectomy for more advanced stages, where conservative surgery is still an option (for the last category we used to utilize the term atypical toilet mastectomy). (11)

As a direct result of contradictions we identified in various terminologies, there is another problem arising, that has not been entirely clarified, and we are talking about the extent of the breast peritumoural excision as well as the exact indication of conservative surgery reported to tumour size and breast volume.

Veronesi is using conservative surgery for breast tumours under 2 cm and is also performing the excision of 2-3 cm of peritumoural healthy tissue together with the above dermal layers and the underlining pactoralis major fascia; this resection, resulting in the removal of one of the breast's quadrants, allows a good local control of the malignancy, but sometimes the cosmetic results are compromised by the extent of the mammary resection. (3,7)

On the other hand, Fisher obtains similar results when it comes to local control by removing the tumour with enough peritumoural tissue to ensure negative resection margins (1 - 1,5 cm) adding better cosmetic results as well, he also manages to extent the conservative surgical indication for tumours above 2 cm and up to 4-5cm in diameter. (5,12)

The protocol we use in our Surgery Clinic is the practice of the excision of the primary tumour together with approximately 1,5 cm of healthy tissue; starting from 2000 we practiced ordinarily the extemporaneous histopathological exam from the margins of the removed piece, but more importantly from the walls of the remaining breast cavity especially if the tumour has been poorly delimited; using this protocol we managed to identify 11 cases where, although conservative surgery was feasible we found invaded margins and remaining microscopic positive tissue in the remaining cavity. In cases where tumour was well delimited from the surrounding glandular tissue and we were sure of the complete tumour excision together with enough healthy tissue (approximately 2 cm) we did not take samples from the walls of the remaining cavity for the histopathological examination. Although there are authors who suggest that the rate of local recurrences is not greater for patients with positive margins compared to those with negative margins or even with borderline margins, especially if the tumour presents estrogens receptors (estrogen-receptor positive), our limited experience and practically the impossibility to determine ordinarily the presence or absence of estrogens receptors in the tumour, have determined us to perform in all of these cases a radical modified Madden mastectomy. (13)

When it comes to the indication of the conservative intervention we guide ourselves not only by the size of the tumour, but rather by the proportion between the size of the tumour and the volume of the breast; the main purpose of the conservative surgery is that of good local control of the malignancy balanced with a satisfactory cosmetic outcome. We had cases where we could extend the indication of the conservative intervention to large tumours (approximately 4 cm in diameter), but we also had cases where we could not perform the intervention for small tumours, of approximately 2 cm in diameter, but for patients with a small breast volume, thus the excision of such a tumour in a breast with a total diameter of approximately 5 cm, would have resulted in a bad cosmetic outcome, wherefore we preferred to perform a mastectomy.

As a practical consequence, the indication for the conservative intervention and the size of the removed fragment are based not on the size of the tumour, but on the proportion between breast and tumour, and afterwards on

the presence of negative resection margins and negative walls in remaining cavity. That is way we prefer the term conservative mastectomy, as an initial quantification does not have necessarily a practical consequence (in a small breast a 3-4 cm tumour treated conservative can lead to a "hemi-mastectomy", while the same size tumour, located in a larger breast can be treated by using a segmentectomy). (11)

Concerning the size of the tumour in proportion to the breast we did not encounter any particular difficulties for those located in central region, considered by some authors as a relative contraindication to conservative surgery, our patients considering the removal of the areola and the nipple (mandatory in this type of localisation) as a more acceptable solution then the mastectomy. (3-5)

Regarding the histologic type of malignancy, we were unable to find reasons against practicing conservative surgery in lobular cancers; it is true that sometimes we found this particular type of cancer in more aggressive local-regional forms (from 50 cases of lobular carcinoma, we found massive lymph node metastases in 21 cases, from these 21 cases, 9 had the primary tumour under 2 cm), but this local and regional aggressiveness might be another argument in favour of using conservative techniques, as the patient's prognosis is not determined by the aggressiveness of the surgical act but rather by the presence or absence of the lymph node invasion. As a matter of fact the recurrences we had were related to a more common type of cancer, invasive ductal carcinoma rather than lobular forms. Given the evidence we cannot find the justification for an aggressive surgical act in the presence of an axillary or systemic disseminated cancer. (9)

We always associated ipsilateral axillar limphadenectomy and post-operative radiotherapy with the conservative breast resection; as suggested by the oncologist we also used adjuvant therapy (chemo and hormonotherapy) for patients with positive axillary lymph nodes or invasive forms (CMF or FEC protocols).

