Perspective

Impact of different type of cancer treatment on the effectiveness of breast reconstruction

Joanna Szloch, Elżbieta Marczyk, Marta Kołodziej-Rzepa, Andrzej L. Komorowski

Department of Surgical Oncology, Maria Skłodowska-Curie Memorial Institute of Oncology, Cancer Centre, Krakow, Poland
Correspondence to: Andrzej L. Komorowski. Department of Surgical Oncology, Maria Skłodowska-Curie Memorial Institute of Oncology, Cancer Centre, Krakow, Poland. Email: z5komoro@cyf-kr.edu.pl.

Abstract: For women undergoing mastectomy as part of their breast cancer treatment, breast reconstruction is an important part of therapy. However, neoadjuvant, adjuvant treatments as well as other patient-related factors can compromise the results of breast reconstruction techniques. In this article we have reviewed current approaches to the management of complications and risks that neoadjuvant and adjuvant therapies pose on breast reconstruction after mastectomy for breast cancer. Non-treatment related factors influencing reconstruction techniques were reviewed as well.

Keywords: Breast cancer; reconstruction techniques; radiation therapy

Submitted Apr 27, 2016. Accepted for publication May 18, 2016.
doi: 10.21037/gs.2016.05.06
View this article at: http://dx.doi.org/10.21037/gs.2016.05.06

Introduction

Breast cancer stands for nearly 12% of all new cancer cases and almost 25% of all cancers in women worldwide with nearly 1.7 million new cases identified each year. A multidisciplinary approach that includes medical oncologist, cancer surgeon and radiation oncologist have considerably reduced mortality caused by breast cancer. A good medical outcome is often reached at an important psychological price associated with post mastectomy depression and lower self-image. Therefore, a significant improvement of patient's quality of life can be obtained thanks to immediate or delayed breast reconstruction. Large proportion of breast cancer patients qualifies for breast conservation therapy comprising excision of the tumor, sentinel node biopsy and radiation therapy. Unfortunately there still exist a range of contraindications for this procedure (i.e., multicentric disease, inflammatory breast cancer, expected unfavorable cosmetic outcome, *BRCA1* and *BRCA2* mutations, previous radiotherapy) which results in several patients requiring mastectomy. Those patients are potential candidates for reconstructive procedures, that can be performed during primary surgery or as an independent procedure. However, during treatment planning one have to take into account that those patients may require other therapeutic steps such as sentinel node biopsy, axillary lymph node dissection, post mastectomy radiation therapy, neoadjuvant and adjuvant chemotherapy or hormonal therapy. All those techniques are burdened with the occurrence of adverse effects that may potentially interfere with reconstructive procedures. Local or general complications in patients, who underwent reconstructive treatment, such as wound breakdown, skin necrosis, infections requiring oral or intravenous antibiotics, could lead to implant loss decreasing chances for a satisfying cosmetic effect. On the other hand, several complications of reconstruction techniques (especially infectious complications) can delay chemotherapy and thus interfere with chances for a long term survival. The negative impact of other factors, such as smoking, age, high body mass index on the results of breast reconstruction techniques should also be taken into account. The aim of this study is to review the impact of different types of cancer treatment on the results of breast reconstruction techniques.

Chemotherapy

Traditionally, neoadjuvant chemotherapy was reserved for more locally advanced breast tumors. Today, we can

observe that the indications for neoadjuvant chemotherapy in patients with breast cancer are increasing. Neoadjuvant chemotherapy can lead to a larger proportion of patients being candidates for breast conserving therapy, even in patients with lobular histology (downstaging in lobular cancers is less frequent than in ductal cancers) (1). Adjuvant chemotherapy is often needed to achieve adequate breast cancer control. It is used in a large proportion of all breast cancer patients with an exception of early Luminal type A tumors. Numerous studies support the opinion that neither neoadjuvant nor adjuvant chemotherapy increase the rate of complications or implant failure in patients undergoing post mastectomy expander/implants breast reconstruction, including in patients who undergo tissue expansion at the time of chemotherapy (2-4). However, there are ongoing discussions on how to choose the ideal moment for a reconstruction procedure, depending on different chemotherapy regimen received by the breast cancer patient. Some authors claim that immediate reconstruction can be safely integrated with chemotherapy without a significant impact on complications (5,6). Recent French report suggests that Skin-Sparing Mastectomy and reconstruction with a latissimus dorsi flap could be safely performed after neoadjuvant chemo- and radiotherapy, with an acceptable rate of flap necrosis in a selected group of patients (7). Patients who receive neoadjuvant chemotherapy are less likely to undergo immediate reconstruction, even though they are no more likely to undergo delayed reconstruction than patients receiving adjuvant chemotherapy (8,9). Also it has been shown that premature removal of a tissue expander occurs more commonly in patients treated with neoadjuvant or adjuvant chemotherapy and is most commonly observed 2–3 months after placement (10). Nevertheless the direct negative influence of neoadjuvant and adjuvant chemotherapy on rate of complications after reconstructive procedures has not been proven. Because of the contradictory data this topic requires further studies.

