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ORIGINAL ARTICLE – BREAST ONCOLOGY

Oncoplastic Level 2 Mammoplasty for Large DCIS: 5-Year Results

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ABSTRACT

Background. Oncoplastic surgery (OPS) allows wider resections with immediate breast reshaping by mammoplasty. This study reviews our experience with level 2 mammoplasties in patients with histology-proven pure ductal carcinoma in situ (DCIS).

Method. From a prospectively maintained database of 392 consecutive oncoplastic level 2 mammoplasties, 68 patients presented with pure DCIS.Involved margin rates and locoregional recurrence rates were calculated, with 76 months (0–166 months) median follow-up.

Results. The mean pathological tumor size was 34 mm (median 26 mm, range 2–106 mm). The mean resection weight was 191 g (median 131 g, range 40–1150 g). Margins were clear in 58 cases (85.3%) and involved in 10 cases (14.7%). Margins were involved in 1 out of 54 (1.9%) cases with tumor size under 50 mm and in 9 out of 14 (64.3%) cases with tumor size higher than 50 mm ($p < 0.001$). On multivariable analysis, only tumor size > 50 mm [odds ratio (OR) 95.400; $p < 0.001$] was independently associated with involved margins. Seven patients had mastectomy. The overall breast conservation rate was 89.4%, and 100% for tumors less than 5 cm. There were three local recurrences. The 5-year cumulative incidence for local recurrence was 5.5% (0–11.5%).

Conclusions. OPS is a safe solution for large DCIS up to 50 mm, with an involved margin rate of only 1.9%, and can thus reduce the mastectomy rate in this group. As margin involvement significantly increases for tumors larger than 5 cm, better preoperative localization and/or wider excisions are necessary in this group.

Ductal carcinoma in situ (DCIS) represents 20–25% of all screening-detected breast cancers and often presents as microcalcifications on screening mammography.[1,2]

Treatment options for DCIS are either breast-conservative therapy (BCT), which consists of lumpectomy followed by radiotherapy, or mastectomy in the presence of extensive or multifocal disease. Overall, 30% of DCIS patients will be treated by mastectomy and 70% by BCT, of whom approximately one in three undergo reexcision.[3–5] However, reexcisions compromise cosmetic outcome and have been associated with a high rate of conversion to mastectomy.

Margin width is one of the modifiable risk factors for ipsilateral breast tumor recurrence (IBTR) and is therefore of great interest to surgeons. The current consensus guidelines of the Society of Surgical Oncology, American Society for Radiation Oncology, and American Society of Clinical Oncology[6] recommend a margin threshold of 2 mm for DCIS.

Oncoplastic surgery (OPS) by mammoplasty combines wide surgical resections with immediate breast reshaping. In 2010 we published a "quadrant per quadrant atlas" based on a two-level classification of oncoplastic techniques.[7] Level 1 OPS techniques include simple advancement or rotation glandular flaps together with nipple–areolar complex (NAC) displacement, which

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allow correction of small volumetric defects (less than 15–20% of breast volume) to reshape the breast. Level 2 OPS is based on mammoplasty techniques and involves resections larger than 15% of breast volume, as well as skin excision. This atlas advocates a specific mammoplasty technique per tumor location, thereby offering a simple and reproducible surgical solution for all clinical scenarios.

The wider resections performed with level 2 mammoplasty techniques can reduce both mastectomy rates and reexcision rates when compared with standard BCT.[8]

There is, however, very little data available on use of OPS for DCIS.[9–11] Only three studies have been published on oncoplastic surgery in DCIS patients, containing 28, 36, and 44 patients, respectively.[10–12]

This study reviews our 14-year experience with use of therapeutic mammoplasties in patients with biopsy-proven large DCIS. To date, this is the largest series with long follow-up on OPS for large DCIS. The rates of positive margin, reexcision, and BCT as well as 5-year local recurrence were evaluated. Patient and tumor characteristics associated with involved margins were analyzed.

PATIENTS AND METHODS

Institutional review board (IRB) approval was obtained to query the prospectively maintained oncoplastic database.

