ORIGINAL ARTICLE

Surgical Closure of Chest Wall in Noninflammatory Locally Advanced Breast Carcinoma with Ulceration of the Skin[1]

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■ **Abstract:** Patients with noninflammatory locally advanced breast cancer with ulceration of skin or muscle or parietal wall infiltration, better named "extended locally advanced breast cancer," may require cancer surgery and plastic reconstruction of the chest wall after multidisciplinary evaluation. The decision is made to improve quality of life, independently of prognosis, and severity of the disease. The aim of this study is to evaluate the best method for surgical closure of the chest wall and to check whether ablative surgery is an appropriate procedure in regards to the treatment of cancer. From October 1997 to June 2006, 27 patients with noninflammatory extended locally advanced breast cancer with ulceration of the skin, who were not candidate or did not respond to a neo-adjuvant treatment, underwent radical mastectomy and reconstructive surgery. Sixteen patients (59%) were affected by primary tumors of the breast, and eleven patients (41%) had local recurrence after mastectomy or conservative breast surgery. Two main techniques were used for breast reconstruction: transverse rectus-abdominis musculo cutaneous flap in 19 patients (70%), and a fasciocutaneous flap in eight patients (30%). The best procedure in each patient was chosen according to the extent of skin loss or previous radiotherapy to the chest wall. Fourteen patients (52%) died during the follow-up and the median length of survival was 16 months (range 3–79) in transverse rectus-abdominis musculo cutaneous group and 4 months (range 2–23) in fasciocutaneous flap group. The median length of follow-up after treatment for patients still alive was 32.5 months (range 0–96) in transverse rectus-abdominis musculo cutaneous flap group, and 18 months (range 8–41) in fasciocutaneous flap group. At the end of the follow-up, 10 patients were alive without evidence of disease and three patients developed metastatic lesion or local recurrence. The longest recorded disease free interval for a patient still alive and tumor free was 96 months. Only three patients (11%) had local complications: two wound infections and one partial necrosis of the transverse rectus-abdominis musculo cutaneous flap. Median hospital stay was 7 days (range 3–13) for transverse rectus-abdominis musculo cutaneous and 6 days (range 3–13) for fasciocutaneous flap. Our results confirmed that transverse rectus-abdominis musculo cutaneous group and fasciocutaneous flap flaps are good reconstructive options in patients with extended locally advanced breast cancer. Quality of life has improved in this group of patients, with acceptable survival periods and in some cases very important survival rates. ■

Key Words: fasciocutaneous flap, locally advanced breast carcinoma, skin involvement, thoracic wall involvement, transverse rectus-abdominis musculo cutaneous flap

Untreated breast cancer may become very large, invade the skin, undergo necrosis and form large ulcers that penetrate the chest wall. Such ulcers are the typical manifestation of breast cancer in populations with limited access to medical care (1).

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[1]Presented at the 9th Milan Breast Cancer Conference, Milan, Italy, June 20–22, 2007.

The Breast Journal, Volume 14 Number 4, 2008 345–352

Since the introduction of the first breast carcinoma staging systems, at the beginning of the last century, cases with extension of tumor to the skin generally have been classified as locally advanced breast cancer (2). This historic significance of skin involvement was perpetuated in the current American Joint Committee on Cancer/International Union Against Cancer TNM staging system, in which noninflammatory breast carcinoma with direct extension to the skin also led to placement in the most unfavorable T category (T4) (3). Locally advanced breast cancer comprises 10–25%

of all breast cancer in developed countries and 40–50% in developing countries (4). Locally advanced breast cancer represents 5–20% of new cases diagnosed every year (5). Brenner et al. (6) defined locally advanced breast cancer as a heterogeneous group of tumors that includes neglected slow-growing tumors and fast-growing tumors.

Surgical treatment of extended locally advanced breast cancer requires large mutilations, and long and sophisticated plastic surgical procedures resulting in severe postoperative inflammatory syndrome, sometimes significant blood loss and prolonged hospital stay. It is therefore questionable whether such surgery could be detrimental for patients' survival and the quality of life in complicated cases.

