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Original Article

Outcomes and Oncologic Safety of Autologous Dermal Fat Grafting in Breast Conservation Therapy

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Abstract

A novel technique of breast reconstruction in breast conserving surgery (BCS) has been introduced by using autologous free dermal fat graft (FDFG). This study is to evaluate the efficacy of using FDFG.

From January 2007 to December 2010, cross-sectional medical records reviewed a total of 96 women who underwent wide excision and breast reconstruction with autologous FDFG from the lower abdomen. Patients and tumor characteristics, complications, and disease recurrence were obtained. Follow-up radiologic imaging was performed.

The majority of patients (95.8%) received immediate breast reconstruction. The average operative time was 94.2 minutes (range 30-180). The staging was mostly in stage I-II disease (70%). The majority of the patients' status (92, 95.8%) at the last follow-up visit was alive without disease. The overall survival was 98.9% at 199 weeks. The FDFG complications were reported in 7 patients (7.3%). No major morbidity and mortality complications were noted. The graft survival rate was 97.8% at 199 weeks. There was no correlation between the FDFG complications and the patient's characteristics, surgical procedure, timing of reconstruction, size, staging, nor adjuvant treatment.

The use of autologous FDFG for breast reconstruction in BCS is efficient for early breast cancer lesions, with minimal complications and no mortality. This method is valid in detection of local recurrence without interfering with the radiologic imaging reports which ensures oncologic safety.

Keywords: **Autologous free dermal fat graft, breast cancer, breast conserving surgery, breast reconstruction, oncoplastic surgery**

Introduction

Breast cancer is a growing national concern. It is the most frequently diagnosed cancer in women worldwide and also the most common cancer found in Thai women. Breast conservation therapy (BCT) has become the standard treatment for early stage breast cancer. It has been accepted that for most women with stage I or II breast cancer that breast conservation therapy (lumpectomy/partial mastectomy plus radiation therapy) is as effective as mastectomy[1-2]. The goals of BCT are to achieve optimal locoregional control together with acceptable cosmesis. To preserve cosmesis and broaden the options for breast conservation therapy, numerous techniques of breast reconstructions were developed[3-8].

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Recently, a novel procedure was introduced by Kijima et al[9-10] aiming at improving the cosmetic results of the treatment of inner and central breast lesions by using autologous free dermal fat graft (FDFG) after breast conservational surgery. The trial results showed that autologous FDFG was useful for reconstruction with good cosmetic effect, achieving better cosmetic results than transposition of residual breast tissue, and was more convenient than muscle flap grafting, and safer than implantation of foreign materials. Also, the FDFG underwent mild resorption and degeneration of fibrous tissue.

In 2007, the Division of Head-Neck and Breast Surgery, Department of Surgery, Siriraj Hospital Mahidol University, has conducted the technique of breast conserving surgery by using autologous free dermal fat graft. The clinical outcomes and results had yet to be determined. A short-term evaluation of the results was essential to confirm the effectiveness of this technique. The aim of this study was to evaluate the short-term outcomes and oncologic safety of using autologous FDFG in breast conserving surgery.

Patients and Methods

Patients

From January 2007 to December 2010, a total of 96 Thai female patients underwent breast conservation therapy with breast reconstruction using autologous free dermal fat graft at the Division of Head-Neck and Breast Surgery, Department of Surgery, Siriraj Hospital. Patients' data and medical records were cross-sectionally reviewed with approval from the Siriraj Institutional Review Board. Table 1 summarizes the patients' and tumors' characteristics. The breast cancer staging, margin status, and definition of menopause were defined according to the NCCN guidelines Version 1.2013. Staging was obtained from the final pathological report.

Operative procedures

Tumor resection

Wide excision was performed to achieve intraoperative surgical margin of at least 1 cm or greater and included the underlying pectoral fascia. The size of the dissected breast volume was obtained from the official pathological report. The breast tissue

Table 1 Patients' demographic data (N=96)

