Curr Surg Rep (2021) 9:2
https://doi.org/10.1007/s40137-020-00280-4

PLASTIC SURGERY (M HANASONO & E CHANG, SECTION EDITORS)

Advances in Autologous Breast Reconstruction

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Accepted: 25 November 2020 / Published online: 18 January 2021

Abstract Autologous breast reconstruction (ABR) in patients undergoing mastectomy is now routinely performed, and associated with high rates of success and minimal donor site morbidity. Compared to alloplastic techniques, advantages of autologous approaches include the ability to confer a lifelong result without the need for additional surgery, superiority in the setting of radiation therapy, and eliminating the possibility of implant-related complications such as anaplastic large cell lymphoma. Moreover, ABR is associated with superior patient-reported outcomes compared to implant-based reconstruction. This article reviews recent advances in ABR, which have refined existing techniques, broadened the array of donor site options available to reconstructive surgeons, and streamlined the management of patients undergoing these procedures.

Keywords Autologous · Diep flap · Breast reconstruction · Postmastectomy

Introduction

There are over 268,000 new cases of breast cancer per year in the USA, making it the second most common malignancy only after nonmelanoma skin cancer [1]. In recent years, rates of mastectomy relative to breast conservation therapy for the treatment of breast cancer have risen [2]. Furthermore, a greater proportion of patients with unilateral breast cancer now elect to pursue bilateral rather than unilateral mastectomies [3]. Patients who undergo breast reconstruction after mastectomy experience significantly greater quality of life compared to patients who undergo mastectomy alone [4].

Autologous breast reconstruction (ABR) is now routinely performed, and associated with high rates of success and minimal donor site morbidity. Compared to alloplastic techniques, advantages of autologous approaches include the ability to confer a lifelong result without the need for additional surgery, superiority in the setting of radiation therapy, and eliminating the possibility of implant-related complications such as anaplastic large cell lymphoma [5]. Moreover, ABR is associated with superior patient-reported outcomes compared to implant-based reconstruction [6]. This article reviews recent advances in the techniques and the management of patients undergoing ABR.

Updating the Gold Standard: Variations on the DIEP Flap

The last decade in ABR has been characterized by widespread adoption and innovation of the perforator flap concept. The deep inferior epigastric perforator (DIEP) flap was first proposed as a muscle-sparing alternative to more conventional abdominally-based ABR procedures like the pedicled or free transverse rectus abdominis myocutaneous (TRAM) flap in 1994 by Allen and Treece [7] and is now largely regarded as the gold standard for abdominally-based ABR. Based on the Healthcare Cost and Utilization Project Nationwide Inpatient Sample (HCUP NIS), DIEP flap breast reconstruction incidence has increased

This article is part of the Topical Collection on *Plastic Surgery*.

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significantly in recent years as compared to free and pedicled TRAM flaps, which have each seen a decrease in utilization [8]. Recent advances in abdominally-based ABR have sought to provide increasingly more natural and functional reconstructions while minimizing donor site morbidity. In addition, reconstructive surgeons have continued to explore and develop alternative donor sites in order to be able to offer the advantages of autologous reconstruction in patients who are not candidates for exclusively abdominally-based ABR.

Enhanced Muscle Preservation: APEX Flap

The complex and widely varying perforator anatomy of the deep inferior epigastric vascular axis can present a substantial obstacle in the completion of a DIEP flap procedure. The proper application of the perforator flap concept—that is, flap harvest with full rectus muscle preservation—allows for the preservation of dynamic abdominal wall motion and depends on the ability to either (a) use a single large perforator to perfuse the entirety of the flap, or barring this, (b) utilize multiple perforators whose locations allow for their inclusion without the disruption of intact muscle, i.e., perforators located within the same "muscular cleavage line." The abdominal perforator exchange (APEX) flap has been introduced as an adaptation to the DIEP flap that preserves muscle by disassembling pedicle anatomy to avoid muscle transection [9]. Although it requires an additional micro-anastomosis, which adds additional time and risk of microvascular complications, the APEX flap shows promise with regard to decreasing the risk of abdominal bulge and hernia while simultaneously decreasing fat necrosis rates. Others have suggested the adaptation of an "intersection-splitting" approach that preserves muscles by dividing rectus abdominis muscles at inscriptions to capture disparate perforators, thereby leaving segmental muscle units intact [10]. Abdominal wall functional outcomes and hernia rates associated with this approach have not been adequately studied to date.

