Oncologic and Cosmetic Outcomes of Oncoplastic Breast Surgery in Locally Advanced Breast Cancer After Neoadjuvant Chemotherapy, Experience from a Developing Country

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Received: 19 February 2017 / Accepted: 1 August 2017 / Published online: 15 August 2017
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Abstract Oncoplastic surgery (OPS) has emerged as a new approach for extending breast conserving surgery (BCS) possibilities, reducing both mastectomy and re-excision rates, while avoiding breast deformities. OPS is based upon the integration of plastic surgery techniques for immediate reshaping after wide excision for breast cancer. This is a prospective feasibility cohort study of oncoplastic breast surgery after neoadjuvant chemotherapy that was carried at the National Cancer Institute, Cairo University and included 70 patients. The primary outcome was the local recurrence rate. Secondary outcomes included survival and margins obtained as well as cosmetic outcomes. Survival analysis was performed. Oncoplastic breast surgery did not compromise oncologic safety in the patients included in the study. It even allowed wider margins of resection which could be associated with better oncologic outcomes. At the same time, it gave a better cosmetic outcome and therefore higher patient satisfaction. Oncoplastic breast surgery includes a wide spectrum of surgical techniques, ranging from the basic level I techniques in breast conserving surgery to the more complex procedures of level II which are broadly classified into volume replace-

ment (therapeutic mammoplasty) and volume displacement procedures. We suggest that oncoplastic breast surgery techniques should be the standard of care in breast surgery. They are the basis for breast conserving surgery techniques in early breast cancer. In our experience, oncoplastic surgery is feasible in locally advanced tumours after downstaging with neoadjuvant chemotherapy without compromising the oncologic safety.

Keywords Breast · Oncoplastic Surgery · Neoadjuvant Chemotherapy · Safety · Egypt

Background

Oncoplastic breast surgery is defined as an approach to allow wide excision without compromising the natural shape of the breast [1]. It is based upon integration of plastic surgery techniques in breast cancer surgery.

It ranges from simple reshaping of breast tissue to more advanced mammoplasty techniques allowing resection of up to 50% of the breast volume.

The evidence for OPS is mostly based on Western published studies and is still lacking randomised trial data. The general consensus is that it is as oncologically safe as standard breast conserving surgery while being cosmetically superior to a mastectomy. There is lack of evidence from the developing countries. This study aims to address the feasibility of OPS in a large Egyptian centre.

It also addresses the feasibility of OPS in locally advanced breast cancer after neoadjuvant chemotherapy, a cohort of patients that would have been traditionally offered a mastectomy.

Electronic supplementary material The online version of this article (doi:10.1007/s13193-017-0689-3) contains supplementary material, which is available to authorized users.

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Methods

A prospective cohort feasibility study was conducted at the Department of Surgical Oncology of the National Cancer Institute (NCI), Cairo University, a major tertiary referral centre for surgical oncology and OPS, from 2013 to 2015.

During this period, 500 patients were seen with locally advanced breast cancer (LABC) at the NCI.

Seventy female patients with locally advanced breast cancer were included in the study.

Inclusion criteria were a histologically confirmed invasive breast cancer, age 18–65 years old, ECOG performance status ≤ 2 and a left ventricular ejection fraction $> 55\%$. Locally advanced breast cancer definition included stages IIb, IIIa and IIb breast cancer according to the AJCC staging system [2].

Pregnant or lactating women, males, patients with inflammatory breast cancer, T4b tumours with skin involvement and oedema and those with previous or concomitant malignancy were excluded.

All patients were treated with neoadjuvant chemotherapy according to the institutional guidelines, followed by evaluation for possibility of surgery. The standard protocol at NCI is the FAC regimen which consisted of 5-fluorouracil 500 mg/m², adriamycin 50 mg/m² and cyclophosphamide 500 mg/m² given in cycles. The cycle was repeated every 3 weeks. Six cycles were given in total.

Surgery was allowed 2 to 3 weeks after completion of chemotherapy.

The planning for surgery was guided by imaging before and after neoadjuvant chemotherapy. A mammogram and $\pm$ MRIs or ultrasound were done to determine the exact site and size of the tumour. Ultrasound of the axilla was routinely performed for nodal staging. Lymph nodes with ultrasound features such as increased cortical thickness and loss of fatty hilum were considered involved. The volume of the breast to be resected was estimated. Glandular density was assessed according to the ACR classification [3].

