



Neoadjuvante chemotherapy and immediate breast reconstruction: a good option?

Quimioterapia neoadjuvante e reconstrução mamária imediata: uma boa opção?

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ABSTRACT

Background: The combination of neoadjuvant chemotherapy and immediate breast reconstruction is a field under discussion. There are doubts whether the association of events could result in an increase of postoperative complications in patients undergoing the surgical procedure. **Methods:** Retrospective study of patients who underwent immediate breast reconstruction from January 2010 to January 2012. Patients submitted to neoadjuvant chemotherapy were compared with those who had not received any form of chemotherapy and those who received adjuvant chemotherapy. **Results:** Fifty-four patients were selected, totalizing 71 immediate breast reconstructions. Thirteen patients received neoadjuvant chemotherapy (15 reconstructions) twenty-three patients did not receive chemotherapy (33 reconstructions) and eighteen received adjuvant chemotherapy (23 reconstructions). Minor complications occurred in 33.3% of breast reconstruction in the group undergoing neoadjuvant therapy. There were 6.7% of major complications in the same group. There was no statistical differences in the number of minor and major complications between groups. **Conclusion:** In the series analyzed, the use of neoadjuvant chemotherapy did not increase the number of postoperative complications in patients undergoing immediate breast reconstruction.

Keywords: Breast cancer. Mastectomy. Mammoplasty. Chemotherapy. Postoperative complications. Reconstructive

RESUMO

Introdução: A combinação de quimioterapia neoadjuvante e reconstrução mamária imediata é um campo em discussão. Há dúvidas se a associação dos eventos poderia resultar em um aumento de complicações pós-operatórias nas pacientes submetidas ao procedimento cirúrgico.

Métodos: Estudo retrospectivo de pacientes submetidas à reconstrução

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mamária imediata no período de janeiro de 2010 a janeiro de 2012. As pacientes submetidas à quimioterapia neoadjuvante foram comparadas com as que não receberam qualquer forma de quimioterapia e com as que receberam quimioterapia adjuvante. **Resultados:** Cinquenta e quatro pacientes foram selecionadas, totalizando 71 reconstruções mamárias imediatas. Treze pacientes receberam quimioterapia neoadjuvante (15 reconstruções), vinte e três pacientes não receberam quimioterapia (33 reconstruções) e 18 receberam quimioterapia adjuvante (23 reconstruções). Complicações menores ocorreram em 33,3% das reconstruções mamárias no grupo submetido à neoadjuvância. Houve 6,7% de complicações maiores no mesmo grupo. Não houve diferenças estatísticas no número de complicações menores e maiores entre os grupos. **Conclusão:** Na série analisada, o emprego da quimioterapia neoadjuvante não resultou em aumento do número de complicações pós-operatórias em pacientes submetidas a reconstruções mamárias imediatas. **Descritores:** Câncer de mama. Mastectomia. Mamoplastia. Quimioterapia. Complicações pós-operatórias. Procedimentos Cirúrgicos Reconstrutivos.

INTRODUCTION

Historically, breast cancer therapy consisted of mastectomy followed by adjuvant treatments such as chemotherapy, radiotherapy, and/or hormone therapy. Breast reconstruction procedures were only performed subsequently, frequently after 5 years of follow-up¹.

However, in the last decades, this practice has been changing, with regard to the timing of reconstruction as well as the sequence of additional treatments.

Immediate reconstruction, conducted at the same time as mastectomy, is being increasingly performed. It has been shown to be beneficial in reducing morbidity (decreasing the number of surgical interventions and recovery time), reducing psychological and social impacts, improving the aesthetic outcome, and increasing the satisfaction of patients about the treatment, without affecting oncological safety^{1,8}.

Chemotherapy has begun to be increasingly used by oncology and mastology teams, as this therapy has been shown to be efficient in reducing the recurrence and mortality of breast cancer, mainly by eliminating or delaying the development of occult micrometastases⁸.

Meanwhile, the timing of chemotherapy has also undergone changes. For patients with locally advanced breast cancer, inoperable cancer, or inflammatory breast cancer, chemotherapy conducted before the surgical procedure (neoadjuvant chemotherapy) has been considered as the standard treatment. In addition to the benefits already described, chemotherapy allows testing the efficacy of the drug

used, and when the patient is responsive, chemotherapy allows the reduction of tumor size, which enables surgery with higher preservation of the skin envelope and facilitates the reconstruction process^{3,4}.

However, although there are many studies in the literature about this topic, the combination of neoadjuvant chemotherapy and immediate reconstruction remains under discussion.

There are doubts about whether the cytotoxic drugs used in chemotherapy and the timing of their application could produce local or systemic adverse effects, affecting the surgery, increasing the incidence of postoperative complications, and resulting in the failure of reconstruction in patients undergoing immediate reconstruction.