Sensory Neurotization of Breast Free Flaps

Sensory reinnervation of breast flaps has been shown to improve patient-reported quality of life after ABR [11] and facilitates the return of erogenous and pressure sensation after breast reconstruction but introduces additional microsurgical complexity that some surgeons may feel is unjustified. In 1999, Blondeel described an improvement in sensation in DIEP flap patients who underwent nerve repair (lateral cutaneous branch of the fourth intercostal nerve [ICN] coaptation to segmental nerve of DIEP flap), with 75% of patients able to detect Semmes–Weinstein monofilament stimulus in all cutaneous segments of the breast as compared to 31% for patients who did not have nerve repair (mean follow-up 21.4 vs. 19.6 months) [12]. However, this approach requires substantial time and skill to isolate and identify segmental nerves within the flap tissue to serve as recipient nerves; in the course of gaining adequate length on these recipient nerves, additional flap donor site morbidity may be incurred. Furthermore, the lateral cutaneous branch of the fourth ICN is routinely injured or divided at the time of the mastectomy, frequently leaving a prohibitively short donor nerve segment. In an effort to minimize operative time and donor site morbidity in ABR with sensory nerve repair, two more recent innovations have been adopted: the use of processed nerve allografts (PNAs) and/or conduits in interposition fashion, and utilization of the anterior branch of the ICN as donor nerve.

Anatomic studies have demonstrated that the lateral cutaneous branches of ICN 2–6 are responsible for sensation to the skin of the breast [13], with ICN 4 most frequently supplying the nipple-areolar complex [14]. Spiegel et al. [15] proposed that the anterior branch of the third ICN—which is frequently encountered during IM vessel preparation—may be able to provide some sensory benefit preserved and used for flap neurotization. In a series of thirty-five patients (fifty-seven flaps), they demonstrated a statistically significant improvement in sensation for patients who underwent flap neurotization with the anterior third ICN. Interestingly, the majority of the flaps in this study (33 of 57) were reinnervated using 40 mm nerve conduits to bridge gaps, and the nerve conduit technique resulted in significantly better sensation when compared to direct coaptation. This is surprising in light of earlier data suggesting diminishing success rates with conduits used to bridge gaps greater than 6 mm [16], but is nonetheless promising if these outcomes are replicable. Alternatively, Ducic et al. [17] endorse the utilization of PNAs to bridge long donor-to-recipient nerve gaps in DIEP flap breast reconstruction, based on data that have emerged from the head and neck reconstruction and hand surgery literature: PNAs have been successfully used to bridge gaps of greater than 5 cm in the inferior alveolar nerve [18, 19], and digital nerve repair with PNA demonstrates improved sensory outcomes when compared to repair with hollow conduits [20]. In the context of ABR and breast flap neurotization; however, further study is required to more comprehensively assess the efficacy of PNAs.

Alternatives to Abdominally-Based Free Flaps

Although the free DIEP flap—along with its abdominally-based variants—is widely accepted as the gold standard in autologous breast reconstruction, patient-specific considerations such as slender body habitus or prior abdominal surgeries may prohibit its use for some patients. As a result, numerous alternative donor sites have been considered in an effort to provide autologous options for all breast cancer patients. Other perforator flaps such as the profunda artery perforator (PAP), transverse upper gracilis (TUG), and superior gluteal artery perforator (SGAP) flaps are well-established alternatives to abdominally-based flaps, and have been in clinical use in substantial volumes for many years, but the last five years have seen an interest in innovating and popularizing other flap alternatives.