Surgery was performed for the responding patients. Patients who did not respond to chemotherapy were not included in the study as they had mastectomy.

Surgery was either type I or type II OPS of volume displacement or volume replacement technique using flaps (e.g. LD) according to the Clough classification [4].

The type of surgical procedure was determined according to the volume of breast tissue to be resected, the site of the tumour and the glandular density of the breast.

Patients were counselled and informed consent obtained. Pre-operative marking and photography were done in the standing position.

Axillary staging procedure was determined according to the pre-chemotherapy status; thus, axillary clearance was performed in node-positive patients.

Adjuvant radiotherapy indication and fields were based upon the pre-chemotherapy tumour characteristics. Hormonal treatment was given when indicated.

Patients were followed up according to the standard NCI protocol with clinical examination every 3 months and mammogram every year. The median follow-up period was 42 months with a range of 24 to 60 months.

The primary outcome was the local recurrence rate. The secondary outcomes included overall survival (OS), disease-free survival (DFS), margins obtained and cosmetic outcomes.

The data for the selected patients was collected in a sheet designed for the study. Statistical analysis was done to illustrate correlation or significance.

Data was analysed using IBM SPSS advanced statistics version 22 (SPSS Inc., Chicago, IL).

Survival analysis was done using Kaplan-Meier method and comparison between two survival curves using log-rank test. All tests were two-tailed. A *p* value < 0.05 was considered significant.

Results

Seventy patients were included in this study. All were diagnosed with locally advanced breast cancer between September 2012 and January 2015 at the NCI, Cairo University. The median age was 46 (range 22–70). The anatomical site of the tumour within the breast varied between upper outer quadrant (UOQ) (40%), LOQ (22.5%), LIQ (20%) and UIQ (2.5%). The stage grouping is shown in Table 1.

Seventy-five percent of the tumours showed positivity for oestrogen and progesterone receptors, and 12.5% showed Her-2 receptor positivity. All patients received neoadjuvant chemotherapy with FAC regimen. In two patients, the regimen was changed to a taxane-based regimen when no response was noted.

Following neoadjuvant chemotherapy, 90% of patients showed marked clinical response, while 10% showed minimal response. When the pathological response was assessed in the final histology of the specimen, 27.5% of the cohort showed complete pathological response, whereas 2.8% (two patients) showed no response. There was no statistically significant relationship between the pathological and the clinical response. The patients who had marked clinical response showed complete pathological response in 30.6% of cases. While 25% of the cases with minimal clinical response showed a complete pathological response (*p* = 1.0).

Of the patients, 57.1% had a level I OPS procedure, 24.2% had a level II procedure and 18.7% had a volume replacement procedure with latissimus dorsi flap (Table 2). Level II procedures included therapeutic mastopexy whether superior or inferior pedicle or round block and Grisotti flap for central tumours.

Table 1 Stage group in the study

TN stage	Number	Percentage
T2 N1	32	45.7%
T2 N2	4	5.7%
T3 N0	16	22.8%
T3 N1	10	14.2%
T3 N2	4	5.7%
T4 N0	1	1.4%
T4 N1	2	2.8%
T4 N2	1	1.4%

All patients received adjuvant radiotherapy as a standard component of breast conserving treatment. Some 4.2% of patients needed to continue chemotherapy after surgery as decided by the MDT.

Three patients (4.2%) had local recurrence and needed mastectomy at a later stage after initial treatment, at 11, 13 and 16 months, respectively. Of those, one patient (1.4%) developed distant metastasis in the bones associated with contralateral breast metastasis.

The cumulative DFS for the whole cohort was 90.2%.

The OS was 100% as there was no mortality reported in any patient during the period of the study

The cumulative DFS for patients who had level I surgery was 85.4%, while for those who had level II and volume replacement, it was 100% with no statistically significant difference ($p = 0.2$) because of small number of events (only three local recurrences) (Fig. 1).

Wider margins were obtained with level II and volume replacement than with level I ($p = 0.025$).