Characteristics	Mean (SD), Frequency (percent)
Age (yr)	44 (7.8) (26-66)**
BMI (kg/m^2)	22.9 (3.9) (15.7-36.7)**
Menstruation status	
Premenopause	70 (73)
Menopause	27 (27)
Family History	
Breast cancer	11 (11.5)
Ovarian cancer	1 (1)
Medical disease	
Diabetes mellitus	1 (1)
Hypertension	6 (6.3)
Dyslipidemia	4 (4.2)
Clinical presentation	
Breast mass	77 (80.2)
Abnormal mammography	14 (14.6)
Breast pain	1 (1)
Delayed breast reconstruction	4 (4.2)
Breast lesion	
Right breast	49 (51)
Left breast	47 (49)
Location	
Upper outer	48 (50)
Upper inner	14 (14.6)
Central	4 (4.1)
Lower outer	21 (21.9)
Lower inner	9 (9.4)
Axillary surgery	
None	9 (9.4)
SLNB	50 (52.1)
ALND	37 (38.5)
Resected breast tissue	
Length (cm)	7.3 (1.8) (3.3-13) **
Width (cm)	5.8 (1.7) (2-11.5) **
Thickness (cm)	3.4 (0.9) (2-5.5) **
Volume (cm^3)	174.3 (121.3) (24-569.2) **
FDFG volume (cm^3)	87.2 (62.53) (10.3-298.1 **)
Timing of reconstruction	
Immediate	92 (95.8)
Delayed	4 (4.2)
Operative time (minutes)	94 (33.5) (30-180) **

SD= Standard Deviation, ** = range

length, width, and thickness were measured in centimeters and calculated into cm^3 for volume of breast defect. In patients who had a prior incisional or excisional biopsy done, the breast volume was omitted for calculation. All surgeries were performed by surgeons from the Division of Head-Neck and Breast Surgery.

Reconstruction

Breast reconstruction was performed using autologous FDFG harvested from the lower abdominal area. Elliptical skin incision was performed and de-epithelialization of the graft was done by sharp dissection. Further dissection of the abdominal fat was done in an elliptical contour down to the abdominal sheath. The graft size was approximated to the breast volume defect, although the graft size was not routinely documented. The excised FDFG was tailored to achieve the best contour for the breast. Then, FDFG was turned over to allow the graft's dermis in direct contact with the pectoralis muscle so that revascularization may occur. Suture fixation of the graft to the muscle 2-4 corners was performed, followed by skin closure. Placement of closed suction drain was not routinely placed in the breast. A supportive dressing was applied to the graft site without applying excessive pressure. The resected breast volume was calculated using the ellipsoid volume formula as follows: volume (cm^3) = $\pi/6 \times$ length (cm) $\times$ width (cm) $\times$ thickness (cm).

Follow up

Patients who required adjuvant treatment, oncologist and radiologist were consulted. Routine post operative follow-up of radiologic imaging with ultrasound and mammogram was done at six months after completion of adjuvant treatment. Medical records were reviewed up to January 2012 with a median follow-up time of 45 months (range 13-60). Complications of the FDFG were reported as mastitis and further categorized into subgroup of treatment, which were medical treatment alone, incision and drainage, or graft removal. Seroma at the graft was not included as a complication since patients did not require any treatment. Seroma at the abdomen was reported as some patients required aspiration, and some patients had prophylactic closed suction drainage placed in the abdomen. Disease recurrence was classified to recurrent to the ipsilateral breast, contralateral breast, the axilla, and distant metastasis. One patient had recurrence in both ipsilateral breast and bone and was then categorized separately. The status of patients up to the last time of visit was categorized into four groups: alive with no evidence of disease; alive with disease; dead with disease; and dead due to other causes.

Statistical Analysis

Statistical analysis was performed using SPSS statistical software, version 15.0; SPSS, Inc., Chicago, IL, USA. For categorical variables, the Fisher's exact test was applied. Mann-Whitney U test was calculated for each association between continuous variables. Kaplan-Meier curve was used to calculate the survival rate.

RESULTS

A total of 96 female patients underwent BCS with wide excision and reconstruction with autologous FDFG. The patients' demographic data are shown in Table 1. The average age of patients was 44.2 years (range 26-66). All of the patients had disease located in one breast. The average volume of resected breast tissue was 174.3 cm^3. The average calculation for FDFG size was 87.3 cm^3, using the ellipsoid volume formula. The timing of reconstruction was mainly immediate; done in 92 patients (95.8%) and delayed in 4 patients (4.2%). There was no correlation of the timing of reconstruction with the FDFG complications (P= 0.394). The average operative time was 94 minutes (range 30-180), which included the axillary surgery.

The histopathologic features are demonstrated in Table 2. The majority of patients were diagnosed with invasive cancer. There was no correlation of the tumor size to the FDFG complications (P= 0.638). The margin of excision was free of tumor in 69 patients (71.9%), 22 (22.9%) had close margin, and 5 (5.2%) had a positive margin. Eleven patients needed a second operation; 7 (7.3%) underwent re-excision without removal of the FDFG, 1 (1%) needed re-excision twice without removal of the FDFG, and 3 (3.1%) required total mastectomy.

