

Advantages of Transoperative Cytology of Surgical Margins in Breast Cancer Conservative Surgery

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Summary

Today, the success of conservative surgery in breast cancer depends not only on an appropriate selection of patients, but also on the combination of adequate surgical margins with an acceptable aesthetic result. Multiple causes, can influence the probability that these borders are affected by tumor, so in this work cytology of the section margins was performed at the time of the freeze biopsy, achieving as a fundamental purpose of the study, to guarantee the advantages of cytology Transoperative, as a safe tool in breast cancer conservative surgery, among other possibilities, which in the last decade have enabled, the decrease in reinterventions caused by this cause and improve the survival of patients.

Keywords: Breast cancer; surgical margins; margin cytology

Introduction

Breast cancer represents the first cause of morbidity - mortality from malignant tumor in women. Approximately one in ten women will develop this condition throughout their life. Despite being a tumor very studied in all its aspects, it has not yet occurred, a great improvement in the survival rate, and yes in the increase in overall survival due to surgery and adjuvant treatments [1,2].

This disease represents a serious health problem for women. The International Agency for Research on Cancer (IARC) estimates that in 2018 more than 15 million people became ill with cancer and more than 8.2 million died from this cause [2,3].

During the last decades, breast cancer management has undergone substantial changes. The therapeutic of the disease is based on several pillars; the local surgical procedure on the mammary region, which has undergone major changes, from radical Halsted surgery (early 20th century), to conservative surgery, which already has more than 4 decades of employment, on the other hand systemic treatment, which includes chemotherapy, radiotherapy, hormone therapy and more recently the use of monoclonal studies according to tumor marker studies. The surgical procedure is based on removing the primary tumor and fatty-lymphatic tissue from the axillary region to determine the extent outside the mammary gland [3,4,5]

The so-called "conservative surgery" is the removal of the breast tumor, which can be limited only to this or include the quadrant of the gland, depending on the variables of the tumor and the lymphatic tissue of the armpit.

At the beginning of this new century, the early diagnosis of the disease allows an important group of women to be intervened by conservative

techniques, in most cases on an outpatient basis, which allows them to preserve the breast and incorporate into their personal activity, family and work in the shortest possible time [4,6,8]

Now, in parallel to these changes and to obtain the best results, the tumor must be removed in block in order to avoid contamination of healthy breast tissue by tumor cells, hence the need to have reliable surgical margins, which today are It recommends its measurement at least one centimeter [9,10] There are multiple reports that provide different margin measures, but Cuban regulations have adopted the measurement described above. Other techniques are performed, which allow to offer the success of conservative surgery, among which are:

- Intraoperative ultrasound.
- Location with harpoon
- Radio guided probe location

All these methods are aimed at providing certainty to the acting surgeon, especially in non-palpable lesions, but in tumors of greater diameter, the diagnostic firmness of the cellular state of the surgical section edges is also essential, thus the execution arises of transoperative cytology in the margins of the surgical section, which adds one more possibility, to guarantee the satisfactory results desired with this procedure, which has marked a milestone in the history of surgical treatment of breast cancer.

Goals:

- ① Identify if there are advantages in performing cytology of section borders in conservative surgery.
- ② State the results regarding the measurement of surgical margins and describe the recurrences found in the first 5 years, after surgery

Methodological design

An observational, descriptive, cross-sectional study was carried out in a group of patients with the diagnosis of Breast Cancer, treated in the General Surgery service of the Dr. Salvador Allende Teaching Clinical-Surgical Hospital, in the municipality Cerro, Havana, Cuba, in the period from January 2013 to December 2018, both inclusive.

The study universe consisted of 76 patients who at the time of their clinical diagnosis, were classified according to TNM [9] as Stage 0, I or II – a, and of course they were surgically operated.

The measurement of the surgical margins was performed, that is, the distance between the tumor and the sectional edge of the surgical piece, it was marked with non-absorbable suture threads at its upper, lower, external and internal edge, being sent to the department of pathological anatomy where the pathologist examined this piece by measuring the surgical margins, cytology to the sectional edges, and of course the tumor freezing biopsy. Voucher Note that stage 0 cases (diagnostic imaging) were previously marked before surgical excision.

All patients also underwent the paraffin study of the surgical section edges, allowing the sensitivity and efficacy parameters of the margins cytology to be performed.

Validation Parameters

Sensitivity: It translates the ability of the test to detect the process and indicates the proportion of positive cytology in patients with a malignant process.

$$VP \\ SENSITIVITY = \frac{VP}{VP + FN + Deferred + Suspects} \times 100$$

Specificity: It is the proportion of patients without malignancy in which cytology is benign.

$$VN \\ SPECIFICITY = \frac{VN}{VN + FP + Deferred + Suspects} \times 100$$

Positive predictive value: It is the probability that a positive cytology corresponds to a malignant process.

$$VP \\ POSITIVE PREDICTIVE VALUE = \frac{VP}{VP + FP} \times 100$$

Negative predictive value: It is the probability that a

$$VN \\ NEGATIVE PREDICTIVE VALUE = \frac{VN}{VN + FN} \times 100$$

Efficacy: It is the proportion of results that are correct

Regarding the total cases. Indicates the diagnostic accuracy.

$$VP + VN \\ EFFECTIVENESS = \frac{VP + VN}{VP + FP + VN + FN + Suspects + Deferred} \times 100$$

VP + FP + VN + FN + Suspects + Deferred

Results and Discussion.