When it comes to surgical technique elements, we approached the tumour without actually respecting a strict rule, as Veronesi is using for example, but we rather tried to adapt the incision type to every particular case. There were situations where a tumour located in the upper outer quadrant was removed using the same incision used for the lymphadenectomy (either the same radial incision, or a curved incision used initially for the breast tumour and extended afterwards in a "rocket tale" to perform lymphadenectomy). For the other quadrants we used a curved incision. For tumours located in a central position we removed them using a circumareolar incision.

The problem of lymphadenectomy in the conservative surgery of breast cancer

Axillar lymphadenectomy is performed ordinarily in all conservative interventions, no matter the histologic type of the tumour.

We entered the axillary region through a vertical incision on the external margin of the pectoralis major, adapting the length to every case; the guidance for the axillary dissection was the axillary vein, performing the axillary dissection and lymphadenectomy at once, starting from the top and moving towards the base of the axillary region, marking the stations, considering their prognostic significance. We avoided the lateral thoracic nerve and thoracodorsal nerve, and whenever possible we kept the subscapular vascular pack (when we could not find any adenopathies along those vessels). We usually perform the axillary drain after lymphadenectomy, with 3-4 drain tubes arranged in "pan flute" according to Chiricuta, without connecting the tubes to an aspiration system. Lymphorrhagia lasts usually around 10 days, after which we begin the progressive removal of drain tubes. We do not use the post-operative immobilizing of the arm, but on the contrary, we recommend an early and active mobilizing. Without having done any statistic measurements on this, we can say from our own experience, that this technique is more satisfying than the one we previously used, until 1986, that usually ended up in more frequent development of axillary lymphoceles, that involved repeated drainage techniques.

We perform ordinarily this dissection method of all the axillary lymph node stations, because it offers both significant prognostic elements (invasion of lymph node station III - bad prognostic element), but it also allows a qualitative local control over the malignant process.

The concept of sentinel lymph node derives from the hypothesis that the lymphatic fluid from the anatomical region that hosts the tumour drains in a particular lymphatic region, and afterwards sequentially draining in other lymph nodes.

Whenever lymphatic dissemination of the malignancy occurs, the invasion occurs firstly in one lymph node (rarely more than one) located on the drainage way. This lymph node, which is the first one to be invaded, was named sentinel lymph node. It represents the mirror of the state of regional lymph nodes. (14)

To establish a lymphadenectomy indication and to avoid an unnecessary procedure (N-), the only correct method is identifying and dissecting the sentinel lymph node, something that can be obtained by using vital dye, radioactive tracer or associating the two techniques.

The technique of identifying and dissecting the sentinel lymph node with radioactive tracer implies: pre-operative lymphoscintigraphy, identifying the sentinel lymph node and excisional biopsy; intra-operative histopathological examination both with paraffin inclusion and immunohistochemic of the sentinel lymph node. (14)

Our attitude towards the sentinel lymph node, and we add that we were unable to find in our literature search, one common attitude, is that performing a selective axillar lymphadenectomy, is a dangerous practice because:

- pTNM stadialization is based on the status of axillary lymph nodes that dictates both the prognosis and the consequent therapeutic approach (chemotherapy).
- recurrence on the remaining breast is easier to diagnose and treated surgically compared to axillary recurrence which is diagnosed later and on many

occasions the lymphadenectomy is difficult and even impossible to perform;
- sentinel lymph node does not have a 100% specificity and sensibility;
- arm swelling as a complication of lymphadenectomy is not a solid argument for the conservative attitude towards the axillary region, because according to our data, the incidence of this occurring is very small (2,3&).