The median margin in level I was 10 mm, while in level II it was 25 mm. When a volume replacement technique was needed due to larger tumour size or involved margins, the median resection margin was 15 mm. The statistically significant difference in margins between the procedures was observed when level I and II were compared to each other in terms of margins obtained ($p = 0.028$) and when the three different categories were compared to each other ($p = 0.035$).

Table 2 Type of OPS performed

Surgical procedure	Number	Percent
<i>Level 1</i>	40	57.1%
<i>Level 2</i>		
Therapeutic mastoplastic	15	21.4%
Grisotti flap	2	2.8%
<i>Volume replacement</i>		
LD flap	9	12.8%
Mini LD flap	4	5.7%
<i>Total</i>	70	100%

LD latissimus dorsi

Although volume replacement allowed greater margins compared to level II techniques, the difference was less statistically significant ($p = 0.2$) (Table 3, supplementary).

The cumulative DFS when the median resection margin obtained was less than 20 mm was 86.3%, whereas when the median margin was equal or more than 20 mm, it was 100%. This difference was not statistically significant ($p = 0.2$) (Fig. 2).

The complications in our series varied between minor wound infection (10%), fat necrosis (5%) and NAC partial necrosis (2.5%). No patient needed re-operation as all complications were managed conservatively.

The cosmetic outcomes ranged between excellent result (61.4%), very good (21.8%), good (10%) and poor results (5.7%) on a very simplified scale that was used for the purpose of the study. This was modified from the Breast-Q scale of the EORTC-1801 trial [5] (Table 4, supplementary).

Discussion

Oncologic Safety

In our study, all breast conserving surgery was performed using OPS technique. Most of the patients had wide local excision with level I technique which included volume displacement with a local glandular flap +/- nipple areola complex re-centralization (Fig. 3).

When the volume to be excised was larger, a level II (therapeutic mastoplastic) technique was performed. This included a Grisotti flap for central tumour (Fig. 4), a superior pedicle mastoplastic for a lower pole tumour and an inferior pedicle mastoplastic for an UOQ tumour (Fig. 4 and 5).

When the volume of breast tissue to be excised was larger than a level II technique or when the margins were involved by intra-operative frozen section analysis, a more complex and extensive volume displacement technique was performed. This meant a latissimus dorsi myocutaneous flap with its variations (Fig. 6 and 7).

All those techniques allowed a wider margin to be obtained. Level II techniques allowed the widest margins. Despite the volume replacement techniques being more extensive and theoretically allowing a wider margin, they were always performed for larger more extensive tumours or for histologically involved margins. This explains why the median margin obtained with volume replacement techniques was less than with level II (Fig. 8).

The difference in margins between the techniques was statistically significant. This is acceptable and expected because level II allows for more extensive resection and ample tissue to reconstruct the defect. This backs up the fact that therapeutic mastoplastic is not only a better technique in terms of cosmetic outcomes, but it also allows wider margins of

Fig. 1 DFS with types of OPS

tumour resection and thus is oncologically more favourable [1]. When therapeutic mammoplasty is used (with or without a contralateral breast reducing procedure), a larger specimen size can be achieved with more likelihood of adequate tumour free margins (Fig. 7) [6].

A complication rate with therapeutic mammoplasty between 15 and 30% is quoted in the literature [7]. Complications include skin/flap or nipple-areolar complex necrosis, seroma, infection, haematoma, wound dehiscence and fat necrosis. In our cohort, the complication rate was within

that range. There was no delay of adjuvant radiotherapy in any of the patients in the study (Fig. 8).

Neoadjuvant Chemotherapy

Neoadjuvant therapy refers to the systemic treatment of breast cancer prior to definitive surgical therapy. The primary objective of neoadjuvant therapy is to improve surgical outcomes in patients for whom a primary surgical approach is technically

Fig. 2 DFS with margins

Fig. 3 Cosmetic outcome after level I OPS

not feasible and in patients with operable breast cancer who desire breast conservation.

In our study of 70 patients with locally advanced breast cancer, neoadjuvant chemotherapy allowed all of them to avoid having mastectomy as their surgical treatment. Only three patients developed local recurrence which necessitated a mastectomy at a later stage of their treatment.