Lumbar Artery Perforator Flap

First described in 2003 in the form of a single case report by de Weerd et al. [21], the lumbar artery perforator (LAP) flap has gained more widespread acknowledgment recently as a useful approach to ABR [22] in patients with suboptimal abdominal donor sites. The LAP flap approach utilizes redundant skin and fat of the lumbar flank, which is reliably perfused by perforators originating from lumbar arteries branching directly off of the aorta. The surgical technique involves identification of the perforator, most typically originating from lumbar arteries at the L3 or L4 level [23], and subfascial dissection beneath the thoracolumbar fascia [24]; CT arteriography can help to identify the dominant perforator in the preoperative setting. Intramuscular dissection proceeds between the quadratus lumborum and paravertebral muscles, but should not be carried out beyond or between the vertebral transverse processes in order to avoid injury to lumbar spinal nerve roots.

This flap can be innervated using the superior cluneal nerves, which accompany the perforators, and may incorporate additional subcutaneous fat using superior and inferior beveling. Donor site closure lies in a plane that is continuous with a typical abdominoplasty closure. According to Opsomer et al., who have published the largest series of LAP flaps to date [22], pedicle length is short, averaging 4.5 cm, and caliber is frequently smaller than recipient vessels if internal mammary vessels are to be used. As such, interposition vein grafts are routinely used to limit donor site morbidity and facilitate recipient vessel anastomosis. Flap bulk is comparable to or larger than other nonabdominally-based alternatives, and secondary revision procedures occur with a frequency similar to the DIEP flap [25]. With regard to complications, incidence of arterial and venous thrombosis is higher in LAP flaps than DIEPs, likely due to small vessel caliber, and total flap loss rates are slightly higher but do not reach statistical significance.

Lateral Thigh Perforator Flap

The tensor fasciae latae (TFL) myocutaneous free flap was first proposed as a method of ABR by Elliott et al. in 1990 [26], and was refined into a perforator flap (based on the ascending branch of the lateral femoral circumflex artery) in subsequent years [27]. More recently, cadaveric and radiologic studies have documented the reliable presence of septocutaneous perforators traveling in the intermuscular septum between TFL and gluteus [28–30], suggesting that superolateral thigh skin and adipose tissue can be relatively easily harvested using a septocutaneous dissection.

Perhaps due in part to this revelation, the septocutaneous TFL free flap—simplified to "lateral thigh perforator" or LTP flap for ease of patient comprehension—has experienced increasing popularity in recent years. According to Tuinder et al., who have published a prospective series of 138 septocutaneous TFL free flaps—or, more simply, "lateral thigh perforator" or LTP flaps—this flap can be rapidly harvested for breast reconstruction, with total median operative times of 277 min for unilateral and 451 min for bilateral breast reconstructions [31]. In their series, flap weight was comparable to moderate-sized abdominally-based free flaps, ranging from 175 to 814 g with a median weight of 348 g, and pedicle length was 6 to 8 cm. The authors made reference to an initially very high rate of donor site wound complications (40%), which was substantively decreased to 6.3% by limiting flap width to 6 cm; total flap loss rates were similar to abdominally-based flaps at 1.4%.

Stacked and Bi-pedicled Flaps

Another strategy for ABR for patients whose body habitus does not permit conventional abdominally-based free flaps is the use of multiple free flaps for reconstruction of a single breast, either as "stacked" flaps placed one on top of the other, or as abdominally-based conjoined bi-pedicled flaps.

