

Influence of Neoadjuvant Chemotherapy on Outcomes of Immediate Breast Reconstruction

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Background: Immediate breast reconstruction following neoadjuvant chemotherapy raises concerns about increased perioperative complications and has the potential to delay planned adjuvant radiotherapy. This study examined the effect of neoadjuvant chemotherapy on reconstructive outcomes and the commencement of postoperative radiotherapy.

Methods: A retrospective review of a single surgeon's immediate breast reconstructions performed from 2000 to 2007 was undertaken. The recipients of neoadjuvant chemotherapy were compared with nonrecipients (controls).

Results: One hundred seventy-one patients underwent 198 immediate breast reconstructions comprising 64 free tissue transfers, 74 pedicled flaps (latissimus dorsi and transverse rectus abdominis musculocutaneous), and 60 implant-only procedures. Fifty-three patients (29 percent), with a mean age of 47.8 years (range, 29 to 68 years), received neoadjuvant chemotherapy before mastectomy and reconstruction (58 reconstructions; 91 percent with flaps). The control group consisted of 118 patients (140 reconstructions; 61 percent with flaps) with a mean age of 50.4 years (range, 29 to 69 years), making them older ($p = 0.08$). The failed reconstruction rate was 2 percent (one of 58) for the neoadjuvant group and 2 percent (three of 140) for the control group, whereas the reoperation rates for major complications were 9 percent (five of 58) and 9 percent (13 of 140), respectively. Minor complications occurred in 10 percent (six of 58) of neoadjuvant reconstructions versus 6 percent (nine of 140) of controls ($p = 0.380$). Three-quarters of neoadjuvant patients received postoperative radiotherapy, compared with only a quarter of the controls. The commencement of radiotherapy was delayed in 10 percent (four of 39) of the chemotherapy recipients versus 11 percent (three of 28) of controls ($p = 1.00$).

Conclusion: In this series, neoadjuvant chemotherapy did not appear to increase the risk of major surgical complications following mastectomy and immediate breast reconstruction or inordinately delay the institution of adjuvant radiotherapy. (*Plast. Reconstr. Surg.* 126: 1, 2010.)

Immediate breast reconstruction is now routinely offered to breast cancer patients undergoing mastectomy as part of their standard treatment.¹⁻⁴ It has been shown to significantly reduce the negative

psychosocial impact of and the body image alteration related to mastectomy.^{5,6} Its oncologic safety is also well established; it does not increase local or distant recurrence, nor does it adversely affect disease-free or overall survival.⁷⁻¹⁴ Furthermore, there is no significant delay in detection of cancer recurrence.⁷⁻¹⁴

The combination of immediate breast reconstruction and preoperative chemotherapy is a relatively new innovation in the management of breast cancer. This systemic therapy before surgery (commonly referred to as neoadjuvant chemotherapy) was introduced in the 1980s¹⁵ initially

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for locally advanced disease and inoperable and inflammatory breast cancer, and later in the hope of improving survival in patients with operable disease.

The current focus of neoadjuvant chemotherapy for breast cancer is for locally advanced disease and in the context of clinical trials to assess the effectiveness of different treatment regimens and to study the biological response to systemic therapy.¹⁶⁻¹⁸ Given that, there is no convincing survival benefit of neoadjuvant chemotherapy over adjuvant chemotherapy^{16,19-21}; its use before primary breast reconstructive surgery therefore needs to be approached with caution. Preoperative cytotoxic chemotherapy can theoretically have adverse effects on surgical outcomes, principally by delaying wound healing and increasing susceptibility to infections, thus raising concerns about the possible increased incidence of complications postoperatively.^{22,23} Surgical complications may in turn delay the commencement of adjuvant therapies, principally radiotherapy, which has been shown to reduce local recurrence rates.^{24,25} This could potentially compromise oncologic outcomes.²² Although this has indeed been shown to be the case in some tumor types,²⁶ previous studies in breast cancer, including randomized trials,²⁷ have not shown a detrimental effect in breast cancer. However, these studies did not specifically focus on reconstructive surgery. The much greater extent of tissue dissection and additional donor sites, sometimes in combination with the use of implants, potentially makes patients undergoing breast reconstruction after neoadjuvant chemotherapy much more susceptible to its possible detrimental effects.

The primary aim of this study was to compare the incidence of postoperative complications in patients undergoing breast reconstruction following neoadjuvant chemotherapy with those having primary surgery within a consecutive series of patients undergoing reconstruction performed by a single plastic surgeon. A secondary aim was to assess the impact of breast reconstruction on commencement of adjuvant radiotherapy.

PATIENTS AND METHODS

A retrospective case note review of a single surgeon's (C.M.M.) immediate breast reconstructions performed between January of 2000 and December of 2007 was undertaken. Patients were identified from the Addenbrooke's Hospital records, the operating theater register, the surgeon's log book, and the oncology database. The study was confined to patients operated on by a

single surgeon to eliminate interoperator variability. No patients were excluded. The recipients of neoadjuvant chemotherapy were identified and then compared with nonrecipients (controls) with respect to age, indication, reconstructive technique, surgical outcome, and time to commencement of adjuvant postoperative radiotherapy.