This result is concordant with the literature regarding neoadjuvant chemotherapy as it is well established that its major effect is the reduction in the rate of mastectomy with no effect on survival [8].

Assessment of Response

The assessment of the response to neoadjuvant chemotherapy is an area of controversy.

The results from this study are in the same line with the literature as there was no relationship between the pathological and the clinical response. It is important to be aware of

Fig. 5 Cosmetic outcome after mini LD flap for volume replacement

such lack of correlation when assessing the patients who are treated with neoadjuvant chemotherapy for surgical options.

One measure to help in assessment is repeating the mammographic imaging at the end of chemotherapy. Some centres use MRI and it was even suggested to use PET scan. There is no method of imaging that is standard yet [9].

Another measure is the pre-treatment marking of the tumour with metal clips. This allows localising the tumour after completion of chemotherapy and guiding the surgical procedure.

We did not use the marking method in our study. However, a post-chemotherapy mammogram was always performed or sometimes an MRI with contrast guided the surgical decision.

A routine intra-operative frozen section analysis was done to ensure adequate clear margins of resection. In many occasions, a more extensive surgery was performed based on the frozen section results. Involved margins were the basis to proceed to a more extensive volume replacement procedures in

Fig. 4 Cosmetic outcome after level II OPS. Superior pedicle therapeutic mammoplasty

Fig. 6 Cosmetic outcome after level II OPS. Grisotti flap for central tumour and immediate nipple reconstruction

Fig. 7 Cosmetic outcome after level II OPS. Inferior pedicle therapeutic mammoplasty (*left*) and contralateral reduction mammoplasty

four patients. The patients have been consented to this prior to surgery.

At the time of conducting this study, trastuzumab was not yet licenced by the Egyptian Ministry of Health for use in the neoadjuvant setting. Therefore, it was not used in our study, even though there was a percentage of patients with Her-2 receptor positivity.

Cosmetic Outcomes

The cosmetic and psychological merits of breast conservation in comparison to mastectomy are well documented [10]. The EORTC Trial 10801 [5], a multi-centre randomised trial of functional quality of life and cosmesis after breast conserving therapy versus mastectomy, found significant benefit in body image and satisfaction with treatment in breast conserved patients. Amichetti [11] demonstrated that breast conservation surgery preserves patients' body image.

Fig. 8 Cosmetic outcome after level II OPS. Volume replacement with mini LD flap for UIQ tumour who had minimal clinical response

Bajaj et al. [12] noted that breast conservation therapy patients had significant treatment-related asymmetry. They reviewed 21 patients and all of them noted asymmetry. Bulstrode et al. [13] examined the feasibility of breast volume estimation as a predictor of cosmetic outcome. Their assessment revealed that excision of more than 20% of the breast tissue resulted in a poor cosmetic score. There is a need for oncoplastic techniques if excellent cosmetic outcome is to be achieved.

Of the patients, 5–14% have a poor cosmetic outcome following OPS [14]. Our results are very similar to the published literature in this aspect. This far less than the possible poor cosmetic outcome associated with wide local excision with no attempt at breast reconstruction.

The use of neoadjuvant chemotherapy as a primary treatment for locally advanced tumours allowed breast conserving surgery in those patients instead of mastectomy. When performed with an oncoplastic approach, the improvement in the quality of life is multiplied.

This is the first study looking at oncological safety and cosmetic outcomes of OPS in a developing country. It was conducted in prospective way which gives more strength to the data available.

The study has many limitations, mainly the small number of cohort. This is a feature of most of OPS studies where randomised trial data are still lacking. The other limitation of our study is the very simplified cosmetic outcome scale. This is due to the social and demographic properties of the study population and the relatively new concept of cosmetic preservation in breast cancer surgery in developing countries and the fact that all the available cosmetic assessment scales are developed from the West. We acknowledge the need to develop a local cosmetic outcome scale specific to the population of the study.

We also recognise the limitation of our study with regards the follow-up time. Since the majority of the patients' cohort are those with T2 and T3 ER positive tumours, longer follow-up may be needed to ascertain local failures. We continue to monitor our patients for further results.

More than 80% of the patients fall in the T2N1, T3N0 and T3N1 group and are ER positive; this could represent a select group among those with LABC who may be suitable for breast conservation surgery.

