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A Clinical Algorithm for Breast Cancer Patients: Exploring Reconstructive Options after Radiation

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Abstract

Purpose of Review As radiation therapy is used as an adjuvant treatment in an increasing number of women during the management of breast cancer, radiation therapy and its well-known adverse effects pose additional challenges for breast reconstruction. The purpose of this review is to examine recent data on outcomes of various breast reconstruction methods in the setting of radiation therapy and help surgeons and oncologists as well as patients with their decision-making process.

Recent Findings Breast reconstruction methods can be categorized into autologous-, implant-, and tissue expander/implant-based, each with its distinct advantages and disadvantages. Autologous and tissue expander/implant are preferred when radiation therapy is expected based on surgical, aesthetic, and patient satisfaction. Use of latissimus dorsi flaps and acellular dermal matrix with tissue expander/implant has shown several advantages to traditional methods.

Summary For patients who have a high likelihood of requiring postmastectomy radiation therapy, choosing a breast reconstruction method depends on multiple factors. Patients and surgeons should be aware of the impact of radiation therapy so that they can make a well-informed decision.

Keywords Breast reconstruction · Radiation therapy · Implant · Autologous flap · Tissue expander

Introduction

Breast cancer is the most common malignancy in women worldwide and contributed to over 30% to new cancer cases in the USA in 2017 according to American Cancer Society. As an increasing number of women are diagnosed with and surviving breast cancer, a growing number of women who undergo mastectomy elect to have breast reconstruction. The quality of life and psychosocial benefits of breast reconstruction are well known. While there are many benefits from breast reconstruction, postmastectomy radiation therapy or other treatments for advanced-stage breast cancer can further complicate breast reconstruction. The use of postmastectomy radiation therapy has been steadily increasing in the USA. Traditionally, radiation therapy was recommended in cases of 4 or more positive lymph nodes, positive margins or margins closer than 1 mm, or tumor > 5 cm in size according to the National Comprehensive Cancer Network. However, more patients with fewer positive lymph nodes and smaller tumor size are offered radiation therapy by many institutions due to the publication of clinical trials exploring benefit in these subsets. In this case, the management of patients receiving postmastectomy radiation therapy and breast reconstruction requires a multidisciplinary team of oncologists and reconstructive surgeons.

The potential need for radiation therapy has become a critical component of the decision-making process in breast reconstruction. The addition of breast reconstruction has been shown to improve various aspects of a patients' quality of life including emotional, mental, and functional well-being [1]. However, the reconstructed breast can increase the complexity of radiation therapy delivery. Conversely, even though postmastectomy radiation therapy has established oncologic benefits in patients with advanced breast cancer, it can negatively impact the breast reconstruction. Current methods of reconstruction in patients who have undergone mastectomy and may require radiation therapy involve various types, techniques, and timing for individual patients. Broadly, types of breast reconstruction can be categorized into autologous flap-, implant-, and tissue

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expander/implant-based. Reconstruction using autologous flaps or implants can be done before or after radiation therapy. Various methods of reconstruction have different outcomes in terms of complications, cosmesis, and patient satisfaction (Table 2). As each technique is also impacted by variables such as patient anatomy and preferences, the optimal approach for combining postmastectomy radiotherapy and breast reconstruction is different for each patient. This review examines surgical, aesthetic, and patient satisfaction outcomes of current breast reconstruction methods to help with the decision-making process for each patient and to aid in patient counseling.