Neoadjuvant chemotherapy patients were defined as those who had received chemotherapy in the 12 weeks immediately before surgery. Neoadjuvant chemotherapy was indicated in patients with some of the following features: large tumors, young patients, high-grade breast cancer, locally advanced disease, and inflammatory breast cancer.

At the Cambridge Breast Unit of Addenbrooke's University Hospital, we were involved in the National Institute for Health Research National Cancer Research Network Neo-tAnGo trial (Table 1). This was a phase III, randomized, controlled trial of sequential epirubicin/cyclophosphamide and paclitaxel with or without gemcitabine in the treatment of high-risk early breast cancer with prospective molecular profiling and candidate gene analysis.²⁸ Patients ineligible or declining the study were treated with epirubicin, cyclophosphamide, methotrexate, and fluorouracil or cyclophosphamide, methotrexate, and fluorouracil; or recruited into the Anglo-Celtic 2 Trial (a randomized trial of Adriamycin and Taxotere versus Adriamycin and cyclophosphamide in early breast cancer).²⁹

The following variables were recorded: patient factors (age, body mass index, smoking, comorbidity), indication for mastectomy (tumor size and grade), and reconstruction type (free flap, pedicled flap, or implant only). In addition, the following treatment timings were noted: date of diagnosis, date of definitive surgery, time from end of chemotherapy to surgery, time from surgery to the start of adjuvant radiotherapy, and the reconstructive outcomes. Statistical analysis was per-

Table 1. Neo-tAnGo Trial Elements in the Cambridge Breast Unit

| Treatment | Regimen |
|-----------|---|
| A1 | EC × 4 cycles, followed by paclitaxel × 4 cycles |
| A2 | Paclitaxel × 4 cycles, followed by EC × 4 cycles |
| B1 | EC × 4 cycles, followed by paclitaxel plus gemcitabine × 4 cycles |
| B2 | Paclitaxel plus gemcitabine × 4 cycles, followed by EC × 4 cycles |

EC, epirubicin/cyclophosphamide.
*All patients received chemotherapeutic agent preoperatively, and there were no placebo arms of the trial.

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Table 2. Demographic Data for the Two Patient Groups

| | Neoadjuvant Group (%) | Nonrecipients (%) | <i>p</i> |
|-----------------|-----------------------|-------------------|----------|
| No. of patients | 53 (29) | 118 (71) | NA |
| Age, years | | | |
| Mean | 47.8 | 50.4 | |
| Range | 25–60 | 33–69 | 0.08 |
| BMI | | | |
| Mean | 27.7 | 27.1 | |
| Range | 24–35 | 20–40 | 0.15 |
| Smokers | 6 (11) | 58 (49) | <0.001 |

NA, not applicable; BMI, body mass index.

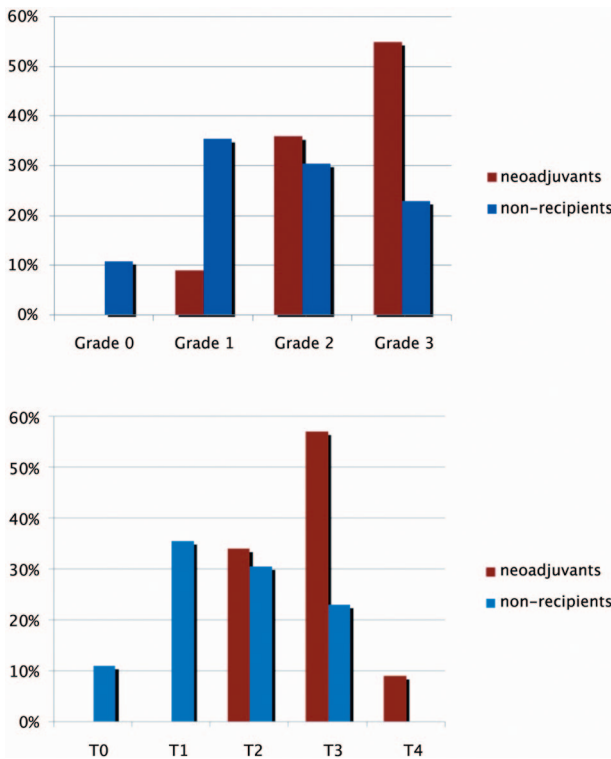


Fig. 1. (Above) Tumor grade for recipients and nonrecipients. (Below) Disease stage in recipients and nonrecipients.

formed using SPSS for Windows, version 17.0 (SPSS, Inc., Chicago, Ill.). Continuous variables were examined using an unpaired *t* test (for ages). The Mann-Whitney *U* test was used for body mass index. Proportions were compared using Fisher’s exact test (for reconstruction outcomes).