From a consecutive cohort of 392 oncoplastic level 2 mammoplasties performed between January 2004 and February 2018, 68 patients were identified with biopsy-proven pure DCIS. All patients presenting with final diagnosis of DCIS with invasive or microinvasive carcinoma were excluded for this series.

Patient and Tumor Characteristics

The following patient and tumor characteristics were recorded: patient age, radiological tumor size, date of surgery, indication for oncoplastic reduction, type of mammoplasty technique, resection weight and volume, contralateral reduction (immediate or delayed) and technique, pathological tumor size and grade, reexcision rate, presence of comedo necrosis, nodal treatment and involvement, and postoperative radiotherapy.

A small subgroup of patients had small tumor size but desired simultaneous reduction mammoplasty given their large breast size, asymmetry, and/or ptosis. Their indication was registered as "oncocosmetic."

Patients were followed up every 4 months for 3 years, then every 6 months until 10 years postoperatively, then yearly. The last date of follow-up was registered.

Surgery, Histopathology, and Adjuvant Treatment

All lesions were localized preoperatively with a radiologically guided hooked wire. In selected cases, two or more wires were placed to bracket the tumor.

Preoperative markings for mammoplasty were done with the patient in standing position. Based on the tumor location, the appropriate mammoplasty technique was applied according to our previously published atlas.[7,13]

When the resection volume resulted in a noticeable asymmetry in size between the two breasts, immediate contralateral breast reduction was performed.

Tumor resection was a large full-thickness glandular excision, from the skin to the pectoralis fascia. No systematic shavings of the cavity were performed, but a specimen X-ray was always performed peroperatively. If calcifications were identified close to any radial margin, immediate reexcision was carried out. Clips were systematically placed into the defect for radiotherapy planning.

Multifocal DCIS was defined as multiple foci of DCIS within the same quadrant of the breast. These were removed en bloc. The size of these separate foci were added to calculate the total tumor size.

Sentinel lymph node biopsy was performed in case of large-sized high-grade DCIS or a radiological mass lesion with suspicion of invasive disease. Axillary surgery was performed either through a separate incision or an extension of an upper outer quadrant incision.

Histopathological examination was done as previously described.[9]

Resection volumes were abstracted from the pathology report by multiplying specimen height × length × width (in cm^3). Positive margins for DCIS were defined as presence of tumor cells within 2 mm of the cut edge of the specimen.

All patients had postoperative radiotherapy to the breast (50 Gray) with a boost to the tumor bed.

Statistics

Data are presented as mean with associated median and range, or as relative and absolute frequencies. The data were analyzed for factors associated with margin involvement. Univariable analysis with χ^2 and Fisher's exact tests was used to compare differences in percentages between groups. Two-sided $P < 0.050$ was considered statistically significant. All variables with $P < 0.500$ on univariable analysis were included in a binary logistic regression model for multivariable analysis.

Estimates of local recurrence, regional recurrence, and distant metastases were performed. Patients were censored when they were last seen, or, for the purposes of local recurrence and distant recurrence cumulative incidence, at

time of death. R (version 3.0.2 for Linux) and SPSS® software version 23.0 (IBM, Armonk, New York, USA) were used for data compilation, validation, and analysis.

RESULTS

Sixty-eight consecutive DCIS patients underwent level 2 OPS mammoplasty. Patient and tumor characteristics are presented in Table 1.

The mean pathological tumor size was 34 mm (range 2–160 mm). The mean patient age was 59 years (range 20–86 years).

The indications for OPS were tumor size (42.6%), positive margins after prior standard breast-conserving surgery (20.6%), poor tumor location with high risk of postoperative deformity (17.6%), oncocosmetic (16.2%), and multifocality (3%).