Type and Timing of Breast Reconstruction Techniques

Autologous Flaps

Current autologous tissue reconstruction techniques involve several flap designs from the abdominal wall, hip/buttocks, thighs, and back. The abdominal wall as a donor site has been popularized because its soft texture has a close resemblance to the feel of normal breast tissue. In addition, women who need breast reconstruction are often at an age where they have excess soft tissue overlying the abdomen and by using the abdominal wall flap, it has an added benefit of cosmetically pleasant outcomes at the donor site [2]. Abdominal wall flaps include transversus rectus abdominis muscle flap (TRAM) and deep inferior epigastric perforator (DIEP). DIEP flap is a free fasciocutaneous lower abdominal flap based on perforators of the deep inferior epigastric vessels, identified suprafascially and traced through the anterior rectus sheath and rectus abdominis muscle. TRAM refers to the use of transversus rectus abdominis myocutaneous flap for breast reconstruction. A classification system of TRAM flaps developed by Nahabedian et al. in 2002 takes muscle-sparing into consideration as it had become a widespread practice to spare some of the rectus abdominis muscle [3]. A degree of muscle-sparing (MS) of the rectus abdominis muscle by Nahabedian et al. includes MS-0 to 3. They were classified as the sacrifice of full width (MS-0), preservation of a lateral strip (MS-1), preservation of both lateral and medial strips (MS-2) while sacrificing a cuff of muscle around the perforators, and preservation of the entire muscle (MS-3) which is equivalent to DIEP flap. Primary choices for autologous breast reconstruction today are muscle-sparing techniques including DIEP and MS-2 TRAM flaps. Donor site morbidity has been minimized especially with the advent of perforator flaps. Currently, several studies have shown that there is no appreciable difference between DIEP and MS-2 TRAM flaps as both techniques maximize the donor site function by maintaining vascularity, innervation, and continuity of the rectus abdominis muscle [4]. As such, both techniques are widely used for autologous breast reconstruction.

Other donor sites are preferred when the lower abdominal wall is not a suitable, due to prior abdominal wall surgery, insufficient abdominal skin or fat, or high-risk comorbidities such as smoking, diabetes, or obesity [5]. There are several other options such as superior (SGAP) and inferior gluteal artery flaps (IGAP) from hip/buttocks; transverse upper gracilis flaps (TUG) and profundal artery perforator flaps (PAP) from thighs; or latissimus dorsi flaps (LDF) from the back. TUG flaps are less utilized because of a modest amount of obtainable volume, short pedicle length, and high rates of donor site breakdown and seroma [6, 7]. PAP offers several advantages to TUG including a longer pedicle, relatively plentiful and soft tissue, and less visible donor site scar. Unlike TUG, the dissection does not sacrifice muscle and is distant from the lymphatics, reducing the risk of seroma. However, PAP is a challenging flap to raise, requiring advanced microsurgical skills. LDF is a good candidate as it supplies tissue volume and a reliable vascular pedicle. LDF is often used as a hybrid form, as implants are necessary for women with moderate to large breast size. Any of the autologous flaps can be used for reconstruction immediately at the time of mastectomy or delayed until after radiation therapy (Fig. 1(a, b)). Despite improvements and introduction of various autologous flap techniques, its use is constrained by greater microsurgical expertise necessary to carry out flap transfer.

Implants

Prosthetic implants were first used for breast reconstruction in the 1960s and are currently used in various reconstruction techniques. The use of implants for breast reconstruction has steadily increased and surpassed the use of autologous flaps in 2002 as the most common method of breast reconstruction performed in the USA [8]. Several factors have contributed to the growth of implant use including greater long-term safety data, greater varieties of shapes and sizes, and decreased operative time as well as post-operative recovery when compared with autologous tissue reconstruction [9]. Introduction of adjunctive procedures such as acellular dermal matrix and fat grafting has also contributed to its popularity as they provide greater control and flexibility over the mastectomy space. Currently saline and silicone gel implants are available for use in reconstruction. Silicone gel implants tend to be softer and more natural-appearing relative to saline implants [10]. Implant reconstruction can be done immediately at the time of mastectomy or in a staged fashion with the use of tissue expander (Fig. 1(a, c)). Prosthetic implants can be used in one-stage during which implants of appropriate volume replace the resected breast tissue. Implants have a limited lifetime and may need to be replaced, generally about 10–20 years after the insertion as recommended by the American Society of Plastic Surgeons.

