Evaluation of Lipofilling Safety in Elderly Patients with Breast Cancer

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**Background:** Lipofilling is widely used in breast reconstruction after mastectomy with reconstruction or breast conserving surgery in patients with breast cancer. The aim of this study is focused on complications associated with lipofilling in elderly breast cancer patients with breast defects after breast conserving surgery or reconstruction.

**Methods:** A total of 137 patients older than 60 years who underwent 153 lipofilling procedures were included. All patients had undergone breast lipofilling using Coleman’s technique. Estimated breast defect volume, lipofilling volume, and complications after lipofilling were obtained for analysis.

**Results:** Most patients (67%) had only 1 lipofilling procedure. The median lipofilling volume to breast defect volume ratio was 1.5. No severe complications were found after treatment. Liponecrosis was detected in 10 of 153 breasts (7%) or 9 of 137 patients within 2 weeks after lipofilling and required surgical drainage in 2. No local recurrences were noted.

**Conclusions:** The incidence of liponecrosis after lipofilling in elderly patients was relatively high, requiring surgical drainage in some cases. As a rough guide, the lipofilling volume should not exceed 1.5 times the defect volume, and close postoperative follow-up within the first 2 weeks is suggested for these patients. (Plast Reconstr Surg Glob Open 2015;3:e441; doi: 10.1097/GOX.0000000000000411; Published online 1 July 2015.)

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the atrophy of the adipose tissue at the donor site, complications and failure of the procedure might be more frequent. The aims of our study included estimating the incidence of complications, the volume of breast defects, and determining the ratio of the lipofilling volume to breast defect volume. These measures might help reduce necrotic complications at the recipient breast and reduce excessive fat harvesting at the donor site.

**MATERIALS AND METHODS**

We used the European Institute of Oncology Breast Cancer Database to identify patients 60 years or older (elderly patients) who were operated on for breast cancer from March 2007 to June 2013 and had subsequently undergone lipofilling procedures. We retrospectively selected 137 elderly patients who underwent 153 procedures. Patients’ age, smoking history, and associated comorbidities (diabetes mellitus, hypertension, and dyslipidemia) were recorded as patient factors. All had secondary defects occurring after quadrantectomy or mastectomy with reconstruction. Patients who received radiotherapy before lipofilling were also included in this study.

All patients were evaluated preoperatively with clinical breast examination, and bilateral mammography and breast ultrasonography. We estimated the fat tissue requirement (breast defect volume) by preoperative photographic assessment in 30 breasts of 25 patients who underwent mastectomy with reconstruction. Preoperative photographs were taken in these cases, and all the parenchymal defects were measured by 2-dimensional quantitative measurement system using a caliper on its 2 major axes and the depth by estimation and empirical measurement. In 45 breasts of 43 patients who previously underwent quadrantectomy, the defect volume was estimated by multiplying the measured length, width, and thickness of resected specimens and reported as cubic centimeter. We evaluated the success rate by clinical examination and comparison of photographs taken in the postlipofilling period with those taken before lipofilling.

We performed the lipofilling procedure as follows. We infiltrated the selected donor site with Klein’s solution. Its composition included 1 mL of 1:200,000 epinephrine mixed in 500 mL of lactated Ringer’s solution. If the surgeon performed the procedure under local anesthesia, we added 50 mL of 2% mepivacaine to this solution. The procedure for fat harvesting and lipofilling was performed using Coleman’s technique, as published in 1995.7 The fat was harvested with negative pressure applied to a blunt-tipped Coleman’s cannula, attached to a 10-mL syringe, and passed through the tissues at the abdomen or other selected donor sites. The fat-aspirate obtained was processed in a centrifuge at 3000 rpm for 3 minutes.2 Centrifugation could separate the serum, oily component, lysed cells, and blood residuals from the purified adipocytes. The purified fat was injected into the recipient area through a 17 G blunt Coleman’s cannula. Multidirectional injections were performed with thin-layer and multiple-tunnel technique. If we hit a fibrotic scar, especially in irradiated tissues, we underlined it with a 17 G needle to create a space for the recipient site.

Subsequent repeated procedures were performed as needed until satisfactory augmentation was achieved. We usually performed lipofilling after the completion of breast surgery and/or reconstructive procedure, and after adjuvant chemotherapy and radiation. If the patient received adjuvant radiation therapy, we delayed the lipofilling for at least 6 months after completion of radiation treatment.

