

LOCAL RE-OPERATION AND RECURRENCE IN ONCOPLASTIC BREAST SURGERY

Reoperação e recidiva local em cirurgia oncoplástica mamária

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ABSTRACT

Introduction: In addition to a surgical option, the oncoplastic surgery (OP) is a new philosophy in the mammary oncologic therapy, since it combines concepts of oncologic surgery and plastic surgery. There was a concern that plastic surgery techniques would compromise the oncologic radicalism, leading to an increased risk of tumor recurrence and damage to the patients' survival. The main purpose of the breast conservative surgery (BCS) is to obtain disease-free surgical margins, with a great esthetic-functional result. However, since the advent of this approach, the search for negative margins has been a problem. Despite the efforts to avoid compromised margins, they occur in 20 to 40% of the cases in the traditional BCS, and in many cases leading to the need of re-excision or even to mastectomy. **Objective and method:** In the analysis of recent studies, the OP role as a reduction factor of new surgeries and local recurrence is questioned. The aim of this paper is to analyze it based on literature review. **Conclusion:** According to recent studies, the OP became a safe oncological surgical technique that improves both the esthetic result and the disease local control, decreasing the compromised margins with impact on the mitigation of new surgeries rate.

KEYWORDS: Mammoplasty; Local recurrence of neoplasia; Reoperation; Margins of excision; Segmental mastectomy.

RESUMO

Introdução: A cirurgia oncoplástica (OP) além de opção cirúrgica é uma nova filosofia no tratamento oncológico mamário, pois combina os princípios da cirurgia oncológica com os da cirurgia plástica. Existia um temor de que as técnicas de mamoplastias redutoras pudessem comprometer a radicalidade oncológica, levando a um risco aumentado para recidivas tumorais e prejuízo na sobrevida das pacientes. O objetivo primário da cirurgia conservadora de mama (CC) é obter margens cirúrgicas livres de doença, com bom resultado estético-funcional. Entretanto, desde o advento dessa abordagem, a busca por margens negativas tem sido problemática. Pois, apesar do esforço para se evitar margens comprometidas, elas ocorrem em 20 a 40% dos casos na CC tradicional, levando, em muitas situações, à necessidade de reexcisão ou até mesmo mastectomia. **Objetivo e método:** Analisando estudos recentes, questiona-se o papel da OP como um fator redutor de reoperações e recidiva local. O objetivo desse artigo é fazer uma discussão embasada em revisão da literatura. **Conclusão:** Conforme estudos recentes, a OP consagrou-se como técnica cirúrgica oncológica segura, com melhora tanto no resultado estético como no controle local da doença, diminuindo margens comprometidas e impactando na atenuação da taxa de reoperações.

DESCRIPTORIOS: Mamoplastia; Recidiva local de neoplasia; Reoperação; Margens cirúrgicas; Mastectomia Segmentar.

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INTRODUCTION

An oncoplastic surgery (OP) is considered a well-conducted tumor resection followed by immediate breast reconstructive surgery, which evaluates the symmetry with the contralateral breast in the same surgery^{1,2}. In addition to a surgical option, this is a new philosophy in the mammary oncologic therapy, since it combines concepts of oncologic surgery and plastic surgery. There was a concern that plastic surgery techniques would compromise the oncologic radicalism, leading to an increased risk of tumor recurrence and damage to the patients' survival. However, contrarily to this initial concern, a combination of mammoplasty techniques to mammary oncologic surgery showed to be positive. It could even add safety regarding margins, and at the same time reduce the risk of a poor esthetic-functional result¹.

OP techniques are more complex and require more time than the traditional conservative surgery (BCS). From the oncologic, aesthetic, and psychological point of view, the selection of patients is essential³. Some points are crucial for the obtainment of satisfactory results, among which:

- proper surgery to resect each type of tumor;
- immediate reconstruction using the proper techniques; and
- handling of contralateral breast⁴.

Several factors may influence the decision of the surgical technique that will be used, such as obesity, diabetes, smoking habits, autoimmune diseases and previous radiotherapy. Essentially, obesity, smoking habits, and previous radiotherapy may cause an increase in the number of complications, regardless of the adopted technique. Obesity may increase the rate of complications in 12 times. Smoking habits may also interfere due to the vasoconstrictor effect. It reduces blood flow in the capillary through inhibition of catecholamine measured by nicotine, thus increasing the chances of necrosis in tissue flaps. Previous radiotherapy may change tissue vascularization due to fibrosis, which may also be accompanied by healing disorders. Although diabetes as an isolated factor does not increase the complication rates, its impact is seen when associated with obesity or previous radiotherapy, increasing the rates of infection and cutaneous necrosis⁵.

