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Locoregional recurrence of breast cancer in patients with conservative surgery and radical surgery

Recurrencia locorregional de cáncer de mama en pacientes con cirugía conservadora y cirugía radical

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Keywords:
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Palabras clave:
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ABSTRACT

Introduction: locoregional recurrence after breast cancer surgery occurs most of the time in the first five years after treatment, and its occurrence is related to the development of distant disease in a subgroup of patients, which determines a worse prognosis. **Objective:** to evaluate the prevalence of locoregional recurrence of breast cancer in mastectomized patients and conservative surgery. **Material and methods:** a descriptive, retrospective case series study was carried out, with clinical, humoral, and imaging analysis in patients with breast cancer recurrence in five years plus a literature review. The purpose was to analyze the type of surgery, recurrence, and clinical and imaging data most frequently associated with this disease and treatments. **Results:** the highest number of patients with a high recurrence rate was in clinical stage IIIB, located mainly in the right breast. Radical surgery, with 18 cases, was the most frequent, mainly after four years. **Conclusion:** the appearance of a recurrence of breast cancer is considered an adverse prognostic factor and decreases the survival rate in patients.

RESUMEN

Introducción: *la recidiva locorregional, luego de una intervención quirúrgica por cáncer de mama se presenta la mayoría de las veces en los primeros cinco años después del tratamiento y su aparición está relacionada con el desarrollo de enfermedad a distancia en un subgrupo de pacientes, esto determina un peor pronóstico.* ***Objetivo:*** *evaluar la prevalencia de la recurrencia locorregional de cáncer de mama en pacientes mastectomizadas y cirugía conservadora.* ***Material y métodos:*** *se realizó un estudio descriptivo, retrospectivo de serie de casos, con análisis clínico humoral, de imágenes, en pacientes con recurrencia de cáncer de mama en un periodo de cinco años más revisión de la literatura. La finalidad fue analizar el tipo de cirugía, su recurrencia, los datos clínicos y de imagen más frecuentemente asociados a dicha enfermedad, además de los tratamientos.* ***Resultados:*** *la mayor cantidad de pacientes con índice elevado de recidivas fue en la etapa clínica IIIb, localizados fundamentalmente en la mama derecha. La cirugía radical con 18 casos fue el de mayor aparición, fundamentalmente después de los cuatros años.* ***Conclusión:*** *la aparición de una recurrencia del cáncer de mama es considerada como un factor pronóstico adverso y disminuye el índice de supervivencia en las pacientes.*

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INTRODUCTION

Breast cancer is the accelerated, disordered, and uncontrolled proliferation of cells with mutated genes, which generally suppress or stimulate the continuity of the cell cycle belonging to different tissues of a mammary gland.[1]

Breast cancer is the most frequent malignant tumor in women, especially in Western countries. There has been a progressive increase in incidence in recent years, which is more significant among women under 40. The World Health Organization reports that about one in 12 women will develop breast cancer during her lifetime, and it is currently the leading cause of death in women.[2]

Breast pathology has been known to humankind since ancient times. The Ancient Egyptians were the first to observe the disease more than 3,500 years ago. The condition was described in the papyri of Edwin Smith and George Ebers. Smith was the first to describe breast cancer, and Ebers was the first to perform a breast tumor resection. In 460 BC, Hippocrates described in his book "Diseases of Women" nipple discharge as a late sign of breast cancer and postulated that the body consisted of four humors: blood, phlegm, yellow bile, and black bile.[3] Frenchman Francois de la Boe Sylvius later refuted this in 1680, who presumed that cancer did not come from an excess of black bile. He proposed that cancer came from a chemical process transforming the lymphatic fluids from acidic to acrid.[3]

Galen (2nd century) described breast cancer as looking like a "crab" whose legs corresponded to the veins emerging from the tumor. This description is probably the origin of the name "cancer". He explains that only by being operated on in the early stages when it is small is there a possibility of a cure.[2]

William Halsted of New York made radical breast surgery the gold standard for the next 100 years. He developed radical mastectomy, removing the entire breast, axillary nodes, and both chest muscles as the only procedure to prevent the spread of breast cancer.[2]

This procedure has been perfected up to the present day, where Auchincloss and Madden (1972) introduced the current technique of modified radical mastectomy, with preservation of both pectoral muscles and complete or partial axillary lymph node dissection.[3]

Breast cancer, in which cancerous cells develop in the tissues of the breast, is the most frequent neoplasm in women worldwide, responsible for approximately one of the 10 million neoplasms diagnosed each year in both sexes.

