

## Immediate Breast Reconstruction for Stage III Breast Cancer Using Transverse Rectus Abdominis Musculocutaneous (TRAM) Flap

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**Background:** The management of stage III breast cancer is challenging; it often includes multimodal treatment with systemic therapy and/or radiation therapy and surgery. Immediate breast reconstruction has not traditionally been performed in these patients. We review the results of immediate transverse rectus abdominis musculocutaneous (TRAM) flap in 21 patients treated for stage III breast cancer.

**Methods:** Data have been collected retrospectively on 21 patients diagnosed with stage III breast cancer between 1987 and 1994. All patients had mastectomy and immediate TRAM reconstruction. Thirteen patients received primary systemic therapy, 10 patients received postoperative consolidation radiotherapy to the operative site, and 3 patients received preoperative radiation.

**Results:** Mean follow-up for the group was 26 months. Two patients died with disseminated disease: neither of them developed local disease recurrence in the operative site; 82% of the patients followed for at least two years are free of disease. Sixty-two percent of the patients received preoperative chemotherapy, the remaining patients received postoperative multiagent chemotherapy and/or radiation therapy. Two of the patients received autologous bone marrow transplants after their adjuvant therapy. Ten patients had postoperative radiotherapy for consolidation; three patients received preoperative radiation.

**Conclusions:** Immediate TRAM reconstruction for stage III breast cancer is not associated with a delay in adjuvant therapy or an increased risk of local relapse. It facilitates wide resection of involved skin without skin grafting. Radiation therapy can be delivered to the reconstructed breast when indicated without difficulty. Breast reconstruction facilitates surgical resection of stage III breast cancer with primary closure and should be considered if the patient desires immediate breast reconstruction.

**Key Words:** Stage III breast cancer — Breast reconstruction — TRAM flap.

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Stage III breast cancer is frequently associated with occult systemic metastases at the time of initial diagnosis (1). The addition of multimodal therapy, including systemic chemotherapy and radiation ther-

apy to surgery, has improved the survival of these patients and decreased local recurrence (2-4). The surgical treatment of patients with stage III breast cancer is usually mastectomy and axillary lymph node dissection (5,6). Immediate breast reconstruction after mastectomy, although frequently performed for early-stage breast cancer (7,8), has generally not been performed in patients with locally advanced breast cancer. The reasons for delaying or eliminating breast reconstruction in these patients include: concerns regarding potential delay in adjuvant chemotherapy or radiation therapy after reconstruction, the possibility of morbidity associated with primary chemotherapy with additional surgery,

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the requirement for simultaneous oncologic and reconstructive surgeons, and the increased cost and use of operating room time and hospitalization. The advantages of immediate transverse rectus abdominis musculocutaneous (TRAM) flap reconstruction in stage III breast cancer are the elimination of a second major operative procedure for those patients who desire breast reconstruction and the primary closure of wide resections of involved skin without skin grafting.

We reviewed the medical records of 21 patients with stage III breast cancer who had immediate breast reconstruction after mastectomy and axillary lymph node dissection, to assess the role of immediate TRAM reconstruction in the surgical management of stage III breast cancer.

### MATERIALS AND METHODS

Between 1987 and 1994, the tumor registry identified 72 patients who had surgery as part of their therapy for stage III breast cancer. Breast cancer patients presenting with locally advanced primary tumors classified as T<sub>3</sub>, T<sub>4</sub>, N<sub>2</sub>, or N<sub>3</sub> without distant metastases were included in this study if they had mastectomy, axillary dissection, and immediate TRAM reconstruction. Patient selection criteria for immediate TRAM reconstruction was based on the patient's response to chemotherapy, the patient's desire for reconstruction, and performance status. All patients were classified by the American Joint Commission TNM classification (9). Patients were initially staged for distant disease with diagnostic studies that included: bone scan, computed axial tomography scan of abdomen and pelvis, and complete blood count and chemistry. This staging evaluation was repeated in patients receiving preoperative chemotherapy and/or radiotherapy, and patients were excluded from the study group if they developed distant disease before surgery. All patients underwent surgical therapy and follow-up at Emory University. Overall survival and disease-free survival data are available for all patients. The median follow-up is 1.66 years (20 months). Recurrence or death were recorded during follow-up. Kaplan-Meier survival curves were used to estimate overall and disease-free survival. Formal statistical analysis could not be performed because of early follow-up and sample size.