Conclusion

This is a feasibility study of OPS techniques in locally advanced breast cancer patients after downstaging the tumour with neoadjuvant chemotherapy.

The lack of randomised trial data makes comparison of techniques very difficult; most studies (like this one) involve

small cohorts of patients assessed for outcome in a multitude of ways.

Despite the available worldwide evidence, validation of the published evidence for OPS in developing countries is still lacking. To the best of our knowledge, this is the first study looking at the oncologic safety and cosmetic outcomes of OPS in the developing countries.

The results from the study are concordant with the available literature on OPS, its oncologic safety and cosmetic outcomes.

It is therefore concluded that OPS is safe oncologically and feasible in locally advanced breast cancer downstaged with neoadjuvant chemotherapy.

We recommend OPS as the standard of care in early breast cancer and in selected cases with locally advanced breast cancer showing good response to neoadjuvant chemotherapy.

OPS is an emerging subspecialty in developing countries which still needs further studies. More research is needed to add to the current evidence.

Compliance with Ethical Standards

Conflict of Interest The authors declare there is no conflict of interest in this article.

Funding There was no funding source involved in the writing of this article.

Ethical Approval Ethical approval was obtained by the Ethics Committee at the National Cancer Institute, Cairo University, April 2011.

References

1. Clough KB, Lewis J, Couturaud B et al (2003) Oncoplastic techniques allow extensive resections for breast-conserving therapy of breast carcinomas. *Ann Surg* 237(1):26–34
2. AJCC (American Joint Committee on Cancer) (2002) Cancer staging manual, 6th ed. Greene FL, Page DL, Fleming ID, et al (Eds), Springer-Verlag, New York. p. 223
3. American College of Radiology (2003) Breast imaging reporting and data systems (BI-RADS). American College of Radiology, Reston, VA
4. Clough KB, Kaufman GJ, Claude N et al (2010) Improving breast cancer surgery: a classification and quadrant per quadrant atlas for oncoplastic surgery. *Ann Surg Oncol* 17:1375–1391
5. Curran D, van Dongen JP, Aaronson NK et al (1998) Quality of life of early-stage breast cancer patients treated with radical mastectomy or breast-conserving procedures: results of EORTC Trial 10801. The European Organization for Research and Treatment of Cancer (EORTC), Breast Cancer Cooperative Group (BCCG). *Eur J Cancer* 34:307
6. Asgeirsson KS, McCulley SJ, Pinder SE et al (2003) Size of invasive breast cancer and risk of local recurrence after breast-conservation therapy. *Eur J Cancer* 39:2462
7. Munhoz AM, Montag E, Arruda EG et al (2006) Superior-medial dermoglandular pedicle reduction mammoplasty for immediate conservative breast surgery reconstruction: technical aspects and outcome. *Ann Plast Surg* 57:502
8. Wolmark N, Wang J, Mamounas E, et al. (2001) Preoperative chemotherapy in patients with operable breast cancer: nine-year results from National Surgical Adjuvant Breast and Bowel Project B-18. *J Natl Cancer Inst Monogr* 96
9. Segara D, Krop IE, Garber JE et al (2007) Does MRI predict pathologic tumour response in women with breast cancer undergoing preoperative chemotherapy? *J Surg Oncol* 96:474
10. Al-Ghazal SK, Fallowfield L, Blamey RW (2000) Comparison of psychological aspects and patient satisfaction following breast conserving surgery, simple mastectomy and breast reconstruction. *Eur J Cancer* 36:1938
11. Amichetti M, Caffo O (2001) Quality of life in patients with early stage breast carcinoma treated with conservation surgery and radiotherapy. An Italian monoinstitutional study. *Tumori* 87:78
12. Bajaj AK, Kon PS, Oberg KC et al (2004) Aesthetic outcomes in patients undergoing breast conservation therapy for the treatment of localized breast cancer. *Plast Reconstr Surg* 114:1442
13. Bulstrode NW, Shrotria S (2001) Prediction of cosmetic outcome following conservative breast surgery using breast volume measurements. *Breast* 10:124
14. Baildam A, Bishop H, Boland G et al (2007) Oncoplastic breast surgery a guide to good practice. *Eur J Surg Oncol* 33(Suppl. 1):S1