Hormonal therapy

Adjuvant hormonal therapy is recommended for at least five years in patients with hormone receptor-positive breast cancers. The available options include tamoxifen, aromatase inhibitors, and fulvestrant (11-16). A prospective randomized trial performed in 1995, comparing modified radical mastectomy to hormone therapy followed by modified radical mastectomy found that there was no significant difference in the risk of complications and that immediate breast reconstruction was not an independent predictor of complications (17). This opinion has been maintained by a study from 2016, even though it has been observed, that the group of patients who received adjuvant hormonal therapy after mastectomy, were initially presenting more advanced stage of the disease, were more likely to receive post mastectomy radiation therapy and had a greater risk of axillary lymph node dissection (11).

Anty HER-2 therapy

The adjuvant therapy with trastuzumab, a fully humanized monoclonal antibody developed to target the extra cellular domain of HER-2 (human epidermal growth factor receptor-2, a gene whose amplification was estimated to be present in 15–20% of breast cancer patients, playing role in epithelial cell mitosis, invasion, and antiapoptosis) was suggested to coincide with the timing of tissue-implant exchange in patients who have undergone immediate prosthetic breast reconstruction. This suggestion was associated with the fact that treatment with trastuzumab may require receiving ongoing infusions for up to 12 months. However, since patients with HER2-overexpression have a relatively higher risk of local recurrence, they are less likely to receive immediate breast reconstruction in general (18). Further investigations are required to specify the impact of trastuzumab on the possibility of post-mastectomy reconstructive surgery.

Radiation therapy

Post-mastectomy radiation in a subset of node-positive and/or small tumor-free margin patients has a significant impact on reducing the rate of mortality and local recurrence. On the other hand, radiotherapy is associated with increased complications and poorer aesthetic outcomes following both autologous tissue and implant-based breast reconstructions (19-21). The long-term effects of radiation therapy include microvascular damage, fibroblast dysfunction, decreased and disorganized collagen deposition, decreased angiogenesis and decreased wound tensile strength. These factors can lead to difficulties such as an increased risk of wound breakdown, infections requiring oral or intravenous antibiotics, additional surgical procedures, implant exposure or implant loss (22). Also nipple necrosis after nipple-sparing mastectomy has been associated with preoperative irradiation.

The optimal timing of radiotherapy and breast reconstruction is still a subject of debate (11). Patients receiving the alloplastic prosthesis, form a distinct group than those treated with autologous tissue reconstruction. The sequence and timing of tissue expansion and implant exchange with regard to post mastectomy radiation therapy may influence complication rates. For instance, some authors suggest that delaying expander-implant exchange for at least six months after the completion of post mastectomy radiation therapy can reduce the risk of expander-implant failure (21). Moreover, patients who undergo post mastectomy radiation therapy generally wait longer for their tissue expander—implant exchange, which means that there is a greater window for physicians to start hormonal therapy in these patients (11). In general, an irradiated field poses important challenges to implant-based breast reconstruction. Therefore, patients should be carefully screened for all risk factors and selected for this procedure accordingly having in mind its limitations in this particular group of patients (23).

A slightly different scenario appears when autologous reconstruction with microvascular flaps is performed. Some authors state that autologous breast reconstruction can be performed safely regardless of preoperative or postoperative radiation therapy. Indeed, there are no significant differences in complication rates or number of surgical interventions depending on the type of free flap (24). Multiple studies have demonstrated reduced complications and failure rates after autologous reconstruction as compared to implant-based reconstructions. However, irradiation continuously causes a wide range of effects, such as stromal atrophy, fat necrosis, contracture and breast asymmetry. Nevertheless it is believed that in patients, who have had tissue expanders placed and underwent unanticipated post mastectomy radiation therapy, delayed-immediate autologous reconstruction may be offered after radiation therapy has been completed (25). If these patients ultimately undergo tissue expander implant exchange, the use of implants that are smaller than expander volume is suggested to decrease wound tension and skin stress and facilitate wound healing. Again, the timing of the reconstructive procedure remains controversial. Delayed or delayed-immediate autologous reconstructions are proposed as an effective options for reducing the risk of radiation-induced contour-irregularities (11,19). Some studies suggest 12 months interval as a safe period after primary surgical treatment, after which significant decrease in rate of complications is observed (26).

