

Review Article

Post-mastectomy breast reconstruction: an overview of the state of the art, challenges, and prospects

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ABSTRACT

Breast cancer, which affects approximately 12% of women worldwide, is a leading cause of death and morbidity, and the majority of cases are treated surgically. The loss of one or both breasts to cancer can be devastating and it often has negative physical and psychological impact on women. In order to maintain an outward breast contour, some women turn to temporary solutions, such as breast pads, which are often unsatisfactory. Over the years, patients' perceptions of their bodies, self-esteem levels and quality of life have all improved as a result of less radical breast cancer surgeries and the growing popularity of post-mastectomy breast reconstruction. Therefore, it is recommended that women undergoing breast cancer surgeries be given the choice of breast reconstruction. Nevertheless, accessibility, acceptability, and affordability of breast reconstruction still pose a challenge. Although these limitations exist globally, they are most noticeable in low- and middle-income nations. This article gives an overview of the various considerations and surgical options for breast reconstruction after breast cancer surgery. In addition, it examines some of the challenges to breast reconstruction faced worldwide and discusses recent and future trends which are bound to improve post-mastectomy breast reconstruction techniques and outcomes globally.

Keywords: Breast reconstruction, Breast cancer surgery, Mastectomy, Autologous reconstruction, Implant-based reconstruction

INTRODUCTION

The breasts are a very important defining female characteristic, and they are regarded as a symbol of femininity, sexuality, beauty, and motherhood. Breast cancer is the most prevalent malignancy in females with an increasing incidence among young women in developing countries.^{1,2} It affects about 12% of the women population.³ In 2017, according to a population-based national cancer institute's surveillance, epidemiology, and end results database study, breast cancer incidence was projected to exceed all cancers by 2020.⁴

Although there are multiple treatment modalities available, surgery remains the mainstay of breast cancer treatment. With improvements in breast cancer screening, diagnosis, and treatment, disease prognosis and patient survival have significantly improved. Thus, nowadays, the emphasis of care is not only on the oncological outcome but also on cosmesis and return to normal functionality post-surgery.⁵ This has resulted in the evolution of surgical techniques from radical mastectomy to breast-conserving surgeries like lumpectomy and quadrantectomy and now to more technical skin- and nipple-sparing mastectomies which have better reconstructive outcomes. These procedures have been shown by multiple short-term follow-up studies to be

oncologically safe with comparable outcomes to standard mastectomy.^{5,6}

Prophylactic mastectomy with breast reconstruction has also gained popularity among women at high risk of developing breast cancer, especially in developed countries, where studies have reported a rise in bilateral prophylactic mastectomies among young, healthy women and a concordant rise in rates of immediate breast reconstruction.⁷ This practice is however unpopular in developing countries. A study done in South-Western Nigeria found a high level of awareness about breast cancer but low awareness about-and consequently low disposition (25.6%) toward- prophylactic mastectomy.⁸

Breast reconstruction after mastectomy is crucial to restoring normal physical appearance and improving the quality of life of women. It is an important determinant of patient satisfaction, function, and well-being following mastectomy.⁹ Based on the importance of breast reconstruction, the women's health act and cancer rights act (WHCRA) was passed in 1998 in America, which mandated universal health insurance coverage for breast reconstruction as part of the medical and surgical treatment of breast cancer.^{10,11}

Breast reconstruction is rarely practised in low-resource settings like Nigeria because of limitations such as delayed patient presentation, inoperable tumours, high surgical costs, incorrect information about reconstructive options, and a lack of sufficient manpower.¹² According to some researchers, reconstruction may not be as important in these settings given the high cost of reconstructive surgeries.¹³

This article reviews existing options for post-mastectomy breast reconstruction, explores particular difficulties with breast reconstruction in resource-limited and resource-rich environments, and also offers a look into reconstructive breast surgery's potential future directions.