We also have to mention that axillary lymphadenectomy has more prognostic significance, and from a therapeutic point of view it is important because of local and axillar control of the disease and because it helps with the indication of adjuvant chemotherapy. The radical intent of the axillary lymfadenectomy is sometimes questioned, when it comes to treating breast cancer, but the exclusion of one of the main lymph stations - internal mammary lymph nodes. There are authors that have showed that the invasion of axillary lymph nodes is proportional to the invasion of internal mammary lymph nodes. Veronesi thinks that, no matter the localization of the tumour, and especially if the tumour is located in the centre of internal quadrants, the chances of metastases in internal mammary lymph nodes are similar to those of this happening in ipsilateral axillary lymph nodes. (9,10,15,16,17)

When it comes to post-surgical complications following the conservative techniques, we encountered a complication that we believe is very specific to this type of intervention: the post-surgical oedema of the breast. The post-surgical oedema of the breast has been noticed at variable intervals following the primary conservative intervention, intervals that have ranged anywhere up to 1 year. The majority of the cases were noticed in the first 3 months after surgery and this was always triggered or accentuated by the radiotherapy. The intensity of this complication was variable, in most of the cases there was a moderate swelling of the breast, but we also had cases where clinical picture mimicked a true "carcinomatous mastitis". In the first 2 cases, that presented in this manner, impressed by the general aspect of the breast, we decided to do a mammography, followed by puncture of denser area (as we would do for a carcinomatous mastitis), but the results were negative; not to mention, that one of the patients, with this type of clinical picture, presented herself to be assessed in a surgical unit, that did not perform conservative surgery, and where, due to a possible diagnosis of carcinomatous mastitis they performed mastectomy (probably after inconclusive puncture results). Later the histopathological examination failed to reveal any malignant tissue in the removed breast.

We believe that this complication, specific to conservative techniques, has a lymphatic pathogenesis, relating to the interference with the lymphatic axillary drainage of the breast. This probably happens during the lymphadenectomy; we relate different presentations of this kind of complication to the individual variability of the disposition of the lymphatic system in the breast (the compensation of the lymphatic circulation via the internal mammary and accessory drainage system of the breast, left untouched).

Breast oedema signaling, 3 months after the primary surgical intervention, so after the beginning of the radiotherapy, also pleads for the hypothesis that this oedema could be more a complication of the radiotherapy rather than the initial conservative surgery.

The intensity of the oedema, decreases gradually, sometimes helped, without having enough data to support this, by anti inflammatory medication and vascular trophic medication (Detralex).

The arm oedema ("thick arm") following surgery, has not been a significant problem in our case – only 7 cases (2,3%), but of low intensity, without any problems related to the therapeutic approach or the use of the arm; more, this complication cannot be a associated with conservative techniques, as it is seen following all surgical techniques that involve axillary lymphadenectomy (including radical interventions in breast cancer).

The problem of local recurrences following conservative breast surgery

Post-surgical follow-up must consist of: clinical examination every 3 months for the first 2 years, every 6 months for the following 3 years and once a year after this period, also mammography and breast ultrasound, imagistic investigations for symptomatic patients (CT, MRI, bone scintigraphy), CA 15-3, puncture with citology or biopsy followed by histopathologic examination where there is a high suspicion of recurrence. (18)

If regarding the overall long-term survival rates, all authors agree that there are no significant differences between the radical mastectomies and the conservative techniques for cancers in stages I and II, when it comes to local recurrences, most of the authors who practice conservative techniques, admit the higher rate of local recurrences linked with this surgical technique. (1,3,4,5,6)

Still, even in this case, there are important differences between the reports of the surgeons that use conservative breast surgery, when it comes to the frequency of recurrences. More so, there are differences in defining local recurrences: Veronesi defines as local recurrence only tumours that appear, following surgery, on the same site as the primary tumour (on the post-surgical scar or 2 cm around it), while tumours that develop in different quadrants, other than the one the patient has surgery on, are considered primary ipsilateral tumours (as an argument, from the statistic data of the same author, the fact is that the incidence of tumours in a different quadrant from that operated on, is similar with tumours occurring in the counter-lateral breast). (3,7)

No matter how they define local recurrence, all authors agree that the incidence of this happening in the same breast, is higher if the patient has not received radiotherapy after surgery, compared to cases where post-surgical radiotherapy was performed (*Table 4*). The differences can be explained by both different manners of defining local recurrences and the type of primary intervention the surgeon practices (quadrantectomy - Veronesi, lumpectomy - Fisher). In conclusion, it is obvious that the risk to develop a local recurrence is higher for patients

Table 4. *The incidence of local recurrences with/without post-operative radiotherapy in conservative surgery*

Author	Recurrences without RT	Recidive after RT
Veronesi	8,8%	0,3%
Fisher	39,2%	14,3%

who have not benefited by post-surgical radiotherapy.