RESULTS

Demographic Data

Over the 8-year period, a total of 198 immediate breast reconstructions were performed in 171 patients by one surgeon (C.M.M.). Fifty-three patients (29 percent) had surgery following neoadjuvant chemotherapy. Patient characteristics

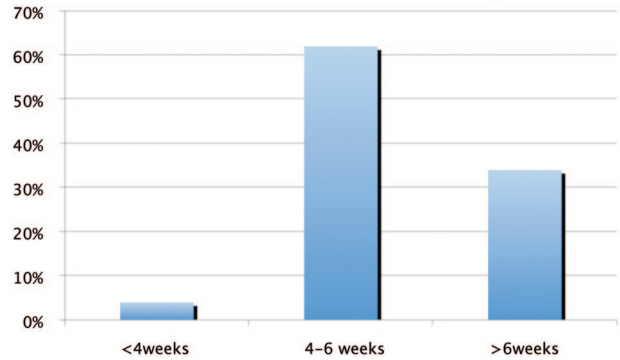


Fig. 2. Time from end of chemotherapy to surgery (percentage of patients).

are summarized in Table 2. There was a nonsignificant trend for neoadjuvant chemotherapy patients to be younger than patients having primary surgery alone (mean age, 47.8 years versus 50.4 years; *p* = 0.08) (Table 2). Their mean body mass indices were comparable, but the percentage of smokers in the control group (49 percent) was significantly higher than in the neoadjuvant group (11 percent) (*p* < 0.001).

Tumor Characteristics

The neoadjuvant group consisted of a higher grade and stage of tumor compared with the controls (Fig. 1). The grade 0 and T0 subgroups comprised those undergoing prophylactic mastectomies and those with ductal carcinoma in situ. Most of the tumors in the neoadjuvant group were grade 2 or 3 or T2 or T3. Neoadjuvant patients had tumors with notably worse prognostic characteristics. All T4 patients received neoadjuvant chemotherapy. The T0 to T4 subgroups were defined according to the American Joint Committee on Cancer tumor-node-metastasis system.

Chemotherapy

In the neoadjuvant group, 47 patients were enrolled in the Neo-tAnGo trial; two were in the Anglo-Celtic II trial; and four received epirubicin, cyclophosphamide, methotrexate, and fluorouracil or cyclophosphamide, methotrexate, and fluorouracil outside trials. The median interval between the final cycle of chemotherapy and surgery was 37 days (range, 32 to 49 days) (Fig. 2). Two patients had their final cycle of neoadjuvant chemotherapy less than 4 weeks but more than 3 weeks before surgery.

Reconstruction Type

The 198 reconstructions included 64 free tissue transfers, 74 pedicled flaps (65 latissimus dorsi

Table 3. Breakdown of Reconstruction Type in Both Groups

| Reconstruction Types | No. of Patients (%) | No. of Operations |
|----------------------------|---------------------|-------------------|
| Neoadjuvant group | 53 (29) | 58 |
| Pedicled flap | | 2 |
| Pedicled flap plus implant | | 23 |
| Free flap | | 28 |
| Implant only | | 5 |
| Nonrecipients | 118 (71) | 140 |
| Pedicled flap | | 13 |
| Pedicled flap plus implant | | 36 |
| Free flap | | 36 |
| Implant only | | 55 |
| Totals | 171 | 198 |

Table 4. Reconstructive Complications of Immediate Breast Reconstruction in Recipients and Nonrecipients of Neoadjuvant Chemotherapy*

| Complication | Recipients (n = 58) | Nonrecipients (n = 140) | p |
|-----------------------|---------------------|-------------------------|-------|
| Minor | | | |
| Wound infection | | | |
| Slow healing | | | |
| Wound breakdown | | | |
| Clinical fat necrosis | | | |
| Total | 10% (6/58) | 6% (9/140) | 0.380 |
| Major | | | |
| Flap loss | 1 (2%) | 3 (2%) | 1.00 |
| Partial flap necrosis | 2 | 3 | |
| Hematoma | 0 | 1 | |
| Infected implant | 1 | 3 | |
| Wound breakdown | 1 | 2 | |
| Pulmonary embolism | 0 | 1 | |
| Total | 9% (5/58) | 9% (13/140) | 1.00 |

*The major complications required surgical treatment or readmission. The minor ones required conservative treatment and no readmission.

flaps and nine transverse rectus musculocutaneous flaps), and 60 implant-only reconstructions. The patients in the neoadjuvant group had far fewer implant-only reconstructions and proportionately more flaps, as they were expected to receive postoperative radiotherapy (Table 3). In contrast, in the controls, one-third were implant-only reconstructions.

Reconstructive Outcomes

In the neoadjuvant group (53 patients; 91 percent with flaps), the failed reconstruction rate was 2 percent (one of 58). The reoperation rate for major complications including flap failure and severe periimplant capsular contracture was 9 percent (five of 58). The incidence of minor complications (not requiring surgical intervention or readmission to the hospital) such as delayed healing was 10 percent (six of 58) (Table 4). In the control group (118 patients; 61 percent with flaps), the

Table 5. Breakdown of Delay of Start of Adjuvant Postoperative Radiotherapy in Recipients and Nonrecipients of Neoadjuvant Chemotherapy

| | Received RT | Delayed RT (%) |
|-------------------------|-------------|----------------|
| Recipients (n = 53) | 39 | 4/39 (10) |
| Nonrecipients (n = 118) | 28 | 3/28 (11) |

RT, radiotherapy.

rate of failed reconstructions was 2 percent (three of 140), that of reoperations was 9 percent (13 of 140), and that of minor complications was 6 percent (nine of 140). These outcomes (Table 4) were not significantly different from the neoadjuvant chemotherapy group (Fisher's exact test, $p = 1.00$, $p = 1.00$, and $p = 0.380$, respectively). Despite this, the incidence of minor, troublesome complications in the neoadjuvant group was almost double that among the controls. The length of stay for both groups was similar at 7 days.

