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Breast Reconstruction and Adjuvant Therapy: A Systematic Review of Surgical Outcomes

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Background and Objectives: The impact of adjuvant therapy on the surgical outcomes following breast reconstruction is poorly understood. The purpose of this systematic review was to evaluate surgical outcomes following autologous and prosthetic reconstruction in the setting of post-mastectomy radiation therapy (PMRT) and adjuvant chemotherapy.

Methods: A systematic review of the English literature published from 2000 to 2015 in the Pubmed/MEDLINE database was performed to identify all manuscripts reporting outcome of breast reconstruction in patients receiving PMRT and/or adjuvant chemotherapy.

Results: Sixty-two manuscripts met the criteria for inclusion. This included 56 manuscripts (5437 patients) evaluating patients treated with PMRT and 11 manuscripts (820 patients) evaluating patients treated with chemotherapy. Pooled analysis of the PMRT cohort revealed significantly higher weighted incidences of re-operation ($P < 0.0001$), total complications ($P < 0.0001$), and reconstructive failure ($P < 0.0001$) in prosthetic reconstruction compared to autologous. There was little evidence to suggest that postoperative chemotherapy is associated with poorer overall outcomes.

Conclusions: PMRT was associated with an increased incidence of adverse events when compared to chemotherapy. There was little evidence to suggest that adverse events following breast reconstruction were related to adjuvant chemotherapy. Manipulating the method and timing of reconstruction may mitigate some of the undesirable outcomes associated with PMRT.

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KEY WORDS: **mammaplasty; radiotherapy; chemotherapy; complications**

INTRODUCTION

Adjuvant therapy in women with locally advanced breast cancer has been demonstrated to improve patient survival and reduce local recurrence [1–3]. With our enhanced understanding of tumor biology, surgical, medical, and radiation oncologists have been able to optimize treatments by working in harmony with one another. Medical oncologists have a variety of chemotherapeutic agents that disrupt cellular functions and effectively shrink or eradicate tumors. Radiation oncologists are able to fractionate delivery systems and optimally target tumors of the breast. Surgical oncologists have emphasized tumor and parenchymal resection focused on margin control with optimal preservation of the skin and nipple areolar complex.

Breast reconstruction following partial or total mastectomy has further enhanced the overall outcome of the breast cancer patient; however, the effects of adjuvant therapy, such as chemotherapy and radiation therapy on the reconstructed breast remain controversial. Studies evaluating these therapies on the oncologic and aesthetic outcomes following breast reconstruction are mixed [4–6]. Several studies have demonstrated that breast reconstruction can improve patient satisfaction and quality of life, particularly in regard to psychological and aesthetic domains of validated patient reported outcomes [7,8]. Other studies have demonstrated that PMRT following breast reconstruction may compromise aesthetic outcomes as well as increase complication rates for both implant and autologous reconstructions [6,9–12]. Despite the oncologic benefits of adjuvant chemotherapy, it is associated with varying degrees of toxicity, immunosuppression, and compromised wound healing. Other untoward effects, such as postoperative infection, delayed healing, and fat necrosis have also been associated with adjuvant chemotherapy after breast reconstruction but much of the literature is conflicting [6,13,14].

Reconstructive surgeons have used a variety of algorithms in order to mitigate the impact of adjuvant therapies on breast reconstruction, yet controversy remains over how to best optimize outcomes [10,15,16]. Options for autologous reconstruction are based on whether the reconstruction is performed immediately or on a delayed or staged delayed basis. Delayed autologous and two-staged delayed-immediate autologous reconstruction have been utilized by some surgeons to decrease the soft tissue effects of PMRT [16–18]. Immediate autologous reconstruction is also performed because some plastic surgeons do not feel that the PMRT effects are deleterious to the reconstruction [19]. Device-based reconstruction can be offered to patients as a single or two-stage procedure. Advocates for the two-stage technique cite the ability to revise any asymmetries or radiation effects following tissue expander removal, and because patients can change their mind from autologous to implant-based reconstruction or vice versa prior to the second procedure [20].