There are indications established for the OP, which include mammary resection with a volume higher than 20% and patients with macromastia, in which the result of a skin-saver mastectomy technique is not satisfactory. Relative contraindications are the following:

- extensive tumors located in the medial breast region;
- small mammary volume or with no ptosis;
- previously irradiated breasts;
- smoker patients or those with decompensated diabetes; and
- patients with excessive or disproportional expectations regarding the esthetic result³.

There are several reduction mammoplasty techniques that may help in the BCS. Reductive mammoplasty based on a superior vascular pedicle consists of a mammary reduction with periareolar and vertical scar (which may also include horizontal scar in T), also known as Lejour or Pitanguy technique. It may be used in cases of tumors located in the lower quadrants, and an average or large volume breast is necessary, with a minimum of ptosis. Reductive mammoplasty based in the changed lower vascular pedicle is based on the inferoposterior areolar vascular pedicle, and it may be applied to tumors located in the upper quadrants of the breast⁶. Double vascular pedicle mammoplasty is a technique combining vascular pedicle for the areola and a lower glandular vascular pedicle. This technique is especially indicated for cases of very superficial tumors located in upper-external quadrants, which need a tumor resection with skin margin⁶. Mixed pedicles for excisions out of the area commonly used in breast reduction techniques may allow for tumor resections in almost any place of the breast⁷. Periareolar techniques, such as the round-block ones, allow resections in all quadrants and are most indicated for small or average volume breasts with minimum or moderate ptosis.

Evaluation of oncologic efficacy is done based especially on the overall survival, disease-free survival, and disease local control rates through local recurrence rates². The OP is an innovative methodology. However, it needs further studies comparing different surgical techniques and evaluating oncologic and repairing results in a more objective way^{2,8-10}.

LOCAL RECURRENCE AND RE-OPERATING RATE

The majority of local recurrence appears in the initial tumor site, which indicates that it derives from residual tumor cells. Compromised margins require a new subsequent operation to avoid remaining tumor cells, which may lead to a new mastectomy, depending on each case¹¹. Therefore, the surgical margin status is a critical factor for the disease local control¹².

The determining factors for local control were considered to be the tumor size, the presence or not of metastasis in axillary lymph nodes, and hormonal receptors status (estrogen and progesterone). However, with the new concepts of tumor biology, the determining factors are currently more related to the molecular biology of the tumor and adjuvant therapy than with the size of the resection margin. Such concept was popularized as "bigger is not better"^{13,14}.

Factors such as histological degree, components of noninvasive carcinoma, lobular histology, and multicentricity are predictive of conservative surgery failure and conversion to mastectomy¹⁴.

There are countless risk factors associated with a high rate of new surgeries due to compromised margins. Among which, we may point out the following:

- tumor size;
- tumor multifocality;
- extensive *in situ* component; and
- increased mammary density showed through mammography¹¹.

There is also the factor associated with regional variations in histopathological definitions:

- margins status;
- capacity of imaging and locating non-palpable tumors;
- 3D perception of the tumor by the surgeon; and
- desire to keep a good esthetic result¹⁵.

Systemic treatments reducing the incidence of distant metastasis also decrease the risk of local recurrence¹³.

Previous studies showed a local recurrence rate in five years (60 months) after the OP varying from 8.5 to 9.4%. Most literature reviews have an average time of follow-up (average of 4.5 years) with a local recurrence rate ranging from 0 to 1.8% per year¹⁶ (Table 1).

Although the purpose of a new surgery is to reduce the risk of local recurrence and the mortality, its actual benefit remains undetermined, since approximately 50% of new surgeries do not show a residual tumor in the anatomopathological test, creating doubt about its real need, as it does not change the mortality rate¹⁷. Similarly, although the OP allows for a larger resection of the tumor and reduces the compromised margin rates, its value in the local recurrence still needs to be confirmed^{16,18}.

There is a lack of standardization and protocols on the approach and handling of compromised margins among surgeons, despite the significant psychological, physical, and financial effects of re-excision in the patients¹⁷.