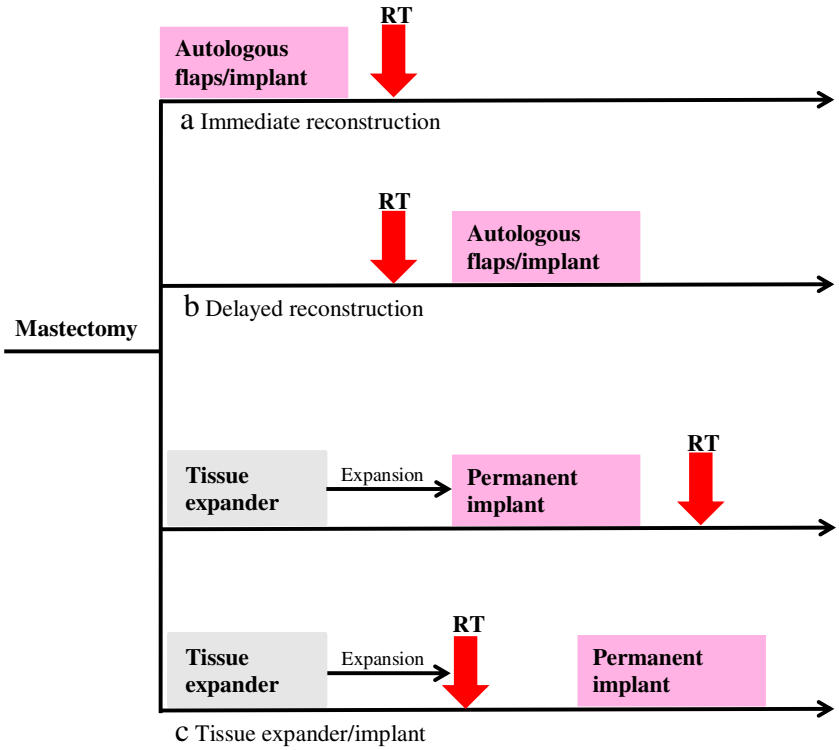

Fig. 1 Timeline of various breast reconstruction techniques in the setting of postmastectomy radiation therapy: (a) immediate reconstruction using either autologous flaps or implants, (b) delayed reconstruction using either autologous flaps or implants, and (c) the use of tissue expander and final implant exchange at a second surgery. Latissimus dorsi flaps or acellular dermal matrix can be added. RT radiation therapy

Tissue Expander/Implant

Although one-stage reconstruction has a benefit of completing the reconstruction within one surgery, high complication rates and poor outcomes have popularized two-stage reconstruction when radiation therapy is required as part of the treatment plan. This technique involves the use of a tissue expander followed by a second surgery for exchange of the expander with an implant. When a tissue expander is placed at the time of mastectomy and before radiation therapy, it helps preserve the integrity of the breast skin flaps such as shape and thickness. The expander can be placed in either a total submuscular pocket or a partial subpectorial position for superior pole coverage with various techniques for inferior pole coverage [11]. A total submuscular pocket is commonly achieved by using the pectoralis major muscle carried down to the rectus fascia or using the pectoralis major and separate serratus anterior and rectus abdominis for inferolateral coverage [12]. Total submuscular coverage fully covers the tissue expander but requires capsular adjustment during the exchange to make the reconstructive mound cosmetically acceptable. Partial subpectorial coverage also achieves comparable results but can cause expander exposure depending on the variability in mastectomy flap viability [13]. Radiation therapy can be delivered during the tissue expander expansion process or after the exchange for a permanent implant (Fig. 1(c)). The expansion can begin as soon as the mastectomy flaps and incision have healed and is usually performed on a weekly or biweekly basis depending on the patient's comfort and skin tolerance [10]. The entire process of expansion can take anywhere from 3 to 7 months. Once the expansion is complete, the tissue expander is exchanged for final implants. In some clinical situations, the tissue expander can be deflated to allow completion of radiation therapy to the chest wall and regional lymphatics. The expander can be re-inflated on completion of radiation therapy until the second-stage reconstruction is performed.