The incidence rate is highest in developed countries (except Japan), with the United States having the highest incidence. It is the second leading cause of cancer-related death among women in North America and Western Europe; 13% of American women will be diagnosed with this type of neoplasm during their lifetime, and more than 3% will die of this disease, representing more than 400,000 deaths per year. It is already ironic that a malignancy that arises in an organ that is so easily accessible for examination continues to take such a high toll.

In 2021 in Cuba, malignant tumors were the second leading cause of death, with 10,967 deaths, where breast cancer ranked third after ischemic heart disease and cerebrovascular diseases, with 965 deaths and the first cause among malignant tumors diagnosed in that year in patients under 70 years of age. It ranked second overall among all malignant tumors after lung cancer, with a total of 1,904 deaths. In Holguín city, it was the second cause of death after heart disease in terms of morbidity; 2,475 new cases were detected, being the fifth province in the country, after Pinar del Río, Artemisa, Havana, and Villa Clara, with the highest number of cancer cases in women in 2021.[4]

Its early detection is the pillar of the fight against this disease since it aims to improve the prognosis and survival of patients. It has been demonstrated that the survival rate of women diagnosed in early stages is 2.5 times higher than those diagnosed in more advanced stages.[5] Breast cancer does not appear suddenly; it takes years to develop slowly and progressively after a series of

multiple biochemical changes that cause normal cells to transform into cancerous cells. The long time that elapses for the growth of a malignant tumor in the breast offers us a window of opportunity for early detection of this disease.[6]

Multidisciplinary surgical, medical, radiotherapeutic, and hormonal treatment achieves excellent cure rates. However, often, the diagnosis of breast tumor recurrence is more devastating or psychologically tricky than the initial diagnosis of breast cancer. However, depending on the stage of the disease and the treatment administered, between 10 and 35% of women experience an isolated locoregional recurrence.[7,8] About 80% of these recurrences occur during the first two years after primary treatment, which is why it has become a significant health problem, as it is one of the leading causes of morbidity and mortality in the female population and the trend is expected to increase in the coming years.[9]

The appearance of locoregional recurrence in patients with breast cancer treated conservatively or by radical surgery may not be determined by its presence alone, meaning that a decrease in survival is an event that, in addition to being a therapeutic failure, causes the patient and the surgeon a situation of intense anguish, assisting the recurrence of the disease at the same site.[6]

Recurrent breast cancer may occur months or years after the initial treatment. The cancer may come back in the same place as the initial cancer (local recurrence), or it may spread to other parts of the body (distant recurrence).[9]

It is also important to point out that there has been a significant advance in medical and surgical treatment since it is now individualized and based on the patient's stage at the time of diagnosis. In the past, radical surgery was performed to minimize the possibility of recurrence of the disease; in recent years, it has been demonstrated that conservative surgery offers approximately the same chances of survival to the patient and with less aggression to the tissues and, consequently, less psychological impact and better response to the patient's treatment. Breast-conserving surgery is defined as the complete resection of the tumor with a concentric margin of healthy tissue, performed cosmetically acceptable.[7] In appropriately selected patients, it is equivalent to mastectomy in terms of recurrence and survival.[8,9] In Holguin, there are few reports of recurrence of this type of procedure.

Even though breast cancer is not currently perceived as a terminal disease but as a chronic process of long duration, statistics confirm that it is a severe threat to women because of the sequelae it produces, the consequent deterioration of their personal, family, and work life, with significant costs, since its incidence is high in an age group in which women are economically active and at a stage of life of formation and development of their own family.[9]

In Cuba, and especially in Holguin, different types of breast cancer treatment are carried out, such as radiotherapy, chemotherapy, hormone therapy, immunotherapy, and surgery, since there are few studies where the recurrence of breast cancer in patients operated on in our province is known.