OBJECTIVE

To evaluate the rate of complications in patients undergoing neoadjuvant chemotherapy followed by mastectomy and immediate breast reconstruction, when compared with patients not undergoing chemotherapy or those undergoing adjuvant chemotherapy.

METHODS

A retrospective review of records was conducted for patients who underwent breast reconstruction from January 2010 to January 2012. Fifty-four patients whose reconstructions were conducted at the same time as the mastectomy were selected.

All patients signed the written informed

consent form, authorizing the use of their data and treatment information, as well as their photographs, for scientific purposes.

The recommendation of chemotherapy and the timing of chemotherapy (when recommended) were decided by the clinical oncologist, on the basis of the histological characteristics, immunohistochemical characteristics, and tumor stage of each patient.

All reconstructions were performed by the same surgeon. The method of reconstruction performed was selected on the basis of a thorough analysis of the case by the assistant plastic surgeon, along with the personal preference of the patient. All patients were followed-up for at least 5 months postoperatively.

The patients were divided into three groups: those who received neoadjuvant chemotherapy (group 1), those who did not receive chemotherapy (group 2), and those who received adjuvant chemotherapy (group 3).

The characteristics analyzed were age, presence of comorbidities, tumor characteristics, reconstruction methods used, and observed complications.

Minor complications were defined as the presence of seroma, hematoma, small areas of dehiscence, and epidermolysis. Major complications were defined as infection, necrosis, and pulmonary thromboembolism.

Patients who received neoadjuvant chemotherapy (group 1) were compared with patients who did not receive any form of chemotherapy (group 2) and with those who

received adjuvant chemotherapy (group 3).

The results were analyzed with statistical tests (e.g., analysis of variance, Levene, chi-square, and Kruskal-Wallis), and the results were considered significant when $P < 0.05$.

RESULTS

Fifty-four patients were selected, comprising a total of 71 immediate reconstructions, with 13 patients allocated to group 1, 23 to group 2, and 18 to group 3.

The ages of the analyzed patients were from 28 to 73 years (mean, 51.2 years).

Approximately 44.4% of the patients had some type of comorbidity, such as history of smoking, obesity, coronary artery disease (previous myocardial revascularization), or diabetes mellitus.

The groups were considered homogeneous in both age and the presence of comorbidities, according to the statistical tests performed.

The detailed analysis of the patients' characteristics and their distribution in each of the groups is described in Table 1.

A total of 55 breast neoplasia diagnoses were made, and none of the patients had a diagnosis of bilateral neoplasia. The main histologic types found were invasive ductal carcinoma (58.2%) and ductal carcinoma *in situ* (18.2%). Cases of inflammatory carcinoma were not observed.

Table 1—Patient characteristics

	Group 1: patients who received neoadjuvant chemotherapy		Group 2: Patients who did not receive chemotherapy		Group 3: Patients who received adjuvant chemotherapy		Total		Statistical significance
	n	%	n	%	n	%	n	%	
Total no. of patients	13	100%	23	100%	18	100%	54	100%	
Mean age (minimum–maximum), years	44,2	(28 - 67)	54,3	(32 - 73)	52,2	(32 - 69)	51,2	(28 - 73)	0,053 ¹
Comorbidities	6	46%	10	43%	8	44%	24	44,4%	0,972 ²
History of smoking	3	23,1%	6	26,1%	4	22,2%	13	24,1%	
Obesity	1	7,7%	2	8,7%	1	5,6%	4	7,4%	
Coronary artery disease	0	0,0%	1	4,3%	0	0,0%	1	1,9%	
Diabetes mellitus	2	15,4%	1	4,3%	3	16,7%	6	11,1%	

¹ Analysis of variance: value close to significance. Homogeneous variances by the Levene test ($P = 0.679$).

² Chi-square test for the presence or absence of comorbidities.

Table 2—Tumor characteristics

	Group 1: Patients who received neoadjuvant chemotherapy		Group 2: Patients who did not receive chemotherapy		Group 3: Patients who received adjuvant chemotherapy		Total	
Total no. of patients	13	100%	23	100%	18	100%	54	100%
Total no. of diagnoses	13	100%	23	100%	19	100%	55	100%
Lobular carcinoma <i>in situ</i> (LCIS)	0	0,0%	6	26,1%	3	15,8%	9	16,4%
Invasive lobular carcinoma (ILC)	2	15,4%	2	8,7%	0	0,0%	4	7,3%
Ductal carcinoma <i>in situ</i> (DCIS)	0	0,0%	3	13,0%	7	36,8%	10	18,2%
Invasive ductal carcinoma (IDC)	11	84,6%	12	52,2%	9	47,4%	32	58,2%
Inflammatory carcinoma (IC)	0	0,0%	0	0,0%	0	0,0%	0	0,0%