IMPORTANT CONSIDERATIONS FOR BREAST RECONSTRUCTION

Prior to breast cancer surgery, patients should receive adequate information about available reconstructive options. This should correct misconceptions, allay fears, and dispel false beliefs. The optimal reconstruction method depends on patient's preference, comorbidities, radiation exposure, and the presence of appropriate donor sites for autologous reconstruction. Ultimately, the patient's decision must be respected.¹⁴ In patients that opt for post-mastectomy breast reconstruction, important considerations include timing of reconstruction, type of incision, and options for reconstruction.⁹

Timing of surgery

Breast reconstruction can be immediate, delayed-immediate, or delayed. Immediate reconstruction reduces

the total number of operations required, allows the preservation of much of the mastectomy flap (native skin) with or without the nipple, and thus has good reconstructive outcomes. It is cost-effective and ideal for use in healthy patients with low-grade tumours.^{9,15} Delayed-immediate reconstruction is done weeks after mastectomy or breast conservation surgery.¹⁶ Delayed reconstruction occurs several months after mastectomy and is advocated in patients with advanced disease, multiple risk factors, and patients who are yet to decide about reconstruction.⁹

Studies have shown that patients who had delayed reconstruction generally report greater satisfaction and improved quality of life. This is perhaps due to the fact that these patients have lived without breasts for a while and have a tendency to be more accepting and forgiving of subtle differences, unlike patients who have immediate reconstruction and end up comparing the new breast to their natural breast.^{6,15}

Type of incision

The appropriate mastectomy incision is based on the planned timing of reconstruction and the proposed type of mastectomy. In skin-sparing mastectomy, an elliptical excision of the nipple-areola complex leaves a single horizontal scar while in nipple-sparing mastectomy, an incision-inframammary or radial-that allows for preservation of the skin and nipple-areola complex is required.⁹

RECONSTRUCTIVE OPTIONS FOLLOWING BREAST CANCER SURGERY

Breast reconstruction can be alloplastic implant-based or autologous tissue-based.^{9,14} Alloplastic reconstruction uses saline or silicone gel implants to reconstruct the breast mound while autologous reconstruction uses the patients' native tissues to reconstruct the breast mound. With the advent of breast-conserving surgeries, lumpectomy and quadrantectomy defect reconstruction are also important.

Alloplastic and autologous reconstruction can be combined in one patient.⁷ In many patients, adjunct procedures such as implant replacement, contralateral breast reduction/augmentation, mastopexy etc. are required over time in order to achieve and maintain symmetry.

Alloplastic implant-based reconstruction

Alloplastic reconstruction can be immediate/single-staged in which the implant is directly placed beneath the mastectomy flap at the time of mastectomy, usually with a supportive scaffold such as acellular dermal matrix and synthetic mesh. This is called the direct-to-implant approach, and it is only used if healthy skin is present at the time of the surgery.⁹ It is a suitable reconstructive

option in patients with multiple co-morbidities, however, it is associated with an increased risk of mastectomy flap necrosis.¹⁷

More commonly, alloplastic reconstruction is done as a multi-stage procedure.⁹ The first stage is usually the placement of a tissue expander beneath the mastectomy flap which is progressively inflated until the desired size is reached. The second-phase surgery, known as implant exchange, is then performed to exchange the tissue expander for breast implants.^{9,18} Traditional tissue expanders are filled with fixed amounts of saline at regular intervals through skin injections and are associated with pain and increased risk of infection. In recent times, CO₂-filled tissue expanders have been developed. These allow for daily, painless, remote-controlled tissue expansion which the patients can administer.¹⁹

Implant placement can be pre-pectoral or submuscular. A pre-pectoral implant is positioned beneath the mastectomy flap and above the pectoralis major. The implant is wrapped in a scaffold - acellular dermal matrix (ADM) or a mesh-that is sutured to the underlying chest muscles. A submuscular implant is placed partially or completely underneath the anterior chest wall muscles; this is associated with increased post-operative pain and shoulder dysfunction due to the dissection of muscles. Here, ADM or a synthetic mesh can also be used to complete the pocket created for the implant.^{17,19}