Table 3 shows that the patients were mostly at stage I-II disease. One patient was diagnosed of stage IV cancer. This patient was a known case of invasive ductal carcinoma of the left breast, and had a previous wide excision with ALND performed. Two years later,

Table 2 Histopathologic features

Characteristics	Frequency (percent)
Tumor size	
In situ disease	13 (13.5)
≤ 2 cm	40 (41.7)
2.1-5 cm	39 (40.6)
> 5 cm	4 (4.2)
Nodal status	
Negative	68 (70.8)
4-9 nodes	16 (16.7)
4-9 nodes	9 (9.4)
> 9 nodes	3 (3.1)
Histology	
Ductal carcinoma in situ	13 (13.5)
Invasive ductal carcinoma	78 (81.3)
Invasive lobular carcinoma	2 (2.1)
Invasive papillary carcinoma	2 (2.1)
Malignant phyllodes	1 (1)
Cell differentiation	
DCIS	13 (13.5)
Low grade	15 (15.6)
Moderate grade	51 (53.2)
High grade	17 (17.7)
Angiolymphatic invasion present	13 (13.5)
Perineural invasion present	8 (8.3)
Hormonal status	
ER positive	67 (69.8)
PR positive	67 (69.8)
Her2 positive	22 (22.9)

Table 3 Staging, management, and follow up

Characteristics	Frequency (percent)
Staging	
DCIS	12 (12.5)
Stage I	31 (32.4)
Stage II	37 (38.5)
Stage III	14 (14.6)
Stage IV	1 (1)
Malignant phyllodes	1 (1)
Excision margin status	
Free margin	69 (71.9)
Close margin	22 (22.9)
Positive margin	5 (5.2)
Second operation	
None	85 (88.5)
Re-excision	7 (7.3)
≥ 2 re-excision	1 (1)
Total mastectomy	3 (3.2)
Adjuvant treatment	
Chemotherapy	55 (59.8)
Radiotherapy	83 (91.2)
Hormonal therapy	70 (76.9)
BIRADS score at 6 months	
BIRADS 1	4 (5)
BIRADS 2	44 (55)
BIRADS 3	30 (37.5)
BIRADS 4	2 (2.5)
BIRADS score at latest imaging	
BIRADS 2	28 (51.9)
BIRADS 3	24 (44.4)
BIRADS 4	2 (3.7)

this particular patient had a recurrent ipsilateral breast cancer with bone metastasis. She was then treated with wide excision and FDFG followed by palliative adjuvant treatment. She died ten months later. There was no correlation between the staging of the disease and the FDFG complications ($P = 0.675$). More than half of patients received postoperative adjuvant systemic therapy (chemotherapy in 59.8% and hormonal therapy in 76.9%) and breast radiation therapy (91.2%). There was also no correlation between the adjuvant treatments and the FDFG complications ($P = 0.515$).

Disease recurrence occurred in 7 patients (7.3%), as shown in Table 4. Four patients (4.2%) had the disease recurrence to the ipsilateral breast which was treated with total mastectomy. Two patients (2.1%) had distant metastasis occurred: one to the lung; and the other to the liver. One patient (1%) recurred with an ipsilateral breast cancer and bone metastasis. The average time to disease recurrence was 56 weeks (range 21-145). The majority of the patients' status (92, 95.8%) at the last follow-up visit was alive without disease. Three patients (3.2%) were alive with disease. There were three patients with distant metastasis as previously discussed above. One patient (1%) died with disease, which was the same patient as she was diagnosed in the stage IV disease. The overall survival was 98.9% at the median follow-up of 45 months. The disease-free survival was 95.5% at 1 year and 83.7% at 33 months (Figure 1).