The initial diagnosis of breast neoplasm was made at the initial office visit by fine needle aspiration biopsy in 11 patients, the remaining patients had

**TABLE 1.** Therapy for patients with locally advanced breast cancer

	IIIA	IIIB (noninflammatory)	IIIB (inflammatory)
Initial			
Surgery	7		
Cytotoxic	7	3	1
Combined	2		1
Secondary			
Cytotoxic	5	0	0
Hormonal	5	0	0
Combined	1	0	0

incisional biopsy for diagnosis. Initial therapy by stage is listed in Table 1. Of the seven patients initially resected, each had a total mastectomy with axillary node dissection with immediate TRAM reconstruction. Systemic therapy was the primary therapy for 11 patients, and 3 patients were treated with chemotherapy and radiotherapy before surgery. The cytotoxic regimens for these patients are listed in Table 2.

Secondary adjuvant systemic therapy was administered to six patients. Secondary therapy by stage is listed in Table 2. Two patients received consolidation therapy with autologous bone marrow infusion. All patients received cytotoxic chemotherapy except for one (this patient declined). Tamoxifen was prescribed as additional systemic therapy after chemotherapy in five patients with positive hormone receptors. Ten patients received postoperative consolidation radiation therapy to the TRAM and node-bearing areas after mastectomy. Eight patients have received no radiation therapy to date.

### RESULTS

Twenty-one patients had mastectomy with immediate TRAM reconstruction for stage III breast cancer.

**TABLE 2.** Cytotoxic therapy for patients with locally advanced breast cancer

Type of primary chemotherapy	Total no. of patients	Stage IIIA	Stage IIIB
FAC	5	4	1
AC	8	5	3
AC, CM	1	0	1
Type of secondary chemotherapy	Total no. of patients	Stage IIIA	Stage IIIB
FAC	4	4	0
AC	1	1	0
CMF	1	1	0

A, Adriamycin; C, cytoxan; M, methotrexate; F, 5-fluorouracil.

**TABLE 3.** Pathologic response to primary chemotherapy and histologic features

Patient	Response	Type of chemotherapy	Grade	Pleomorphism	Mitosis	Tubul form
1	CR	FAC	—	—	—	
2	PR	FAC	3	3	2	3
3	NR	FAC				
4	PR	AC	3	3	3	3
5	PR	AC, CM	3	3	3	3
6	CR	FAC				
7	PR	AC				
8	PR	AC	3	3	3	3
9	CR	AC	3			
10	PR	AC	3	3	3	3
11	PR	AC	2	1	1	3
12	PR	AC	3	3	3	3
13	PR	AC	2	2	2	2
14	NR	FAC	2	2	2	2

CR, complete response; PR, partial response; NR, no response. For other abbreviations see Table 2.

cer. The median age at diagnosis was 46.5 years. Three of the patients had a family history of breast cancer; the remaining patients had no major risk factors. All patients had mammograms before any therapy. Only seven patients had a prior mammogram performed. All patients had mammographic abnormalities that were highly suggestive of malignancy. There were no false-negative mammograms. Initial treatment included: systemic therapy in 11 patients, chemotherapy followed by radiation therapy in 3 patients, and primary surgical therapy in 7 patients. The clinical response to primary cytotoxic therapy by stage is listed in Table 3. Although 12 of 14 patients demonstrated a partial or complete response to primary chemotherapy, most patients continued to have stage III tumors at the time of their surgery. Three patients had a complete response. The three patients who failed to demonstrate a clinical response to systemic cytotoxic therapy received preoperative radiation therapy to doses of 45–60 Gy to the breast and nodal area. One of these patients had no residual tumor at the time of mastectomy and was included in the complete response group. The histologic grade was intermediate or high by Elston's modified Bloom and Richardson method (10), which included scores of 2 or 3 for cellular pleomorphism, mitotic rate, and tubule formation. All the tumors demonstrated vascular invasion. These histologic features are shown in Table 3.

