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Review

Does post-mastectomy radiotherapy represent a contraindication to skin-sparing mastectomy and immediate reconstruction: An update

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ABSTRACT

The use of skin-sparing mastectomy (SSM) to facilitate breast reconstruction is increasing due to a wide acceptance of improved cosmetic outcomes and evidence of equivalence in oncologic outcomes. The rates of patients undergoing mastectomy for whom post-mastectomy radiotherapy (PMRT) will be recommended is increasing as evidence of decreased loco-regional recurrence and increased survival mounts.

PMRT may adversely effect complication rates and cosmetic outcomes for patients undergoing immediate breast reconstruction and PMRT – although the evidence for this is methodologically flawed.

This article summarises the above evidence and highlights a reconstructive algorithm that may be used to mitigate the possible deleterious effects of PMRT on results.

Contents

Introduction

Breast-conserving surgery (BCS) for breast cancer has been shown to be safe [16]; and its role continues to expand through the use of newer volume displacement techniques, such as therapeutic mammoplasty [27]. For some patients a mastectomy is still advised or requested by the patient [45]. For those patients, breast reconstruction is often possible. This can be done via an immediate or delayed approach using either implants, autologous tissue or both. An immediate reconstruction has some advantages – the native skin envelope may be used and the number of operations can be minimised.

Many patients whose disease warrants mastectomy are at high risk of local recurrence and will also need post-mastectomy radiotherapy (PMRT) [45]. This has been shown to compromise both implant-based and autologous immediate breast reconstructions [3]. It is not possible to predict all patients that will need PMRT pre-operatively. Many surgeons therefore delay reconstruction if PMRT may be needed. Randomised trials such as 'SUPREMO' are currently investigating the benefit of PMRT in patients judged to be at intermediate risk of local recurrence, so the proportion of patients recommended to have it may increase further [33].

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Skin-sparing mastectomy (SSM) provides a way of preserving the native skin envelope for immediate breast reconstruction [66] and produces better cosmetic outcomes relative to standard mastectomy [34]. SSM is usually performed to facilitate immediate breast reconstruction and so this option may be denied to patients undergoing mastectomy where PMRT is a possibility.

The aims of this article are to provide an update on the oncological safety of SSM, to summarise the evidence for PMRT in terms of effect on loco-regional recurrence and survival, to outline the available evidence on the effects of PMRT on breast reconstruction and to describe surgical algorithms which are in use to mitigate these effects.

Post-mastectomy radiotherapy

Oxford Overview data from trials of patients undergoing either BCS or mastectomy with and without radiotherapy reported in 1995 and updated in 2000, showed a reduction of two thirds in local recurrence with radiotherapy and a reduction in breast-cancer specific deaths. This was offset by an increase in deaths from other causes. No overall survival benefit was therefore seen, perhaps reflecting the toxicity of the older radiotherapy schedules given to patients in the trials that made up the meta-analyses (EBCTCG [84,85]).

In 2005, the group reported updated data from 42,000 women (EBCTCG [86]). Analysing comparisons in treatments where the difference in local recurrence between treatment groups was greater than 10%, a significant difference in breast-cancer specific mortality was demonstrated. Where the differences were less than 10%, there was no significant difference. This seemed to show that breast-cancer specific mortality was proportional to local recurrence, but not to overall survival and again there was an excess of non breast-cancer mortality in the radiotherapy-treated patients.

A survival benefit of radiotherapy in the treatment of high risk breast cancer patients has since been demonstrated. Firstly; two large randomised studies from a Danish group confirmed there was a significant reduction in loco-regional recurrence with PMRT and a significant increase in overall survival in high risk pre-menopausal patients undergoing mastectomy who also underwent chemotherapy with CMF, and in high risk post-menopausal patients who were treated with Tamoxifen [46,47]. Secondly, a meta-analysis of breast-cancer trials that involved node-positive pre and post-menopausal women also undergoing systemic treatments for their breast-cancer and randomised to PMRT or none showed significant reductions in recurrence and overall survival in the PMRT group [70]. Thirdly, the British Columbia study of high risk pre-menopausal women undergoing CMF chemotherapy, where half were randomised to PMRT, showed a significant benefit of PMRT in terms of loco-regional recurrence and disease-free survival when first reported, and at 20 years showed significant overall survival benefit [52]. The survival benefit of PMRT that could be expected in patients treated today may have been overestimated by these trials, which used systemic therapies that are now thought to be outdated.

