

## Evolving Management Options for Breast Cancer in Era of Oncoplastic and Reconstructive Breast Surgery: Where Do We Stand?

Abubaker Shafiq Ahmed; Safia Zahir Ahmed; Noman Zaib

**IMPORTANCE** Recent advances in oncoplastic techniques have revolutionized concepts in the management of breast cancer. Numerous oncoplastic and reconstructive surgery options are available to oncoplastic breast surgeons to meet the needs of variation in character and stage of the disease. To employ these available surgical and non-surgical strategies, a holistic and comprehensive understanding of the disease and treatment modalities is pivotal. In this essay, we would describe various surgical options available and would critically evaluate them in light of a typical case scenario.

**KEYWORDS** Oncoplastic Breast Surgery; Breast Reconstruction; Implant-Based Reconstruction

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### Critical Review

**Author Affiliations:** Author affiliations are listed at the end of this article.

**Corresponding Author:**

Abu Baker Shafiq Ahmad  
Shalamar Medical & Dental  
College, Lahore  
([abubaker\\_shafiq@yahoo.com](mailto:abubaker_shafiq@yahoo.com))  
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Breast reconstruction has become an integral part of breast cancer treatment<sup>1</sup>. Both autologous and implant-based reconstructions are effective but need to be individualized to the needs of patients. Annually, more than 80, 000 reconstructions in the US are implant-based, however, the utility and satisfaction of the implant-based reconstruction are gradually reducing owing to multiple reasons<sup>2,3</sup>. Capsular contracture, infection, the feeling of being unnatural, and finally breast implant-associated (BIA) lymphoma are the few reasons for reducing the popularity of implant-based reconstructions and the gradual shift to autologous reconstruction<sup>4</sup>.

### IMPLANT-BASED RECONSTRUCTION

Implant-based reconstructions are the most commonly performed breast reconstructions all over the world<sup>5,6</sup>. Nipple-sparing and skin-sparing mastectomies associated with implants are being increasingly performed and are associated with up to 7% recurrence rate over a period of 10 years, which is comparable with cancer risk in contralateral normal breast<sup>7,8</sup>. Implant-based reconstructions are quite suitable for small and medium-sized breasts where ptosis is limited. Round and anatomical implants with or without surface texturing are available and are associated with good aesthetic outcomes<sup>7</sup>. Immediate reconstructions are well suited with implant-based reconstructions. Small inframammary or lateral incisions are used for mastectomy and insertion of implants. The implants are mostly placed in a subpectoral plane with or without the use of acellular

### CASE SCENARIO

A 46-year-old woman underwent previous WLE for a 15mm triple-negative Grade-3 breast cancer 1 year ago. Her surveillance mammography has shown a local recurrence, confirmed on core biopsy. She has just moved to the local area and is a single working mother to three daughters aged 6-17. She is a non-smoker and exercises regularly. Her previous medical history includes Laparoscopic cholecystectomy and emergency C-section. She is keen to undergo immediate breast reconstruction. Although she has some concerns about implants as she is aware of some risks following recent news reports but is open to any suitable option available. Please provide a comprehensive management plan for this case including a discussion on the following issues: Further investigations, management options for breast and axilla, appropriate clinical trials, reconstructive options including limitations, social and lifestyle factors, consent process, adjuvant therapy, surveillance, and follow-up, PROMS, medico-legal issues. Your plan should reference and critique relevant evidence and guidelines, and you are encouraged to cite relevant examples from your clinical practice to support your response.

dermal matrix (ADM) depending upon the availability of the coverage<sup>9</sup>.

Implant-based reconstructions can be done either in an immediate setting or it may be bridged by using expandable Becker's prosthesis. The patients who require adjuvant chemoradiation are best treated in two stages involving

Becker's prosthesis. This, however, leads to poor aesthetic outcome<sup>5,3</sup>.