Statistical analysis was performed using Stata version 12 (Stata Corp, College Station, Tx.). Quantitative variables were summarized as mean and SD or median and range as appropriate. Categorical variables were summarized as counts and percentage. Differences in quantitative variables between groups were tested using unpaired t test or Wilcoxon rank-sum test as appropriate, and Fisher’s exact test was used for categorical variables. Linear correlation between quantitative variables was measured using Pearson’s correlation coefficient. Statistical significance was defined as a 2-sided P value less than 0.05. We assumed all units of primary analysis (breasts) to be independent.

**RESULTS**

The mean age of patients in this study was 64.8 years (range 60–78 years), with comorbidities presented in Table 1. The median follow-up time was 16 months (range 5–74 months). All patients had a history of breast cancer. Types of breast reconstruction before the lipofilling procedure are shown in Table 2. Lipofilling was performed after BCT in 58 breasts (52 patients) and after mastectomy with reconstruction in 95 breasts (85 patients). Among the 137 patients, 78 patients (57%) or 86 breasts had previously received locoregional radiotherapy before lipofilling procedures.

The median initial estimate of fat tissue requirement (or breast defect volume) of the defect per breast in the available data (n = 75) was 60 mL, with a range from 5 to 495 mL. The estimated breast defect volume in mastectomy patients was lower than in quadrantectomy patients because of reconstruction of the breast with silicone implants in that group.
The median total volume of injected fat was 81 mL, varying from 6 to 460 mL (Table 3), with an average total volume of 102 mL; these data were available for all breasts (n = 153). There was a low correlation between the estimated breast defect volume and total lipofilling volume (Pearson’s correlation coefficient = 0.123; n = 75). The majority of patients required only 1 procedure (103 of 153 breasts or 67%; 92 of 137 patients or 67%). Forty-five patients (33%) underwent more than 1 procedure and 1 required 5 procedures.

Irradiated breasts had significantly more repeated lipofilling procedures (44% or 38 of 86 breasts) than those without irradiation (18% or 12 of 67 breasts); P value was equal to 0.001 by Fisher’s exact test. However, the median total volume injected was 84.5 mL in the irradiated group and 80 mL in the nonirradiated group, and this difference was not significant (P value = 0.155 by Wilcoxon rank-sum test).

The smallest ratio of the lipofilling volume to breast defect volume was 0.11, or one-ninth of the estimated defect volume (the estimated defect volume was 111 mL). The largest lipofilling to defect ratio was 34.3, or approximately 34 times the estimated defect volume (P value = 0.833 by Wilcoxon rank-sum test).

Complications at the donor site area were not observed in this series. Types of postoperative complications are shown in Table 4. Postoperative complications were seen in 12 breasts (8%) in 11 patients. Liponecrosis were seen in 10 breasts (7%) in 9 patients. Breasts with complications did not receive more than 2 lipofilling procedures. In fact, 3 of 12 breasts with complications (25%) had 2 injections, whereas 47 of 141 breasts with no complications (33%) had 2 injections (P value = 0.752 by Fisher’s exact test). The median total volume of injected fat in the group with liponecrosis was 98.5 versus 80.0 mL for the group without necrosis (P = 0.647, Wilcoxon rank-sum test). Neither age nor occurrence of comorbidity was significantly different between the groups with complications and without complications (t test, P value = 0.355 and Fisher’s exact test, P value = 0.511, respectively).

Liponecrosis was managed by conservative treatment in 7 breasts, but needed surgical drainage in 2 breasts because of abscess formation, and required needle aspiration in 1 breast. Two breasts with cellulitis were successfully treated with antibiotic therapy. All abscesses and cellulitis occurred within 2 weeks after lipofilling. Among the 12 breasts with postoperative complications, 8 received locoregional...
radiotherapy (8 of 78 or 9% complication rate in the radiation group) and 4 did not receive this treatment (4 of 67 or 6% in the non-irradiated group). This difference was not statistically significant (P-value = 0.552 by Fisher’s exact test).

All patients underwent both preoperative and postoperative mammography and ultrasound. Several imaging changes were noted in 13 breasts (Table 5). They were all reported as benign findings not requiring further interventions. The oncological follow-up was based on physical examination and mammographic findings. No local recurrence was found within the period of follow-up. Thus, there were 126 of 137 patients with reasonable cosmesis but without lipofilling complications and no local recurrence within the follow-up period, providing a success rate of 92%.