Table 3—Reconstruction methods

	Group 1: Patients who received neoadjuvant chemotherapy		Group 2: Patients who did not receive chemotherapy		Group 3: Patients who received adjuvant chemotherapy		Total	
Total no. of patients	13	100%	23	100%	18	100%	54	100%
Total no. of unilateral reconstructions	11	84,6%	13	56,5%	13	72,2%	37	68,5%
Total no. of bilateral reconstructions	2	15,4%	10	43,5%	5	27,8%	17	31,5%
Total no. of reconstructions	15	100%	33	100%	23	100%	71	100%
Local flaps	0	0,0%	1	3,0%	1	4,3%	2	2,8%
Prosthesis	0	0,0%	2	6,1%	0	0,0%	2	2,8%
Expanders	6	40,0%	21	63,6%	10	43,5%	37	52,1%
TRAM	5	33,3%	5	15,2%	9	39,1%	19	26,8%
LD	4	26,7%	4	12,1%	3	13,0%	11	15,5%

The detailed analysis of tumor characteristics is described in Table 2.

The methods of reconstruction involved the use of local flaps, prosthesis, expanders, myocutaneous flap from the rectus abdominis muscle (TRAM), and myocutaneous flaps from the latissimus dorsi muscle associated with the prosthesis (LD).

Concerning the method of reconstruction, 68.5% of patients underwent unilateral reconstruction and 31.5% underwent bilateral reconstruction. The main method used when all the groups were analyzed was the use of an expander (52.1%), followed by TRAM (26.8%) and LD (15.5%).

The detailed analysis of the reconstruction methods used in each group is described in Table

3.

A mean percentage of 38% reconstructions with complications was observed. In the evaluation of minor complications, the mean incidence was 25.4%, reaching up to 33.3% in group 1. Among the major complications, the mean incidence was 12.7%, being higher in group 3 (21.7%).

The incidence of complications, regardless of severity, was not significant between the groups ($P = 0.407$). Statistically significant differences were not found between minor and major complications. ($P = 0.667$ and $P = 0.280$).

The detailed analysis of the observed complications in each studied group and its respective percentages is described in Table 4, and in Figures 1 and 2.

Table 4—Complications

	Group 1: Patients who received neoadjuvant chemotherapy		Group 2: Patients who did not receive chemotherapy		Group 3: Patients who re- ceived adjuvant chemotherapy		Total		Statistical significance
Total no. of patients	13	100%	23	100%	18	100%	54	100%	
Total no. of reconstructions	15	100%	33	100%	23	100%	71	100%	
Total incidence of complications	6	40%	10	30,3%	11	47,8%	27	38,0%	0,407 ¹
Minor	5	33,3%	7	21,2%	6	26,1%	18	25,4%	0,667 ²
Seroma	2	13,3%	5	15,1%	4	17,4%	11	15,5%	
Hematoma	0	0,0%	0	0,0%	1	4,3%	1	1,4%	
Dehiscence	2	13,3%	0	0,0%	1	4,3%	3	4,2%	
Epidermolysis	1	6,7%	2	6,1%	0	0,0%	3	4,2%	
Major	1	6,7%	3	9,1%	5	21,7%	9	12,7%	0,280 ³
Infection	0	0,0%	1	3,0%	2	8,7%	3	4,2%	
Necrosis	1	6,7%	2	6,1%	3	13,0%	6	8,5%	
PTE	0	0,0%	0	0,0%	0	0,0%	0	0,0%	

¹Chi-square test for the presence or absence of complications.

²Chi-square test for the presence or absence of minor complications.

³Kruskal-Wallis test for the distribution of the presence or absence of major complications.



Fig. 1 - Patient with dehiscence and infection in the right immediately reconstructed breast that required the removal of the expander and a subsequent secondary breast reconstruction.



Fig. 2. Patient with necrosis in the reconstructed right breast .

DISCUSSION

The World Health Organization estimates that every year, >1 million of new cases of breast cancer occur worldwide, which makes this cancer the most common among women⁹. Accord-

ing to data from the Ministry of Health, the situation is similar in Brazil⁹.

In light of the aging population in Brazil and the higher prevalence of the risk factors for this condition, there is a tendency for an increase in the incidence of the breast cancer in the country. However, the mortality rate of breast cancer in Brazil is stable, despite being high^{10,11}.

This is mainly attributed to improvements in the diagnosis and therapeutics of the disease, which have allowed earlier diagnoses and treatments that are increasingly more effective.