The surgical procedures performed are summarized in Table 4. In patients treated with primary chemotherapy and/or radiation, the median time to operation was 130 days. All patients were staged at the time of diagnosis and before operation. If surgery was the primary treatment, the median time to oper-

ation was 15 days. All patients had mastectomy and axillary dissection. One patient requested an elective contralateral mastectomy. Total mastectomy included wide resection of involved skin. Although autologous blood was available for most patients, it was used in only seven patients. The median operative procedure was 244 min. All TRAM flap reconstructions were either unipedicle (3 patients) or bipedicle (18 patients). It is the authors' preference to perform pedicled TRAM reconstruction for most patients. Free tissue transfer is performed with less frequency, and was not performed in any of these patients. Free tissue transfer is not without complication (11) and pedicled TRAM may tolerate radiation therapy (XRT) better. A vertically oriented skin island is much more reliable than a transverse skin island (12,13). This approach is used for the majority of pedicled TRAM reconstructions, regardless of skin resection during mastectomy (Fig. 1). Two operative teams were used in 18 cases. Postoperative complications included fever and atelectasis in two patients; one patient developed flap ischemia that required closure with a latissimus dorsi flap 2 months postoperatively. There were no operative deaths. The median length of hospitalization was 7 days. Six patients received postoperative systemic therapy; one patient received systemic therapy and adjunctive radiotherapy. Ten patients received postoperative radiation therapy to the chest wall (TRAM) and supraclavicular and internal mammary nodes for consolidation. Radiation was well tolerated without significant complication. Surgical margins were free of microscopic disease in all patients.

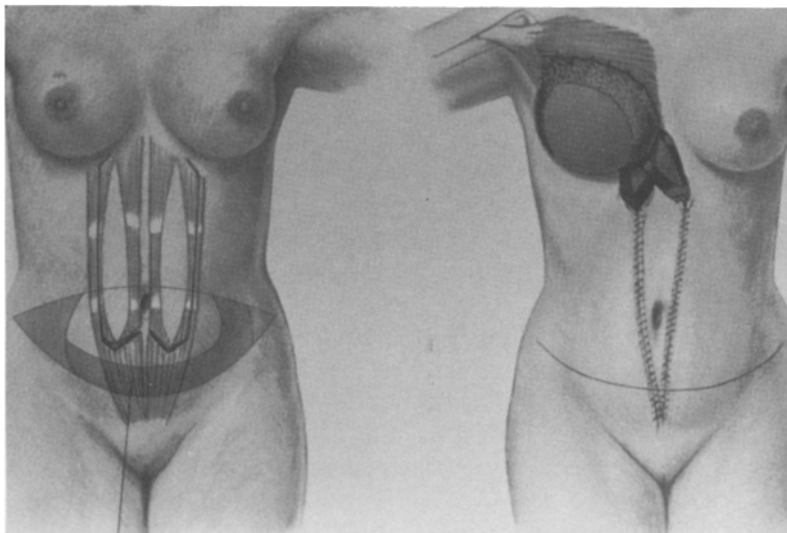
**TABLE 4.** Operative procedures, blood loss, transfusion requirements, tumor margins on surgical specimens, and length of hospitalization