**DISCUSSION**

Complication rates after different techniques of lipofilling in all age groups have been reported to be small but quite variable.\(^8,9\) In this study, we reported one of the largest series of lipofilling performed in elderly patients. The present 8% early complication rate should be compared with the 4% rate in our 2011 publication, in which we reported the results of lipofilling done in patients of all age groups.\(^2\) Liponecrosis was seen in 10 breasts (7%) in this study and needed surgical drainage in 2 patients because of high fever, which did not respond to systemic antibiotics, compared with 5 breasts (3%) with liponecrosis in our previous report, which did not need surgical intervention.

To reduce the occurrence of liponecrosis, we performed lipofilling according to Coleman’s technique in which we injected the fat graft from a separated column of fat to maximize the surface area of contact between the grafted fat and available healthy tissue.\(^4\) This technique is technically easy and safe. Thus, liponecrosis, evident on mammography in 5 cases, was not clearly related to excessive amount of fat grafting in this study. In our strategy, we did not perform overcorrection of the breast defects that might impair the viability of adipose tissue leading to liponecrosis. However, this study, done in a large group of elderly patients, had a relatively higher liponecrosis rate that was still comparable with those reported in the literature for a wide range of age groups (Table 6).

Previous studies suggested that the surgeon should be more cautious in performing lipofilling in patients with irradiated breasts. The study by Losken et al\(^20\) suggested that radiation therapy might increase the number of repeated injections because of less compliance of the covering soft tissue. Rigotti et al\(^22\) also reported multiple injection sessions in irradiated patients but with excellent results. Serra-Renom et al\(^16\) showed that fat grafting in patients who received radiotherapy achieved better outcomes with the formation of new subcutaneous tissue because of the angiogenic capacity of preadipocytes or stem cell in the adipose tissue. Sarfati et al\(^15\) demonstrated the benefits of fat grafting to the irradiated chest wall before implant placement. Although our study also did not clearly show increased adverse effects of prior radiation therapy, there was a clear increase in the number of repeated lipofilling procedures in elderly patients with breast irradiation.

There has been no study showing the correlation between the volume of breast defects and the lipofilling volume, in both breast conserved patients and patients with mastectomy and reconstruction. For example, Del Vecchio and Bucky\(^18\) evaluated breasts treated with fat grafting, by 3-dimensional volumetric imaging or magnetic resonance imaging to quantify required breast volumes for patients with micromastia, postexplantation deformity, tuberous breast deformity, and Poland syndrome. We decided to do a study in elderly breast cancer patients because with fatty fibroglandular breasts and atrophy of adipose tissue at the harvesting area, and greater potential for fat resorption after grafting, there might be higher complication rates or lower success rates after lipofilling, or multiple repeated procedures might be required in these patients.

We found poor correlation between breast defect volume and total lipofilling volume (a linear correlation coefficient of 0.123). This could be because of inaccurate or inadequate pregraft estimation methods or the unpredictable nature of graft-taking in the elderly, or both. The volume of fat needed to be grafted also varies depending on the shape and surface area of the defect, which we did not take into account. Delay et al\(^14\) reported that 30–40% of the volume gained by fat transfer would gradually be lost within a period of 3–4 months. This loss could be even higher for elderly patients. Missana et al\(^9\) injected an average of 75 mL of fat after breast conservative surgery. In our study, we injected an average of 102 mL of fat, or a median of 81 mL, both of which seemed to be higher than those reported.
elsewhere. Thus, it is still very difficult to predict the
fat volume required before performing lipofilling,
and experimental studies have shown that no prep-
aration or harvesting techniques seem to be more
advantageous or have more predictable effects on
transplanted fat grafts within the first 3 months.23

Because of the poor correlation between estimat-
ed breast defect volume and total lipofilling volume,
the lipofilling to defect volume ratio in our study was
highly variable (Table 3). Nonetheless, a median li-
pofilling to defect volume ratio of 1.5 could be used
as a rough guide to avoid excessive lipofilling. To
prevent a high incidence of liponecrosis, total lipo-
filling volume should not exceed 1.5 times the esti-
mated defect. Although, in our study, the difference
in the median total lipofilling volume between pa-
tients with liponecrosis (98.5 mL) and those without
(80.0 mL) was not statistically significant, this differ-
ence (18.5 mL) was clinically meaningful. However,
the graft-to-capacity ratio theoretically maximizes at
100% if proper diffusion of graft is to successfully
occur.24 Fat failure is because of over grafting of the
recipient site. In cases of high graft-to-capacity ratio,
volume maintenance appeared to diminish; in cases
of low graft-to-capacity ratio, better percentage vol-
ume maintenance was demonstrated.