The author of this paper considers that despite the efforts made by our country, especially in our province, to maintain a high standard of living for its inhabitants, the scientific evidence on this subject is scarce. This prevents us from carrying out a more detailed review of the recurrence of this disease in the province's teaching scenarios, updating our knowledge, and performing a better follow-up of this entity.

RESULTS

Examination of the available literature describes apparent differences in the pattern of breast cancer recurrences depending on the type of surgery performed, whether a modified radical mastectomy or conservative surgery and the adjuvant provided so that in the present study, we had a higher incidence of breast tumor recurrences in patients who underwent radical mastectomy than in those who underwent conservative surgery. We believe that this could be related to the fact that the universe of patients treated

Table 1: Distribution according to age and sex.

Age, years	Sex		Total n (%)
	Male	Female	
20-39	0	50	50 (6.3)
40-59	1	195	196 (24.7)
60-79	4	280	284 (35.7)
80 and over	0	265	265 (33.3)
Total	5	790	795 (100.0)

Source: medical record.

had more advanced stages of the disease (stages II and III), which contributed to its recurrence.[10-12]

Table 1 shows the distribution of patients according to age, where a predominance was observed between 40 and 59 years of age, followed by those between 60 and 79 years of age, which represented 47.05 and 35.29%, respectively, in general accumulating the highest percentage in those between 40 and 79 years of age, where 82.34% of the patients studied were found.

This study is not different from the literature concerning sex and age. Again, it shows that the ages between 40 and 59 years have the highest incidence rates and that women are more likely to suffer from breast cancer, which mutilates their productive life at a social and psychological level and can cause death, which is why it is considered a severe health problem that has led to determine the recurrence of breast cancer.

The incidence of locoregional recurrences for breast cancer in our universe was 3.14%, as shown in *Table 2*. The incidence of locoregional recurrences in breast cancer is highly variable depending on the stage of the disease and the treatment administered. Between 10 and 35% of women experience an isolated locoregional recurrence.[13] In our study, we had only 3.14% locoregional recurrences, possibly due to the high percentage of radical mastectomies performed. Bergamo[13] reports that only 2% of 167 cases were operated with radical surgeries for one year and followed for 36 months. On the other hand, Spinetti D and collaborators[14] report 14.8% local recurrence and 27% distant recurrence at ten years, with periodic follow-up.

According to the clinical stage of diagnosis, the greatest number of cases was diagnosed in stage II, as shown in *Table 3*, with 440 patients who did not relapse. The same occurred with stage III patients who did relapse, with a total of 21 patients representing 84%. Only four patients who relapsed were diagnosed with stage II of the disease, which represented 16% of the total number of relapses.

Similar findings were observed in other studies, such as that of Silvina Malvasio[15] and collaborators, where the distribution by stage was as follows: stage I 23 patients (21.5%); stage II 47 patients (44%); stage III 33 patients (31%), and stage IV four patients (3.5%). The author of this research thinks that the increase in stage III recurrences is because the patients are coming late to the established medical consultations.

Regarding the histological type, as shown in *Table 4*, similarities were found with what was reported regarding breast cancer in different studies, where the infiltrating ductal histological type predominates. In 2017, a study conducted in Mexico City showed similar results, where this histological type was the most prevalent at 80.13%.[16] Similar data were found in other studies performed.[17,18] In this study, infiltrating ductal carcinoma was propitious, and the highest percentage of locoregional recurrence was found at 44%.

As can be seen in *Table 5*, the more significant number of patients diagnosed with breast cancer and operated on have a greater location in the upper external quadrant, which agrees with other studies; it was more frequent in the right breast, which represented 60% of the total. These results differ slightly in the study carried out by Dr. Diosdado Cruz del Pino[19] in Holguin Province in 2010, where left breast cancer predominated, despite carrying out the study in the same province, where also in these last years of the study no tumor was found in the

axillary projection; there were no patients who had been diagnosed with cancer in the contralateral breast, that is, all the patients who participated in the study had cancer only in one breast.