Latissimus dorsi flaps (LDF) and acellular dermal matrix (ADM) have been used as an adjunct to traditional immediate tissue expander/implant techniques, often resulting in improved cosmesis and amelioration of irradiation-induced contracture. LDF includes latissimus dorsi muscles, along with skin and fat that covers the muscle. The entire flap is elevated off the back and brought to the front of the chest wall with its main blood vessels still attached. Since many women do not have enough fatty tissues on the back, LDF is commonly combined with a tissue expander/implant to achieve the desired volume. When LDF is used with implants, it provides enough soft tissue to completely cover the underlying implant. LDF can be used for patients with wound healing problems or soft tissue failure and patients who have had previous radiation.

ADM has been increasingly used in implant-based breast reconstruction due to its ability to provide soft tissue support and regenerative potential. ADM is used to provide support for the tissue expander and placed as a sling between the inferior edge of the pectoralis muscle and the inframammary fold. Therefore, the expander is covered completely or mostly

by a muscle above and acellular dermal matrix below. This coverage provides not only soft tissue support but also additional elasticity, stabilization of the pectoris major muscle, and device compartmentalization [14]. ADM can be used in both one-stage and two-stage reconstructions with implants. The benefits of acellular dermal matrix for implant-based reconstruction over traditional, submuscular placement include improved implant pocket control, faster expansion, less patient discomfort, and superior aesthetic outcomes [15–18]. However, there is a concern of ADM use in the setting of radiation therapy as it has been shown to predispose to higher complication rates including infection, mastectomy skin flap necrosis, and seroma formation [19, 20].

Outcomes

One-Stage Reconstruction: Autologous Flaps

Types

Major concerns with radiation therapy and immediate autologous reconstruction are radiation-associated flap complications including fat necrosis, fibrosis, poor wound healing, flap shrinkage, and volume loss. Because of the harmful effects of radiation and well-documented concerns, the general consensus is to delay autologous tissue reconstruction until after radiation. In one review, when the outcomes of immediate autologous breast reconstruction with and without postoperative radiotherapy were compared, there were no significant differences in reported satisfactory outcomes, overall complication rates including fat necrosis, and need for revision surgery [21]. This systemic review did not compare different types of autologous flaps. The majority of autologous reconstruction uses DIEP and muscle-sparing TRAM flaps due to lower complication rates, lower donor site morbidity, and higher physical well-being compared with other types of TRAM flaps [22]. Although Macadam and colleagues did not consider the role of radiation in this report, they showed that DIEP and muscle-sparing TRAM flaps lead to better abdominal well-being and lower morbidity compared with other types of autologous reconstruction. Therefore, they may be preferable in the setting of radiation use as well.

Another option for autologous tissue reconstruction is with latissimus dorsi flaps, which continue to be used in various breast reconstruction techniques as it provides sufficient tissue volume for autologous reconstruction and reliable vascular pedicle for implant-based reconstruction. In addition, when compared with DIEP and TRAM flaps, latissimus dorsi flaps show lower donor site morbidity and complication rates, even in obese and overweight patients as well [5]. Latissimus dorsi flaps are also often used as a secondary or salvage flap after a failed previous reconstruction. Several other groups showed no differences in clinically significant surgical complications including fat necrosis, wound healing, or the number of revisions among various types of autologous flaps when used for either preoperative or postoperative radiation therapy [23–28]. Furthermore, another study reported no significant differences in total complication rates between the irradiated and unirradiated autologous tissue reconstructions [29]. This suggests that immediate reconstruction in patients undergoing radiation therapy can be without significant complications and morbidity with improvement in quality of life and body image compared with initial mastectomy with delayed reconstruction. Yet, it should be acknowledged that immediate reconstruction can still lead to complications including wound contracture, volume loss, fat necrosis, and interference with radiation delivery to all target volumes.