ONCOPLASTIC SURGERY AND SURGICAL MARGINS

The primary purpose of BCS is to obtain disease-free surgical margins, with an excellent esthetic and functional result. However, since the advent of this approach, the search for negative margins has been a problem. Despite the efforts to avoid compromised margins, they occur in 20 to 40% of the cases in the traditional BCS, and in many cases leading to the need of re-excision or even to mastectomy^{19,20}. This is associated with an increase in the therapy cost and the morbidity, and delay to begin adjuvant therapies^{13,17}.

The OP showed to be effective in several series (Table 1), allowing larger excisions and keeping the effective local control rates. Since the mammoplasty techniques involve flaps rotation and displacement of the mammary glandular tissue, the concern with surgical margins is essential, considering that if a second surgery is needed to extend them, this may be even more complex²¹⁻²³. In a systematic review from Piper et al. (2016), the new surgery rate in the OP was of 3.5% and the mastectomy rate was 3.7%. When the OP is compared with the traditional BCS, the new surgery rates are lower and the mastectomy rates are equivalent. Thus, the reductive mammoplasty allows larger tumor resections, resulting in an improvement of the margins control²³.

Among the pathology laboratories, there is a lack of standardization in the processing of samples, especially in the accuracy of the microscopic margins evaluation, which subsequently creates a difficulty to study the effect of millimetric differences between the margins size^{13,14}.

The consensus of the Society of Surgical Oncology (SSO) and from the American Society for Radiation Oncology (ASTRO) emphasizes the importance in reaching free-tumor margins

Table 1. Literature series comparing oncological results in patients treated with oncoplastic breast surgery.

| Author/year | Rate of compromised margins (%) | Number of patients | Average follow-up time (months) | Distant metastasis rate (%) | Re-operating rates (%) | Local recurrence rate (%) | Rate of mastectomies (%) |
|------------------------|---------------------------------|--------------------|---------------------------------|-----------------------------|------------------------|---------------------------|--------------------------|
| Kaur et al. (2005) | 16 | - | - | - | - | - | - |
| Rietjens et al. (2007) | 3 | 148 | 74 | 13 | - | 3.4 | - |
| Munhoz et al. (2009) | 5.5 | 218 | - | - | - | - | - |
| Meretoja et al. (2010) | 16.2 | 90 | 26 | 3.3 | - | 8 | - |
| Fitoussi et al. (2010) | 18.9 (comprometidas ou exíguas) | 540 | 49 | - | - | 6.8 | 9.4 |
| Hamdi (2013) | 2.5 | 119 | 48 | - | - | 1.7 | - |
| Haloua et al. (2013) | 0-10 | 998 | 74 | - | - | - | 3- 16 |
| Losken et al. (2014) | 12 | 3116 | 37 | - | 4 | 4 | 6.5 |
| Kaviani et al. (2014) | 5 | 258 | 26 | 3.3 | - | 2.9 | - |
| Rezai et al. (2015) | - | 944 | 62 | - | - | 4 | 7.2 |
| De Cruz et al. (2016) | 9.8 | 6011 | 50.5 | 8.7 | - | 3.2 | - |
| De Lorenzi (2016) | - | 454 | 86.4 | 9.9 | - | 7.5 | - |

to optimize local control, and they highlight that no tumor cells touched the dye (in invasive carcinomas and *in situ*) as a negative criterion. This is based on the Houssami et al. (2014) meta-analysis outcomes, which showed that margins of one, two, or five millimeters were not associated with different risks for local recurrence^{14,24}. This fact corroborates the results of the clinical trial from the American College of Surgeons Oncology Group (ACOSOG), which provides more evidence on the concept that, in this current era of multiple therapies, minimizing the subclinical tumor margin is not essential to reduce local recurrence. Therefore, the concept that the resection margin of invasive carcinoma should have from two to five millimeters should be abandoned. Hopefully, this will bring a decrease in the re-excision rates. This is also in line with the concept of the negative margin from the National Surgical Adjuvant Breast and Bowel Project (NSABP), which is no tumor cell touching the dye²⁵.

When the OP is associated with the intraoperative evaluation of the margins, there is an even higher decrease in the new surgery rates, if compared to traditional BCS²³. Intraoperative evaluation of the margins provides a safe resection of the tumor, minimizing possible surgeries to extend the resection margins²¹.

Intraoperative techniques commonly used in the margins evaluation are the following:

- freezing;
- cytology;
- intraoperative ultrasonography; and
- sample radiography.