Local recurrence in the previously irradiated field, although rare, could be a devastating event. Surgical treatment may frequently require large resections including part of thoracic cage with complicated reconstructions with microvascular autologous flaps or contralateral breast and always require excision of the implant (27). The cosmetic outcomes of such operations are poor.

Axillary lymph node dissection

Axillary dissection was considered as the gold standard for all patients with positive sentinel lymph node. In 2011, a bold study by Giuliano *et al*. showed that in patients with T1-T2 tumors with no palpable adenopathy and with 1 to 2 positive lymph nodes on sentinel node biopsy axillary dissection is not superior to no axillary dissection. All patients received appropriate systemic and radiation therapy and showed no statistical difference in overall survival and in disease free survival after a median of 6.3 years (28). Based on these data it has been suggested that the routine use of axillary lymph node dissection could be safely omitted in women with early diagnosed breast cancer who have only one or two positive sentinel nodes. The debate whether sentinel lymph node biopsy with radiation therapy may achieve the same long-term oncologic outcomes as axillary lymph node dissection for a selected group of patients is ongoing as well as several randomized studies aiming at evaluating this approach (11,29-33). If indeed the axillary dissection could be spared for a large group of patients it would be beneficial for them not only in terms of avoiding typical short and long term complications associated with this procedure but also, it would mean lower risk of implant loss for those undergoing reconstruction (11). In patients with positive sentinel node undergoing a mastectomy without radiotherapy, a complete axillary node dissection remains the standard of treatment (34).

When planning further reconstructive treatment in patients with breast cancer who had been qualified for mastectomy with axillary lymph node dissection, complications associated with primary surgical treatment must be considered. These complications include such side effects as breast cancer-related lymphedema, postoperative wound infection, seroma and paresthesias (11,35-37). Postoperative lymphedema, a condition in which fluid and protein accumulate in the extravascular interstitial spaces, is a well known risk factor for poor wound healing. In addition, axillary lymph node dissection has been shown to increase the risk of wound breakdown, infections requiring

oral antibiotics that might ultimately lead to implant loss and failure of the reconstructive procedure (11,38). Consequently to high probability of this complication same authors recommend autologous reconstruction instead of tissue expander-based reconstruction in patients who require mastectomy and axillary lymph node dissection (11). Other authors however, while discussing prolonged drain usage as an independent source of infection causing delayed healing, suggest early tissue expansion, associated with earlier drain removal as a way to avoid infectious complications (39). It has to be underlined that postoperative rehabilitation including exercises and self-massage could be a way of preventing and managing secondary lymphedema thus minimizing the risk of failure of reconstruction process due to this complication. Physicians should be able to identify this complication early and provide basic patient education on the subject (38).

Other factors

There are also some other patient-related factors that influence outcome of reconstructive breast surgery. Better short and long term reconstructive surgery results have been achieved in non-smokers *vs.* smokers (40), in patients younger than 45 years *vs.* older than 45 years (41), in non-obese *vs.* obese patients (40). To minimize these factors patients should be advised to maintain correct Body Mass Index and cease smoking before undergoing breast reconstruction.

Conclusions

The impact of each type of cancer treatment on breast reconstructive techniques requires further studies. Radiation therapy and axillary dissection seem to have higher inherent danger for reconstructive failure than other treatment modalities. The optimal sequence of cancer treatment and reconstructive surgery remains unclear.

Acknowledgements

None.

Footnote

Provenance: This is a Guest Perspective commissioned by the Section Editor Rong Tang (Breast Surgery, Hunan Tumor Hospital, Changsha, China; Surgical Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, USA).
Conflicts of Interest: The authors have no conflicts of interest to declare.