Adjuvant Radiotherapy

After reconstruction, almost three-quarters of patients in the neoadjuvant group (39 of 53) received adjuvant radiotherapy, in contrast to just under a quarter (28 of 118) of those in the control group ($p < 0.001$). Oncologically, the ideal time from surgery to the start of radiotherapy was 6 weeks. However, some patients in the control group needed adjuvant postoperative chemotherapy before undergoing adjuvant radiotherapy. We considered delay as deviation from the anticipated commencement date of adjuvant radiotherapy. The start of radiotherapy was delayed in some cases because of nonhealing surgical wounds. This delayed start was found in a nearly similar proportion in the two groups in those who required radiotherapy: 10 percent (four of 39) of the chemotherapy recipients versus 11 percent (three of 28) of the controls ($p = 1.00$) (Table 5). Median time to adjuvant radiotherapy was 46 days (range, 21 to 76 days) in the neoadjuvant chemotherapy group and 43 days (range, 19 to 69 days) in the control group.

Follow-Up

The median follow-up in this study was 21 months (range, 7 to 64 months). Representative reconstructive outcomes are shown in Figures 3 through 6.

DISCUSSION

The present, relatively large study of immediate breast reconstruction in recipients of neoad-

T3

T5

T4

F3-6

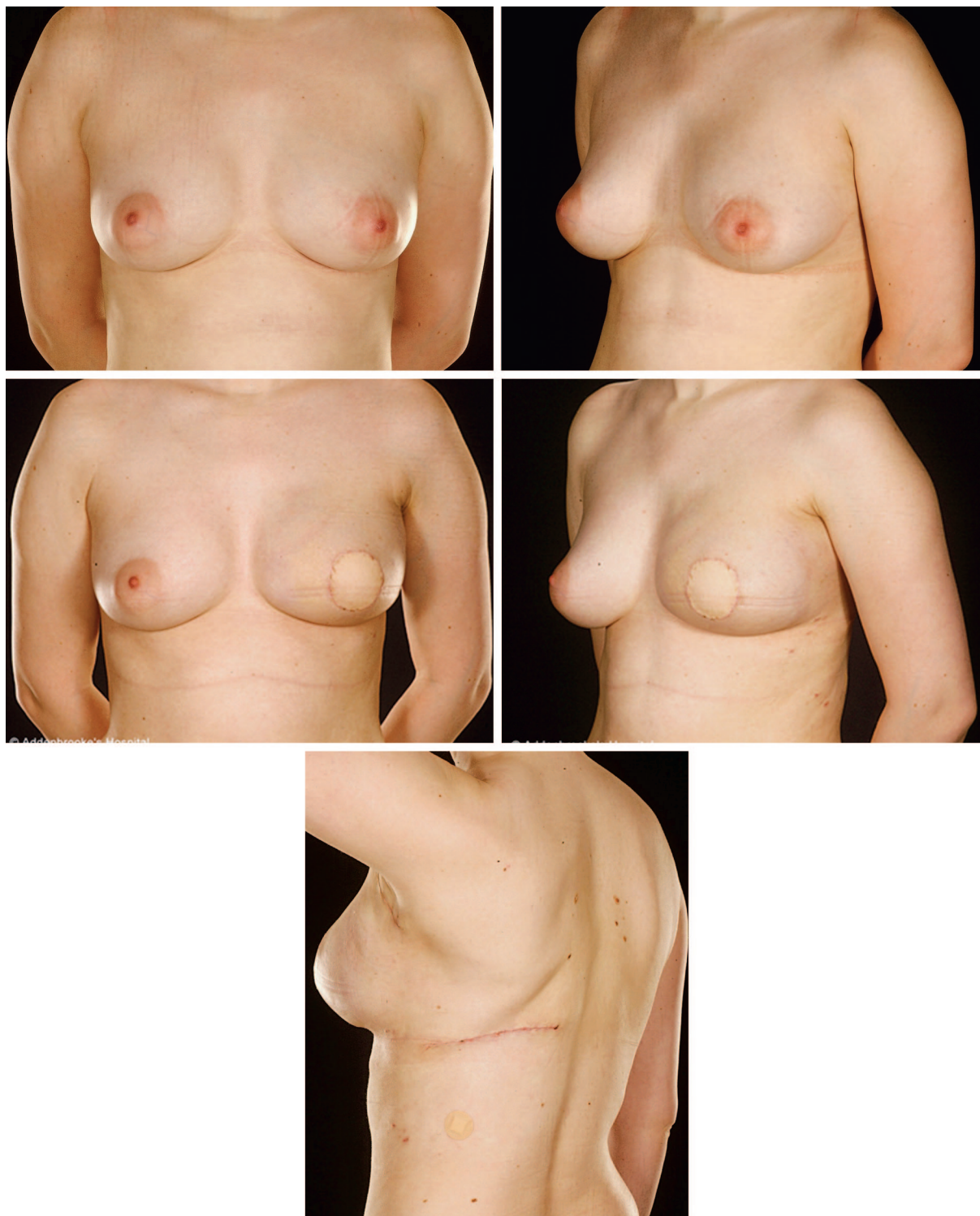


Fig. 3. A 29-year-old patient received neoadjuvant chemotherapy for a T4 tumor of her left breast. She had an immediate reconstruction with a latissimus dorsi flap and permanent expander. Her appearance is shown preoperatively (*above*), as is the good healing at 4 weeks postoperatively (*center and below*), just before starting radiotherapy. This patient elected not to have nipple reconstruction.