They all present limitations, and no specific technique has become universal in the international practice up to now. Pathological anatomy techniques are operator-dependent; therefore, they need resources and usually have a slow response. Only some sample points may be used for freezing, and the tissue may suffer from artifacts. Cytology techniques do not allow distinguishing one *in situ* tumor from an invasive tumor, and they do not provide information on the sample edge. Intraoperative ultrasonography is also operator-dependent, requires specific training, and suspected calcifications may not be visualized. Sample radiography is not capable of detecting noncalcified lesions, and benign calcification may be wrongly interpreted as malign^{15,26}. Among them, the intraoperative evaluation technique of higher accuracy margins, according to St. John et al. (2016) meta-analysis, is freezing (sensitivity of 86% and specificity of 96%), along with cytology¹⁵.

Some oncoplastic series in the literature are summarized in Table 1. Kaur (2005) obtained in his comparative study between the OP and traditional BCS a 16% rate of compromised margins with the OP, while the compromised margins rate in the BCS technique was of 43%²⁷. Rietjens et al. (2007), in a retrospective cohort study of 148 patients subjected to bilateral OP, found

a compromised margins rate of 3%⁶. In the series of Munhoz (2009), 218 patients subjected to OP were evaluated, and 5.5% of them showed positive resection margins in the final pathologic evaluation by paraffin, that is, a false-negative of the assessment through margins freezing²⁶. In the series of Meretoja (2010), a compromised margins rate of 16.2%²⁸ was showed.

In the retrospective study of Fitoussi (2010), with an average follow-up of 59 months, the low or compromised margins rate was of 18.9%²⁹. In the series of Hamdi (2013), with 119 patients subjected to the OP, a 2.5% rate of margins compromised by the tumor was obtained³⁰. In 2013, in the systematic review of Haloua et al., the rate of compromised margins in the group treated with BCS ranged from 20 to 40%. Use of OP resulted in a rate of 78 to 93% of tumor-free margins and compromised margins, ranging from 0 to 10%, leading to the mastectomy need in 3 to 16% of all OP cases¹⁹.

In the series of Kaviani (2014), 258 patients were included, all subjected to OP and prospectively followed-up, and in 95% of the cases, free margins were obtained³¹. At Losken (2014) meta-analysis, the compromised margins rate was significantly lower in the group treated with OP (12 *versus* 21% of the group treated with BCS; $p < 0.0001$)¹⁸.

In 2015, in the study of Rezai et al., in only 7.2% of the cases there was a need of later mastectomy (associated with multicentricity, large tumor size, and repeatedly undetermined margins). In addition, the lobe histological types, multicentricity, and multifocality are predictive factors of a subsequent mastectomy, although there is no impact on the overall survival³². In 2016, in the De Cruz's systematic review, the compromised margins rate was of 9.8%⁹.

ONCOPLASTIC SURGERY AND THE *IN SITU* CARCINOMA

The increase in early detection of breast cancer, due to tracing with mammography, lead to an increase in the incidence of ductal carcinoma *in situ* (DCIS), which corresponded to an average of 20% of all breast tumors. It should be ensured that there are no residual tumor cells, and at the same time, there must be a concern on removing the smallest margin possible to minimize breast deformities. There is no evidence that larger margins provide better rates of the disease local control³³.

Currently, radiotherapy is the gold standard in therapy after BCS for DCIS³³. Randomized studies evaluating the breast conservative post-surgery radiotherapy in DCIS therapy found high levels of local recurrence, with half of them being diagnosed as invasive carcinomas. The local recurrence rates in patients with DCIS treated with BCS range from 26 to 36% in those not treated with radiotherapy; from 9 to 23% in those treated with adjuvant radiotherapy – according to randomized prospective studies with 13 to 20 years of follow-up³⁴.

There are no randomized prospective series in literature with groups including only patients with DCIS that evaluate the oncoplastic surgery. Only in one descriptive and retrospective Polish study from Szynglarewicz (2016), a series of 36 patients diagnosed with DCIS treated with the reductive mammoplasty techniques was described, in which a new surgery rate of 8.3% was seen in patients showing near margins (1 mm or less)³⁵.

CONCLUSION

In the analysis of recent studies, the OP role as a reduction factor of new surgeries and local recurrence is questioned. According to recent studies, the OP became a safe oncological surgical technique that improves both the esthetic result and the disease local control, decreasing the compromised margins with impact on the mitigation of new surgeries rate.

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