The most common level 2 technique used was lateral mammoplasty for upper outer quadrant tumors (23/68 cases, 33.8%), followed by a superior pedicle technique for lower pole DCIS (17/68 cases, 25.0%) and J-mammoplasty for lower outer quadrant lesions (8/68 cases, 11.8%) (Table 2).[7]

TABLE 1 Baseline characteristics and surgical outcome of 68 patients treated with OPS for DCIS

Characteristic	*n*	%
Mean age (years)	59 (median 60, range 20–86)	
Mean radiological tumor size (mm)	33 (median 30, range 5–100)	
Mean pathological tumor size (mm)	34 (median 26, range 2–106)	
Focality		
Unifocal	63	92.6
Multifocal	5	7.4
Pathological T size (mm)		
≤ 20	29	42.6
21–50	25	36.8
> 50	14	20.6
Final histology		
Pure DCIS	68	100
Nuclear grade		
Low	3	4.4
Intermediate	23	33.8
High	42	61.8
Comedo necrosis		
No	19	27.9
Yes	49	72.1
Mean specimen weight (g)	191 (median 131, range 40–1150)	
Mean specimen volume (cm^3)	375 (median 300, range 45–3483)	
Margins		
Clear	58	85.3
Involved	10	14.7
Treatment of involved margins		
Conservative reexcision	2	20.0
Completion mastectomy	7	70.0
Radiotherapy alone	1	10.0
Axilla		
No surgery	30	44.1
SLN	37	54.4
ALND	1	1.5
Nodal status		
N0	68	100

SLN sentinel lymph node, *ALND* axillary lymph node dissection

TABLE 2 Level 2 OPS techniques applied to 68 DCIS cases according to the "quadrant per quadrant atlas"—orientation for left breast[7]

Tumor location	Level II OPS mammoplasty techniques 2	*n* (%)
Upper outer quadrant	Lateral mammoplasty	23 (33.8)
Lower pole	Superior pedicle	17 (25.0)
Lower outer quadrant	J mammoplasty	8 (11.8)
Lower inner quadrant	LIQ-V mammoplasty	8 (11.8)
Upper pole	Inferior pedicle	5 (7.4)
Upper inner quadrant	Round block	2 (2.9)
Central subareolar	Inverted T or vertical scar mammoplasty with NAC resection	2 (2.9)
Miscellaneous	Other	3 (4.4)
Total		68 (100)

LIQ lower inner quadrant, *NAC* nipple areolar complex

The mean resection weight was 191 g (median 131 g, range 40–1150 g), and the mean resection volume was 375 cm^3 (median 300 cm^3, range 45–3483 cm^3).

Margin Status

Margins were clear in 58 cases (85.3%) and involved in 10 cases (14.7%). Of the ten patients with an involved margin, two underwent conservative reexcision, seven underwent mastectomy, and one was treated with radiotherapy alone because she had minimal margin involvement and refused further surgery. The overall breast conservation rate was 89.7%.

When analyzing the ten patients with positive margins, they were more likely to have younger age ($\leq$ 45 years, $P = 0.037$) and tumor size larger than 50 mm ($P < 0.001$). Margins were involved in 1 out of 54 (1.9%) cases with tumor size under 50 mm and in 9 out of 14 (64.3%) cases with tumor size higher than 50 mm ($P < 0.001$) (Fig. 1). Margins were involved in 3 out of 6 (50%) patients with age $\leq$ 45 years and in 7 out of 62 patients (11.3%) with age $>$ 45 years ($P = 0.037$). High tumor grade and comedo necrosis were not associated with a positive margin ($P > 0.05$).

On multivariable analysis, only tumor size larger than 50 mm (OR 95.400, 9.952– 914.552; $P < 0.001$) was independently associated with involved margins.