In our series, patients were selected clinically by the presence of edema (including peau d'orange) or ulceration of the skin or satellite skin nodules confined to the same breast, or soft tissue and thoracic wall involvement regardless of size of the tumor. In certain cases, the enormous extension of the tumor associated with extremely offensive smell cannot explain why the patients accepted such difficult social and family life without looking for medical advice. Most selected cases of our series were desperate, without expectation of long survival. All of them required cancer surgery and plastic reconstruction of the chest wall after multidisciplinary evaluation.

Radical surgical extirpation in these patients produced extensive loss of skin with large defects requiring plastic surgical procedures for the closure. In the literature, many methods are used to close the defects: skin grafts, local flaps, omental flaps, abdominal flaps, and myocutaneous flaps (7–9). The aim of this study was to analyze the criteria of the surgical indications for the extended locally advanced breast cancer and to define the best technique of reconstruction in each case.

PATIENTS AND METHODS

Between October 1997 and June 2006, most patients with locally advanced breast carcinoma received the standard application of preoperative chemo and/or radiotherapy at the European Institute of Oncology of Milan, Italy, to make the tumor more respectable before undergoing surgical operation. We found only 27 who were not candidate or did not respond to a neo-adjuvant therapy. It was interesting for us to expose the difficulties we had in managing these cases. These patients with noninflammatory locally advanced breast cancer with direct infiltration to the skin, with or without pectoralis muscle infiltration or parietal wall involvement, underwent radical resection and reconstructive surgery and were retrospectively included into a database. There were 27 female patients, with median age 51 years (range 28–78). The median time of primary diagnosis of breast cancer was 13.6 months (range 0–52): 16 patients (59%) had primary and 11 (41%) recurrent breast cancer (eight after conservative treatment and three after mastectomy). Tumor characteristics and adjuvant therapies are listed in Table 1. Patient demographic and clinical characteristics, surgical procedures, and the rate of survival or death are recorded in Table 2. All details were obtained from tumor registry data and the patients' medical records.

Most patients had local infection and unpleasant smell at presentation (Figs. 1–3). All these patients were not staged preoperatively. Due to the dramatic clinical situation, most of the patients proceeded with surgery before, and they completed the staging one month later with abdominal ultrasound, positron emission tomography, computer tomography and bone scintigraphy performed in our institute. Distant metastases were not present at this moment. Data based on concomitant diseases included respiratory disease, cardiovascular disease, diabetes mellitus, hypertension, microcytic anemia, hypothyroidism, Sjogren's syndrome and Hepatitis C.

Statistical analyses were performed with "no parametric test." Pathological assessment included evaluation of the histological type of the tumor, lymph node status, tumor grading and perivascular, muscular and chest wall invasion, estrogen receptor, progesterone receptor, and Her2-neu overexpression. In our series, 20 patients had invasive ductal carcinoma, one lobular invasive carcinoma, one mucinous carcinoma, two phylloid tumors, two angiosarcoma and one spinocellular carcinoma. Histopathologic examination confirmed skin infiltration in all 27 patients (100%), vascular invasion in 14 (52%), muscular infiltration in 11 (41%) and chest wall infiltration in three patients (11%).

RESULTS

The surgical techniques consisted of seven modified radical mastectomies and one bilateral modified radical mastectomy (Figs. 8 and 9), six radical mas-