Implant-based reconstruction has no donor-site or associated morbidities, shorter operating time, shorter convalescence, and is less invasive than autologous reconstruction. However, it carries a risk of capsular contracture and implant migration and as such requires long-term monitoring of the implant, possible revision of the procedure and implant exchange.^{9,14} A 2019 study assessing outcomes of immediate implant-based reconstruction with or without mesh found a highly increased risk of complications with immediate reconstruction.²⁰

Autologous tissue reconstruction

In autologous reconstruction, the breast mound is reconstructed using the patient's native tissue. It uses free and pedicled tissue flaps, and fat grafting which gives a more natural appearance and feel to the reconstructed breasts, but is associated with longer operating time, longer convalescence, and donor site morbidities.²¹ Pedicled flaps maintain a connection to their native blood supply, they are situated near the breast and can be easily advanced into the mastectomy defect. They include the transverse rectus abdominis myocutaneous (TRAM) flap and latissimus dorsi (LD) flap. Free flaps are perforator flaps that are separated from their native blood supply, transferred to the breast, and microsurgically anastomosed with vessels in the breast region.^{9,21}

Although tissue from many sites can be used, abdominally-based tissue is preferred because there is an abundance of soft tissue in the area with a similar consistency to breast tissue.^{21,22} The abdominal flaps are based on the superficial and deep inferior epigastric vessels and they include the free and pedicled TRAM flaps, the deep inferior epigastric perforator (DIEP) flap, and the superficial inferior epigastric artery (SIEA) flap. The DIEP flap is the commonest free flap used for breast reconstruction.^{9,22} Abdominally-based reconstruction is associated with deficits in abdominal flexion and extension. These deficits are worse with TRAM flaps than perforator flaps, but there is a gradual return to baseline functionality over time.⁷ TRAM flaps are also associated with a higher incidence of abdominal wall laxity, weakness and hernias.²²

For patients in whom an abdominal-based flap cannot be used-previous abdominal surgery, failed abdominal autologous reconstruction, future prospect of pregnancy, preference of a non-abdominal donor site-alternative donor sites include the chest wall, lower limbs and trunk. Chest wall flaps include the thoracodorsal artery perforator (TDAP) flap and latissimus dorsi (LD) flaps, one of the commonly used flaps.¹⁹ LD flaps are associated with minor limitations in daily activities which generally resolve with time, and limitations in rigorous athletic functions.⁷

Lower limb flaps that have been described include the gluteal artery perforator (GAP) flaps, transverse upper gracilis (TUG) flap, diagonal upper gracilis (DUG) flap, profunda artery perforator (PAP) flap, and the lateral thigh perforator (LTP) flap.^{22,23} GAP flaps are associated with contour deformities at the donor site and pain when sitting. Thigh flaps, particularly the TUG flap, may result in dissection of the neurovascular structures resulting in seromas, lymphedema, donor site breakdown, and paresthesia.²² The DUG flap is a good alternative to TUG because its orientation avoids these complications.²³

Thigh flaps are limited by the small amount of tissue available for harvest and can only be used for small-medium-sized breast reconstruction.^{19,22,23} This may necessitate the combination of multiple flaps to correct a single defect in a process known as 'stacking'.²³ The lumbar artery perforator (LAP) flap is a trunk flap that offers a greater amount of tissue for reconstruction, a hidden donor site, as well as a more breast-like consistency of the adipose tissue.²³

The outcome of autologous reconstruction largely depends on flap perfusion. Therefore, different modalities have been used to examine vascular anatomy and blood flow characteristics before, during and after the operative process. Preoperatively, CT or MR Angiography can be used for localisation of perforators and careful surgical planning, and this has been shown to improve surgeons' efficiency and reduce donor site morbidity and flap complications. Intraoperatively, indocyanine green (ICG)

angiography can be used to assess blood flow to both the donor tissue and mastectomy skin flap thus reducing the likelihood of flap necrosis.^{19,23} Postoperatively, blood flow can be monitored with implantable dopplers (preferably) or external dopplers. This allows for immediate detection of poor flap perfusion and surgical intervention.¹⁹