When autologous reconstruction is compared with immediate implant-based reconstruction in the setting of radiation therapy, autologous reconstruction is generally preferred. This is attributed to less morbidity, superior patient satisfaction, lower rates of reconstruction failures, and lower incidence of complication rates, in both short-term and long-term assessments [30, 31].

Timing

Although recent studies show no significant differences in overall complication rates between immediate and delayed reconstruction, surgeons often choose delayed reconstruction to avoid irradiating the flap, optimizing radiation delivery, and avoiding potential complications [32•, 33, 34]. In addition, delayed reconstruction has been shown to have significantly lower incidences of the need for revisional surgeries [35••]. The optimal time of reconstruction after radiation therapy is still debated due to the paucity of data but appropriate time should be allowed for adequate healing after radiation therapy. Some of the disadvantages of delayed reconstruction are delayed cosmetic results, which can affect patients psychologically. Patients who undergo a reconstructive procedure at the time of mastectomy have reported higher self-esteem, body image, feelings of attractiveness, and sexual functioning [36, 37]. However, several studies have suggested that these benefits are temporary as differences in quality of life, psychological and sexual well-being, and patient satisfaction such as symmetry, softness, and aesthetics between immediate and delayed autologous reconstruction dissipate over time [28, 38, 39].

One-Stage Reconstruction: Implants

Implants alone are often used in the setting of postmastectomy breast reconstruction as it offers the advantages of having a breast immediately after mastectomy in a single procedure and better psychological well-being [32]. Several studies have

Table 1 Advantages and disadvantages of various types of breast reconstruction in the setting of postmastectomy radiation therapy

Types	Pros	Cons
Implant	• Single procedure • Preserves the breast skin envelope • Less complex surgery, shorter recovery time • Weight gain or loss does not change the breast size	• Not a good option if skin has been irradiated; risk of implant rupture/extrusion and capsular contracture • Require implant replacement after 10–20 years • Relatively less natural appearance of breast • Often requires the use of ADM for coverage
Tissue expander/implant	• Allows a flexible plan for patients who are unsure of implant or autologous flaps • Comparable aesthetic outcome to other types • Avoid difficulties associated with radiation delivery	• Two procedures • Risk of implant rupture/extrusion and capsular contracture (lower than implant-alone) • Require implant replacement after 10–20 years • Relatively less natural appearing breast
LDF/Tissue expander/implant	• Very reliable and easy to harvest • Less complicated compared with other flap procedures because the transferred tissue can remain attached to its natural blood supply	• Results in smaller breasts; almost always requires tissue expander/implant under flap to provide adequate breast size • Partial loss of strength or function that makes it hard to lift or twist • The breast feels tighter than the other breast because the fat around the LD is stiffer than fat from the abdomen (i.e., the TRAM or DIEP flap)
Autologous flaps	• Natural-looking breast • Lower risk of insufficient blood supply • Tolerate radiation therapy better than implants	• More complex procedure • Donor site morbidity • Risk of partial/total flap loss or flap failure • Longer hospital stay and recovery time

shown that radiation is a significant risk factor for major complications including implant extrusion and capsular contracture [40, 41]. Severe capsular contracture can require reoperation to remove or exchange the implant. Compared with the reconstruction in the absence of radiation therapy, implant reconstruction led to much higher complication and failure rates due to radiation therapy [42, 43]. As a result, many surgeons opt for using autologous flaps over implants due to poor aesthetic results and a higher risk of complications with implants and radiation therapy [29].