Table 1. Characteristics of 27 Locally Advanced Breast Cancer Patients Evaluated

Locally advanced breast cancer	Primary *n* = 16 (59%)	Recurrent *n* = 11 (41%)	Total *n* = 27 (100%)
Histology			
Ductal	13	7	20
Lobular	1	0	1
Phylloid	1	1	2
Angiosarcoma	0	2	2
Spinocellular	0	1	1
Mucinous	1	0	1
Perivascular invasion			
Yes	8	6	14
Muscular invasion			
Yes	8	3	11
Chest wall invasion			
Yes	2	1	3
Pathologic lymph node status (pN)			
pN0	0	1	1
pN1	5	1	6
pN2	2	0	2
pN3	7	1	8
pNx	2	8	10
Estrogen receptor status			
Positive	11	2	13
Negative	4	5	9
Unknown	1	4	5
Progesterone receptor status			
Positive	9	1	10
Negative	6	6	12
Unknown	1	4	5
Her2-neu			
Positive	9	5	14
Negative	2	2	4
Unknown	5	4	9
Tumor grade			
G 1	—	—	—
G 2	2	1	3
G 3	3	1	4
Unknown	11	9	20
Primary surgical treatment			
Modified radical mastectomy	7	—	7
Total mastectomy	—	8	8
Radical mastectomy	6	—	6
Radical mastectomy and costal resection	1	—	1
Mastectomy and thoracectomy	1	—	1
Bilateral resection of soft tissues of the chest wall	—	1	1
Resection of soft tissues of the chest wall	—	1	1
Bilateral modified radical mastectomy	1	—	1
Resection of soft tissues of the chest wall and thoracectomy	—	1	1
Reconstructive surgery			
Transverse rectus-abdominis musculo cutaneous flap	12	7	19
Fasciocutaneous flap	4	4	8
Treatment			
No treatment	—	1	1
Hormono post	1	1	2
Chemo pre	1	—	1
Chemo post	2	1	3
Radio post and Hormono post	1	—	1
Chemo post and hormono post	1	1	2
Chemo post and radio post	1	1	2
Chemo pre and radio post	1	1	2
Chemo pre and radio pre	—	2	2
Chemo pre and radio post and hormono post	4	—	4
Chemo pre and post and Hormono post	1	—	1
Chemo pre and post and radio post	2	—	2
Chemo pre and radio pre and post and hormono post	—	1	1
Chemo pre and post and radio pre	1	2	3

Table 2. Comparison of Patient Group Based on Reconstructive Procedure

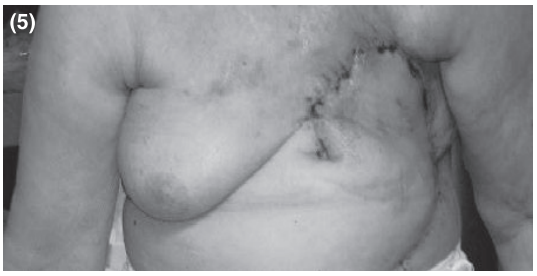
Locally advanced breast cancer	Transverse rectus-abdominis musculo cutaneous flap $n = 19$ (70%)	Fasciocutaneous flap $n = 8$ (30%)
Age (years), median (range)	51 (28–78)	50 (34–60)
Primary cancer	12	4
Recurrent cancer	7	4
Muscular invasion		
Yes	10	2
Chest wall invasion		
Yes	3	0
Comorbidity		
Arterial hypertension	—	1
Cardiovascular disease	1	—
Bronchial asthma	1	—
Arterial hypertension and diabetes mellitus	—	1
Microcytic anemia	—	1
Hypothyroidism	1	—
Sjogren's syndrome	1	—
Arterial hypertension and hepatitis C	1	—
Length of follow-up (months), median (range)		
Alive patients	32,5 (0–96 months)	18 (8–41 months)
Dead patients	16 (3–79 months)	4 (2–23 months)
Complications		
Flap necrosis	1	—
Infections	2	—
Loco-regional recurrences		
Skin	2	3
Skin and pleura	1	—
Skin and lymph node	1	—
Distant metastases		
Bone	1	—
Lung	1	2
Central nervous system	1	—
Pleura	1	—
Larynx	1	—
Contralateral breast	1	—
Multiple sites	3	1
Alive event free	7	3
Alive with metastases or loco-regional relapses	1	2
Dead with disease	10	2
Dead without disease	1	1
Postoperative treatment		
Chemotherapy	6	—
Radiotherapy	1	1
Hormonotherapy	1	1
Chemo and hormonal therapy	2	1
Chemo and radiotherapy	3	1
Radio and hormonotherapy	4	2
Chemo-hormono-radiotherapy	—	—