Secondary procedures

To ensure that the reconstructed breast is similar in size, shape and projection to the contralateral breast, secondary procedures such as fat grafting, nipple-areola complex (NAC) reconstruction and symmetrization procedures may be required.²¹ NAC reconstruction is usually done long after the breast mound has healed. The nipple can be reconstructed using a local skin flap, a contralateral nipple graft, or a three-dimensional (3D) tattoo. Areola pigmentation can also be achieved by tattooing and skin grafting.^{6,9,21} Symmetrization procedures on the contralateral breast, such as reduction mammoplasty and mastopexy, are performed to match the size and projection of the reconstructed breast.²¹

Autologous fat grafting involves extracting fat from different areas of the body via liposuction and injecting the harvested fat into the breast. This fat is biocompatible and rich in stem cells and can be regenerated following adjuvant radiation therapy. It can be used as a primary technique of breast reconstruction or an adjunct to other reconstructive techniques, and to fill partial mastectomy defects.^{9,17} It can also be used to reverse fibrosis and improve skin and soft tissue quality in irradiated mastectomy flaps.^{19,24} While this procedure is relatively easy with low morbidity and complication rates, the postoperative results can be uncertain due to fat resorption and the possibility of fat necrosis which result in significant volume loss in the months following the surgery and may necessitate repeat procedures till the desired breast volume/shape is achieved.^{19,24} Research has shown that enriching the graft with fat-derived stem cells helps to maintain volume and improve graft survival.¹⁹

BREAST RECONSTRUCTION IN THE CONTEXT OF ADJUNCTIVE BREAST CANCER TREATMENTS

Patients who have breast reconstruction may require other treatments such as chemotherapy radiotherapy and hormonal therapy before or after reconstruction. Adjuvant and neo-adjuvant chemotherapy have not been proven to have any significant impact on breast reconstruction. A few studies have found an increased risk of flap loss due to thromboembolism in patients who receive hormonal therapy with tamoxifen.¹⁹

The effect of radiotherapy on breast reconstruction has been widely studied. In pre-radiated fields, alloplastic reconstruction has been associated with a high risk of

postoperative complications (mastectomy flap necrosis, capsular contracture) and reconstructive failure. On the other hand, autologous reconstruction is associated with increased intra-operative vascular complications-due to fibrosed, irradiated surgical bed-and minor post-operative complications.²⁵ In post-mastectomy radiation therapy (PMRT), alloplastic reconstruction has been linked to higher failure rates, although there are mixed results regarding the timing of reconstruction; while immediate autologous reconstruction has been linked to a higher risk of fat necrosis and contour deformity with no difference in the rate of surgical revision.²⁵

There has been a lot of discussion about the integration of reconstruction and radiation therapy. At the 2021 oncoplastic breast consortium (OPBC) consensus conference, an expert panel recommended that surgeons and radiation oncologists work together to determine the right timing and techniques of PMRT and breast reconstruction in individual patients, and they agreed that surgical technique should not be altered for PMRT. The panel preferred immediate or delayed-immediate autologous reconstruction over implant-based reconstruction because the former is associated with a lower risk of complications in the long term; however, they do not consider any form of reconstruction to be absolutely contraindicated by PMRT.²⁶

Oncoplastic breast surgery

Oncoplastic breast surgery is a field of breast surgery that combines the principles of oncological surgery with aesthetic surgery. Using volume displacement, replacement and reduction techniques, every patient gets a customized reconstruction that is determined by the tumour location, amount of excised breast tissue, and natural breast size/volume.¹⁶ While oncoplastic surgery is well established in developed countries, this field is only beginning to gain popularity in some low and middle-income countries (LMICs).^{27,28}