Comment on: Wang F, Peled AW, Chin R, *et al*. The Impact of Radiation Therapy, Lymph Node Dissection, and Hormonal Therapy on Outcomes of Tissue Expander-Implant Exchange in Prosthetic Breast Reconstruction. Plast Reconstr Surg 2016;137:1-9.

References

1. Delpech Y, Coutant C, Hsu L, et al. Clinical benefit from neoadjuvant chemotherapy in oestrogen receptor-positive invasive ductal and lobular carcinomas. Br J Cancer 2013;108:285-91.
2. Alderman A, Gutowski K, Ahuja A, et al. ASPS clinical practice guideline summary on breast reconstruction with expanders and implants. Plast Reconstr Surg 2014;134:648e-55e.
3. McCarthy CM, Mehrara BJ, Riedel E, et al. Predicting complications following expander/implant breast reconstruction: an outcomes analysis based on preoperative clinical risk. Plast Reconstr Surg 2008;121:1886-92.
4. Warren Peled A, Itakura K, Foster RD, et al. Impact of chemotherapy on postoperative complications after mastectomy and immediate breast reconstruction. Arch Surg 2010;145:880-5.
5. Rodby KA, Robinson E, Danielson KK, et al. Age-dependent Characteristics in Women with Breast Cancer: Mastectomy and Reconstructive Trends at an Urban Academic Institution. Am Surg 2016;82:227-35.
6. Shea-Budgell M, Quan ML, Mehling B, et al. Breast reconstruction following prophylactic or therapeutic mastectomy for breast cancer: Recommendations from an evidence-based provincial guideline. Plast Surg (Oakv) 2014;22:103-11.
7. Zinzindohoué C, Bertrand P, Michel A, et al. A Prospective Study on Skin-Sparing Mastectomy for Immediate Breast Reconstruction with Latissimus Dorsi Flap After Neoadjuvant Chemotherapy and Radiotherapy in Invasive Breast Carcinoma. Ann Surg Oncol 2016;23:2350-6.
8. Voineskos SH, Frank SG, Cordeiro PG. Breast reconstruction following conservative mastectomies: predictors of complications and outcomes. Gland Surg 2015;4:484-96.
9. Hu YY, Weeks CM, In H, et al. Impact of neoadjuvant