The concept of the stacked flap is far from novel; double-island bi-pedicled TRAM flaps for unilateral breast reconstruction was described in 1985 by Ishii et al. [32], popularized by Hartrampf in 1991 [33], and further modified by Spear in 1994 [34], when the term "stacked flaps" was coined. Stacked free flaps were first described as being applied to breast reconstruction in 2002 [35], and today represent a commonly used strategy in patients for whom the volume of tissue necessary for breast reconstruction exceeds that which can reliably be provided by a single flap. When multiple flaps are being utilized for reconstruction of a single breast, vascular anatomy can be rearranged in numerous ways: in series (at the branch chain anastomosis, or "daisy-chained") [36]; with a vascular anastomosis at the medial or lateral row takeoff [35]; or with vascular anastomoses to each flap performed using a separate set of recipient vessels, with the secondary flap utilizing vessels including the subscapular system (thoracodorsal vessels and their branches), internal mammary perforators, and retrograde internal mammary vessels [37–39]. Anastomosis to the thoracodorsal vessels requires the preparation of a separate field in the axilla and introduces some difficulty with flap shaping and inset, and internal mammary perforators of adequate caliber are not reliably present. The retrograde internal mammary vessels avoid these pitfalls, and have been demonstrated to be reliable recipient vessels for the purposes of breast reconstruction [39–41]. As such, the antegrade and retrograde internal mammary vessels have become popular recipients for stacked flaps when retrograde vessel caliber is favorable. Among those who underwent stacked flap unilateral breast reconstruction, complications were statistically equivalent between those who had intra-flap anastomoses as compared to those who underwent antegrade-retrograde anastomoses to internal mammary vessels [42].

In light of the evidence supporting use of IM vessels, unilateral breast reconstruction using both hemiabdominal flaps together as a single bi-pedicled free flap has also become an increasingly utilized surgical option for patients with marginal abdominal donor sites. The conjoined bi-pedicled DIEP flap has the benefit of restoring the breast conus in addition to its footprint and skin envelope [43], with similar complication rates when compared to stacked or uni-pedicle flaps [44].

Advances in Preoperative Imaging for Surgical Planning

Advanced imaging techniques such as computed tomography (CT) and magnetic resonance (MR) angiography have contributed significantly to the adoption of flap techniques for autologous breast reconstruction, in part due to their role in facilitating a more comprehensive understanding of vascular anatomy; Rozen et al. performed a number of studies detailing the branching pattern of the inferior epigastric vascular axis which evolved into classification schemes for DIEP flaps [45–47]. In recent years, the utilization of CTA for surgical planning has become common, and is considered by some to be the gold standard for preoperative imaging. Preoperative CTA has been shown to reduce operative time and decrease complications including intraoperative bleeding and postoperative abdominal bulge in abdominally-based perforator flap breast reconstruction, and it has been suggested that it increases cost-effectiveness by driving down the costs associated with lengthy procedures [48–51]. Use of CTA may also result in more frequent use of single-perforator flaps [52], and can also identify patients whose candidacy for flap procedures has been adversely affected by congenital absence or surgical disruption of donor vessels.

Magnetic resonance angiography, or MRA, represents an alternative to CTA that obviates the need for ionizing radiation; contrast-enhanced MRA utilizing 3.0-T MR technology as described by Chernyak et al. [53] is an emerging technique that may represent a new horizon in preoperative imaging for surgical planning, given its ability to enhance both spatial and contrast resolution. However, to date, MRA has been slow to gain acceptance as a standard imaging modality for surgical planning, in part due to its comparatively high cost.

Laser-assisted indocyanine green (ICG) angiography has been widely applied in reconstructive surgery for assessment of perfusion, but has also demonstrated utility intraoperatively in autologous breast reconstruction for identifying the two-dimensional locations of perforators as they reach the skin surface [54]. However, the technology is only capable of illuminating vascular anatomy within millimeters of the skin surface, limiting the capability of ICG to clarifying three-dimensional (i.e., intramuscular) vascular anatomy [55].

Postoperative Flap Monitoring

Postoperative monitoring of breast free flaps, if managed adequately, can detect postoperative complications and create opportunities to salvage compromised flaps. Historically, the gold standard for monitoring involved a combination of clinical examination of the skin and Doppler ultrasound. In recent years, however, adjunctive technologies have been developed to assist with early detection of flap demise.

In the setting of completely buried free flaps, which prohibit the use of clinical examination of the skin, as in breast reconstruction following nipple sparing mastectomy, devices such as the Cook-Swartz Doppler and venous flow coupler devices have been demonstrated to be effective in detecting flap compromise [56]. However, it has been suggested that these devices may contribute to increased false-positive findings resulting in unnecessary reoperations, and that flow couplers in particular may cause vessel kinking, contributing to thrombosis and flap loss [57].