Advantages of the implant-based reconstructions include operative ease; shorter postoperative hospital stay and fewer ischemic complications<sup>7</sup>. Disadvantages include a higher rate of infection, seroma formation, rupture, and displacement in an acute setting. Long-term complications include rupture, infection, anaplastic implant-associated lymphoma, and capsular contracture<sup>10</sup>. The females have a sense of carrying something unnatural which is the most important source of patient dissatisfaction. Hence recently females are preferring autologous reconstructions<sup>11</sup>.

### **BREAST RECONSTRUCTION USING FLAPS / AUTOLOGOUS TISSUE**

Autologous reconstruction depends on the use of women's tissue to achieve the objective of breast reconstruction in either immediate or delayed setting<sup>3</sup>. Immediate reconstruction is associated with higher patient satisfaction with associated decreased overall cost. Delayed setting reconstruction is associated with inferior cosmetic outcomes, patient satisfaction, and a higher degree of graft loss due to arterial or venous thrombosis. The complication rate however is surprisingly equivalent in the immediate or delayed setting as shown in multiple studies<sup>12</sup>.

There are numerous flap options available in the armamentarium of an oncoplastic surgeon, which includes Deep Inferior Epigastric Artery Perforator (DIEP) Flap, Superficial Inferior Epigastric Perforator Artery (SIEP) Flap, Transversus Rectus Abdominus Muscle (TRAM) Flap<sup>3</sup>. Other less utilized options include Transverse Upper Gracilis (TUG) Flap, Superior gluteal Artery Perforator (SGAP) Flap, Inferior Gluteal Artery Perforator (IGAP) Flap, and Profunda Artery Perforator (PAP) Flap. Lower abdominal flaps in the form of DIEP, TRAM, or SIEP are the most favored ones which will be discussed in detail. Autologous reconstruction allows a more natural, aesthetically acceptable, and durable outcome at the expense of donor site morbidity which includes scars, contour deformity, and functional impairment. Wound-related complications occur in around half of the patients suggesting their radical nature<sup>13</sup>.

The most commonly used abdominal flaps for breast reconstruction are TRAM and DIEP<sup>12</sup>. TRAM is associated with fewer ischemic complications as opposed to DIEP. Pedicled flaps like TRAM are associated with bulk loss due to fat decomposition in the long run as contrasted with free flaps like DIEP, especially in obese patients<sup>12</sup>. This ischemic loss can be minimized over the period by neovascularization produced by a vascular delay procedure 2-3 weeks before TRAM or DIEP. TRAM, however, is associated with more donor site complications in the form of a hernia due to loss of rectus muscle. In one study it has been estimated that TRAM is associated with a rate of the herniation that is double to the DIEP. This is the reason that most experienced

micro-surgeons now have started relying on DIEP flap instead of TRAM flap<sup>3</sup>.

If the abdominal flaps are not available due to certain reasons then the thigh and buttocks are the most commonly used sites for harvesting the perforator flaps. For these perforator flaps, the most important thing is the availability of the feeding perforators at the recipient sites. Mostly the perforators of the mammary vessels are utilized. TUG flap has recently been used most efficiently to provide the bulk to the breast. TUG flap is based on a profound artery perforator supplying the Gracilis muscle and the inguinal region extending to the back<sup>14</sup>. It is a very common and definitive site for the perforator and readily provides bulk to the flap. A significant amount of fat can be harvested. Donor site morbidity may be quite significant and the lymphatic leak can be troublesome after harvesting this flap due to loss of lymphatics in the inguinal region.

Gluteal region flaps which include Superior Gluteal Perforator Flap and Inferior Gluteal Perforator Flap are other options. However, they require extensive expertise even in the good hands<sup>15,16</sup>. Loss of Sciatic nerve or posterior cutaneous nerve of thigh and donor site morbidities are the most important hurdles in their consistent use. The perforator sizes are usually small and donor site issues are quite significant including infection, contour deformity, and scar formation<sup>16</sup>.