chemotherapy on breast reconstruction. Cancer 2011;117:2833-41.
10. Dolen UC, Schmidt AC, Um G, et al. Impact of Neoadjuvant and Adjuvant Chemotherapy on Immediate Tissue Expander Breast Reconstruction. Ann Surg Oncol 2016;23:2357-66.
11. Wang F, Peled AW, Chin R, et al. The Impact of Radiation Therapy, Lymph Node Dissection, and Hormonal Therapy on Outcomes of Tissue Expander-Implant Exchange in Prosthetic Breast Reconstruction. Plast Reconstr Surg 2016;137:1-9.
12. Ingle JN. Postmenopausal women with hormone receptor-positive breast cancer: balancing benefit and toxicity from aromatase inhibitors. Breast 2013;22:S180-3.
13. Amir E, Seruga B, Niraula S, et al. Toxicity of adjuvant endocrine therapy in postmenopausal breast cancer patients: a systematic review and meta-analysis. J Natl Cancer Inst 2011;103:1299-309.
14. Kelley BP, Valero V, Yi M, et al. Tamoxifen increases the risk of microvascular flap complications in patients undergoing microvascular breast reconstruction. Plast Reconstr Surg 2012;129:305-14.
15. Dixon JM. Reducing early recurrence with adjuvant aromatase inhibitors: what is the evidence? Breast 2008;17:353-60.
16. Chung CT, Carlson RW. The role of aromatase inhibitors in early breast cancer. Curr Treat Options Oncol 2003;4:133-40.
17. Forouhi P, Dixon JM, Leonard RC, et al. Prospective randomized study of surgical morbidity following primary systemic therapy for breast cancer. Br J Surg 1995;82:79-82.
18. Wu W, Cheng S, Deng H, et al. Impact of Breast Cancer Subtype Defined by Immunohistochemistry Hormone Receptor and HER2 Status on the Incidence of Immediate Postmastectomy Reconstruction. Medicine (Baltimore) 2016;95:e2547.
19. El-Sabawi B, Carey JN, Hagopian TM, et al. Radiation and breast reconstruction: Algorithmic approach and evidence-based outcomes. J Surg Oncol 2016;113:906-12.
20. Ragaz J, Jackson SM, Le N, et al. Adjuvant radiotherapy and chemotherapy in node-positive premenopausal women with breast cancer. N Engl J Med 1997;337:956-62.
21. Peled AW, Foster RD, Esserman LJ, et al. Increasing the time to expander-implant exchange after postmastectomy radiation therapy reduces expander-implant failure. Plast Reconstr Surg 2012;130:503-9.
22. Dormand EL, Banwell PE, Goodacre TE. Radiotherapy and wound healing. Int Wound J 2005;2:112-27.
23. Nahabedian MY. Implant-based breast reconstruction: Strategies to achieve optimal outcomes and minimize complications. J Surg Oncol 2016;113:895-905.
24. Chang EI, Liu TS, Festekjian JH, et al. Effects of radiation therapy for breast cancer based on type of free flap reconstruction. Plast Reconstr Surg 2013;131:1e-8e.
25. Kronowitz SJ. Delayed-immediate breast reconstruction: technical and timing considerations. Plast Reconstr Surg 2010;125:463-74.
26. Baumann DP, Crosby MA, Selber JC, et al. Optimal timing of delayed free lower abdominal flap breast reconstruction after postmastectomy radiation therapy. Plast Reconstr Surg 2011;127:1100-6.
27. Kolodziejski LS, Wysocki WM, Komorowski AL. Full-thickness chest wall resection for recurrence of breast malignancy. Breast J 2005;11:273-7.
28. Giuliano AE, Hunt KK, Ballman KV, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. JAMA 2011;305:569-75.
29. Zervoudis S, Iatrakis G, Tomara E, et al. Main controversies in breast cancer. World J Clin Oncol 2014;5:359-73.
30. Galimberti V, Botteri E, Chifu C, et al. Can we avoid axillary dissection in the micrometastatic sentinel node in breast cancer? Breast Cancer Res Treat 2012;131:819-25.
31. Giuliano AE, McCall L, Beitsch P, et al. Locoregional recurrence after sentinel lymph node dissection with or without axillary dissection in patients with sentinel lymph node metastases: the American College of Surgeons Oncology Group Z0011 randomized trial. Ann Surg 2010;252:426-32.
32. Galimberti V, Cole BF, Zurrida S, et al. Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial. Lancet Oncol 2013;14:297-305.
33. Fu Y, Chung D, Cao MA, et al. Is axillary lymph node dissection necessary after sentinel lymph node biopsy in patients with mastectomy and pathological N1 breast cancer? Ann Surg Oncol 2014;21:4109-23.
34. Rao R, Euhus D, Mayo HG, et al. Axillary node interventions in breast cancer: a systematic review. JAMA 2013;310:1385-94.
35. Lucci A, McCall LM, Beitsch PD, et al. Surgical complications associated with sentinel lymph node dissection (SLND) plus axillary lymph node dissection compared with SLND alone in the American College of

Surgeons Oncology Group Trial Z0011. J Clin Oncol 2007;25:3657-63.
36. Kell MR, Burke JP, Barry M, et al. Outcome of axillary staging in early breast cancer: a meta-analysis. Breast Cancer Res Treat 2010;120:441-7.
37. Nahabedian MY, Tsangaris T, Momen B, et al. Infectious complications following breast reconstruction with expanders and implants. Plast Reconstr Surg 2003;112:467-76.
38. Cheifetz O, Haley L, Breast Cancer Action. Management of secondary lymphedema related to breast cancer. Can Fam Physician 2010;56:1277-84.
39. Hanna KR, Tilt A, Holland M, et al. Reducing Infectious Complications in Implant Based Breast Reconstruction: Impact of Early Expansion and Prolonged Drain Use. Ann Plast Surg 2016;76:S312-5.
40. Chang EI, Chang EI, Soto-Miranda MA, et al. Evolution of Bilateral Free Flap Breast Reconstruction over 10 Years: Optimizing Outcomes and Comparison to Unilateral Reconstruction. Plast Reconstr Surg 2015;135:946e-953e.
41. Komorowski AL, Zanini V, Regolo L, et al. Necrotic complications after nipple- and areola-sparing mastectomy. World J Surg 2006;30:1410-3.

Cite this article as: Szloch J, Marczyk E, Kołodziej-Rzepa M, Komorowski AL. Impact of different type of cancer treatment on the effectiveness of breast reconstruction. Gland Surg 2016;5(4):444-449. doi: 10.21037/gs.2016.05.06