In the period in which this study was executed, 405 patients with breast cancer diagnosis were treated, in the different stages in which the disease is classified (TNM) between 2013 and 2018, of that total 76 were chosen, to which 76 Surgical margins were measured and cytology of the section edges was also performed. These patients were included in stages 0, I and II-a, at the time of their clinical classification. In Stage 0, 3 patients were classified (3.94%); those framed as stage I, represented 63.15%; while 25 women who constituted 32.89% were included in stage II. There are no significant differences in this parameter, since today diagnoses are made at earlier stages, thanks to the different programs established worldwide for this disease [3,6]

Surgical margins occupy a leading place in the subject of conservative surgery and it is very important that the pathologist has information on the clinical and radiological characteristics of the lesion studied in the preoperative period. You should know if the cancer diagnosis has already been established by Fine Needle Aspiration Biopsy (BAAF) or Thick Needle Biopsy (BAG), depending on the size of the lesion. The information through imaging techniques, about the presence of multiple lesions, microcalcifications or suspicious densities that allows a better correlation with the pathological findings.

The first step in the management of the excised piece is performed by the surgeon, who must check the fragment before sending it to the pathologist to determine if the tumor is close to the margin of resection. If the tumor macroscopically appears to be adjacent or contacts the margin, additional tissue will be taken from the exact site during the surgical procedure.

The surgical piece should be spatially oriented with sutures, (as was done in this study) that indicate the situation with respect to the residual cavity in the breast. They can also be marked with Chinese ink as it appears in other investigations. The next step is to send the piece to the pathologist in full and it is up to the expert to measure the surgical margins, which are nothing more than the measurements from the tumor edge, to the surgical incision.

The intraoperative study includes the cytological study (Imprint) or freezing biopsy of the tumor itself. The cytological imprinting procedure is performed on the edges of the surgical section. This simple technique is based on the fact that tumor cells adhere to contact with the lamella, while fat cells do not, they are fixed with alcohol, stained with hematoxylin and eosin and studied. The procedure is fast and cheap.

In the work at hand, there were insufficient margins in 3 patients representing 3.94% and the rest (73 patients), had margins above 1 cm.

The involvement of resection margins has been identified as an important risk factor for local recurrence, so that, in most centers, the expression “affected margins” is synonymous with reintervention with the corresponding negative impact from the point of aesthetic vision in addition to a delay in adjuvant treatment, and the subsequent anxiety of the patients [3,4,6,8].

In this regard, a series of studies, the majority retrospective, published during the last decade have allowed us to identify some factors that independently predict a higher risk of presenting positive margins. These are: young patients (<45-50 years), large tumors (> 20-30 mm), multifocal tumors, absence of preoperative cancer diagnosis, microcalcifications on mammography, stereotactic location of the tumor, presence of component in situ (DCIS) and infiltrating lobular histology [8,9,10,13]

It has also been proposed that as the fixation with formalin and the time elapsed from the extraction of the piece until its pathological analysis could determine an insufficient assessment of the state of the edges and, consequently, a higher rate of positive margins due to the retraction of the fabric [9,10,14].

These arguments have supported the proposal to perform margin cytology to contribute as much as possible to avoid reinterventions.

The cytological imprint was made to the section edges in its 4 orientations (upper, lower internal and external) and in 2 patients it was positive, which was communicated to the surgeon, who proceeded to widen the

margin in the same surgical act, He was informed again about the negativity of this extended margin and was able to conclude the surgery as safely as possible of the subsequent evolution of the patients. As noted, these edges were also studied in the usual paraffin process and 100% efficacy was obtained,

Conservative surgery is closely associated with radiant treatment, so that in the case that there are no possibilities of assuming ionizing therapy, it is then an absolute contraindication of conservative surgery [4,8,17,18].

Autor	Año	Estadio	Nº pacientes	% CC	Seguimiento (meses)	RL(%)
Veronesi	1995	I-II	226	90	36	15
Merajver	1997	II	89	39	60	14
Bonadonna	1998	I-II	536	85	65	7
Favret	2001	II	64	75	51	13
Cance	2002	I -II	59	35	70	10
McIntosh	2003	I-II	166	25	62	2
INOR*	2005	II	160	10	42,2	6,25
Serie Actual	2018	0- I - II	76	59	60	3,94

CC: conservative surgery. LR: local recurrence. * INOR: Institute of Cuban Oncology

In the last decades, treatment with chemotherapy and hormonal therapy has also been incorporated, depending on the tumor markers, but which are also part of the therapeutic set, applied personally to each patient. Regarding the Local Recurrence category, in this study it appeared in two patients at 4 years of the intervention for the first time and at 5 years in another patient

The need to obtain “negative margins” in conservative breast surgery is justified by the impact it has on local recurrence and overall survival. There are numerous studies in the literature in which recurrence rates are compared with and without negative margins. Most of them show a significant benefit when negative margins are obtained, both in patients with infiltrating carcinoma and in situ [4,8,10,14,18]

The time of recurrence, in the literature reviewed it is stated that two thirds of recurrences appear in the first five years after surgery, on the area of the primary tumor and with the same histology, a fact that would explain the origin of the recurrence in the incomplete eradication of the residual tumor in the initial treatment [16,17,18].

Despite this, after the conservative treatment there is a local control deficit of 1% per year. Local recurrence is then its main problem, not only because it represents the failure of the technique, but because of the psychological impact that the possible modification for the patient implies, after a period of time free of the disease.

Different authors consulted provide their statistics regarding local recurrence and the following table shows the results regarding the percentage of recurrences and the period of time of appearance.

Local recurrences in breast cancer patients treated with conservative surgery:

Conclusions

- All the experts consulted agree that surgical margins are the golden key to the success of conservative surgery.
- This work, although it does not have a broad universe, was 100% effective.
- This simple and fast technique could be added as one more **TOOL** for the specialist who performs breast cancer conservative surgery.

Conflict of interests

The authors declare no conflict of interest.

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