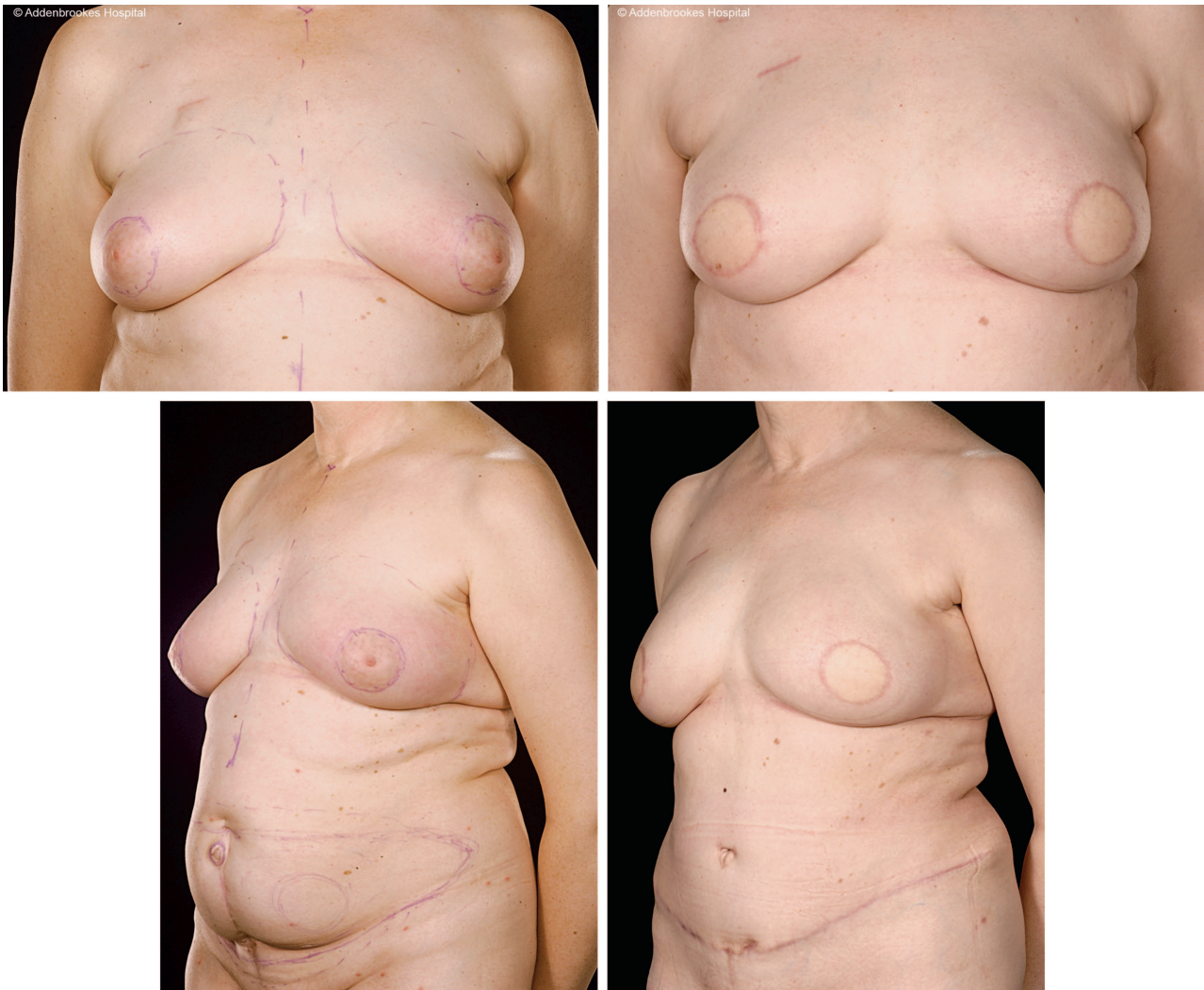


Fig. 4. A 59-year-old woman had bilateral immediate breast reconstruction following neoadjuvant treatment using bilateral free deep inferior epigastric perforator flaps. Note the hair loss preoperatively (*left*). Postoperatively, she had minor abdominal wound-healing problems that settled with dressings only. (*Right*) Appearance at 8 weeks postoperatively.

juvant chemotherapy is unique in that it is a single-operator series and includes “all comers” to avoid selection bias. Other large, landmark series have involved multiple operators,³⁰ been selective,³¹ or have tended to focus on only one type of reconstruction such as free flaps³⁰ or excluded them.³¹ The inclusion of different types of reconstruction in the analysis was deemed desirable, as it allows the results to be more widely applicable to the various situations commonly encountered by most reconstructive surgeons. In any case, it is difficult to obtain two exactly comparable groups because of the nature of the subject being examined. The requirement for neoadjuvant chemotherapy instantly creates two distinct groups, as it is likely to reflect larger and more aggressive tumors. In addition, neoadjuvant chemotherapy tends to be ad-

ministered to patients who can tolerate the side effects of such treatment, who as such tend to be younger and healthier. Furthermore, preoperative chemotherapy is not indicated in ductal carcinoma in situ or prophylactic mastectomy cases.