Two-Stage Reconstruction: Tissue Expander/Implant

Despite the suggestion of improved results with autologous flaps over implants in the setting of radiation therapy, the advent of the two-stage tissue expander-based technique provides a safer alternative for implant-based reconstruction. When implants are to be used, two-stage reconstruction has become the conventional approach due to superior surgical and aesthetic outcomes, especially in the setting of radiation therapy [44]. Two-stage reconstruction also offers a flexible plan for patients who are unsure if they want an implant or autologous-based reconstruction at the time of mastectomy. In addition, this option is beneficial for patients whose lymph node biopsy results are unknown and therefore are uncertain if post-mastectomy radiation is necessary. By placing a tissue expander, the physician can avoid radiating an autologous flap in the event that radiation is needed for cancer treatment.

The two-stage reconstruction in patients receiving radiation therapy showed higher reconstruction failure and complication rates with capsular contracture being the most common complication relative to patients without radiation therapy [45]. Nevertheless, two-stage reconstruction has been shown to have lower complication rates when compared with autologous-alone reconstruction with radiation therapy [46, 47]. In addition, two-stage reconstruction has been shown to achieve similar aesthetic outcomes as one-stage reconstruction [48, 49]. Therefore, two-stage reconstruction may be preferable in the setting of radiation therapy to avoid potential aesthetic and radiation-delivery problems.

Two-stage reconstruction method allows radiation therapy to be delivered during the tissue expander expansion process or after exchanging with final implants. Several studies have shown that the timing of radiation relative to the tissue expander/implant exchange does not affect the rate of overall complications nor the rate of reconstruction failure [12, 48, 50]. However, radiation to the tissue expander leads to a better aesthetic result and lower capsular contracture rates compared with radiation to the final implant [51].

Use of Latissimus Dorsi Flaps

Latissimus dorsi flaps have been increasingly used in one-stage implant-based and two-stage tissue expander/implant-based reconstruction as it has been shown to decrease radiation-related

Table 2 Outcomes of various breast reconstruction techniques in the setting of radiation therapy

Timing relative to RT	Implant	LDF with tissue expander/implant	ADM with tissue expander/implant	Autologous flaps
Immediate	Complications: implant failure or extrusion, capsular contracture, infection Aesthetic outcome: symmetry and contour irregularities, may appear disproportionate after weight gain or loss Patient satisfaction: higher quality of life (lower anxiety and depression, higher self-esteem and body image) for 12–24 months postoperatively (*tissue expander/implant)	Complications: seroma, hematoma, capsular contracture, partial flap loss Functional outcome: partial loss of back muscle strength or function, breast feels tighter due to stiffer fat from the back Aesthetic outcome: natural look, smaller breast	Complications: seroma, expander explantation, infection, and need for reoperation Aesthetic outcome: superior aesthetic outcome in terms of shape, symmetry, and contour	Complications: partial/total flap loss, fat necrosis, delayed wound healing, infection, dehiscence, hematoma Aesthetic outcome: natural look Patient satisfaction: higher general and aesthetic satisfaction compared with implant-based reconstruction; higher general and aesthetic satisfaction than LDF
Delayed	Complications: capsular contracture, skin necrosis, infection, expander/implant failure or extrusion, implant rupture (lower overall complication rates compared with implants) Aesthetic outcome: similar aesthetic outcomes to immediate reconstruction, radiated skin may not stretch during tissue expansion			Complications: partial/total flap loss, fat necrosis, delayed wound healing, abdominal hernia/bulge, wound infection, dehiscence, hematoma, arterial thrombosis Aesthetic outcome: natural appearance Patient satisfaction: similar to immediate autologous flaps

complication rates [34]. In patients who have undergone radiation therapy, LDF can provide well-vascularized tissue to the ischemic chest wall as LDF retains its natural blood supply. When latissimus dorsi flaps are used with implants in one-stage reconstruction, it reduces the incidence of implant loss, reconstruction failure, and complications in irradiated breasts compared with implant-only reconstruction [52]. These patients also achieved complication rates equivalent to those experienced by patients not receiving radiation therapy [53]. However, when latissimus dorsi flaps are used with implants alone, the mastectomy skin envelope imposes a size limit of implants and limits surgical outcomes. If the implant is too large for the skin envelope to accommodate, the implant can put excessive pressure on both the LDF and the mastectomy skin envelope, causing ischemia and wound dehiscence [54].

