**IMPACT OF IMMEDIATE BREAST RECONSTRUCTION ON BREAST CANCER RECURRENCE, PROGRESSION AND SURVIVAL**

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**Summary**

The practice of Immediate Breast Reconstruction (IBR) following mastectomy for primary breast cancer is increasingly adopted. Here, the impact of IBR on disease progression and survival following treatment for invasive breast cancer was assessed. A total of 1697 consecutive patients underwent surgery for operable primary breast cancer between 1996 and 2007. Of those, 691 (41%) received mastectomy of whom 136 (21%) also underwent IBR. Overall survival, local and distant recurrence in patients who underwent mastectomy was compared for those patients who also underwent IBR. No significant difference was found between IBR and mastectomy only, in terms of survival (p= 0.176), time to distant metastasis (p= 0.783) or local recurrence (p= 0.505). There were no significant changes observed when patients were allocated to sub-groups as defined by Nottingham Prognostic Index scores. In terms of post-surgical survival and disease progression, IBR following mastectomy has a similar profile to mastectomy.

[150 words; 150 words max]

**Key words**

Invasive breast cancer, Immediate Breast Reconstruction, Survival, Local Recurrence, Nottingham Prognostic Index1

**Introduction**

Immediate Breast Reconstruction (IBR) following Mastectomy (Mx) for primary breast cancer is being increasingly adopted. The UK National Institute of Clinical Excellence (NICE) recommends that all patients receiving mastectomy should be offered IBR, unless significant comorbidity or adjuvant therapies preclude this option.2 The results of a national audit of primary and delayed breast reconstruction jointly conducted by The British Association of Surgical Oncology (BASO) and The Royal College of Surgeons of England are currently awaited3.

There are potential advantages for IBR over a delayed approach. In one operation both the tumour is removed and body image maintained. This can have a profound positive impact on the patient’s psychological and emotional well being especially in the young4. When reconstruction is delayed some poor prognostic patients may never receive the potential advantages of reconstruction. Other drawbacks associated with delayed reconstruction are the need for large skin paddles required to recreate a symmetrical breast mound, a second anaesthetic and psychological stress for the patient prior to the reconstruction.5

Others have argued in favour of a delayed approach as there is more time for the patient to explore different reconstructive techniques allowing them to opt for reconstructive procedures which may not be available in the primary treatment centre. With a delayed approach there is less adverse effect of radiation on implant based reconstruction. Radiation damage to the skin can be assessed more accurately and any tissues damaged by adjuvant radiation can be discarded at the time of reconstruction.

There are potential oncological safety concerns when IBR is carried out in that more breast tissue may be left behind in an effort to conserve skin especially when an implant only reconstruction is employed. There is also potential delay in starting adjuvant treatments especially chemotherapy and radiotherapy if post operative complications of IBR were to occur. Chemotherapy following IBR may increase the risk of early implant infection affecting continuation of adjuvant treatments. M. Mortenson found that IBR was associated with an increased risk of surgical site complications, but did not delay the initiation of chemotherapy.6 Several other studies have confirmed that IBR does not affect the timing or delivery of post operative chemotherapy.7,8,9,10

Oncological concerns have also included the possibility that the reconstructed breast mound may interfere with targeting of radiotherapy. This is less likely with a subpectoral implant, the pectoralis major is superficial to the reconstruction and tangential beams of radiation are easily targeted. When autologous flaps are employed, pectoralis major may be deep to the flap and implant and so could potentially affect the efficacy of radiotherapy on residual disease in pectoral muscle.11 Current advances in radiation delivery have minimised this effect of IBR on radiation efficacy.

Studies have also examined the aesthetic outcome of IBR following adjuvant radiotherapy It is generally considered that morbidity is increased and aesthetic outcome adversely affected, with outcomes being influenced by the specific type of reconstruction.11 When prosthetic devices are used prior to RT morbidity includes capsular contracture, pain, infection, interstitial fibrosis and breast asymmetry. Autologous flaps can develop fat necrosis and flap shrinkage resulting in breast asymmetry.12,11,5

The aim of this study is to assess the impact of IBR on local recurrence (LR), distant metastasis (DM) and overall survival in a consecutive series of patients requiring treatment for invasive breast cancer. To mitigate against any prognostic bias in the selection of patients for IBR we have also compared results within Nottingham Prognostic groupings.