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The purpose of this systematic review is to assimilate the relevant literature and assess surgical outcomes, reconstructive failures, and the likelihood of adverse events. The goal is to provide surgeons with a foundation of knowledge to assess the risks associated with adjuvant therapy on breast reconstruction following mastectomy. The endpoint was to evaluate outcomes following autologous and device-based breast reconstruction in the setting of PMRT and adjuvant chemotherapy and to determine if there was an optimal timing for breast reconstruction.

MATERIALS AND METHODS

A systematic search of the literature published from January 1, 2000 to June 8, 2015 was performed to identify all relevant articles on PubMed/MEDLINE. The search entry "breast reconstruction AND (radiation OR irradiation OR radiotherapy OR chemotherapy)" was used. Inclusion criteria included studies that reported complications or reconstructive failures following post-mastectomy breast reconstruction in the setting of PMRT and/or adjuvant chemotherapy. Exclusion criteria included studies that contained less than 20 patients and those that lacked relevant extractable data. Studies were excluded if it was not clear whether patients received radiation or chemotherapy after mastectomy. Included studies were screened for potential citations not captured in the aforementioned search.

The specific variables included patient demographics, method of reconstruction, timing of adjuvant therapy, complications, and rates of reconstructive failure. Demographic data were extracted from the PMRT and adjuvant chemotherapy cohorts. When the demographic data for the specific cohorts receiving adjuvant therapy were not specified, the cumulative demographic data were used. For the PMRT studies, a pooled analysis using study size weighted means was performed. If only the median was reported, then a Gaussian distribution was assumed and the medians were equated to means.

Data were reported based on type of reconstruction that was device-based or autologous. Patients that had a combined prosthesis with a flap (i.e., latissimus dorsi and implant) were included in the device-based population. Capsular contracture was defined as a grade III/IV contracture on the Baker or modified Spear–Baker classification. If the grade was not specified, capsular contracture was omitted from data collection. Statistical analysis was performed using a two-tailed chi-squared test with statistical significance defined as a P value less than 0.05.

RESULTS

Results from the initial search identified 1,825 potential studies. Screening yielded 352 studies for abstract review. A total of 159 abstracts were selected for full text review, of which 62 met criteria for study inclusion (Fig. 1).

Post-Mastectomy Radiation Therapy

Fifty-six articles reported findings on breast reconstruction in the setting of PMRT, yielding a total of 5,437 patients. The mean patient age was 47.3 years and the mean body mass index (BMI) was 25.7 kg/m^2. Mean follow-up was 37.6 months. Of these patients, 3,605 underwent implant-based reconstruction. The remaining cohort of patients (n = 1,832) had autologous reconstruction. Patient demographics for the implant-based patients are listed in Table I. Within the device-based cohort, 87.3% of patients had a two-stage reconstruction that included a temporary tissue expander followed by replacement with a permanent implant, 1.8% of patients had a latissimus dorsi (LD) flap combined with an implant, and 0.8% of patients had immediate direct to permanent implant reconstruction. In 10.1% of the device-based patients, the specific method was not specified. PMRT was applied to the tissue expander in 53.3% and to the permanent implant (PI) in 30.5%. The timing of PMRT was not specified in 16.1% of patients.

Patient demographics for the autologous patients are described in Table II. The specific reconstruction in this cohort included a transverse rectus abdominis myocutaneous (TRAM) flap in 54.8%, deep inferior epigastric perforator (DIEP) flap in 19.5%, latissimus dorsi (LD) flap in 1.7%, and an unspecified or other flap (i.e., superficial gluteal artery perforator or superficial inferior epigastric artery flap) in 24.0%. PMRT