The success of any free or pedicled flap lies in the quality of the blood supply and it is more important to focus on it when we are utilizing the perforators which are usually smaller than the named vessels<sup>3</sup>. As the radiological investigations have improved, MRI and doppler are available to assess the quality and diameter of the feeding vessels which is important to know pre-operatively especially when there is a risk to perforators due to previous surgery on the anterior abdominal wall. CT angiography or MR angiography are more reliable as opposed to the hand-held doppler. These are being increasingly used in situations where we need to be sure if the perforators are available for the free flap especially following any abdominal surgery like cholecystectomy and C-section during which perforators or SIE veins and perforators are at more risk of damage. Hence, it is important to note that abdominal surgery is no absolute contraindication for the DIEP or TRAM. Pre-operative evaluation is the key before handling these difficult cases.

### **Immediate or Delayed Reconstruction?**

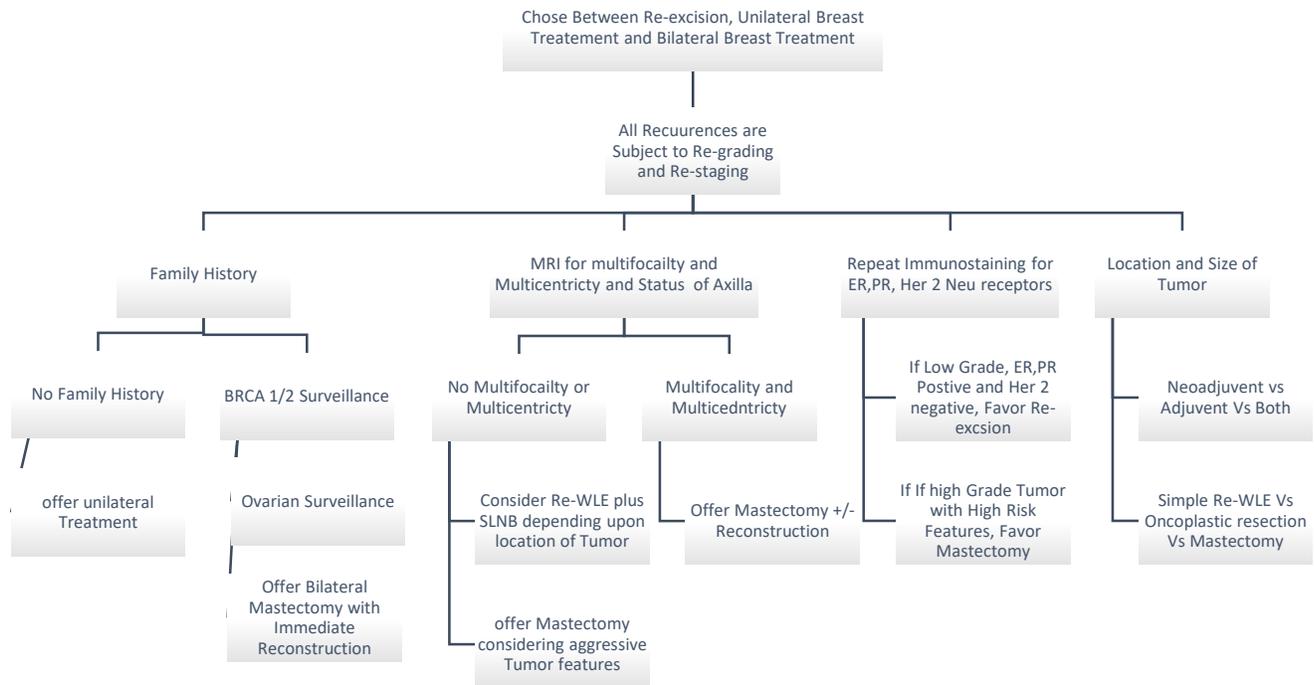
Breast reconstruction can be done along with mastectomy in two ways either immediate or delayed<sup>17</sup>. The greatest advantage of immediate reconstruction is the fewer number of surgeries and low financial burden<sup>18</sup>. The immediate or one-stage reconstructions are better in terms of positive emotional well-being than the delayed or two-stage reconstructions. Patients with immediate reconstructions show low levels of depression and anxiety and because of positive body impression and self-concept, women are more confident and have better sexual fulfillment. A skin-sparing