tectomies, eight total mastectomies for recurrences after quadrantectomy, axillary dissection and radiotherapy, one mastectomy and thoracectomy, one radical mastectomies and costal resections, two resections of soft tissues in the chest wall, one resection of soft tissues in the chest wall and thoracectomy. The criteria for axillary lymph nodes dissection in these patients was clinically palpable or ultrasonographically suspicious lymph nodes. Axillary dissection was performed in seventeen patients. Axillary clearance had already been performed in eight patients with recurrent breast cancer. In those patients who had distant metastasis, seven patients underwent axillary clearance, because of positive lymph node biopsy.

According to the extension of skin loss, the most common procedure performed for the breast reconstruction was transverse rectus-abdominis musculo cutaneous flap in nineteen patients (70%) (Figs. 6, 7, and 10) and fasciocutaneous flap in eight patients (30%) (Figs. 4 and 5). Transverse rectus-abdominis musculo cutaneous flap was performed in patients with large primary carcinoma or in patients with local recurrences after receiving external radiotherapy, in whom the size of defect on the chest wall was too large. There was no perioperative death. Complica-

Figures 1–3. Typical cases of locally advanced breast cancer. **1**. Ulcerated left breast cancer; **2**. Ulcerated right breast cancer: necrosis of the tumour associated with fungus infection; **3**. Ulcerated left breast cancer prior to the mastectomy and chest wall closure with a TRAM flap.

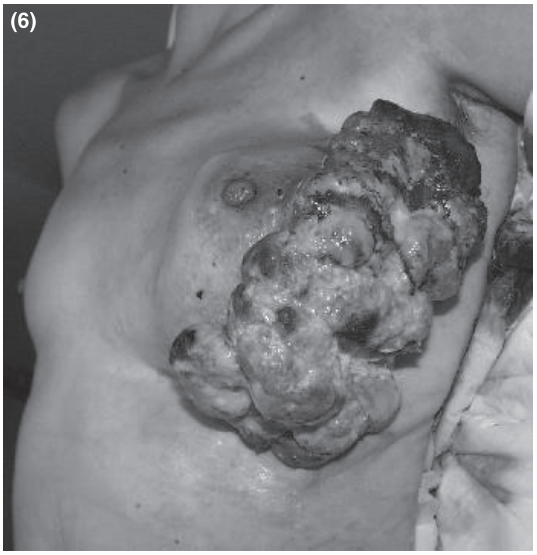
tions were seen in three patients (11%). Of the three patients with complications, two had postoperative wound infections and one had flap necrosis. One patient who developed infection was a recurrent

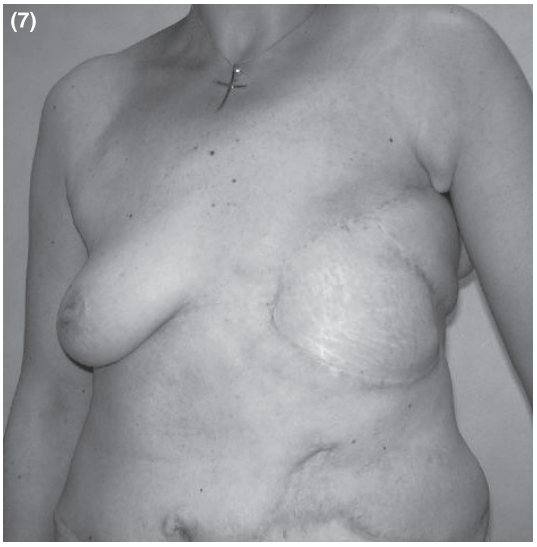


Figures 4, 5. Local fasciocutaneous flap. **4**. Ulcerated left breast cancer prior to surgery; **5**. Post operative aspect after chest wall closure with local fasciocutaneous flap.

breast carcinoma and the other complications were seen in patients with primary carcinoma. None of these patients received neo-adjuvant chemotherapy and/or radiation. Wound infections treated with local care and partial flap necrosis treated under local anesthesia. The median hospital stay was 7 days (range 4–13) for transverse rectus-abdominis musculo cutaneous flap and 6 days (range 3–13) for fasciocutaneous flap.