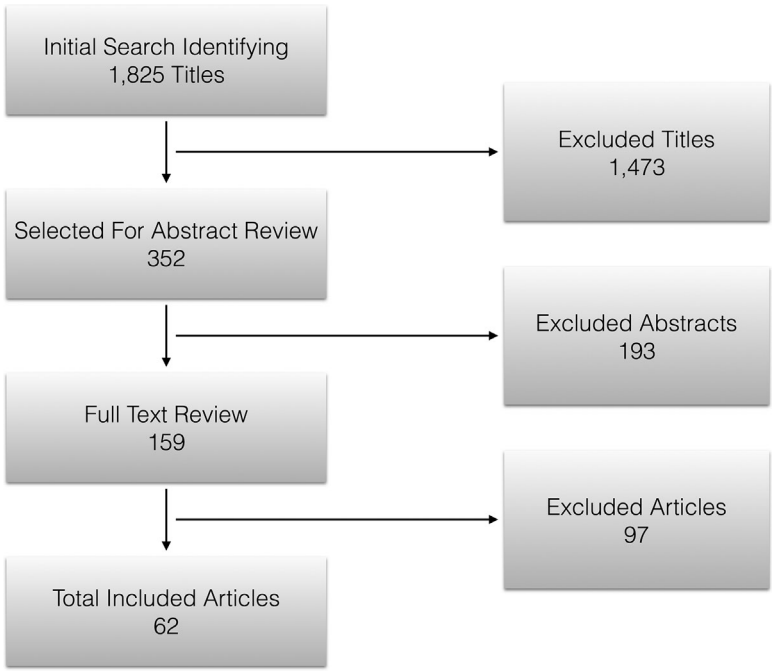

Fig. 1. Flowchart of the selection process for inclusion of articles in the systematic review.

TABLE I. Patient Demographics and Characteristics of Device-based Reconstruction in the Setting of PMRT

Characteristics	Value
No. of patients	3605
Mean age ± SD, yr	46.9 ± 2.2
Mean BMI ± SD, kg/m^2	24.9 ± 0.9
Method of Reconstruction	
TE/I, n (%)	3192 (87.3)
DTI, n (%)	28 (0.8)
LD combined with implant, n (%)	64 (1.8)
Not specified, n (%)	373 (10.1)
Timing of PMRT	
Applied to TE, n (%)	1951 (53.3)
Applied to PI, n (%)	1116 (30.5)
Not specified, n (%)	590 (16.1)
Adj. Chemotherapy, n (%)	1623 (70.8)
Mean follow-up ± SD, mo	38.8 ± 12.6

TE/I, two-stage temporary expander and susbsequent exchange to permanent implant. DTI, direct to permanent implant. PI, permanent implant. LD, latissimus dorsi.

was delivered before definitive reconstruction in 55.2% and after definitive reconstruction in 44.8% of patients.

The weighted mean of reported total complication rates was 35.5%. Thirty-five articles included complications and/or reconstruction failures in device-based reconstructions [4–6,10,11,21–50]. Twenty-seven articles included complications or reconstructive failures in autologous reconstructions [4,5,9,12,15–19,28,39,40,50–64]. A detailed analysis of complications is depicted by method of reconstruction in Table III.

A comparison of complications between device-based and autologous reconstructions in the setting of PMRT demonstrated that device-based reconstruction had a significantly higher incidence of infection (13.5% vs. 5.8%; $P < 0.0001$), mastectomy flap necrosis (10.5% vs. 5.0%; $P = 0.03$), re-operation due to complication (37.0% vs. 16.6%; $P = <0.0001$), and total complications (41.3% vs. 30.9%; $P < 0.0001$). Autologous reconstruction had a significantly increased incidence of wound related complications (5.8% vs. 12.9%; $P = 0.001$), hematoma (2.8% vs. 6.1%; $P = 0.02$), and seroma (6.0% vs. 8.0%; $P = 0.02$).

TABLE II. Patient Demographics and Characteristics of Autologous Reconstruction in the Setting of PMRT

Characteristics	Value
No. of patients	1832
Mean age ± SD	48.1 ± 3.4
Mean BMI ± SD	27.6 ± 1.3
Timing of definitive reconstruction	
Immediate, n (%)	655 (34.9)
Delayed, n (%)	833 (44.3)
Delayed-immediate, n (%)	195 (10.4)
Not specified, n (%)	195 (10.4)
Method of reconstruction	
TRAM, n (%)	1030 (54.8)
DIEP, n (%)	367 (19.5)
LD, n (%)	31 (1.7)
Not specified/other, n (%)	450 (24.0)
Timing of PMRT	
Before definitive reconstruction, n (%)	1037 (55.2)
After definitive reconstruction, n (%)	841 (44.8)
Adj. Chemotherapy, n (%)	266 (68.0)
Mean follow-up ± SD, mo	33.5 ± 14.9

Delayed-immediate, temporary expander placed at time of mastectomy followed by definitive reconstruction after conclusion of PMRT.
Delayed-immediate, temporary expander placed at time of mastectomy followed by definitive reconstruction after conclusion of PMRT. TRAM, transverse rectus abdominis myocutaneous flap.
DIEP, deep inferior epigastric perforator. LD, latissimus dorsi flap.