mastectomy is quite suitable for the small to moderate-size breast without significant ptosis and healthy skin flaps. The bulk can be provided by the free or pedicled tissues. Single-stage methods however are associated with a higher degree of implant extrusion, flap necrosis, and higher infection rate. It is always difficult to obtain symmetry with a one-stage operation. The reconstructed breasts are usually smaller than the contralateral healthy breast.

On the contrary, the delayed reconstruction is associated with the availability of a liberal amount of time for the patient to think about the available options and it provides the surgeons to manage the patient's expectations in terms of the overall outcome of the breast reconstruction<sup>14</sup>. The delayed reconstruction is one of the most commonly used operative options. It can be either in the form of implant-based reconstruction or autologous reconstruction. The

implant-based reconstruction can be a single-stage if there is no fear of having postoperative radiotherapy or a two-stage procedure which comprises of insertion of a Becker's prosthesis at first intervention followed by replacement with a permanent implant<sup>14</sup>. The two-stage approach bridges the period for chemoradiation well and keeps the skin flap healthy and distended for future implant replacement without tight closure. The infra-mammary fold can also be conveniently adjusted in the second intervention and improves the overall outcomes of the reconstructed breast. The two-staged implant-based reconstruction is however associated with the relatively suboptimal aesthetic outcome. In case of low bulk or infection, Latissimus Dorsi (LD) muscle can function as a salvage flap<sup>14</sup>. Autologous flaps however are associated with the absence of implant-related complications<sup>19</sup>.

**ALGORITHM FOR ONCOLOGICAL DECISIONS**



**Radiotherapy & prosthetic breast reconstruction**

Radiotherapy can have a dramatic impact on the reconstructed breast<sup>20</sup>. The reconstruction if avoidable, should be avoided before the radiation therapy. Radiation can affect significantly in acute and chronic setting<sup>s</sup><sup>20</sup>. In an acute setting, about 95% of the patients develop radiation-induced dermatitis characterized by edema, redness,

desquamation, and ulceration. In the chronic setting, it is associated with skin retraction, induration, chest and shoulder pain, and movement restriction in the neck and shoulders<sup>20</sup>. Radiation-induced fibrosis is permanent and is associated with Becker grade III and IV capsular contractures in case of implant-based reconstruction, in about 68% patients<sup>20</sup>. It would be wise to have Becker's implant during the bridging period associated with chemoradiation. If in

few circumstances, the final histopathology report following mastectomy, shows invasive cancer and lymphadenopathy then it would be prudent to tell the patient of higher chances of capsular contractures postoperatively.