Noninvasive near-infrared spectroscopy (NIRS) tissue oximetry for postoperative monitoring of breast free flaps has been adopted in many surgical centers, and early data demonstrated a decrease in flap loss rates and an increase in flap salvage rates [58]. Subsequent study has also showed a decrease in the need for intensive care unit admission and specialized nursing, due to the automation of some monitoring functions and a concordant decrease in the reliance upon experienced nursing care [59]. Cost analysis of NIRS tissue oximetry has shown a cost savings of between $1337 and $1667 per flap when these factors are taken into consideration [59–61], but relatively high material costs and false-positive rates may be preventing widespread adoption of this technique.

Superimposed on these advances in flap monitoring has been a gradual acceptance that free flap monitoring protocols can be effectively shortened without adverse consequences. Numerous independent analyses have demonstrated that circulatory issues contributing to flap compromise are largely identified within the first postoperative day [62, 63], prompting the development of many postoperative care protocols that aim for discharge on postoperative day #2 or #3 [64], facilitated in part by the promotion of enhanced recovery pathways.

Enhanced Recovery After Surgery

Many of the recent advancements in autologous breast reconstruction have pertained to development and refinement of surgical techniques. However, in recent years there has also been an important innovation that has significantly improved the management of patients undergoing autologous breast reconstruction: Enhanced Recovery After Surgery (ERAS) protocols.

ERAS protocols aim to facilitate recovery in surgical patients by means of a multimodal and multidisciplinary approach to the management of analgesia, anesthesia, fluids, mobilization, and nutrition. By employing an array of different analgesic classes that have varying mechanisms of action, postoperative pain management is optimized. Medications that are typically used include acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and gabapentin, usually in combination with regional anesthetic techniques. One important consequence of these regimens is that the need for opioids is greatly reduced. In addition, preoperative optimization of patients including their nutritional status, intraoperative goal-directed fluid management, and early postoperative resumption of diet and mobilization all collectively serve to aid recovery [65].

Patients undergoing cardiothoracic, colorectal, and urologic surgery were among the first to be managed using ERAS protocols. Studies in these subspecialties, which include high levels of evidence such as randomized controlled trials, found that these protocols decreased opioid use and reduced length of stay without increasing readmissions. Soon after, these concepts were applied to patients undergoing breast reconstruction [66]. In the setting of microsurgical reconstruction, ERAS protocols have been found to decrease length of stay, cost, and inpatient opioid use without increasing complications [67, 68]. For example, in a study of 91 consecutive patients undergoing DIEP flap breast reconstruction, Afonso et al. found that these protocols reduced length of stay by one day and opioid consumption by approximately one-third [69]. Earlier hospital discharge is unlikely to have a negative impact on identifying and treating vascular compromise of breast free flaps, which generally occurs within the first 24 h postoperatively [70]. Moreover, these beneficial effects on opioid use and recovery have also been observed to extend into the outpatient setting following hospital charge [71]. Accordingly, ERAS protocols have now rightfully found their place in the standard of care in patients undergoing autologous breast reconstruction [72].

With respect to the relationship between ERAS protocols and cost of care, there have thus far been relatively few studies. However, existing research has found that ERAS seems to overall decrease cost [73]. For example, Mericli et al. pooled five studies involving 986 patients undergoing microvascular breast reconstruction, and reported that even though there were increased costs associated with medications and personnel, that overall costs were lower [74]. Further study is necessary to determine to what degree these cost savings may be offset by new technologies like nerve grafts and monitoring devices.

Timing of Autologous Reconstruction in Patients Receiving Postmastectomy Radiation Therapy

Historically, reconstructive surgeons have often favored delaying autologous breast reconstruction in patients who are at increased likelihood to receive postmastectomy radiation therapy (PMRT) [75]. The rationale for this approach has traditionally been that delayed reconstruction in these patients avoids the potential for radiation-induced fibrosis, fat necrosis, and contracture in a breast reconstruction that can be difficult or impossible to repair. This line of thinking has led to previously described strategies such as delayed-immediate breast reconstruction, as well as use of models that predict the likelihood for PMRT [76].