TABLE III. Complications Based on Method of Reconstruction

Complication	Device-based, % (n)	Autologous, % (n)	*P*-value
Hematoma	2.75 (23)	6.09 (21)	0.02
Seroma	5.95 (52)	8.00 (34)	0.02
Infection	13.51 (141)	5.79 (42)	<0.0001
Wound dehiscence/ delayed wound healing	5.77 (19)	12.89 (46)	0.001
Capsular Contraction[a]	38.02 (511)	—	—
Flap fibrosis	—	30.32 (104)	—
Mastectomy Flap Necrosis	10.49 (82)	5.01 (20)	0.03
Fat necrosis	—	15.15 (137)	—
Partial Flap Loss	—	4.31 (35)	—
Exposure/extrusion	5.19 (46)	—	—
Reoperations	36.95 (470)	16.58 (124)	<0.0001
Reconstructive Failure[b]	16.84 (560)	1.59 (19)	<0.0001
Total Complication Rate	41.32 (380)	30.91 (361)	<0.0001

[a]Includes reported grade III and IV Baker capsular contraction and grade III and IV modified Spear–Baker capsular contraction only.
[b]Reconstructive failure was defined as loss of implant/expander or total flap loss as a result of vascular complication.

Reconstructive failure was defined as loss of the tissue expander or permanent implant in device-based reconstruction or total flap loss in autologous reconstruction. Reconstructive failure had a weighted incidence of 16.8% in device-based reconstruction and 1.6% in autologous reconstruction with PMRT ($P < 0.0001$). A subgroup analysis of reconstructive failure based on the timing of PMRT in relation to device based reconstruction demonstrated a significant increase when PMRT preceded definitive implant reconstruction (radiation to the tissue expander) when compared to PMRT following definitive implant reconstruction (radiation to the permanent implant) (18.8% vs. 14.7%; $P = 0.006$). With regard to autologous reconstruction, subgroup analysis demonstrated a trend towards reconstructive failure when PMRT preceded definitive reconstruction compared to radiation after autologous reconstruction without reaching statistical significance (2.2% vs. 0.6%; $P = 0.07$).

Adjuvant Chemotherapy

Eleven studies (820 patients) met inclusion criteria and reported findings of breast reconstruction in the setting of adjuvant chemotherapy. All were retrospective reviews that varied with respect to the type of chemotherapeutic agent, dosage administered, and timing of administration (Table IV). Mean time of chemotherapeutic administration was unable to be quantified due to a paucity of data and lack of reporting. Compelling evidence to suggest postoperative chemotherapy was associated with diminished overall outcomes was lacking. Eight studies (566 patients) reported total complication rates or reconstructive failure rates that ranged from 16–54% and 0–32%, respectively [6,44,47,48,50,65–67]. Six studies (435 patients) demonstrated no increase in the rate of complications or reconstructive failures when compared to cohorts not receiving adjuvant chemotherapy [44,47,48,50,65,67]. In a single study, an increase in reconstructive failure and overall complication rate was noted in 41 patients that had adjuvant chemotherapy [6]. However, it should be noted that 92.7% of those patients also received PMRT. Four studies (227 patients) reported inconsistent rates of infections ranging from 0–44% [13,65–67]. Three studies (183 patients) reported rates of skin necrosis ranging from 0–15% [65–67]. One study reported a 1.74 odds ratio of mastectomy flap necrosis in women receiving postoperative chemotherapy; however, this did not reach statistical significance with multivariate regression analysis [68]. A relative risk of 4.8 for fat necrosis was reported in women that received adjuvant chemotherapy after

TABLE IV. Studies in Which Patients Underwent Breast Reconstruction in the Setting of Adjuvant Chemotherapy