In Brazil, the guidelines for screening the disease are determined by the Ministry of Health, which recommends an annual clinical breast examination for women from the age of 40 years, and a mammography examination every 2 years in women aged 50 to 69 years^{9,12}. For women from population groups considered to be at high risk for breast cancer (family history of breast cancer in first-degree relatives before 50 years of age, family history of bilateral breast or ovarian cancer in first-degree relatives at any age, family history of male breast cancer, histopathological diagnosis of atypical proliferating mammary lesion or *in situ* lobular neoplasia), clinical breast examination and mammography annually from the age of 35 years are recommended^{9,10}.

There are two alternatives for the surgical treatment of mammary neoplasia: conservative surgery or total mastectomy. Factors that direct the decision for one or the other approach include the size of the tumor, multicentricity, breast volume, and genetic predisposition to the disease¹³. The oncologic treatment may still be multidisciplinary, in which there might be a need for complementation with radiotherapy, chemotherapy, and hormone therapy.

Plastic surgery has also changed, accompanying the changes seen in the diagnosis and therapy of breast neoplasia during the last decades. New methods of reconstruction have been proposed, with optimized results being achieved along with a considerable increase in the expectations of patients.

However, diverse factors can interfere in the process of breast reconstruction and affect the results of this treatment.

The increase in postoperative morbidity among patients undergoing immediate mammary reconstruction is closely related to the previous conditions of the patients, such as age, history of smoking, obesity, arterial hypertension, and diabetes mellitus^{1,5}.

In our work, the studied groups were homogenous from the statistical point of view with regard to the variables studied.

Regarding the histologic type, we observed a higher percentage of patients with ductal carcinoma in our cases, which was expected as this is the most prevalent subtype.

When we analyzed the breast reconstruction methods, we verified that the use of an expander was the main method used by our team, with >50% of cases being reconstructed in this manner.

We attributed this fact mainly to the increasing tendency for an early diagnosis of breast cancer, which allows mastectomies that preserve the skin and allows reconstruction with the use of silicone implants/tissue expanders. Furthermore, we believe that the diagnosis of mammary neoplasia performed in ever younger patients (commonly with restricted donor sites because of the desire to become pregnant in the future, engaging in regular physical activity, and having undergone a previous aesthetic abdominal surgery) decrease the possibilities of reconstruction by using autologous flaps in isolation.

Another important factor about this issue is the increasing number of bilateral mastectomies conducted by mastologists in this subgroup of young patients (because of a more potentially aggressive disease, possible genetic causes, and the possibility of new diagnosis of contralateral neoplasia in the future). In our statistical study, there was a need for bilateral reconstruction in approximately 31% of cases.

Although bilateral reconstruction is still controversial in the literature, we noted that this practice is used with some frequency, which hinders even more the possibilities of reconstruction with uniquely autologous flaps.

Most studies concerning complementary therapy indicate that conducting chemotherapy, either neoadjuvant or adjuvant, does not seem to increase the risk of complications and failures in immediate breast reconstruction⁸.

However, this is controversial. Given the impact of chemotherapy on the patient and its potential local and systemic cytotoxic effects, the combination of surgery and neoadjuvant chemotherapy could result in an increase in the number of complications and failures in patients submitted to immediate breast reconstruction^{6,7}. Some studies suggest that the combination of these processes could cause cicatrization problems in wounds and postoperative infections, causing failures in the reconstruction, mainly when implants are used.

This fact becomes extremely important, because reconstruction with implants is more frequently used in the Brazilian population.

Although several studies have investigated immediate breast reconstruction in the Brazilian

literature, we could not find any study that correlates neoadjuvant chemotherapy and the possible complications arising from the process. We believe that we are pioneers in tackling the topic in the country.

In our analysis, there was no statistically significant increase in the number of complications in patients who received neoadjuvant chemotherapy when compared with those who did not receive any form of chemotherapy, or those who received adjuvant chemotherapy. This applies not only to the analysis of the total number of complications but also after subdivision into minor and major complications.

We believe that the reason for this result was that patients who received neoadjuvant chemotherapy underwent surgery only after a period of bone marrow recovery, and when their immunity had reached a minimum safety level, initiating an increasing curve of recovery and decreasing the chances of postoperative infection.

When we compared these groups of patients (potentially of higher risk) with those who underwent surgery and only subsequently underwent chemotherapy, we found that the lower-immunity condition that occurs at each cycle of medication may compromise the safety of the reconstruction, particularly for patients who received reconstruction with implants.

CONCLUSIONS

A surgeon who performs breast reconstruction should be familiar with the recommendations, mechanisms of action, and possible collateral effects of conducting neoadjuvant chemotherapy.

In our sample of cases, neoadjuvant chemotherapy, when associated with immediate breast reconstruction, did not result in increase in complications. Therefore, we conclude that these are not incompatible procedures and that they can be used together.

This result might be due to the number of young patients studied, which makes our results valid; however, a follow-up is needed to make definitive conclusions and validate our results. The present study serves as a basis for further analysis concerning this topic.

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