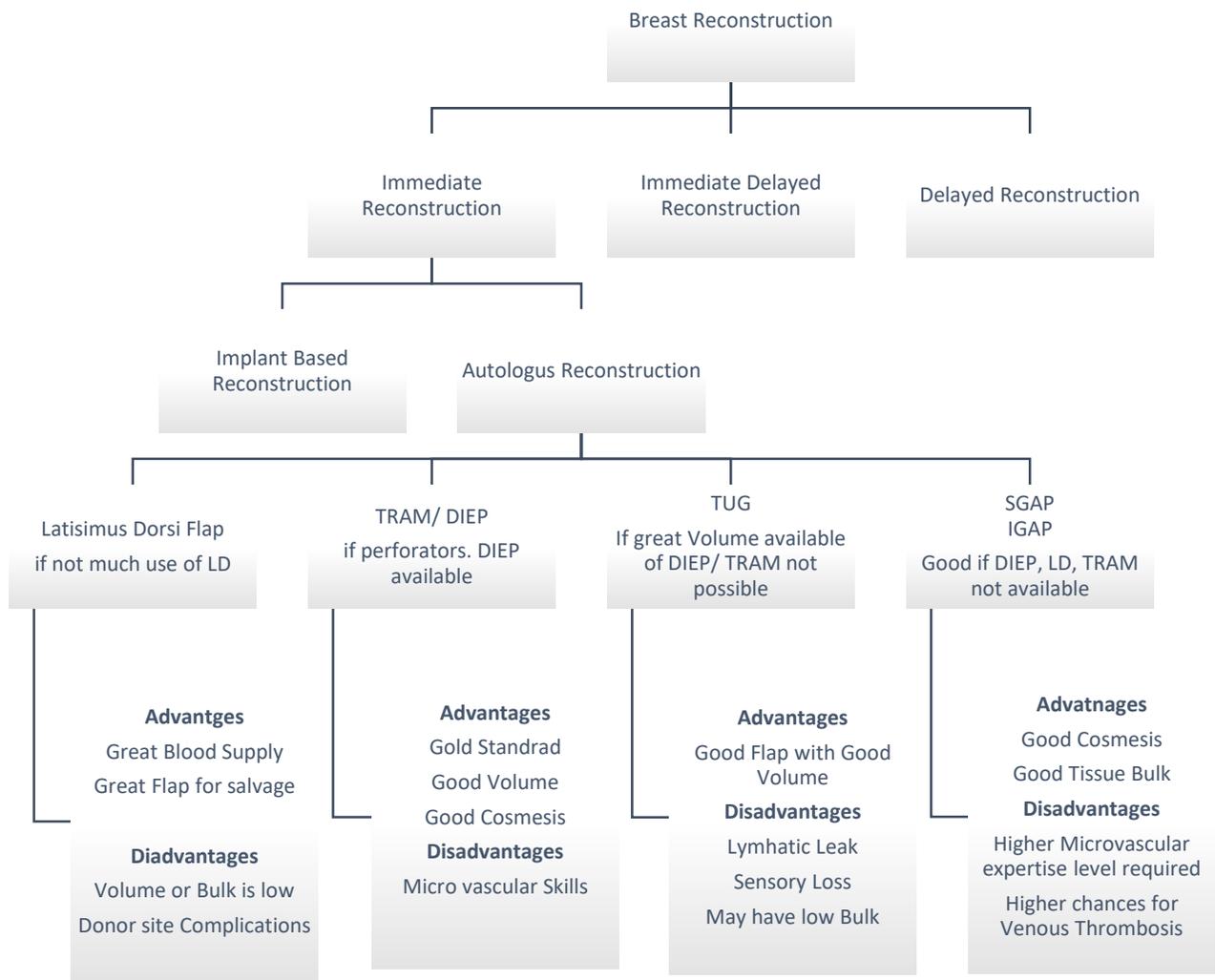
**Complications associated with Implant-Based and Autologous Reconstructions**

Appropriate patient selection is pivotal for the better outcomes of the reconstruction whether implant-based or autologous <sup>21</sup>. Various risk factors have been identified to adversely affect the reconstruction which includes the history of diabetes, increased BMI, smoking,

immunodeficiency, hypertension, certain characteristics of the body habitus, and breast characteristics <sup>3</sup>.

Diabetes is one of the strongest limiting factors in a successful reconstruction without complications <sup>21</sup>. It induces hyperglycemia which is associated with poor blood supply and higher soft tissue infections. The patients need to have a blood sugar level below 200 mg/dl and urine glucose should be absent. Uncontrolled diabetes is linearly correlated with infection and reconstruction failure rates. It promotes poor wound healing and wound dehiscence <sup>7</sup>.

**ALGORITHM FOR BREAST RECONSTRUCTION**



Tobacco use leads to strong vascular constriction compromising the blood supply of the tissues including feeding flaps vessels and is associated with higher ischemic flap complications. The patients need to stop smoking at least 6 weeks before the breast reconstruction in most of the units<sup>7</sup>.