Median time between diagnosis and surgery (range)	
Primary chemotherapy	130 days (34–201)
Secondary chemotherapy	15 days (1–31)
Operative procedures	
Total mastectomy + level III + TRAM	19 patients
Patey modified radical + TRAM	1
Bilateral total mastectomies, unilateral I, II dissection and TRAM	1
Units of blood replacement	
Autologous (range)	Mean: 0.42 (0–2)
Autologous and directed donor (range)	Mean: 0.47 (0–4)
Median length of operation (range)	244 min (162–360)
Tumor margins on specimen	
Negative	21 patients
Positive	0
Length of hospitalization (days) (range)	7 days (4–10)

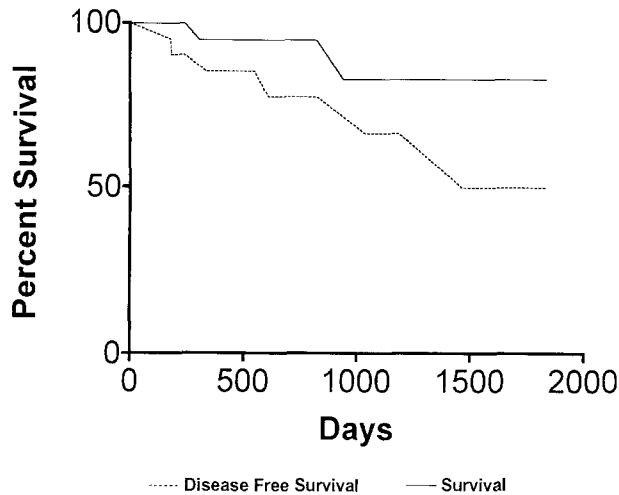
The median follow-up of all patients (21) was 609 days, with a range of 240–1,832 days. The median time to recurrence in six patients was 633 days, with a range of 177–1,460 days. One patient developed a local recurrence in the TRAM at 177 days after diagnosis and 53 days after surgery. She received primary treatment with Adriamycin and Cytosin. She has subsequently developed distant disease. Her current therapy is taxol. Of the other five patients who developed distant disease, two have died as a result of disease progression. Kaplan-Meier survival curves were used to estimate the overall and disease-free survival (Fig. 2).

## DISCUSSION

Mastectomy with immediate TRAM breast reconstruction is an option that allows for wide resection of skin and soft tissues in patients who present with stage III breast cancer (Figs. 3 and 4). It is not associated with a wound complication rate greater than that in our experience with stage I or stage II breast cancer and immediate TRAM reconstruction (14); the risk of fat necrosis was 9% (versus 11%), no abdominal hernias (versus 8%) were identified, and the overall complication rate was 12% (versus 24%). Immediate breast reconstruction can be performed after primary or



**FIG. 1.** Bipedicle transverse rectus abdominis musculocutaneous flap. (Illustration courtesy of Quality Medical Publishing, Inc., *Endoscopic plastic surgery*, p. 857.)

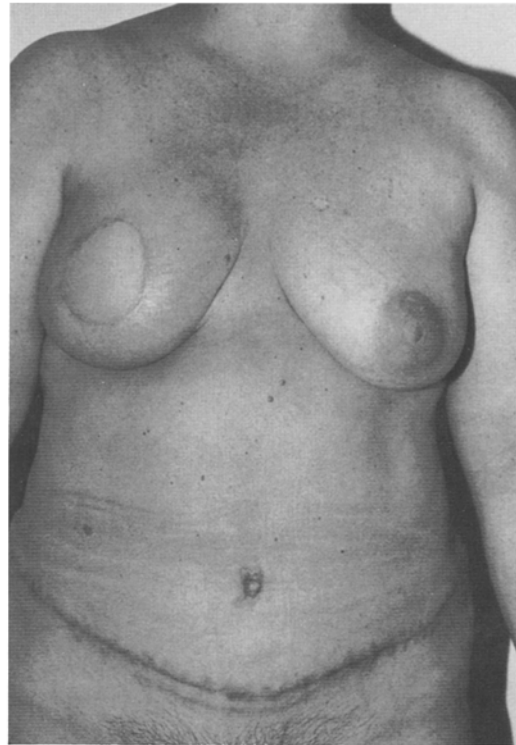


**FIG. 2.** Kaplan-Meier survival.

neoadjuvant chemotherapy without major complication. Eighty-five percent of patients had a response to primary Adriamycin-based chemotherapy. This is comparable to the response in many other series (15–17). Despite a favorable response



**FIG. 3.** A 50-year-old woman 2 years after primary chemotherapy and wide resection and immediate transverse rectus abdominis musculocutaneous breast reconstruction and postoperative radiation therapy.



