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A meta-analysis of implant-based breast reconstruction and timing of adjuvant radiation therapy

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ABSTRACT

Background: Implant-based breast reconstruction is the most common type of reconstruction after postmastectomy radiation therapy (PMRT). The impact of the timing of PMRT to a tissue expander or permanent implant is not well understood. The purpose of this systematic review was to evaluate outcomes in implant-based reconstruction and the timing of PMRT.

Methods: A review of the English literature in the PubMed/MEDLINE database (2000-2016) was performed to identify all articles on implant-based breast reconstruction and PMRT. Cases from each study were grouped by PMRT to a tissue expander or PMRT to a permanent implant. Outcomes of interest included reconstructive failure and capsular contracture as overall rates and associations were pooled. Effect sizes (z values), risk ratios (RRs), and heterogeneity scores (I^2) were calculated on meta-analysis.

Results: There were 20 studies meeting inclusion criteria with 2348 patients identified. Pooled analysis revealed an overall rate of reconstructive failure of 17.6% and Baker grade III/IV capsular contracture of 37.5%. PMRT applied to tissue expanders resulted in higher rates of reconstructive failure compared with PMRT applied to permanent silicone implants (20% *versus* 13.4%, RR = 2.33, P = 0.0083, 95% confidence interval 1.24-4.35), but lower rates of capsular contracture (24.5% *versus* 49.4%, RR = 0.53, P = 0.083, 95% confidence interval 0.26-1.09).

Conclusions: Regardless of timing, PMRT applied to implant-based breast reconstruction was associated with high risk of reconstructive failure and capsular contracture. Surgeons should consider alternative strategies, such as autologous tissue reconstructions, in patients requiring PMRT.

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Introduction

Although there have been significant improvements in breast cancer outcomes, adjuvant therapies are known to adversely affect reconstruction.[1] Studies have demonstrated that multidisciplinary teams involving surgical oncologists, medical oncologists, and radiation oncologists have been associated with a reduction in breast cancer mortality.[2] There has been debate about the timing and usage of adjuvant radiotherapy, hormonal therapy, and chemotherapy, with respect to surgical interventions. Of particular importance to the reconstructive surgeon is the use of postmastectomy radiation therapy (PMRT).[3-6] The use of radiotherapy has increased recently as studies have shown decreased local recurrence and improved mortality rates.[7-9]

Unfortunately, the association between PMRT and poor reconstructive outcomes is well documented. In patients undergoing implant-based reconstruction, PMRT increases rates of infections, capsular contracture, implant loss, and overall reconstructive failure requiring revisional surgeries.[10-12] In patients undergoing autologous reconstruction, PMRT has been associated with fibrosis, distortion of breast shape, volume loss, and fat necrosis.[13,14] More importantly, patient-reported outcomes after reconstruction are lower in women receiving PMRT; these include aesthetic outcome, overall satisfaction, and quality of life.[15,16]

The extent to which radiotherapy ultimately impacts breast reconstruction outcomes is dependent on various factors such as dosing, length of treatment, time separating reconstructive surgery from radiation, and method of reconstruction. Studies have demonstrated that adverse outcomes are higher in patients undergoing concomitant adjuvant systemic therapies with PMRT.[17] One major obstacle to identifying the optimal treatment regimen is that treatment varies widely between centers. This variation has resulted in discrepancies in the literature regarding the outcomes of PMRT on breast reconstruction, with some centers reporting high rates of complications and others reporting few adverse events.[12,18,19] Other factors adding to these discrepancies include the different types of reconstruction: implant and autologous. The most common method of breast reconstruction currently is implant based.[6,20] There are two broad categories: single stage reconstruction where a permanent prosthesis is placed immediately after mastectomy and two-stage reconstruction where a tissue expander is placed at the time of mastectomy and later exchanged for a permanent prosthesis.

To mitigate the negative impact on breast reconstruction caused by PMRT, many centers have implemented an algorithmic approach in patients identified to require PMRT as part of their treatment plan.[11,21] One main factor in these algorithms is the timing of radiation therapy with respect to the sequence of surgical interventions during implant-based reconstruction. This systematic review evaluates the current evidence on how the timing of PMRT affects the outcomes of implant-based breast reconstruction.

Materials and methods

Literature search

A systematic search of the literature published from January 1, 2000, to June 1, 2016, was performed to identify all relevant articles on PubMed/MEDLINE. The search entry "Breast reconstruction AND (Implant or Tissue expander) AND (Radiation OR Irradiation OR Radiotherapy)" was used. Abstract review was performed on studies with pertinent titles. Full article review was performed on studies with pertinent abstracts. The decision to include or exclude each study was made by the first and senior authors on full article review. Included studies were then additionally screened for potential citations not captured in the aforementioned search.

Assessment of methodologic quality

Studies were selected for inclusion based on the following inclusion criteria: (1) the study involved implant-based breast reconstruction in the setting of PMRT; (2) the provided extractable data for reconstructive failure and/or capsular contracture; (3) the study was not limited to case reports or literature reviews; and (4) the study was published in the English language. Studies were excluded if they did not meet the previously mentioned criteria. In addition, studies were excluded if they contained less than 20 patients, patients did not receive radiotherapy, and it was unclear when patients received radiation during reconstruction. Methodologic quality was assessed with the American Society of Plastic Surgeons level of evidence rating scale.

Data extraction

Data extracted included study size, study design, timing of adjuvant radiotherapy relative to reconstructive stage, average length of follow-up (months), and specific outcome rates. Outcomes of interest included reconstructive failure and severe capsular contracture (Baker grade III/IV). Length of follow-up was reported by each individual study as the time from the last surgical intervention until the most recent postoperative visit. Reconstructive failure was defined as tissue expander or permanent implant removal or a failure to progress through all implant-based reconstructive stages for reasons other than cosmetic outcome, such as pain or tenderness. Data from studies reporting capsular contracture rates without grade were omitted from analysis. Only Baker grade III or IV was included because these are symptomatic while Baker I/II could not be analyzed, as it was not reported by every article. Patients undergoing staged reconstruction with radiation were included only if they underwent a both stages, including tissue expander placement and an exchange procedure. No patients with premastectomy radiation treatments were included.

Studies captured in this meta-analysis only used silicone implants for reconstruction. Studies performing both single