Multidisciplinary Approach

In the authors' institution, a tertiary cancer referral center of a large university teaching hospital, immediate breast reconstruction is offered routinely to all patients undergoing mastectomy. All cases are discussed in multidisciplinary team meetings involving specialist breast radiologists, oncologic breast surgeons, histopathologists, radiation oncologists, medical oncologists, plastic surgeons, and specialist nurses. Patients request-

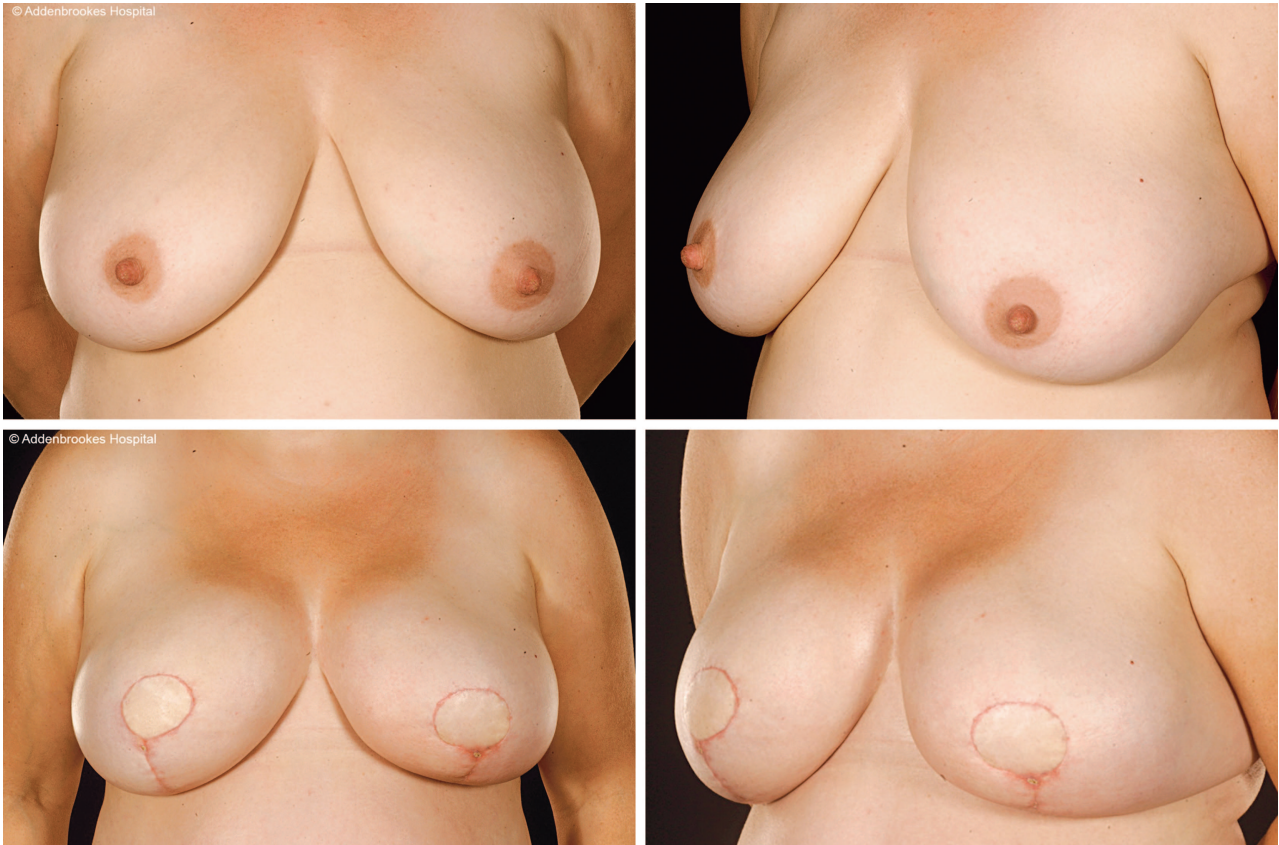


Fig. 5. A 45-year-old control group patient with large grade 2 ptotic breasts (*above*) underwent abdominal free flap breast reconstruction following bilateral prophylactic mastectomy. She developed delayed healing in both reconstructed breasts and the abdominal donor site (*below*) that cleared with 2 weeks of dressings.



Fig. 6. A clinically obese, middle-aged (47 years) neoadjuvant patient (*left*) had immediate breast reconstruction using a totally autologous latissimus dorsi myocutaneous flap and a balancing contralateral Lejour mastopexy. After surgery, she developed significant wound breakdown and partial mastectomy skin flap necrosis (*right*) that were related to the vertical scar mastectomy pattern and the unplanned thin breast flaps. The wound settled with conservative management but caused a delay in institution of radiotherapy. We now recommend early surgical intervention of such wounds to prevent this.

ing immediate breast reconstruction are referred early during their chemotherapy, and their plastic surgery consultation is carried out during the chemotherapy to allow a timely patient assessment

and a thorough discussion of reconstructive options. At this visit, the patients are also given a provisional date for surgery approximately 4 to 6 weeks after the anticipated completion of chemo-

therapy. This is to allow recovery from the myelosuppressive effects of the neoadjuvant chemotherapy drugs.³² In our institution, the median interval between cessation of chemotherapy and surgery was 37 days (range, 32 to 49 days). The aim is for this to be between 4 and 6 weeks.