Recurrences were observed after a median follow-up of 5 months (range 1–15). The median length of follow-up after treatment for patients still alive in transverse rectus-abdominis musculo cutaneous flap group was 32.5 months (range 0–96) and in fasciocutaneous flap group was 18 months (range 8–41). The longest recorded disease free interval for a patient still alive and tumor free at the date of last follow-up was 96 months. At the end of the study period, ten patients were still alive without loco-regional or distant recurrence and three patients developed metastatic lesion. In most of these patients, axillary status correlate with distant metastasis, but distant metastasis developed during follow-up. Of 27 patients 14 patients (52%) died during follow-up and the median length of follow-up for the patients was 16 months (range 3–79) in transverse rectus-abdominis musculo cutaneous flap group and 4 months (range 2–23) in

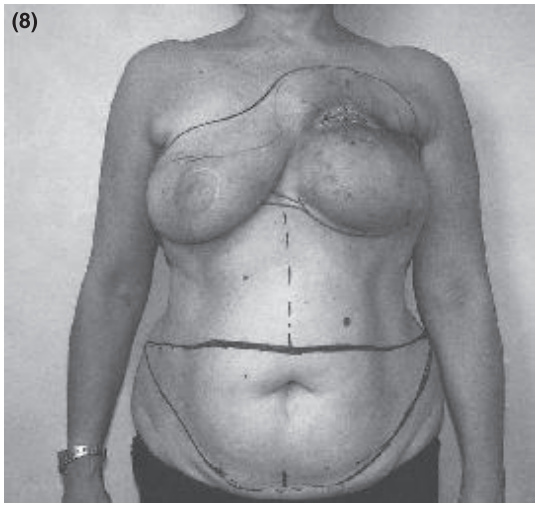


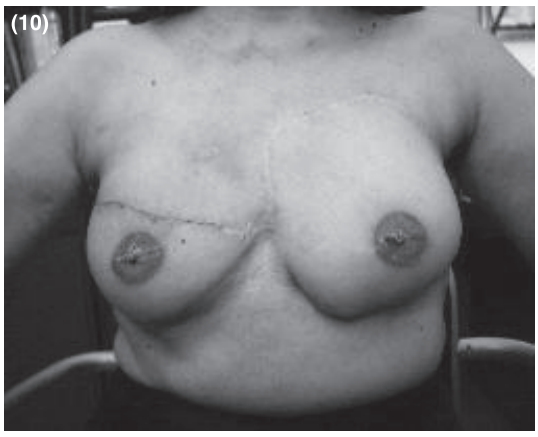


Figures 6, 7. Transverse rectus-abdominis musculo cutaneous flap. **6**. Ulcerated left breast cancer; **7**. The same patient after mastectomy and chest wall closure with a TRAM flap.

fasciocutaneous flap group. Less aggressive histological type of the tumor in fasciocutaneous flap group was associated with the higher survey rate than in transverse rectus-abdominis musculo cutaneous flap group. The follow-up has began in different timing for each group of patients and that is why the fasciocutaneous flap group appears to have a shorter life span than the transverse rectus-abdominis musculo cutaneous flap group. In all, 58% of the patients in transverse rectus-abdominis musculo cutaneous flap group and 38% in fasciocutaneous flap group died during the period of follow-up.