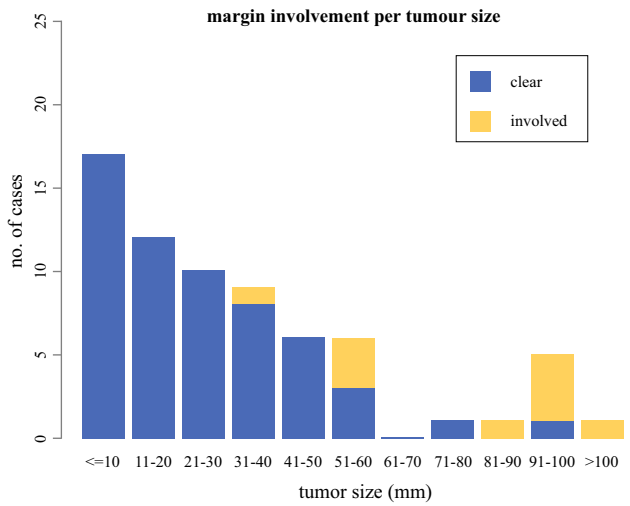

FIG. 1 Margin involvement as a function of tumor size in patients with DCIS

Recurrences and Survival

With median follow-up of 76 months (mean 73 months, range 0–166 months), there were three local ipsilateral breast recurrences, two axillary recurrences, two distant recurrences, and one death. The 5-year cumulative incidence for local recurrence was 5.5% [confidence interval (CI) 0–11.5%], 2.1% (CI 0–6.2%) for regional recurrence, and 1.5% (CI 0–4.5%) for distant recurrence.

DISCUSSION

Oncoplastic surgery allows wider excisisions than standard BCT[8,14] without cosmetic compromise to the breast. In properly selected cases, it is a major tool to reduce margin involvement and to increase breast conservation rates for breast cancer. Very few studies have analyzed the outcome of OPS for large DCIS. In this study of 68 DCIS cases with mean tumor size of 34 mm, margins were involved in only 14.7% of cases. Margin involvement was only 1.9% when the tumor size was under 50 mm and significantly increased (64.3%) when the tumor size was over 50 mm. Overall, the ipsilateral 5-year local recurrence rate was 5.5%.

Margin Involvement of DCIS After Standard BCT Versus OPS

Identifying the extent of carcinoma in situ is more difficult than for a mass lesion since DCIS is not always

visible on imaging and often nonpalpable. This may result in incomplete excision or inadequate clearance margins, which both typically require reoperation. Most studies have reported that about one in three women (31–46%) with DCIS will undergo reexcision for involved margins,[3,15–18] with a median tumor size reported in these historical studies of around 20 mm.[15,16]

OPS could be beneficial for these often underevaluated DCIS lesions, allowing wider resections than standard BCT,[19–22] which should translate into fewer positive margins. This is confirmed in the current series, as our margin involvement rate of only 14.7% with a median tumor size of 34 mm is very low, compared with the higher margin involvement rates mentioned in historical studies, albeit for smaller tumor sizes.

DCIS Size and Margin Involvement

Patients with greater DCIS size have higher risk of positive margins.

Melstrom et al.[18] demonstrated in a retrospective review of 546 DCIS patients treated with BCT that tumor size was independently associated with positive margin status with an odds ratio of 2.38. Tumor size of the margin-positive group was more than twice the size of the margin-negative group (2.1 versus 1.0 cm; $P < 0.001$).

Cheng et al.[23] confirmed this in their study, and found that 77% of patients with DCIS $\geq$ 2.5 cm had positive margins compared with 30% of those with lesions $<$ 2.5 cm.

In the study of Dillon et al., DCIS lesions over 3 cm in size had a risk of compromised margins of over 90%.[15]

Mammoplasty techniques can extend the boundaries of BCT for DCIS, by maximizing resection volumes in these larger-size DCIS lesions. It is notable that, in the current study, none of the patients with DCIS size $\leq$ 30 mm had positive margins. Of the patients with tumor size between 3 and 5 cm, 6.7% (1/15) had positive margins versus 64.3% (9/14) of patients with tumor size over 5 cm.

DCIS and Local Recurrences

Complete excision of DCIS with clear margins is the most important factor in reducing the risk of local recurrence.[24–26] The risk of locoregional recurrence (LRR) in contemporary DCIS patients treated with breast-conserving surgery (BCS) followed by radiotherapy ranges from 5 to 10% at 10 years.[27] Half of the recurrences that do occur are invasive.

The EORTC 10853 trial randomized 507 of 1010 patients with DCIS to local excision followed by radiotherapy. The mean mammographic lesion size was 20 mm. The 4-year local recurrence rate in this group was 8%.[28] Forty percent of this population was poorly differentiated/high grade.