**FIG. 4.** A 45-year-old woman 1 year after primary chemotherapy and immediate transverse rectus abdominis musculocutaneous breast reconstruction and postoperative radiation therapy.

to primary chemotherapy, the majority of these patients had large tumors at the time of surgery. Wide surgical excision and closure without skin grafting was facilitated by TRAM reconstruction. Ten patients have received consolidation radiation to the area of reconstruction without difficulty (Figs. 3 and 4). The quality of TRAM reconstruction after XRT is dependent on technique (overlapping fields and hot spots). Although mild hyperpigmentation over the TRAM has been observed after XRT, there have been no cases of TRAM desquamation. Occasionally, induration of the TRAM has been noted. In our experience, a well-vascularized TRAM (no evidence of fat necrosis) will tolerate XRT as well as native breast. Delivering postoperative radiation therapy to patients with immediate TRAM breast reconstruction is not difficult. Treating the reconstructed breast mound is analogous to treating an intact breast. The field borders and technique are the same for a reconstructed breast and regional nodal areas as they are for a chest wall after mastectomy or an intact breast preoperatively or after lumpectomy. TRAM reconstruction may make delivering a boost to the

chest wall in a homogenous fashion difficult if this is a proposed part of the treatment. However, using tissue compensators, wedges, and treatment planning, the technical challenges associated with TRAM reconstruction are easily solved.

Immediate TRAM reconstruction after mastectomy does increase the length of surgery and hospitalization. In addition, it generally requires both an oncologic surgeon and a reconstructive surgeon during the operation. At our institution, this coordination is facilitated by a multispecialty breast center. The potential complications of TRAM reconstruction after primary chemotherapy or radiation of the TRAM reconstruction have not been problematic. Immediate breast reconstruction with TRAM does not delay the initiation of systemic therapy.

Immediate TRAM breast reconstruction does not increase the risk of local recurrence or prevent detection of local recurrence in patients with early-stage breast cancer (18,19). A comparably treated group of patients with stage III breast cancer was reported by Hortobagyi et al. (1,17). More than half of the recurrences noted in 5 years of follow-up were noted within the first 2 years. In another review, Fowble et al. noted that the majority of local regional recurrences presented within 2 years of surgery, and by 5 years 89–90% had become manifest (20). Although median follow-up for these patients is limited, there does not seem to be an increase in local recurrence after immediate TRAM reconstruction for stage III breast cancer. Immediate TRAM reconstruction may have potential for decreasing the incidence of local recurrence, because it permits wider surgical resection.

Mastectomy and immediate breast reconstruction using TRAM is not recommended for all patients with stage III breast cancer. Patients should be good surgical candidates, and surgery usually should be performed with curative intent. A surgical team experienced in breast reconstruction is a requirement. For appropriate patients, TRAM breast reconstruction for stage III breast cancer is a reasonable and safe alternative if the patient requires extensive surgical resection and desires immediate breast reconstruction.