Reconstructive Outcomes

In this study, the reconstructive complications were classified into either major or minor ones. The major complications required operative intervention or readmission to the hospital and thus altered the planned course of treatment. The minor complications included delayed wound healing requiring antibiotics or prolonged wound care. There was no difference in the rate of major complications between the two study groups. The incidence of minor complications was 10 percent in the neoadjuvant chemotherapy group but only 6 percent in the control group. The excess of minor complications in the neoadjuvant chemotherapy group could be explained simply by the higher frequency of flap reconstructions. Although the difference in minor complications between the two groups was not statistically significant, they are clinically important. They constitute a general irritation for the patients and their families as they involve multiple visits to the hospital or general practice nurse for dressings and possibly a delay in return to work. Patients undergoing neoadjuvant chemotherapy and considering immediate breast reconstruction should therefore be warned that they may be almost twice as likely to suffer these problems with reconstruction, but the overall reconstructive success should be unaffected.

A direct comparison of our complications with other studies is limited by inconsistencies. For example, other authors do not consider having a seroma as a complication unless it requires surgery or is complicated by an infection. In one study, it was suggested that immediate breast reconstruction would decrease the risk of seroma from axillary dissection and mastectomy because it reduces the dead space compared with cases of mastectomy alone.³³ Furthermore, we did not assess the incidence of radiologic fat necrosis. The main areas of concern of the study were the failed reconstructions, the reoperation rates, and the effect on adjuvant radiotherapy. It is important to note that the failed reconstructions were included in the reoperation rate figures in our study; the flap loss rate and rate of major complications were identical in both groups.

Mehrara et al. presented a multioperator series of 1195 free flap breast reconstructions in 952 patients.³⁰ Of these, 70 patients (7.7 percent) had neoadjuvant chemotherapy. In our study, the percentage of neoadjuvant chemotherapy recipients among free flaps reconstructions was much higher (44 percent), possibly reflecting the involvement of the university unit in several neoadjuvant trials during the study period. They recorded an overall complication rate of 27.9 percent (minor complications, 21.7 percent; major complications, 7.7 percent), including six total flap losses (0.5 percent). In our study, the minor complication rates were lower, possibly because radiologic and asymptomatic fat necrosis were not formally assessed. Indeed, after exclusion of asymptomatic fat necrosis, the minor complication rate of Mehrara et al. dropped to 15 percent, which was comparable to ours. It is also important to state that this study consisted entirely of free flaps, whereas our study included all types of reconstruction, although 52 percent of our reconstructions (28 of 53) were with free flaps in the neoadjuvant group.

A number of investigators have studied the effect of other risk factors on the outcomes of reconstruction.^{30,34,35} These include previous scars, smoking, obesity, and other medical conditions. Neoadjuvant chemotherapy has also been identified as an independent predictor of complications. A direct comparison of the effect of chemotherapy is difficult, as these other articles also included delayed breast reconstruction.

In a study of 79 randomized cases of mastectomy with or without systemic therapy, Forouhi et al. concluded that systemic therapy (i.e., neoadjuvant chemotherapy and hormone therapy) did not increase the complication rate of surgery.³¹ In contrast, in another study of 31 patients with locally advanced breast cancer who had received neoadjuvant therapy before mastectomy and immediate reconstruction with the transverse rectus abdominis musculocutaneous (TRAM) flap, Deutsch et al. found that 55 percent of them developed postoperative complications.²²

In our study, there appeared to be some increase of complications among smokers; however, the number of complications was too small for statistical analysis. It is important to note the high percentage of smokers (49 percent) in the control group at the time of surgery. This was possibly attributable to the neoadjuvant chemotherapy patients having the time and opportunity to heed our encouragement to stop smoking while undergoing chemotherapy. Similarly, a reduction in smok-

ing in the neoadjuvant group may have helped in reducing their complication rate.

Oncologic Aspects

Useful consequences of neoadjuvant chemotherapy include enhanced surgical ability to eradicate the tumor and possible reduction of the extent of required surgery.^{20,36–38} Clinical regression may be achieved in 70 to 80 percent of patients.³⁹ In addition, because breast cancer is considered to be a systemic disease, such primary systemic chemotherapy could help in eradication of micrometastases⁴⁰ and thus reduce the incidence of distant metastases.³⁸ Neoadjuvant chemotherapy may indicate better survival and thus is considered to be of prognostic value.^{40,41} Clinically significant resistance may also allow earlier identification of cases that require an alternative approach with non-cross-resistant or novel therapies.⁴¹

