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Post-mastectomy radiation therapy after breast reconstruction: Indications, timing and results

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ABSTRACT

Around 50% of women undergoing mastectomy choose to pursue breast reconstruction to improve their psychological, social and sexual well-being, and many of them will require subsequent radiotherapy. The optimal integration of mastectomy and radiotherapy may create a therapeutic challenge. This review addresses selected aspects of this problem.

1. Introduction

Within the past decades breast-conserving therapy has largely replaced mastectomy for the treatment of breast cancer. However, up to 40% of women with breast cancer undergo mastectomy due to more advanced local and regional disease, or individual preferences [1]. Around 50% of women undergoing mastectomy choose to pursue breast reconstruction in order to improve their psychological, social and sexual well-being [1]. Breast reconstruction may be performed at the time of mastectomy (during the same anesthesia), or as a separate procedure, after several months or even years. An increasing number of patients, even in the setting of post-mastectomy radiotherapy, opt for immediate breast reconstruction to cope with the cosmetic and psychological consequences of breast loss [2]. Immediate, compared with delayed breast reconstruction has also other advantages, such as avoiding another surgery, better esthetic outcome by limiting scars and using natural skin envelope, and lower cost. However, some patients undergoing breast reconstruction may require adjuvant radiotherapy, which in this setting may create some problems [3,4].

Postoperative radiotherapy in breast cancer significantly reduces the risk of relapse and death, and the indications for its use are broadening [5]. This method has traditionally been administered for all patients with tumor size 5 cm or greater, and for those with four or more positive axillary nodes. More recently, radiotherapy has also been recommended for selected patients with one to tree positive lymph nodes [6,7].

The optimal integration of mastectomy and radiotherapy creates a therapeutic challenge. Current knowledge regarding the use of radiotherapy after breast reconstruction is mainly based on single-institutional observational studies which lack controls and long follow-up, and do not account for confounding variables. There is also a significant heterogeneity in the literature owing to differences in definitions of complications and patient-related outcomes, patient characteristics, radiation doses, fractionations and techniques. Owing to the paucity of high-quality evidence-based data, recommendations on the optimal use of radiotherapy in patients undergoing breast reconstructions are based on lower-level evidence.

1.1. Types of breast reconstruction

Breast reconstruction can be accomplished with a prosthetic device, autologous tissue transfer or a combination thereof. The choice between prosthetic and autologous breast reconstruction depends on individual anatomical conditions, the size and configuration of the contralateral breast, comorbidities, prior therapies and patient preferences. Additionally, there are apparent institutional preferences of one modality over the other, with autologous reconstruction favored by academic institutions [8].

1.1.1. Prosthetic reconstruction

Prosthetic reconstruction constitutes around 80% of all reconstructions [8]. This option may be accomplished using immediate placement of permanent implant (one-step procedure) or insertion of tissue expander prior to implant placement (two-step procedure). Compared to autologous, prosthetic reconstruction is less complex, shorter, cheaper, reversible and allowing for quicker postoperative recovery. With improved implant technology and the

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use of acellular dermal matrices, prosthetic reconstruction has become the most commonly used method of reconstruction [2,9]. However, in the setting of radiotherapy, this approach is associated with increased risk of complications which may affect cosmetic effect or cause implant failure [10–13]. Despite a large body of literature data, there are currently no consistent factors predictive for the risk of complications in patients irradiated after implant-based reconstruction. To decrease morbidity, immediate prosthetic reconstruction has traditionally been discouraged in patients likely to receive postoperative radiotherapy. On the other hand, avoiding breast reconstruction or its postponement for months or even years commits patients to more distress and poorer well-being during the recovery period. Patients may also be reluctant to undergo another complicated surgery at the end of treatment. Finally, tissue expansion following post-mastectomy radiotherapy may be restricted and painful due to extensive fibrotic changes [14]. In consequence, despite some risks the use of immediate implant-based reconstructions in patients with indications for radiotherapy has been gradually increasing, to become the most common form of reconstruction [2].

In some patients the need for postoperative radiotherapy cannot be definitively determined until the final pathologic results are available. In such cases, as well as in patients who are unsuitable for autologous tissue reconstruction or prefer prosthetic option, some authors recommend the two-step "delayed-immediate" reconstruction [15]. This method includes a skin-sparing mastectomy with a sub-pectoral insertion of a saline filled temporary tissue expander to preserve the shape and dimensions of the breast envelope. After reviewing the pathology sections, patients who do not require radiotherapy are subjected to breast reconstruction within two weeks of mastectomy, whereas those who require radiotherapy are allowed to complete it with the expander deflated on the chest wall to optimize treatment planning and delivery. After the completion of radiotherapy, the expander is replaced with a permanent implant or converted into an autologous flap reconstruction. Another postulated option, to avoid ulceration and decrease implant exposure to radiotherapy, is protective lipofilling on irradiated expanders [16].