In the NSABP B-17 study, 410 DCIS patients were randomized to lumpectomy followed by radiotherapy. Of these patients, 91.5% had tumor size $\leq$ 20 mm.[29] The 8-year cumulative incidence of ipsilateral breast recurrence was 12.1% in this group.[29]

In the current study, the median tumor size was 34 mm. Our population was a high-risk DCIS population, with 62% high grade and 72% with comedo necrosis. However, the 5-year local recurrence rate was only 5.5%. Moreover, out of 14 patients with BCT for DCIS larger than 5 cm, only 1 patient developed a local recurrence, and there were no regional recurrences or distant metastases in this subgroup.

In a metaanalysis by Wang et al.,[4] comprising 21 studies and 7564 patients, a negative margin was associated with a lower risk of IBTR (OR 0.46).[4] This study suggests that surgeons performing first BCS should target the widest possible negative margin within cosmetic constraints. OPS facilitates this. By attaining wider negative margins with the initial surgery, surgeons improve quality of care and minimize ipsilateral breast tumor recurrence, as well as decrease the risk of reexcision, resulting in better long-term outcomes without further cosmetic compromise.

OPS Literature on DCIS

Despite extensive literature on OPS, very few studies have evaluated OPS for DCIS.[9,20,30–34] Song et al.[10] described a series of 28 patients with DCIS treated with oncoplastic BCS. They reported a positive margin rate of 32%, despite the extensive resection associated with the oncoplastic approach ($>$ 250 g). The women in this positive-margin group who required reoperations were overall younger (mean age 45.6 years) than those in whom oncoplastic surgery was the definitive procedure (mean age 57.8 years). After median follow-up of 32.4 months, there was one local recurrence.

In the study of Szynglarewicz et al.,[11] 36 women with DCIS and average tumor size of 29 mm underwent OPS. Three out of 36 women had close margins and underwent successful reexcision. Median follow-up and local recurrence rates were not reported. Both studies defined a free margin width as at least 1 mm.

In the recent European Institute of Oncology study by De Lorenzi et al.,[12] 44 DCIS patients treated by level 1 and 2 OPS techniques followed by radiotherapy were matched with 375 patients treated with standart BCT. They reported a 6-year local recurrence rate of 22%. Our 5-year local recurrence rate is 5.5% despite the higher grade and mean tumor size of 34 mm in the current study.

To the best of the authors' knowledge the current study is the largest series on DCIS treated with OPS

mammoplasties, reporting the results of 68 patients with median tumor size of 34 mm, in a high-risk population (72% comedo necrosis, 62% high grade). The positive margin rate of 14.7% in the current study compares favorably with the data above, as does the overall breast conservation rate of 89.4% (100% for tumors 5 cm or less).

Study Limitations

The results of this study are limited by its retrospective nature. Although the number of patients in this study was low, our population appears to be a high-risk group of DCIS patients with 72% comedo necrosis and 62% high grade.

The measurable outcomes of oncoplastic surgery are margin involvement and breast conservation rate, complication rate, survival and local recurrence rates, cosmesis, and patient satisfaction.[35] In this study, we focused on the oncological results, since the cosmetic outcomes have been reported in our previous publication.[13]

CONCLUSIONS

The current study is the largest series on oncoplastic breast reductions for DCIS, confirming that level 2 mammoplasties allow wide resections with free margins in patients with large DCIS. Despite a median tumor size of 34 mm, the breast conservation rate was 89.7% with a 5.5% 5-year local recurrence rate.

OPS is thus a safe and excellent solution for large DCIS lesions, at least up to 50 mm, with an involved margin rate of only 1.9% for tumors below 50 mm. As margin involvement significantly increased for tumors larger than 5 cm, patients considering BCT should be informed about the significantly higher risk of margin involvement, even with OPS techniques. Better preoperative localization and/or wider excisions are necessary to extend OPS possibilities and allow breast conservation in this group.

DISCLOSURE There were no conflicts of interest for any of the authors.

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