Author	Study type	No. of cases	Follow up (mo)	Patient age	Method of reconstruction	PRMT	Timing of Chemotherapy	Timing of Chemotherapy	Complication
Baschnagel et al. 2012	Retrospective	48	24.1*	45*	TE/I	100%	N/A	N/A	21% reconstruction failure
Rey et al. 2005	Retrospective	23	12.3	44	76% definitive implant, 16% TE/I	69.50%	High Dose Chemotherapy	After immediate reconstruction; prior to exchange if exchange occured	13% infection, 21.7% capsular contraction, 0% local necrosis 36% complication rate
		67	12.9	46	70.7% definitive implant, 18.6% TE/I	70%	Conventional Chemotherapy	After immediate reconstruction; prior to exchange if exchange occured	2.9% infection, 16.4% capsular contraction, 0% local necrosis. 16% total complication rate
Nahabedian et al. 2003	Retrospective	44	29	48.2	TE/I	N/A	N/A	N/A	11.4% infection,
Abedi et al. 2014	Retrospective	147	N/A	N/A	pTRAM, DIEP TE/I, definitive implant	N/A	N/A	N/A	19.0% mastectomy flap necrosis
Peled et al. 2010	Retrospective	41	19.2	48.2	78% TE/I, 20% pTRAM, 2% DIEP	N/A	67% doxorubicin hydrochloride/ cyclophosphamide followed by paclitaxel.	4-6 weeks after immediate reconstruction	0% Hematoma, 44% infection, 15% skin necrosis, 22% loss of implant/expander, 0% flap loss, 32% unplanned return to OR
Li et al. 2014	Retrospective	48	14.9*	42*	TRAM or DIEP	N/a	include anthracyclines, cyclophosphamide,taxanes FU, paclitaxel	After breast reconstruction	52.1% fat necrosis
		15	14.9*	42*	TRAM or DIEP	N/a	include anthracyclines, cyclophosphamide, taxanes, FU paclitaxel	Before breast reconstruction	13.3% fat necrosis
Berry et al. 2010	Retrospective	181	N/A	50.3	LD, fTRAM, p TRAM, DIEP	N/a	N/a	Post-operative	29.3% total complication rate
Tallet et al. 2003	Retrospective	41	25*	51.5	TE/I	92.70%	N/A	Prior to exchange	32% reconstruction failure, 54% total complication rate
Fowble et al. 2015	Retrospective	44	45.6*	44*	TE//I	100%	primarily doxorubicin or taxane-based regimens	N/a	15.9% reconstruction failure
Jimenz-Puente et al. 2011	Retrospective	69	25.5	49.6	Permanent expander or TE/I	N/A	AC, FEC, AC-T	N/a	21.5% reconstruction failure
Caffo et al.	Retrospective	52	N/a	48	48.1% permanent expander or 53.9% TE/I	N/A	57.7% CMF, 40.4% EPI/CMF, 1.9% FEC	during expansion	0% necrosis, 0% infection, 0% contraction, 0% extrusion, 7.7% seroma, 0% loss, 3.8% rupture

FU, fluorouracil; AC(-T), adriamycin, cyclophosphamide (docetaxel); FEC, fluorouracil, epirubicin, and cyclophosphamide; CMF, cyclophosphamide, methotrexate, fluorouracil; EPI/CMF, epirubicin followed by CMF.
*Median.

immediate free flap reconstruction [14]. Overall, the majority of studies indicate that breast reconstruction preceding adjuvant chemotherapy can be well tolerated; however, the heterogeneity amongst the studies included makes it difficult to draw any definitive conclusions.

DISCUSSION

Breast reconstruction following mastectomy is increasing at the rate of 5%/year and has provided a significant improvement in most quality of life measures [7,8,69]. Adjuvant therapies have become an integral component in the treatment of breast cancer as they have provided a significant reduction in local recurrence and increase in disease free survival [1–3]. Understanding the dynamics between these management strategies is important for clinicians and patients in order to facilitate the decision making process and provide the best possible outcome. The purpose of this study is to review the existing literature with regard to breast reconstruction, PMRT, and adjuvant chemotherapy and to highlight differences in outcome between device-based and autologous breast reconstruction in the setting of these adjuvant therapies.