The two-stage reconstruction technique addresses difficulties of one-stage reconstruction, including low satisfactory aesthetic outcome and inadequate tissue volume. The two-stage reconstruction involves the insertion of LDF with the tissue expander during before radiation therapy or LDF with the final implant placement after radiation therapy. The most common complication is associated with donor site morbidity, most commonly seroma formation followed by dorsal hernia and loss of shoulder range of motion, strength, and functioning [5]. When LDF is used with the tissue expander before radiation therapy, there is a risk of damaging the flap with radiation. Irradiation of the tissue expander with subsequent delayed LDF placement with implants yields favorable outcomes, addressing the difficulties of high post-irradiation tissue contracture, relative to irradiated tissue expander/implants [34]. The advantage of adding a flap to the final implant was more dramatic when radiation therapy was done during expansion. When a flap was added to the final implant after radiation therapy, the cosmetic outcome was equivalent to that in unirradiated patients [55].

Use of Acellular Dermal Matrix

During both one-stage and two-stage implant-based reconstruction, many surgeons opt to use acellular dermal matrix (ADM) in about 80% of cases to ensure sufficient coverage of the inferior implant [56]. Not only does an acellular dermal matrix help the surgeon to better shape the new breast and provide lower pole coverage, but it also facilitates the regeneration of blood vessels in the surrounding tissue [57]. In several studies, the use of an ADM for one-stage implant-based reconstruction has shown to result in low overall complication rates and extremely low rates of capsular contracture relative to implant reconstruction without an ADM [58, 59]. These studies support that the use of an ADM is safe and reliable and furthermore, superior aesthetic outcome from higher ratings on the length, symmetry, and contour of the inframammary fold and decreased mechanical shift of the implant [60]. These results suggest that the use of an ADM decreases the risk of overall complications and improves the aesthetic outcomes of implant-based reconstruction.