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**Patients and methods**

The study population is derived from a consecutive series of 1697 patients who received surgery for primary invasive breast cancer at the North Cumbria Breast Unit, Carlisle, UK between 1st January 1996 and 31st December 2007. Patients who received neoadjuvant chemotherapy and neoadjuvant endocrine treatment were excluded. 1006(59%) received breast conservation. 691 (41%) underwent mastectomy. Of the mastectomy group 555(80%) had mastectomy alone. 136(21%) patients received IBR of which 82(60%) had reconstruction employing Latissimus Dorsi myocutaneus flap and 54(40%) had subpectoral implant alone.

Only patients presenting below age 75 were included in the analysis of survival and recurrence leaving 135 in the IBR group (Group A) and 452 in the mastectomy alone group (GroupB).The axilla was staged in all patients and lymph node positive patients received clearance or radiotherapy to the axilla. Post mastectomy radiotherapy and adjuvant systemic treatments were employed as per local protocols. Patients were reviewed in designated follow up clinics 3 monthly for the first year, 6 monthly for the second year and annually thereafter. Time to local / regional recurrence and distant metastasis was recorded prospectively on a computerised database as was overall survival. Patients received annual contra-lateral mammograms for 10 years. During follow up staging investigations were carried out based on symptoms alone.

**Statistical Analysis**

The following outcomes were recorded for all patients: local recurrence, distant metastases and survival. These data were analysed for all patients and separately within patient groupings based on the Nottingham Prognostic Index (NPI) scores. The NPI scores were categorised into NPI ‘good group’ (a score of less than 3.4), NPI ‘moderate group’ (3.4 to 5.4) and NPI ‘poor group’ (higher than 5.4). Survival and recurrence analysis were conducted using the Kaplan-Meyer method, with log rank tests for assessing statistical significance. All statistical analyses were performed using SPSS (version 15, SPSS, Woking, UK).

**Results**

Of the 587 patients studied, only 8 patients (1.4%) were lost to follow up. Median age for group A was 47 (range 23-75) and group B was 59 (range 28-75). Patients were followed up for a median of 55 (range 16-148) months. There was no significant difference between the numbers of patients receiving adjuvant treatments in the two groups although a trend occurred for a lower radiotherapy rate in the IBR group (see Table 1).

[comment for journal Editor: Table 1 to be inserted here]

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During the 10 year study period there was a gradual change in the method of IBR adopted with increasing numbers of patients opting for reconstruction employing autologous tissues. Figure 1 shows the type of reconstruction carried out in each year during the study period.

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Over the study period, 12 patients (9%) developed local recurrence in the IBR group compared to 38 (8%) in the mastectomy only group. Mean time to local recurrence was 26 (range 3-131) months in group A and 22 (range 3-133) months in Group B. 7 out of 12 (60%) in group A and 22/38 (57%) in group B developed distant metastasis following local recurrence. Annual local recurrence rate of patients, for those who completed 36 months of follow up, was similar in the two groups. Thirty-nine patients (29%) developed distant metastasis in group A and 89(20%) in group B. Mean time to distant metastasis was 36(2-136) months for group A and 24(3-132) months for group B (see Table 2).

[comment for journal Editor: Table 2 to be inserted here]

**Survival analysis**

No significant difference in survival was found between group A and group B (p = 0.18, Log rank test), although there was a trend towards improved survival amongst IBR patients. Similarly there was no disadvantage for IBR patients in terms of local recurrence (p = 0.51) and distant metastases (p = 0.78). Figure 2 summarises the data by means of Kaplan-Meier plots.