According to different authors, the average time to recurrence is within the first two years of follow-up in 80-90% of cases.[14,20]

The recurrence rate at five years after surgery is highly variable. The incidence following modified radical mastectomy ranges from 3 to 48%.[21] In the present investigation, the overall incidence of recurrence was 3.14%, as explained in *Table 2*. Some authors report in an extensive review that the incidence of recurrence ten years after mastectomy is 13% and that 35% of these cases present synchronous systemic disease.[21] Nine to 25% of these cases will have distant metastases or extensive disease at the time of diagnosis of recurrence.[22,23]

In the present study, the time of onset of recurrence showed that four patients (16%) relapsed before 24 months, nine patients (36%) between 24 and 48 months, and 12 patients (48%) after 48 months, very similar to studies carried out in other countries, as shown in *Table 6*.

It is essential to point out that four of the five recurrences had a modified radical mastectomy as a previous surgery, representing 80% of the recurrences. As seen in *Table 7*, modified radical mastectomy prevailed with 81.37%. Modified radical mastectomy still has an essential place in the primary treatment of breast carcinoma.

Table 2: Recurrences in operated patients.

	Sex		Total n (%)
	Male	Female	
With recurrences	1	24	25 (3.14)
No recurrences	4	766	770 (96.86)
Total	5	790	795 (100.0)

Source: medical record.

Locoregional relapse after mastectomy varies widely from 5 to 40% in the literature.[24,25] In the present work, we had a higher incidence of breast tumor recurrence in patients who underwent radical mastectomy than in those who underwent conservative surgery. We believe that this could be related to the fact that the universe of patients treated had more advanced stages of the disease (II and III), which contributed to the recurrence of the disease.[26]

This result differs from the studies of Veronesi and Fisher, which suggest a slight increase in local recurrences in cases of breast-conserving surgery, with no change in overall survival or disease-free interval. Regardless of the technique to be used, whether radical or breast-conserving, the negativity of the surgical section border is a fundamental principle in all oncological surgery.[15] In recent years, this has been a much-debated topic by different authors such as Sheik,[12] Sabel[27] and Borgen.[28]

DISCUSSION

Breast cancer is the primary malignant pathology in women, which, due to its multiple etiological factors, has become an epidemiological problem in women of increasingly younger ages and is prevalent in older women. In addition, inadequate diagnosis due to delay or quality of the diagnostic process itself is reflected in the patient's prognosis.[29]

Breast cancer is a systemic disease in which breast tissue cells begin to form malignant tissues with a capacity to metastasize to neighboring tissues or distant organs of the body. A breast cancer cell doubles every 100-300 days. The 1 cm breast neoplasm makes about 30 duplications before reaching this size, so this cancer has at least seven years of evolution. This simple estimate shows us the usefulness of early detection, with diagnostic methods capable of visualizing (subclinical) alterations of less than one centimeter in size.[10,30] Thus, we can prevent possible future locoregional recurrences.

Local recurrence can be defined as the reappearance of the cancer either in the

Table 3: Relapses according to clinical stage.

Stage	Relapse		Total n (%)
	No n (%)	Yes n (%)	
0	15 (1.94)	–	15 (1.94)
IA	93 (12.39)	–	93 (12.39)
IB	11 (1.42)	–	11 (1.42)
IIA	260 (33.7)	3 (12)	263 (33.1)
IIB	180 (23.3)	1 (4)	181 (22.8)
IIIA	97 (12.5)	3 (12)	100 (12.5)
IIIB	102 (13.2)	18 (72)	120 (14.3)
IIIC	12 (1.55)	–	12 (1.55)
Total	770 (100.0)	25 (100.0)	795 (100.0)

Source: medical record.

Table 4: Distribution of patients according to histologic variant.