Similarly, higher BMI is associated with poor reconstruction outcomes. The patients need to have BMI below 30 for any reconstruction<sup>7</sup>. Planned weight reductions are hence important preoperatively to handle the disadvantages of higher BMI. Hypertension needs to be controlled<sup>7</sup>.

Patients having tissue disorders and immune deficiency need to be optimized or preferably should avoid such reconstructions<sup>7</sup>.

Mammary hypertrophy associated with grade III or beyond ptosis is associated with the poor blood supply of the flaps hence are not good candidates for the skin-sparing mastectomy and these patients need to have reduction mammoplasties along with resection of the tumors<sup>7</sup>.

Infections can hamper both implant-based and autologous reconstructions of the breast. Implant infection is the leading cause of reconstruction failure<sup>7</sup>. Pre-operative and post-operative broad-spectrum antibiotic prophylaxis is used routinely to avoid infection in these settings, otherwise, exclusion of implant or tissue reconstruction may be the rule. Extended antibiotic use should be avoided to limit the development of resistant organisms. Topical antibiotic use could reduce the contracture rates but not the infection rates.

Rates of seroma formation have been reported from 0.2-20%<sup>7,22</sup>. Obesity, insertion of foreign body, lymphatic destruction, postoperative inflammatory response, large dead space, and ADMs are the most common risk factors for seroma formation. Seroma may lead to higher infection rates also.

Implant extrusion and exposure is a serious complication of implant-based reconstruction<sup>7,23</sup>. The flap thickness in this regard is very important and the role of radiotherapy is significant. The flaps need to be thick enough to have a good blood supply and avoid ischemic complications and secondly should be able to withstand the effects of the radiotherapy which are real. Radiotherapy may lead to complete necrosis of the flap and an explanation of the prosthesis would be required in these circumstances.

Anaplastic Large Cell Lymphoma (ALCL) is one of the most important complications which have come to light recently. Various type of lymphomas has been attributed to be associated with implant-based reconstruction including T cell lymphoma, follicular lymphoma, marginal zone B cell lymphoma, primary effusion, lymphoplasmacytic type. However, these types are mostly curable<sup>24</sup>.

## CRITICAL APPRAISAL OF THE CASE SCENARIO

1. Before devising a plan for this particular patient many questions need to be asked in history and clinical examination. It would be important to get information regarding previous oncological workup, surgical interventions, details about radiotherapy, family history, and patient aspirations and expectations about the future treatment plan. Signs and symptoms of the metastasis would require scrutiny.

o Family history is important because a patient may be having BRCA 1/2 mutation for which she might be requiring an ovarian work up and may alter the management plan altogether. If a patient is positive for BRCA 1/2 mutations then she would be offered and possibly opting for a bilateral prophylactic mastectomy with immediate reconstruction instead of local WLE or single breast treatment.

o The previous history of radiotherapy would make the surgeon cautious about future wound complications and the choice of local or distant flaps.

o Similarly, the need for postoperative adjuvant radiation would also be an important determinant of future surgical interventions.

2. On clinical examination, it would be important to know the size and location of the tumor, its relationship with NAC, and also, we need to know the clinical status of the axillary lymph nodes. It would be important to re-stage and know the current stage of the disease. Likewise, it would be important to know the size and location of the tumor if a patient opts for a breast-conserving option in form of traditional WLE or oncoplastic resection. If a patient has positive clinical nodes then metastatic workup would be required and this also shows the need for future radiation therapy in the adjuvant setting. It would also be important to preoperatively know the degree of ptosis and size of the breast. Moreover, the aspirations and expectations of the patients regarding the reconstruction need to be known and tailored accordingly in the management plan.

3. It would also be important to re-grade and re-stage this patient. This would require the use of trucut biopsy, US, mammogram, and perhaps MRI. I would also like to immunostain the trucut blocks to know the molecular oncological features of the disease.