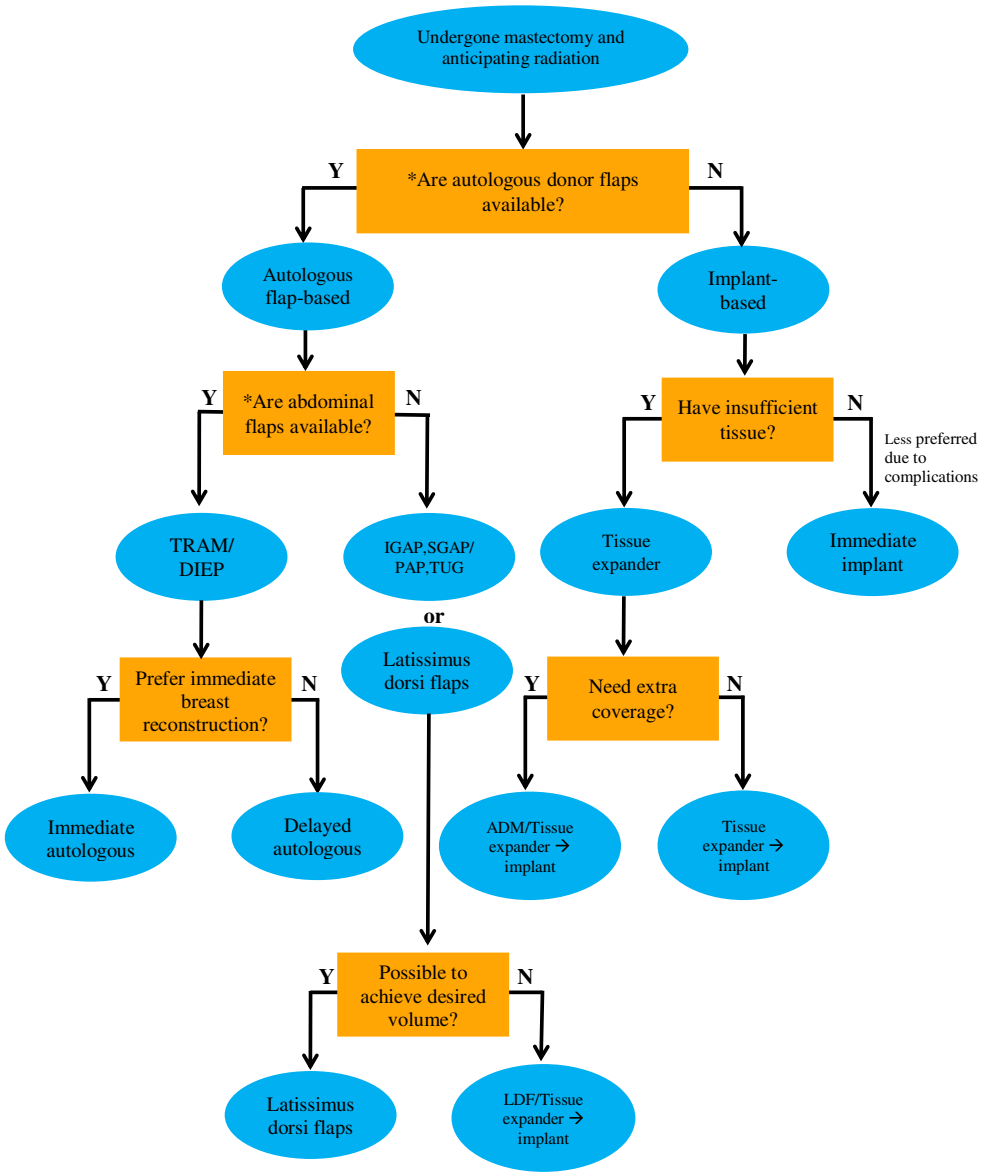

Fig. 2 A clinical algorithm of patient evaluation for various types of breast reconstruction in the setting of postmastectomy radiation therapy. Asterisk symbol means the choice of reconstructive option depends on multiple factors: Surgeon experience/preference, patient preference, and patient specifics (BMI, age, and history of XRT, previous use of flaps)

Despite these perceived benefits, conflicting studies have reported that the use of an ADM in postmastectomy reconstruction has been associated with higher complication rates. The complications associated with ADM include expander explantation, infection, seroma formation, and reoperation. Furthermore, in patients whose newly reconstructed breast weighed greater than 600 g, the ADM group showed higher rates of infection compared with the non-ADM group [56, 61]. Collectively, these studies indicate that while the use of ADM may lead to a lower rate in capsular contracture and improved aesthetic outcomes, the potential tradeoff is a higher risk of seroma, infection, and reconstructive failures [62]. Further studies are needed in order to elucidate the safety and efficacy of acellular dermal matrices in implant-based reconstructive procedures.

Conclusions

With the increased use of radiation therapy in the management of breast cancer, successful integration of breast reconstruction and postmastectomy radiotherapy has become an important yet challenging process. Various breast reconstruction techniques have been extensively studied and reviewed and yet, there is no consensus for defining the best method due to surgeon-related (preference, experience, and expertise) and patient-related factors (preference, body habitus, comorbidities). Choosing a specific type of breast reconstruction is a multifactorial decision among surgeons, oncologists, and patients that requires a careful preoperative planning based on risks and benefits (Tables 1 and 2). Here, we review various types and timing of breast reconstruction methods to help surgeons and patients choose the optimal method that best suits unique personal goals and preferences (Fig. 2).

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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