During breast-conserving surgery, tumour excision may result in unsightly breast defects and significant size reduction when compared to the contralateral breast. Thus, intraoperative rearrangement of the breast tissue and/or reduction mammoplasty or mastopexy of the contralateral breast may be required in order to maintain symmetry between the two breasts.^{9,16} These defects can also be reconstructed through autologous fat grafting and the use of free or pedicled flaps. Immediate oncoplastic reconstruction of defects is favoured because delayed reconstruction is more difficult due to the presence of scar tissue and may be more expensive in low-resource settings.^{9,16,27} However, patients who had immediate reconstruction may have positive post-operative tumour margins or develop local tumour recurrence and require a completion mastectomy with flap-based reconstruction. Therefore, abdominal flaps should be preserved as much as possible during oncoplastic breast surgery.¹⁶

CHALLENGES TO BREAST RECONSTRUCTION ACROSS THE GLOBE

In high-income countries, post-mastectomy breast reconstruction (PMBR) rates are affected by race, income, insurance, level of education and location.²⁹ People residing in provincial areas are less likely to have breast reconstruction due to lack of access to the required facilities.¹¹ High cost of breast reconstruction procedures or low indemnification by insurance companies has further worsened the poor rates of breast reconstruction.¹¹ Other reasons for low PMBR rates include advanced age, presence of other major comorbidities, fear of undergoing additional surgeries, regarding breast reconstruction as unnecessary, and the fear of implants.³⁰

The adoption of health insurance schemes by developed countries with mandatory post-mastectomy reconstruction coverage has increased the rate of PMBR.^{11,31,32} These programs increase the access to reconstruction services provided. In the US for example, it is compulsory to offer all mastectomy patients breast reconstruction. Awareness creation, formation of interest groups, and media campaigns (internet, television, radio, advertisements) have helped to spread information about PMBR,³³ thus increasing the knowledge of reconstructive options and improving attitude towards these procedures.

PMBR data from LMICs are few since the option is not routinely offered to mastectomy patients. This has been ascribed to a shortage of plastic surgeons coupled with an increased workload.^{34,35} In LMICs, breast cancer cases typically present in advanced stages when surgical intervention is limited. This results in low rates of immediate breast reconstruction.³⁶ Low socio-economic status, cultural beliefs and taboos, misinformation about the prognosis, and lack of information on oncoplastic breast reconstruction are linked with the sluggish development of breast reconstruction in these countries.²⁸ Surgical equipment needed for reconstruction is usually very costly and unavailable. Majority of the population in LMICs do not have access to medical insurance while those who have are not covered for breast reconstruction as it is considered cosmetic and not part of the clinical management of breast cancer. This has restricted breast reconstruction to only the upper class of society who can afford out-of-pocket payment.²⁷

Ideally, breast reconstructions are done by plastic surgeons, but in low-resource settings, general surgeons carry out these procedures with the aid of plastic surgeons. These general surgeons are more concerned about the oncological outcome of cancer management rather than aesthetics, as they aim to reduce the risk of recurrence and hence are less inclined towards breast reconstruction in breast cancer patients.³⁶ There is also a lack of training programs on breast reconstruction to increase surgeons' confidence in handling oncoplastic surgery.^{27,28}

In Turkey, oncoplastic surgeries are performed successfully by general (breast) surgeons with or without plastic surgeons, and it is suggested that training in oncoplastic surgery be included in mainstream surgical training.³⁷ Indian researchers have proposed a "one surgeon, dual role" concept in which one surgeon is trained to perform both the oncologic and plastic surgery as a way to reduce the cost of care and make up for the dearth of plastic surgeons.²⁷ In fact, Oncoplastic surgeons in India and the United Kingdom have created a comprehensive, multidisciplinary Oncoplastic Surgery Training Program. This may be a worthy cause in other low-resource countries with a huge patient-specialist ratio like Nigeria, where it may be impossible for all reconstructive surgeries to be performed by plastic surgeons.