Several groups have published guidelines on PMRT following these major trials. The American Society of Surgical Oncology in 2001, published their guidelines after two meetings by an expert panel [54]. They recommended PMRT for patients with more than 4 positive axillary nodes, and tumours larger than 5 cm because of the proven reduction in loco-regional recurrence and overall survival in these groups. The benefit for smaller tumours and patients with 1–3 positive nodes was thought to be unclear.

There is limited data from a sub-group analysis of the Danish trials [48] suggesting a survival benefit in patients with 1–3 nodes. The 'SUPREMO' trial has been designed to address the benefit in this patient group and in other patients thought to be at intermediate risk of local recurrence [33].

Hypofractionated PMRT regimes are likely to increase in proportion as high profile trials of hypofractionation such as the START A and B trials (in which 15% and 8% of patients underwent mastectomy respectively) report 5 year follow-up data suggesting the results in terms of loco-regional recurrence are at least as good as standard regimes [63,64].

NICE recommends PMRT for women thought to be at high risk of loco-regional recurrence (more than 4 involved lymph nodes, large tumours, involved margins), and recruitment into 'SUPREMO' is suggested for those at intermediate risk (patients under 40 years, 1–3 nodes, lymphovascular invasion, grade III and ER negative tumours) [45].

The second annual report of the national mastectomy and breast reconstruction audit [28] reported a rate of PMRT of 40%.

Radiotherapy and breast reconstruction

There have been no large, randomised controlled trials reporting the effects of PMRT on breast reconstruction. A number of studies reporting comparative complication rates have been published, but these have been either small, non-randomised or were retrospective reviews. They report increased morbidity after both autologous and implant-based reconstruction with PMRT and in general implant-based reconstructions fared worst in terms of complications [6]. The results are difficult to interpret as the reporting of complications is not standardised and in many studies is not complete. A recent systematic review of 42,000 women from 134 trials of breast reconstruction reported that complications were defined in only 20% and that definitions tended to be inconsistent [51].

A recent meta-analysis [3] has been published. The authors identified 11 suitable studies reporting the effect of radiotherapy on complication rates after breast reconstruction. The 1105 patients were split into three cohorts for analysis.

Firstly, the impact of PMRT on implant-based reconstruction was assessed. Of 424 patients undergoing immediate implant-based reconstruction with or without PMRT higher rates of capsular-contraction, infection, skin-necrosis and re-operation were noted in the PMRT patients with an odds ratio of 4.2.

Secondly, the impact of PMRT on immediate implant versus autologous reconstructions was assessed in 380 patients. In this group, the implant-based group had a rate of 33% for complications (capsular-contraction, infection, fibrosis, re-operation) versus 7.8% in the autologous group (capsular-contraction, infection, fibrosis, fat necrosis, re-operation). This suggests that the morbidity from autologous reconstruction with PMRT is less than implant-based reconstruction for the parameters studied (odds ratio 0.20, 95% CI 0.1–0.4).

Thirdly, the impact of radiotherapy on immediate versus delayed reconstruction was assessed (although the authors only included TRAM reconstructions). They found no significant difference in complications between the immediate and the delayed group (fibrosis, fat necrosis, infections, re-operation rates), but there were small numbers in the immediate group suggesting a high chance of type II error.

The comparison of studies reporting complication rates with PMRT following immediate reconstruction is complicated by the fact that differing radiotherapy schedules and implants are used (many of which are now regarded as out of date) and that complications are reported inconsistently. For example, the rates of significant capsular-contracture after immediate implant-based reconstruction with & without PMRT vary from 15 to 50% & 0 to 20% respectively. The difference in capsular-contracture rates with & without PMRT was significant in all the studies, but salvage