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We further analysed disease-free survival in subgroups defined by their Nottingham Prognostic Index. The IBR patients suffered no excess local recurrence in the good (p= 0.79), moderate (p= 0.77) or poor (p= 0.84) prognostic groups compared to mastectomy alone. Similarly there was no significant difference in the time to distant metastasis either in the good (p= 079), moderate (p= 0.26) or poor (p= 0.48) prognostic groups. There was a trend towards improved overall survival, in the IBR group. (Graph7). We analysed overall survival within Nottingham Prognostic groups in order to mitigate against any prognostic bias that might have occurred in the selection of patients for IBR, A small but significant improved overall survival for IBR patients in the good prognostic group was found. This may be due to the higher mortality from non breast cancer related events in the relatively older GroupB patients compared to groupA patients. In the poor prognostic group with higher breast cancer specific deaths there is no survival disadvantage for the IBR patients (Figure 3)

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**Discussion**

This study compares survival in mastectomy surgery patients who had IBR with those who had no IBR. Patient data was collected retrospectively and neither were patients randomised to one of the two treatments assessed. No fixed policy governed which patients were offered reconstruction. For this reason results in terms of recurrence and survival were analysed after subdivision of patients according to NPI. By doing this any prognostic bias involved in decision making to offer patients IBR is reduced.

There was no significant difference in the time to local recurrence between the two groups (25 versus 22 months) implying IBR doesn’t delay detection of local recurrence. The annual local recurrence rate of patients who completed 36 months follow up was also similar between the two groups (1.7 % in group A versus 2.1 in group B).

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A number of other studies have looked at the impact of IBR on local recurrence and mortality and concluded that immediate reconstruction is safe. However most of these series were based on small retrospectively collected data without a control population. There have been no reported randomised studies comparing IBR versus no IBR. Such a study would not be possible for ethical reasons. The use of Nottingham Prognostic Index goes someway to avoid bias of patient selection for IBR when comparing outcomes in the two groups of patients studied.

The main limitations of this study are that the number of patients is small and minimum follow up is only 16 months even though the study population is selected from a consecutive series over 10 years. Literature search revealed 3 studies with larger number of patients but the control groups were not matched for prognostic factors. Michael Bezuhly et al compared 3620 IBR patients to 46177 control patients who had mastectomy alone using the data from US National Cancer Institute’s Surveillance, Epidemilogy and End Results (SEER) registries and found that IBR is associated with improved surviva129. However the IBR patients used in this analysis were more likely to be younger with early stage lymph node negative cancer. Colleen M. Mccarthy compared 309 IBR patients with 309 controls matched for age and TNM staging and found that there was no excess locoregional recurrence in the IBR group30. TNM staging is not as accurate as NPI as a marker of prognosis and therefore control group is not a good match for IBR patients. Petit et al compared 518 IBR patients to 159 controls who had mastectomy alone in a consecutive series of 677 patients and confirmed the safety of IBR in terms of disease free and overall survival31. Again the control group was not matched for prognostic factors.

**Conclusion**

The data presented here shows that IBR after mastectomy for breast cancer is safe and is not associated with an increased risk of local or distant recurrence, or death either overall or within Nottingham Prognostic Groups. Patients should be counselled about the option of post operative RT and the risk of implant related complications.

*Ethical approval*: Ethics approval was not deemed necessary as this concerns a retrospective evaluation in which no identifiable data is disclosed..

*Funding*: None.

*Conflicts of interest*: None.

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**Figure 1**. Distribution of types of surgery methodology applied in patients undergoing IBR. 

**Figure 2**. Survival (a), recurrence (b) and metastasis (c) following breast surgery.

**A**



**B**



**C**



**Table 1**. Demographic overview of and completion rate in the two study groups

|  |  |  |
| --- | --- | --- |
| Adjuvant treatments | IBR group | Mastectomy only group |
| RT to chest wallp= 0.06\* | 44(33%) | 213(47%) |
| Endocrine treatmentp = 0.20\* | 96(71%) | 260(58%) |
| Chemotherapyp =0.40\* | 59(44%) | 169(37%) |

\*Determined by analysis of variance.

**Table 1**. Local recurrence of breast cancer following surgery

|  |  |  |  |
| --- | --- | --- | --- |
|  | 1st year | 2nd year | 3rd year |
| IBR | 2(1.5%) | 2(1.5%) | 3(2 %) |
| Mx alone | 11(2.4%) | 9(2%) | 9(2%) |