## REFERENCES

- Hortobagyi GN. Comprehensive management of locally advanced breast cancer. *Cancer* 1993;66:1387–91.
- Armstrong DK, Fetting JH, Davidson NE, Gordon GB, Huel-skamp AM, Abeloff MD. Sixteen week dose intense chemotherapy for inoperable, locally advanced breast cancer. *Breast Cancer Res Treat* 1993;28:277–84.
- Zucali R, Uslenghi C, Kenda R, Bonadonna G. Natural history and survival of inoperable breast cancer treated by radiotherapy and radiotherapy followed by radical mastectomy. *Cancer* 1976;37:1422–31.
- Swain SM, Sorace RA, Bagley CS, Danforth DN Jr, Bader J, Wesley MN, et al. Neoadjuvant chemotherapy in the combined modality approach of locally advanced nonmetastatic breast cancer. *Cancer Res* 1987;47:3889–94.
- Singletary SE, McNeese MD, Hortobagyi GN. Feasibility of breast conservation surgery after induction chemotherapy for locally advanced breast carcinoma. *Cancer* 1992;69:2849–52.
- Perez CA, Graham ML, Taylor ME, Levy JF, Mortimer JE, Philpott GW, Kucik NA. Management of locally advanced carcinoma of the breast. I. Noninflammatory. *Cancer* 1994;74(suppl 1):453–65.
- Elliott LF, Eskenazi L, Beegle PH Jr, Podres PE, Drazan L. Immediate TRAM flap breast reconstruction: 128 consecutive cases. *Plast Reconstr Surg* 1993;92:217–27.
- Jacobsen WM, Meland NB, Woods JE. Autologous breast reconstruction with use of transverse rectus abdominis musculocutaneous flap: Mayo Clinic experience with 147 cases. *Mayo Clin Proc* 1994;69:635–40.
- American Joint Committee for Cancer Staging and End-results Reporting. *Manual for staging of cancer*. Chicago: American Joint Committee, 1977:101.
- Elston C. Grading of invasive carcinoma of the breast. In: Page D, Anderson T, eds. *Diagnostic histopathology of the breast*. Edinburgh: Churchill Livingstone, 1987:300–11.
- Banic A, Boeckx W, Greulich M, Guelickx P, Marrchi A, Rigotti G, Tschopp H. Late results of breast reconstruction with free TRAM flaps: a prospective multicentric study. *Plast Reconstr Surg* 1995;95:1195–206.
- Robbins TH. Rectus abdominis myocutaneous flap for breast reconstruction. *Aust NZ J Surg* 1979;49:527–30.
- Dinner MI, Labandter HP, Dowden RV. The role of the rectus abdominis myocutaneous flap in breast reconstruction. *Plast Reconstr Surg* 1982;69:209–15.
- Watterson PA, Bostwick J, Hester TR, Bried JT, Taylor GI. TRAM flap anatomy correlated with a 10 year clinical experience with 556 patients. *Plast Reconstr Surg* 1995;95:1185–94.
- Loprinzi CL, Carbone PP, Tormey DC, Rosenbaum PR, Caldwell W, Kline JC, Steeves RA, et al. Aggressive combined modality therapy for advanced local-regional breast carcinoma. *J Clin Oncol* 1984;2:157–63.
- Schwarz GF, Cantor RI, Biermann WA. Neoadjuvant chemotherapy before definitive treatment of stage III carcinoma of the breast. *Arch Surg* 1987;122:1430–4.
- Hortobagyi GN, Amers FC, Buzdar MD, Kau SW, McNeese MD, Paulus D, Hug MD, et al. Management of stage III primary breast cancer with primary chemotherapy, surgery and radiation therapy. *Cancer* 1988;62:2507–16.
- Slavin SA, Love SM, Goldwyn RM. Recurrent breast cancer following immediate reconstruction with myocutaneous flaps. *Plast Reconstr Surg* 1994;93:1191–204.
- O'Brien W, Hasselgren PO, Hummel RP, Coith R, Hyams D, Kurtzman L, Neale HW. Comparison of postoperative wound complications and early cancer recurrence between patients undergoing mastectomy with or without immediate breast reconstruction. *Am J Surg* 1993;166:1–5.
- Fowble B, Schwarbold F. Local regional recurrence following definitive treatment for operable breast cancer. In Fowble B, Goodman R, Glick J, Rosato E, eds.: *Breast cancer treatment*. St. Louis: Mosby Year Book, 1991:373–402.