Recent studies have rekindled the debate on whether immediate versus delayed autologous breast reconstruction should be performed in patients receiving PMRT. Kelley et al. performed a systematic review of 20 articles that examined autologous breast reconstruction in patients receiving PMRT [77]. They found similar pooled rates of flap loss, fat necrosis, and wound healing complications between patients who underwent reconstruction before versus after PMRT. However, they did identify a 27% rate of flap contracture and fibrosis in flaps that were exposed to radiation therapy. In a prospective study utilizing the Mastectomy Reconstruction Outcomes Consortium (MROC) study data, Billig et al. examined 108 patients who underwent immediate and 67 patients who underwent delayed autologous breast reconstruction in the setting of PMRT [78]. After a follow-up of 2 years, they found that complication rates were similar between the two groups, as were patient-reported outcomes as measured by the BREAST-Q questionnaire. Collectively, these studies indicate that immediate autologous breast reconstruction in patients who will receive PMRT may be reasonable, and that each case should be considered individually, including the availability of autologous donor sites and patient preferences.

Epidemiologic Trends in Autologous Breast Reconstruction

Breast cancer incidence continues to climb in the USA, with projections suggesting that it will surpass all other cancers during this calendar year, according to the National Cancer Institute's Surveillance, Epidemiology, and End Results study [79]. Retrospective analysis of surgical management of breast cancer from 1998 to 2011 demonstrated a significant increase in mastectomy rates, even among early-stage cancer patients eligible for breast conservation surgery (BCS) [2]. Data from the Nationwide Inpatient Sample database show that immediate postmastectomy reconstruction rates have also trended higher over a similar time period, rising from 20.8 percent in 1998 to 37.8 percent in 2008, representing a 78 percent increase [80]; this is credited in part to successful legislative initiatives supporting breast reconstruction awareness [81]. Nonetheless, despite a growing body of evidence supporting improved quality of life and patient-reported outcomes with autologous reconstruction techniques [82–84], there has been a relative decline in the proportion of patients pursuing autologous breast reconstruction (ABR): the number of ABR procedures performed in recent years has plateaued [80], while implant-based reconstructive techniques have become significantly more prevalent [85].

The explanation for this paradoxical trend is likely multifactorial. Modern autologous reconstructive techniques require microsurgical expertise and specialized equipment, and as such, they exist predominantly at academic centers [86]; the number of academic centers capable of performing these procedures, and thus the capacity for performing them, is unlikely to have changed appreciably over this time period. Physician reimbursement is a possible contributing factor to stagnating autologous reconstruction rates; on an hourly basis, average physician reimbursement for autologous reconstruction is two-thirds lower for autologous reconstruction than for implant-based procedures [87]. On a per-procedure basis, ABR reimbursements have plateaued, whereas implant-based reimbursement has trended upward [88, 89]. Emerging data also suggest a more recent increase in incidence of BCS including oncoplastic approaches to partial mastectomy, with a corresponding decrease in mastectomy incidence [90]. Additional study is required to quantify the impact of this trend on the incidence of ABR.

Conclusions

Autologous techniques remain a cornerstone of breast reconstruction in patients undergoing mastectomy. Recent advances in ABR have refined existing techniques, broadened the array of donor site options available to reconstructive surgeons, and streamlined the management of patients undergoing these procedures. Plastic surgeons continue to work toward being able to offer all patients undergoing mastectomy the prospect of a natural and functional breast reconstruction outcome with minimal morbidity.

Author Contributions Geoffroy C. Sisk, MD, and Albert H. Chao, MD, both contributed significantly to literature review and manuscript preparation.

Funding None.

Compliance with Ethical Guidelines

Conflict of interest All authors declare that they have no conflict of interest.

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Recently published papers of particular interest have been highlighted as:
• Of importance
•• Of major importance

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