In our center, tumor response to neoadjuvant chemotherapy is monitored objectively using magnetic resonance imaging. The local clinical response to neoadjuvant chemotherapy is thought to theoretically correlate with response of micrometastases or distant metastases.¹⁷ The prevention of these metastases is thought to be a major rationale for the use of neoadjuvant chemotherapy over adjuvant chemotherapy. Nevertheless, one of the concerns over the use of neoadjuvant chemotherapy is that it may affect accurate estimation of tumor size and axillary node involvement at the time of surgery and thus result in loss of important prognostic information. In our institution, this concern is addressed by ensuring that tumor size is estimated by multiple imaging modalities and all axillae are staged by sentinel lymph node biopsy before commencement of neoadjuvant chemotherapy.⁴²

Effect on Adjuvant Treatment

A major concern of immediate breast reconstruction in recipients of neoadjuvant chemotherapy is the possible delay in instituting any adjuvant radiotherapy. Gouy et al. retrospectively investigated whether reconstruction following neoadjuvant chemotherapy and mastectomy for large operable breast cancer affected the interval between surgery and adjuvant treatment and thus had an effect on survival.²³ The study compared three groups, namely, mastectomy without reconstruction, mastectomy with nonimplant reconstruction, and mastectomy with implant reconstruction. It found that immediate reconstruction did not delay the commencement of adjuvant therapy and had no significant effect on local relapse-free or distant disease-

free survival.²³ Although there may be no benefit to earlier initiation of radiotherapy, a delay of greater than 3 months could be associated with higher overall mortality.⁴³ This occurred regardless of the cause of the delay.⁴³ This prompted a suggestion to delay breast reconstruction in patients who were preoperatively deemed to require radiotherapy (stage III breast cancer) to avoid complications associated with administration of radiation following immediate breast reconstruction.⁴⁴

In the Cambridge Breast Unit, the radiotherapy protocol⁴⁵ recommends that radiotherapy should be initiated ideally within 4 weeks of surgery and no later than 8 weeks. The indications for chest wall irradiation are listed in Table 6. In our study, following reconstruction, 39 of 53 patients (74 percent) in the neoadjuvant group received radiotherapy, although 28 of 118 (23 percent) of those in the control group received adjuvant therapy in the form of radiotherapy. This difference is explained by patient selection: those receiving neoadjuvant chemotherapy had higher grade and stage of tumors compared with the controls, and the latter also included those with ductal carcinoma in situ and prophylactic mastectomy patients, who were unlikely to receive adjuvant therapy. The start of radiotherapy was delayed in a nearly similar percentage in the two study groups. However, it is vital to note that reconstructive choices were somewhat affected by the need for postoperative radiotherapy. There was an obvious infrequency of implant-based reconstructions in the neoadjuvant group to prevent the occurrence of severe periimplant capsular contracture following adjuvant radiotherapy.^{45–47} Autologous tissue reconstructions are, however, not immune from the effects of radiotherapy,^{48,49} despite tolerating radiation better than prostheses. There may be an unpredictable volume, contour, and symmetry loss with immediate TRAM flap breast reconstruction followed by postoperative irradiation. Contracture of pedicled TRAM flaps,^{50–52} free TRAM flaps,^{51,53} and even deep inferior epigastric perforator flaps⁵⁴ following radiotherapy has been reported, although this may be partially compensated for by deliberate use of larger flaps. Other authors have reported less con-

Table 6. Indications for Chest Wall Radiotherapy in the Cambridge University Unit

- Tumor size ≥ 50 mm (T3)
- Any T4 tumor
- High risk of local recurrence because of tumor characteristics: histologic grade, multicentric, vascular or lymphatic invasion
- Inadequate tumor excision
- Skin involvement

tracture of free TRAM flaps or totally autologous latissimus dorsi flaps.⁵⁵ A two-stage delayed-immediate reconstruction technique of preserving the mastectomy skin flaps with a temporary expander while waiting for the definitive histopathologic assessment of the mastectomy specimen and final oncologic decision on the need for subsequent radiotherapy has been proposed by Kronowitz et al.^{56,57} Those who do not require radiotherapy proceed to reconstruction 2 weeks later, whereas those needing radiotherapy undergo delayed reconstruction. This concept, although interesting, has yet to gain widespread acceptance. Although radiotherapy has significant effects on long-term immediate breast reconstructive outcomes, neoadjuvant chemotherapy remains an important factor, especially in the early outcomes of immediate breast reconstruction. By association with postoperative radiotherapy, neoadjuvant chemotherapy has an additional indirect effect on aesthetic outcome of immediate breast reconstruction (but only to the extent that its indications overlap those for adjuvant radiotherapy).

This article focused on the reconstructive complications of immediate breast reconstruction following neoadjuvant chemotherapy, although no aesthetic disadvantages in those undergoing adjuvant radiotherapy were reported. This may be explained by the differing radiotherapy regimens used in the United Kingdom that differ from the higher total doses and fractionations administered elsewhere.

CONCLUSIONS

In our series, neoadjuvant chemotherapy did not appear to statistically increase the risk of major surgical complications following mastectomy and immediate breast reconstruction or inordinately delay the institution of adjuvant postoperative radiotherapy. Our data suggest a higher incidence of minor complications in the neoadjuvant group which, although clinically important, did not attain a statistically significant difference. It is concluded that neoadjuvant chemotherapy and immediate breast reconstruction are not incompatible and that successful reconstruction can be achieved in this group of patients.

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