Each patient was evaluated in a multidisciplinary meeting attended by breast surgeon, medical oncologist, radiotherapist, and pathology specialists. In our series, only a few patients received neo-adjuvant treatment because of the heterogeneous histology of the patients' tumor (ductal, lobular, mucinous and spino-





Figures 8–10. Bilateral mastectomy and transverse rectus-abdominis musculo cutaneous flap. **8**. A case of bilateral locally advanced breast cancer; **9**. Surgical aspect after bilateral extended mastectomy; **10**. After breast reconstruction with a bipedicled TRAM flap and right side grand-dorsal flap.

cellular carcinoma, philloid, and angiosarcoma tumors). Considering tumor histology and grade, estrogen and progesterone receptor status, Her2-neu overexpression some patients were evaluated to receive neo-adjuvant chemotherapy. The usual chemotherapy used for selected patients was 5-FU + Epirubicin + Cyclophosphamide or Taxanes. But during the treatment, the clinical situation of these patients was worsened and no effect was seen on respectability of the tumor. These patients were permanently exposed to neotoxicosis, sepsis and hemorrhage, so that 11 patients proceeded with extensive "mutilating" surgery upfront.

Sixteen patients received adjuvant treatment. Of 11 recurrent breast cancers, six had adjuvant therapy after initial surgery. A total of 23 patients were evaluated for adjuvant medical treatment. Among these patients 10 received monotherapy (chemotherapy in six, hormonal treatment in two, radiotherapy in two), and 13 had combined therapy (chemotherapy and radiotherapy in four, radiotherapy and hormonal therapy in six, chemotherapy and hormonal therapy in three).

Malignancy-related deaths were censored in the statistical analyses for 12 patients. Metastases were found in the lung ($n = 3$), bone ($n = 1$), central nervous system ($n = 1$), pleura ($n = 1$), larynx ($n = 1$), contralateral breast ($n = 1$), multiple sites ($n = 4$). Loco-regional recurrences occurred in seven patients.

DISCUSSION

Large soft tissue defects following radical surgical resection of extended locally advanced breast cancer require plastic surgical procedures for closure. Those are to eliminate the tumor macroscopically as much as possible for local control and to allow an acceptable survival with a better quality of life. Our study was retrospective and during the follow-up 14 of 27 patients died making difficult to apply a database about the quality of life. After surgical operation, medical visit has been performed by different surgeons, and simple questions regarding patient's actual lifestyle were asked to. During the medical visit, patients affirmed their better lifestyle saying for example that after months of isolation they were able to leave the house and socialize with friends and family members.

Transverse rectus-abdominis musculo cutaneous flap and fasciocutaneous flap were used to cover extensive chest wall defects resulting from resection of extended locally advanced breast cancer, and there was no statistically significant difference in parameters between the transverse rectus-abdominis musculo cutaneous flap and the fasciocutaneous flap groups, regarding morbidity, hospital stay, time of adjuvant therapy, quality of life and survival rates. The two procedures had similar complication rates and the choice was only determined by the extension of the tissue resection. These procedures resulted in no perioperative mortality, and an acceptable morbidity, and they were successful in palliating physical and psychological distress. Our study confirms that plastic surgical reconstruction allows more radical cancer resection in extended locally advanced breast cancer. However, we cannot assess that radical surgery provides any improvement in the cure rate of these patients. The number of patients is very less and the prognosis in each of them is very different, as suggested by Brenner (6).

Sutherland and Marther (10) analyzed the prognostic factors of 308 patients with regional breast carcinoma (with skin, muscle, and/or chest wall attachment). Lymph node status and peau d'orange were found to be significant prognostic factors, whereas ulceration and tumor size, among other factors, had no effects on survival (10). In our study group, we did not make any distinctions among the clinical signs. Ten cases are event-free survival, four cases alive with metastases; and one case had an 8-year survival rate, with excellent quality of life. Numerous studies have observed a 5-year survival of 36–67% in relation to the stage of the disease (2–6), taking into account that women over the age of 65 and operated for breast cancer die for reasons other than the disease (11,12).

In conclusion, our results confirmed that transverse rectus-abdominis musculo cutaneous flap and fasciocutaneous flaps are excellent reconstructive options in the reconstructive management of patients with extended locally advanced breast cancer to improve the quality of life. However, the survival improvement depends more on the specific biology of the tumor than on the surgical indications. Such indications of extensive surgery with reconstructive techniques are particularly indicated in case of the so-called "slow growing tumors" (13).

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