1.1.2. Autologous tissue reconstruction

Autologous tissue reconstruction uses transverse rectus abdominis myocutaneous flap, latissimus dorsi flap or others tissue flaps. This method is not prone to post-radiation capsule formation, induces less morbidity and, compared to immediate prosthetic reconstruction, is less likely to fail. However, it is more invasive and often contraindicated due to patient anatomical conditions or comorbidities, such as obesity, poorly controlled diabetes mellitus or tobacco smoking. Autologous reconstruction is also not devoid of same radiotherapy complications, such as flap fibrosis or shrinkage, fat necrosis or wound dehiscence [10–13]. Postponement of autologous reconstruction until after radiation may minimize these complications, although most recent data suggest that this may not be the case [17].

2. Timing and technique of radiotherapy

The optimal timing and sequence of reconstruction and adjuvant radiotherapy remains debatable. Two-stage implant based reconstruction can be accomplished in two ways: with radiation being administered to the temporary tissue expander or to the permanent implant. The optimal treatment algorithm and the time to perform the exchange to permanent implant remains a matter of debate. In the case of adjuvant chemotherapy there is enough time for the exchange procedure, and patients may receive irradiation to permanent implant. However, performing the exchange preferably 4 weeks after chemotherapy and 4 weeks before irradiation may considerably delay radiotherapy. If postoperative chemotherapy is not required or a patient underwent preoperative chemotherapy, there is insufficient time to undergo the exchange procedure before radiotherapy, and irradiation includes the expander. In patients managed with one-step procedure, radiotherapy is given to the implant, irrespective of adjuvant chemotherapy.

The recommendations regarding post-mastectomy radiotherapy after breast reconstruction are generally the same as in the case of mastectomy without reconstruction. The delay of postoperative radiotherapy in breast cancer may affect its efficacy [18]. Hence, radiotherapy should not be intentionally postponed, except for patients managed with postoperative chemotherapy. The standard median dose is 50 Gy, five days a week for 5 weeks or, more recently, the dose of 40 Gy with modest hypofractionation (five days a week for 3 weeks) [19].

The chest wall is the most common site of recurrence after mastectomy, therefore should be included in all irradiated patients. A boost dose may be reasonable in some situations (e.g. T4 tumor or close/positive surgical margins). In patients with T3 or T4 primary disease or positive axillary lymph nodes, clinical target volume is usually extended to supraclavicular area, and not infrequently to internal mammary lymph nodes and axillary apex. To ensure the delivery of prescribed dose to all tissues included in the clinical target volume, some margin for the planning target volume is added to account for breathing motion and treatment set-up uncertainties.

In the case of implant-based reconstruction, clinical target volume should include the tissues between the skin and the expander or implant, encompassing the pectoralis muscle, whereas the prosthetic device should be spared. To secure set-up stability and avoid deviations from the prescribed radiation dose, expander filling should not be performed during the radiotherapy period. In patients with partially inflated tissue expander, its volume should be kept constant during radiotherapy. In the case of autologous reconstruction, the flap is usually placed ventral to the pectoral muscle and should be included into clinical target volume.

Irrespective of its type, immediate reconstruction may compromise radiation treatment planning, particularly in patients with left-sided tumors or bilateral reconstruction [13,20,21]. Left-sided patients administered internal mammary treatment may be exposed to a non-negligible dose to the heart [22]. However, modern radiotherapy techniques, such as breathing control, intensity modulated radiotherapy, arc therapy or helical tomotherapy, allow satisfactory dose distribution, and effective sparing of implant and normal tissues [20,23]. Internal high-density metallic ports through which saline is injected into tissue expanders may result in difficulties in imaging and perturbation in dose distribution around the port [24]. This problem may be partially alleviated through the implementing a metal artifact reduction image reconstruction algorithm [25].

3. Results

According to a metaanalysis including 1105 patients, radiotherapy after prosthetic reconstruction is associated with over four times higher risk of complications compared to reconstruction without radiotherapy (OR 4.2; 95% CI, 2.4–7.2) [3]. The most common complications include infections, post-radiation capsular contraction, pain and distortion [10–13]. The reported complication rates in patients managed with radiotherapy after prosthetic reconstruction vary between 10 and 70%, and some type of revision surgery is mandated in 18–30% of patients [10–12,26–28]. However, with the use of modern radiotherapy techniques, these rates are likely to be lower. Different implant failure rates in particular

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