In our series, only 33% of the patients were given
further, repeated lipofilling sessions. This percentage
of repeated lipofilling was probably an underestimate,
as there were a few patients who did not undergo fur-
ther sessions because of lack of donor sites, not be-
cause the defect was treated to full satisfaction. We
also needed to adequately estimate the oncological
risk in elderly patients after lipofilling because fat
transfer into a previous breast cancer site might stim-
ulate a local recurrence. There are studies that sug-
gest that adipocytes and preadipocytes are involved
in cancer–stromal interaction through autocrine,
paracrine, and exocrine secretions.25–27 The potential
core of fat transfer in this clinical setting is that it

Table 6. Comparison of Liponecrosis Rates and Management after Lipofilling in All Age Groups

| Author                  | Mean Age (y) | No. of Patients (Breasts) | Technique                                                                 | Complications                  | Management                        |
|-------------------------|--------------|---------------------------|---------------------------------------------------------------------------|--------------------------------|-----------------------------------|
| Delay6                  | NR           | 200                       | Lipomodeling (centrifugation at 3200 rpm for 3 min)                       | Fat necrosis (3 of 200)        | None                              |
| Spear et al10           | NR           | 37 (47)                   | Low-pressure syringe lipoaspiration system with repetitive saline washing | Superficial lumps (3 of 47)   | 2 excisional biopsies: liponecrotic cysts |
| Missana et al9          | 51 (21–73)   | 69 (74)                   | Coleman with minimal modifications                                        | Cytosteatonecrosis (5 of 74)  | None                              |
| Yoshimura et al11       | 35.8         | 40                        | Cell-assisted lipotransfer                                                | None                           | None                              |
| Zheng et al12           | NR (20–62)   | 66                        | Centrifugation at a low 600 rpm speed (26g) for 2 min                    | Fat necrosis (11 of 66)        | None                              |
| Zocchi and Zuliani13    | 33 (19–39)   | 181                       | Bicompartamental breast liposculpturing, using vibrating table (not centrifugated) | Liponecrosis (2 of 181)       | None                              |
| Delay et al14           | NR           | 880                       | Lipomodeling                                                              | Focal clinical fat necrosis (28 of 880) | None                              |
| Illouz and Sterodimas15 | 45.6 (19–78) | 820                       | Decanting of fat (not centrifugated)                                      | None                           | None                              |
| Serra-Renom et al16     | NR (34–62)   | 65                        | Coleman                                                                   | None                           | None                              |
| Ueberreiter et al17     | NR           | 85                        | Water-assisted liposuction (Bodyjet, human med, AG, Schwerin, Germany) and separate by the Lipocollector (human med, AG) | None                           | None                              |
| Del Vecchio and Bucky18 | NR (21–60)   | 25 (46)                   | Low-g-force centrifugation                                                | None                           | None                              |
| Sarfati et al19         | 45 (29–61)   | 28                        | Blunt-tip liposuction cannula and a “fat trap,” centrifugation at 3000 rpm for 3 min | None                           | None                              |
| Losken et al20          | 52 (34–73)   | 107                       | lipiVage system, Telfa pads, sedimentation alone, and centrifugue          | Fat necrosis (12 of 107)       | None                              |
| Petit et al1            | 52.1 (27–86) | 513 (646)                 | Coleman                                                                   | Liponecrosis (13 of 646)       | None                              |
| Irani et al21           | 52 (38–70)   | 25                        | Coleman                                                                   | Fat necrosis (2 of 25)         | Needle aspiration                 |

NR, not recorded.
has been proposed that engrafted cell may not be as stable to local tissue cues as intrinsic cells.25 Direke et al26 demonstrated that mesenchymal stem cells can engraft within, and contribute functionally to, cancer associated stroma. Experimental report suggests that cancer associated stroma may be capable of progression of epithelial tumors. Manabe et al30 demonstrated that adipocytes increased proliferation of breast carcinoma cells in vitro. Iyengar et al31 found that adipocytes increased cell proliferation and the invasive potential of malignant breast epithelial cells in vitro. We were unable to detect any local recurrence using conventional clinical and radiologic examinations within a median follow-up period of 16 months. However, longer follow-up times and more patients are needed for more definitive conclusions.

CONCLUSIONS

Despite a relatively higher postoperative complication rate and unclear oncologic risk after lipofilling in elderly patients, lipofilling remains an option for correcting defects after BCT or reconstruction in appropriately selected patients with breast cancer. To reduce early necrotic complications of lipofilling, a total lipofilling volume not exceeding 1.5 times the estimated defect volume is recommended as a rough guide in the elderly patients.

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