Another factor associated with higher risk of developing recurrences, was in all studies, the young age of the patient (under 45 years). Regarding this, Veronesi gets after performing simple quadrantectomy a recurrence rate for 10 years of 17,5%, for patients under 45, compared to only 3,5%, for patients over 45. This aspect raises two problems: explaining the phenomena and necessity of post-surgical radiotherapy for elderly patients. Probably, the higher incidence of recurrences in young patients is due to some biologiocal features of breast cancer, as we now it tends to be more aggressive when diagnosed in young patients, but at the same time it can be due to a more limited resection, hoping to obtain a better cosmetic result.

Other factors that predispose to developing local recurrences, after conservative breast surgery, but less evident in their role, are: the large size of the tumour, positive resection margins (variable parameter, according to some statistic data only this becomes a risk factor if it is associated with a lack of estrogens receptors in tumour cells and not receiving radiotherapy as part of the treatment); the presence of vascular and lymphatic invasion, the low degree of tumour differentiation; the invasion of axillary lymph nodes (variable parameter as it is involved in recurrences after radical mastectomies as well). (3,5,6,7,9,12,16)

As far as we are concerned, we considered as local recurrence, a tumour developing in the operated breast, no matter the localization: we had a total number of 12 "true" local recurrences from 210 patients we followed for intervals ranging from 10 to 16 years after surgery (3,9% recurrence rate). In all cases patients did not follow the complete therapeutic protocol, not having radiotherapy. The recurrences where noticed at variable intervals after the primary intervention, ranging from 8 months to 2 years.

The treatment option for local recurrences was modified radical Madden mastectomy. We found cases in literature, where authors have opted for re-excision (conservative technique) plus radiotherapy to treat the recurrence. (3,5)

False local recurrences can become a problem as they can compromise the confidence of the patient in the conservative surgery; we encountered this situation in 2 cases, in both the outcome was performing unnecessary mastectomies, which were requested by the patient for there on mental comfort offered by the perspective of being clear from an oncologic point of view. In one case there was a sanguinolent nipple discharge after surgery and in the other case there was the presence of mastalgia associated with a degree of breast oedema that frightened the patients. In both cases the histopathological examination failed to identify any malignant tissue in the breast removed following the second intervention. We encountered false local recurrences in other 5 cases, which were represented by tumour masses with sizes ranging from 2 cm to 4 cm. The diagnosis was established using a histopathologic exam (in 4 of the cases, following the removal of the mass, and in 1 case a combination of negative citology following surgical puncture and tumour disappearing after anti inflammatory medication).

Looking at the mortality rates, we had 2 deaths (0,6% deaths due to breast cancer), in patients that had undergone conservative surgery for what it was assumed to be a stage II cancer, but later it developed rapidly with a true "explosion" of metastases both bone and visceral, which have lead to fatalities; we cannot blame these deaths as surgical technique (whether we use conservative or radical techniques the case was already inoperable at the time of intervention), being more an error of pre-surgical stadialization, both due to the disease itself and the lack of pre-surgical investigations.

We had 5 more deaths (1,65%) caused by other factors than cancer, but it would be reckless for us to come up with the conclusion about the global mortality rate, as we only followed a small number of cases, for a long period (only 83 cases were followed at 16 years post-intervention).

Discussions about the indication of conservative surgery in breast cancer management

Until now there were a number of studies published, regarding the indication for conservative surgery in stages I and II of breast cancer; all conclude that using conservative surgery does not influence in a negative way, the overall survival rate at long distance after the primary intervention, and that although a higher rate of local recurrences, compared to mastectomies, this does not have a negative impact on the overall survival rate, and therefore does not justify abandoning the techniques. More so, the results of the study that Veronesi, performed, over 20 years has allowed him to say: "This result (referring to the similar survival rate at 20 years interval between conservative surgery and Halsted mastectomy) should shatter every doubt that still hangs around the use and safety of conservative surgery as treatment for breast cancer". (3,4,5)

We consider that at the present day, based on important data provided by different authors, and on our modest experience, conservative surgery should become the elective treatment option for stages I and II of breast cancer, the surgical attitude towards cancer in these stages dividing surgeons into "radicals" and "conservatives".