The post operative mammogram at 6 months had a BIRADS score of mostly 2 (44, 55%) (Figure 2) and 3 (30, 37.5%). Two patients (2.5%) had BIRADS score of 4. The first patient was diagnosed of DCIS, and was treated with wide excision with SLNB followed by adjuvant radiotherapy. Two years later, she complained of scar contracture and breast asymmetry. Therefore, the scar excision and delayed FDFG was performed. This patient developed mastitis and was treated with

Table 4 Status, recurrence, and complications

Characteristics	Frequency (Percent)
Status	
Alive without disease	92 (95.8)
Alive with disease	3 (3.2)
Dead with disease	1 (1)
Disease recurrence	
None	89 (92.7)
Ipsilateral breast	4 (4.2)
Distant metastasis	2 (2.1)
Ipsilateral and distant metastasis	1 (1)
FDFG complications	
None	89 (92.7)
Mastitis, medical treatment	2 (2.1)
Mastitis, incision + drainage	1 (1)
Mastitis, graft removal	2 (2.1)
Mastitis + drainage, scar excision and re-DFG	2 (2.1)
Abdominal complications	
None	85 (89.5)
Seroma	8 (8.4)
Bleeding	2 (2.1)

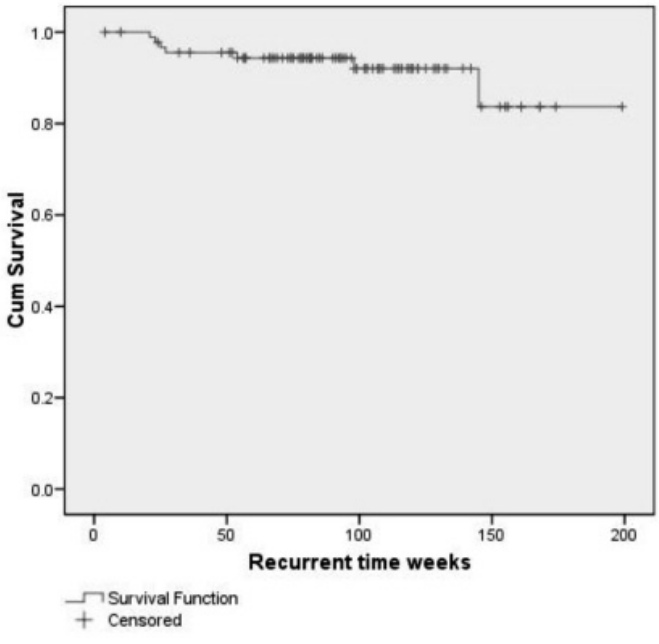

Figure 1 The disease-free survival was 95.5% at 1 year and 83.7% at 145 weeks.