4. In this particular patient it would be appropriate to do an MRI of the breast and axilla and do metastatic workup if required. If a patient has a strong family history then it would be appropriate to get genetic testing for BRCA 1/2 mutations as it would alter the decision tree.

5. Management Options for Breast & Axilla: Patients with early recurrent breast cancer may opt for WLE again on oncoplastic resection if the disease is confined and tumor aggression is low. This may be contested by few experts however few surgeons may still have reasons to go for this

option. If the patient has high-risk tumor features on a re-work-up, it would be appropriate to choose mastectomy with SLNB. This patient is having triple-negative cancer and a grade 3 tumor, which would be better treated aggressively. However, WLE and oncoplastic resection may be feasible if the disease is limited and confined.

6. **Reconstructive Options:** There are many reconstructive options available. The reconstruction can be immediate, immediate-delayed, and delayed. It may be implant-based or autologous or a combination of the both. This patient has been in favor of autologous reconstruction. If the patient does not have significant use of LD flaps, then LD flaps may be utilized. Other options include TRAM, DIEP, TUG, IGAP, SGAP flaps. History of cholecystectomy and C-section is not absolute contraindications for the TRAM or DIEP. The patient may be all right to have these flaps if the CT angiogram shows good perforators and blood supply.

7. **Social and Lifestyle Issues:** All the flaps have pros and cons and must be carefully chosen to meet the requirements of the oncological perspectives, aesthetic outcomes, and patient desires. For example, although LD can function as a great salvage flap it may be inappropriate to go for the LD flap in patients requiring strenuous activity like dancers, swimmers, climbers, etc. DIEP is considered a gold standard in these circumstances.

8. **Consent Process:** Consenting process should include information regarding the failure of a flap, redo surgery, take-backs, and the complications associated with the flaps especially the thrombosis, infection, and loss rates, and the modalities that would be used in case of failure.

9. **Adjuvant Therapy:** Adjuvant therapy can influence the outcomes of the reconstruction and overall treatment. The postoperative need for the radiation is very important to assess before the operative intervention so that the reconstructed breast suffers the least.

10. **Surveillance and Follow-up:** Surveillance and follow-up differ among the patients, severity, and type of the disease, and the surgical modality used for the reconstruction.

11. **Patient-Reported Outcome Measures (PROMS):** Breast-Q has important measures to know the outcomes of the reconstructed breast and they should be incorporated into the practice.

12. **Medicolegal Factors:** Several factors are involved when planning and executing a breast reconstruction.

## CONCLUSIONS

With recent advancements in the field of microsurgery, surgeons can recruit many perforator-based flaps which used to be not available in the past. The surgeons are shifting very rapidly towards the autologous route because of their increasing experience in microsurgery and also because of increasing patient satisfaction with reconstructions that are more natural and acceptable. DIEP and other perforator flaps are rapidly replacing TRAM because of the higher incidence of herniation. TUG, SGAP, and IGAP are other acceptable alternatives but they require more expertise. For choosing any flap pre-operative evaluation of the donor's vessels through CT angiography or color doppler is important. Microsurgery skills would be of pivotal importance in the future for reconstructions. Implant-based reconstruction still is quite effective and popular. Nipple and skin-sparing mastectomies have shown great promise to immediate breast reconstructions especially in cases of DCIS or for cancer prophylaxis. Anatomical and rounded implants can be individualized to the demands of the patients. Anaplastic implant-associated lymphoma needs careful research and scrutiny in the future. Oncoplastic resections can also be an important alternative to reconstructions and have been recently advocated by many with good oncological safety principles and aesthetic acceptability. The treatment plans in the future have to be individualized or personalized according to the needs and demands of the patients.

## ARTICLE INFORMATION

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Author Affiliations: Department of Surgery, Shalamar Medical & Dental College, Lahore, Pakistan (Ahmed, Ahmed, Zaib)

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