Once the surgical indication for stages I and II is established, there is also the issue of the indication of conservative techniques (conservative mastectomies and axillar lyumphadenectomy) for more advanced stages such as stage IIIa and IIIb - the notion of palliative conservative mastectomy. (11)

We consider this as being logic, especially in stages with large lymph node blocks and small tumour, where we can use conservative surgery, or for smaller tumours in stage T_{4b}.

The first argument for using these techniques, in these

inoperable cases, is not so much an aesthetic one, but rather a surgical one - a more limited intervention, shorter in length and with fewer post-surgical complications, for patients are often very frail medically and try and avoid such complications (as ulcerated, infected and bleeding tumours); similar for lymphatic blocks that can share the same complications.

Also, sometimes, palliative conservative mastectomy seems a necessity, offering a way to deal with some technical intra-operative problems (having to solve large skin defects, as a consequence of radical mastectomies, that would imply future skin grafts).

In stage IIIa cancers (small tumour and axillar lymphatic block, and even T3 tumours that respond well to chemotherapy and decrease in size), the use of conservative surgery can again have curative intent, especially if the initial response to chemotherapy was a good one, situation where we can hope for a better therapeutic result.

In cases with small tumour and axillar lymph block there is no indication that mastectomies are superior to conservative surgery, as the main issue is "cleaning" the axillary region, something that can be addressed just as well by using conservative surgery.

Usually when we aim for a good aesthetic result we recommend conservative mastectomy; in this way we consider radical mastectomy (modified or not) as an alternative to conservative surgery, when this is contraindicated, and the main contraindication for conservative surgery is a poor aesthetic result, obtained after ensuring negative resection margins. In this case using reconstructive breast surgery seems a viable alternative. (19,20)

Our attitude in stage IV breast cancer is: when the malignancy spreads outside the breast area (pulmonary, hepatic, bone, brain metastases etc.) and the breast/tumour proportion is a favourable one, we think that radical mastectomy does not bring further benefits for the patient compared to the conservative surgery, as the prognosis in this case is dictated by the metastasis and not by local tumour.

Summarizing we can say that there are still a few mismatches in the treatment of breast cancer, due to relative things related to:

- the width of the mammary excision, that we discussed earlier and we made our point of view clearly: we prefer conservative approach, no matter the size of the tumour, if the aesthetic result is good after ensuring negative resection margins (an aspect that is dictated by the tumour/breast size proportion);
- mismatches related to the pre and post-operative stadialization: pre-operative palpable adenopathies or intra-operative apparently invaded lymph nodes are nor always confirmed by the histopathologic examination, which leads to a supra-stadialization, not always also, the size of the tumour is directly related to the degree of regional or systemic extent;
- the manner where extemporaneus histopathological examination is carried out and even inclusion paraffin techniques are very important for an accurate evaluation of the resection margins, and especially the impossibility to do the examination of the post-segmentectomy cavity walls is important;
- the correctness of the stadialization is relative and usually retrospective. Anyway it is almost impossible, even with histopathological arguments, to ensure a truly radical surgical act; radicality and stadialization are usually determined retrospective.

Conclusions

1. The conservative treatment of stages I and II of breast cancer represents a viable option that offers patients same post-surgical survival chances as more mutilant surgery.
2. The essential element that needs to be considered in applying conservative surgery in the treatment of breast cancer, besides the patient's option, is the proportion between size tumour and breast size; therefore, an arbitrary attitude is avoided where there are maximum tumour sizes that indicate conservative breast surgery; no matter the size of the tumour, the important thing is, to offer the patient a combination between a good aesthetic results and oncologic safety, if this is impossible to provide, than the option should be radical mastectomy, followed by breast reconstruction.
3. Post-operative radiotherapy aimed at the breast is mandatory in order to obtain a satisfactory local recurrence rate.
4. The use of pre-operative complex oncologic treatment can allow the conversion of some cases toward "conservative operability" as well as consolidating good surgical results in early cases.
5. Conservative surgery for stages I and II of breast cancer should become "gold standard" in the management of breast cancer, the results we have so far, fully supporting this statement.
6. The notion of palliative conservative mastectomy is an original idea, which still needs further reflection from our part.

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