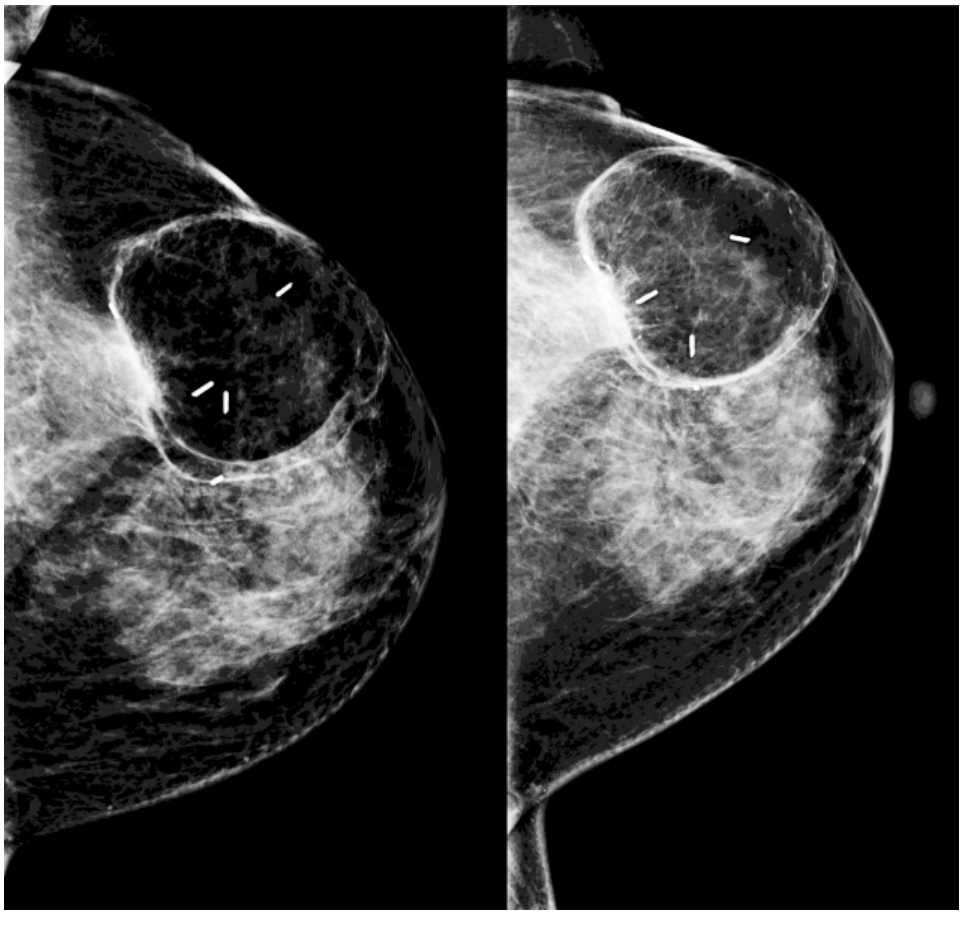

Figure 2 Mammography at 6 months (left) and 24 months (right) post adjuvant treatment. BIRADS score 2

incision and drainage. Her mammogram at 6 months post operation was 4B. The core-needle biopsy was invasive ductal carcinoma. She was diagnosed of disease recurrence to the ipsilateral breast and was treated with total mastectomy.

The second patient with a BIRADS score of 4 was diagnosed of invasive ductal carcinoma of breast and had wide excision with SLNB performed, followed by adjuvant treatment. She then presented with scar contracture and had delayed breast reconstruction performed with FDFG. At 6 months post operation BIRADS score was 4a, core-needle biopsy showed chronic inflammation and fat necrosis. Among the 96 patients, 54 had further follow-up mammogram. The majority score were still BIRADS 2 and 3. The average time to second mammogram was 109 weeks (range 41-190).

The FDFG complications were not seen in the majority of cases (89, 92.7%). Two patients had mastitis which was successfully treated with antibiotics. One patient had mastitis that required incision and drainage while keeping the DFG in situ. Two patients had mastitis which turned into graft necrosis and had FDFG removed. Two patients underwent wide excision and FDFG, and later developed mastitis which was treated with incision and drainage, and later developed scar contracture which was treated with scar excision and re-FDFG. There was no skin flap necrosis, nor nipple-areolar complex complications. No major morbidity and mortality complications were noted at 30-day post operative period. The graft survival rate as detected by ultrasonography was 97.8% at last follow-up visit with excellent patients' satisfaction in term of cosmetic outcome.

Abdominal complications were found in 10 patients. Eight patients had seroma in the donor site, which were treated with aspiration. Due to frequent seroma found in the abdomen, some surgeons preferred to place a prophylactic closed-suction drain in the abdomen in cases of large-size graft. Two patients had bleeding problem at the abdominal wound which was treated with sutures under local anesthesia.

Discussion

Breast conservation therapy (BCT) has become the standard treatment for early stage breast cancer, achieving optimal locoregional control together with acceptable cosmesis. A novel procedure reported by Kijima et al, used the autologous FDFG for immediate breast reconstruction in early breast cancer patients who underwent partial mastectomy, with the disease mainly in the upper inner quadrant of the breast. In this study, the technique of using autologous FDFG was performed in 96 Thai female patients with defects in any quadrant of the breast. We did not find any correlation between the disease location of the breast to the complications, and the cosmesis was satisfactory in all patients. The size of the tumors did not have correlation with FDFG complications such as mastitis.

In this study, about a quarter of the pathological margins were close or positive margins. A large number of cases with close margins were at the anterior or posterior aspect, which sometimes cannot achieve a greater margin. Suggestions for wide excision of the tumor in this study were at least ≥1 cm during dissection. It is possible that, to reduce the rate of close or positive margins during the operation, the margins may be examined histologically to ensure that the margins were free of tumor. The dissection of at least 2 cm beyond the tumor edge was also an option, but a larger FDFG graft would be required and the cosmesis have yet to be determined. All cases with a second operation of re-excision or total mastectomy did not report any FDFG complications. There were also no 30-day morbidity and mortality in this study.

There was no correlation between the timing of reconstruction and FDFG complications. No correlation between adjuvant treatment and FDFG complications was also found. Although a few patients developed disease recurrence in the breasts, all of the recurrence could be detected by radiologic imaging. This implied that the use of FDFG did not interfere with the interpretation of BIRADS score and could detect local recurrence of the ipsilateral breast.

In conclusion, BCS with the use of autologous FDFG for reconstruction is efficient in early breast cancer lesions with minimal complications. This method did not interfere with the radiologic imaging reports to detect local recurrence, which ensures oncologic safety in a short-term period. Evaluations of the long-term aesthetic outcome are warranted in future studies.

Conflict of interest statement: Pornchai O-charoenrat and other co-authors have no conflict of interest.

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