FUTURE TRENDS IN BREAST CANCER SURGERY

Breast cancer surgery has evolved from previously radical techniques to more conservative techniques, and in recent times, more focus has been on improving surgical techniques and reconstructive options in order to give patients a better quality of life post-surgery.^{19,31} To improve the outcomes in existing autologous reconstruction techniques, neurotization of free flaps is being used to restore breast mound innervation and vascularized lymph node transfers and lymphovenous anastomoses are being studied as ways to manage lymphedema associated with breast cancer surgery or reconstructive surgery.²³

In recent years, there has been research on applying tissue engineering and regenerative medicine principles towards breast reconstruction and augmentation.^{19,38,39} Adipose tissue regeneration, from fat-derived stem cells, is guided and supported with engineered scaffolds which may be custom-made to fit individual patients' characteristics through 3D imaging and computer-aided design and manufacturing (CAD/CAM).^{38,39} However, breast tissue engineering is limited largely by the high costs of production of biocompatible scaffolds and inadequate volume of regenerated adipose tissue due to poor vascularization.³⁹ Researchers are working to find ways to improve scalability by ensuring sustained adipogenesis in clinically relevant volumes and also reducing the cost of production of the engineered constructs.

In 2015, Chhaya et al reported sustained angiogenesis and adipogenesis in rats over a period of 24 weeks.³⁸ Using CAM/CAD technology, the authors produced a highly porous synthetic scaffold that was first seeded with human umbilical cord perivascular cells and cultured in-vitro for 6 weeks, and then seeded with human umbilical vein endothelial cells before it was finally implanted into the rats' subcutaneous tissue. Similarly, Visscher and colleagues have also demonstrated regeneration of a large volume of adipose tissue in pigs.³⁹ By implanting biodegradable aliphatic

polyester-based scaffolds and then injecting lipoaspirate either immediately or after a 2-week period (to allow pre-vascularisation), the authors recorded a 6-fold increase in adipose tissue in the delayed group over 24 weeks. To scale down the cost of scaffold production, Visscher et al advocate for the use of degradable aliphatic polyesters that are already FDA-approved for implantation and can be customised and mass-produced via additive manufacturing.³⁹

Although many of the reported proof-of-concept/principle studies are of in-vitro and animal trials, breast tissue engineering could potentially be an exciting alternative to current reconstructive methods. By offering patient-centred customized reconstruction and avoiding complications of current surgical options, it could become an option for patients who may be uncomfortable with current techniques.³⁹ Despite being promising, the safety of use of these stem cells has not been guaranteed as they can serve as a stromal network for the cancer cells due to their regenerative abilities and as such could cause a cancer recurrence.^{19,39} Hence, it is very important that the use of this technique is approached with caution.

Robotic-assisted reconstruction has also gained some popularity over the years. This technique is minimally invasive and it has been used in harvesting flaps for breast reconstruction.⁴⁰ Due to its less invasiveness, it causes minimal scarring during harvesting of the flap and it also shortens hospital stays. However, the high maintenance cost presents a huge setback for its use. When compared to the traditional methods of breast reconstruction, there is no statistical data to back up its effectiveness. There is no data providing the long-term complications associated with its use due to cost limitations. As of now, the only indication for using a robot for reconstruction is if a latissimus dorsi flap harvest is needed for reconstruction.⁴⁰ There is still a long way to go before approval, further research has to be done to standardize its use and to also compare its complications, and long and short-term costs with the traditional open breast reconstruction methods.

CONCLUSION

To improve aesthetic and surgical results while ensuring oncological safety, the surgical management of breast cancer has moved from radical mastectomy to more sophisticated conservative surgeries. Breast reconstruction offers some women a return to normalcy following breast cancer surgery. Although these reconstructive surgeries are largely available in developed countries, there are some racial and socioeconomic disparities in access to the surgeries. In low-resource settings, PMBR is in the nascent stages due to limited resources, late patient presentation (advanced breast cancer), and poor socio-economic factors.

Exciting advances have been described in the field of post-mastectomy breast reconstruction. Neurotization of

free flaps, vascularised lymph node transfer, and lymphovenous anastomosis will improve existing reconstructive techniques by restoring sensation and reducing lymphedema. Regenerative medicine could potentially revolutionise breast reconstruction by combining adipose tissue regeneration with CAD/CAM techniques. Robotic surgery has also been described as a minimally invasive method of breast reconstruction. However, the short and long-term outcomes and safety of these techniques are yet to be proven.

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