Histological variant	Sex		Total n (%)	Relapses n (%)
	Male	Female		
Ductal carcinoma *in situ*	1	210	211 (26.5)	7 (28)
Infiltrating ductal carcinoma	3	422	425 (53.4)	11 (44)
Infiltrating lobular carcinoma	–	45	45 (5.6)	3 (12)
Medullary carcinoma	–	32	32 (4.1)	1 (4)
Metaplastic squamous cell carcinoma	–	39	39 (4.9)	2 (8)
Other histological variants	1	42	43 (5.5)	1 (4)
Total	5	790	795 (100.0)	25 (100)

Source: medical history.

operated breast, in the operative scar, or the skin covering the rib cage after surgery. Regional recurrence is the anatomical situation in which the tumor involvement invades the axillary, infraclavicular, ipsilateral supraclavicular, or internal mammary chain nodes.[31,32]

In 2016, Elsayed et al. published an article in which 238 patients who underwent conservative surgery were studied. After five years of follow-up, 16 patients (6.72%) had locoregional recurrence, while ten patients (4.2%) had distant recurrence.[28] In 2016, Choi and his group released the results of a study that included 322 patients; the follow-up period was 57 months. During this time, 19 patients (5.9%) had a recurrence in the ipsilateral breast, and six patients had a recurrence in the contralateral breast.[17,33] In 2015, Manning and Sacchini concluded an analysis involving 413 patients, with an average follow-up of 49 months, who underwent nipple-sparing mastectomy; 402 of 413 were alive with no evidence of disease. Four patients died, one with regional and distant recurrence 15 months after surgery.[14] In 2016, Warren et al. reported a study that included 753 patients with nipple-sparing surgery, with a follow-up

Table 5: Location of the primary lesion and specific location.

Specific location	Location of lesion (breast)	
	Right	Left
Quadrant:		
Superior external	4	4
Lower internal	5	2
Superior interno	2	1
Lower external	3	2
Central or retroareolar	1	1
Axillary projection	0	0
Total	15	10

Source: medical record.

Table 6: Distribution of cases according to time elapsed between initial diagnosis and the onset of recurrence.

Time to onset of recurrence	Sex		Total n (%)
	Male	Female	
Before 2 years	0	4	4 (16)
From 2 to 5 years old	1	8	9 (36)
More than 5 years	0	12	12 (48)
Total	1	24	25 (100)

Source: medical record.

Table 7: Surgical technique used.

Technique used	Sex		Total n (%)
	Male	Female	
Conservative surgery	0	6	6 (24)
Radical mastectomy	1	18	19 (76)
Total	1	24	25 (100)

Source: medical record.

of 41 months where there was a recurrence prevalence of 5%.[34]

These results coincide with those of Professor Soler Vaillant,[25] who indicates a higher incidence between 45 and 60 years of age, with the highest contribution of data to the research work carried out. Other authors, such as Kelly K. Hunt and Elizabeth A. Mittendorf, both from the Department of Oncologic Surgery of the University of Texas,[35,36] differ slightly in these results, showing a higher incidence between 75 and 85 years of age, which in the present work only represented 14.70% of the patients studied.

Many studies in Mexico found an analogous result: the histological type that prevailed in their study was infiltrating ductal carcinoma for 89% of the cases.

Between 80 and 90% of recurrences appear in the first five years after surgery, and the remaining 10% appear between five and 10 years after surgery.[21] Other studies indicate that between 10 and 20% of patients will have recurrent disease in the breast between one to nine years after conservative surgery and radiotherapy.[18] When analyzing this information, we observed that the periods and the percentage of recurrence prevalence are very similar to that found in our research.

CONCLUSIONS

As was seen in the study, patients in the 60-79 age group predominated, with 284 patients for 35.7%; of these, 280 patients were female; there were also 25 patients with recurrences out of 795, representing 3.14%. Stage IIIb was predominant in the preoperative stage for 72%, which led to modified radical mastectomy being the most frequently performed surgical intervention in 19 patients for 76%, where the most frequent histological type was infiltrating ductal carcinoma. Most of the patients had a relapse after more than five years, with a more significant localization towards the right breast. The occurrence of breast cancer recurrence is considered an adverse prognostic factor and decreases the survival rate in patients.

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