Device-based reconstruction is now the most common method of reconstruction in patients who receive PMRT [70]. Despite improvements in surgical technique and device manufacturing, complications requiring reoperation were 37% and reconstructive failure was 16.8% in this study. Strategies to reduce the incidence of unplanned reoperation and reconstructive failure have been implemented and are principally focused on the timing of PMRT relative to the type of device. In a study focused on the timing of PMRT, Cordeiro et al. compared 94 patients that had PMRT in the setting of tissue expanders to 210 patients that had PMRT in the setting of permanent implants [37]. The reported reconstructive failure rates were 18.1% with PMRT to tissue expanders and 12.4% with PMRT to permanent implants. The group with the irradiated permanent implants had significantly increased Grade III and IV capsular contracture rates (44.6% v. 15.9%). In a similar study, Nava et al. compared PMRT in the setting of tissue expanders and to permanent implants and reported reconstructive failures in 40% and 6.4%, respectively [33]. These statistics are consistent with our pooled analysis demonstrating that PMRT to permanent implants reduces the rate of reconstructive failure (18.8% vs. 14.7%).

The timing of PMRT is also relevant to patients receiving autologous reconstruction; however, this has been marred with controversy. Some surgeons feel that, immediate autologous reconstruction should not be performed when PMRT is anticipated because of the potential for radiation induced flap fibrosis and contracture [12,51]. Other surgeons feel that the addition of well-vascularized tissue to the radiation field does not pose undesirable aesthetic or functional consequences [19]. In a comparative study, Tran et al. studied 32 patients with immediate free TRAM flap reconstruction before PMRT to 70 patients with delayed reconstruction after PMRT [17]. The immediate cohort had increased late complications including contracture (75% vs. 0%), volume loss (87.5% vs. 0%), and fat necrosis (43.8% vs. 8.6%), while the delayed group had a slightly higher incidence of partial flap loss (7.1% vs. 0%) and total flap loss (1.4% vs. 0%).

The delayed-immediate approach to autologous reconstruction was introduced in 2004 and has demonstrated success [71]. The principle governing the technique is that the PMRT should be directed to a temporary tissue expander that is placed at the time of the mastectomy constituting the immediate portion. Following the PMRT, the tissue expander is removed and replaced with a flap constituting the delayed portion. The goal of this strategy is to minimize the adverse PMRT consequences to the flap and to optimize the aesthetic outcome of the breast. To test the validity of this strategy, Patel et al. compared outcomes from two cohorts of patients. The first cohort had delayed-immediate reconstruction and the second had delayed autologous reconstruction [16]. The incidence of flap related complications in patients who underwent delayed-immediate reconstruction was similar to that of the delayed cohort; however, the rate of revision surgery was less with the delayed-immediate cohort, suggesting an improved overall aesthetic result. Other studies have demonstrated that delaying microvascular autologous reconstruction by at least one year following PMRT may result in decreased flap-related complications [54].

The impact of adjuvant chemotherapy on breast reconstruction remains unclear. The immunosuppressant and cytotoxic effects of chemotherapy have raised concerns of post-operative infection and compromised wound healing [72–74]. Of the studies included in this review, two reported a higher rate of infection in patients who received adjuvant chemotherapy as compared to those that did not [13,65]. Peled et al. found that 44% of 41 patients who received adjuvant chemotherapy after immediate breast reconstruction developed postoperative infections, significantly higher than those that received neoadjuvant chemotherapy or none at all [65]. Nahabedian et al. reported an 11.4% rate of infection that required prosthesis removal in 44 patients who received chemotherapy after implant-based reconstruction [13]. Although the rate was elevated as compared to the control, the difference was not statistically significant. Conversely, Caffo et al. evaluated 52 patients that received adjuvant chemotherapy during breast expansion and demonstrated no risk of infection and no added risk of device based morbidity. [67].

It is known that chemotherapy has adverse effects on normal host immunity [75]. Risk of infection may be related to the dose of adjuvant chemotherapy. Rey et al. compared outcomes of 23 patients who received a high-dose regimen of adjuvant chemotherapy with 67 patients who received conventional adjuvant chemotherapy [66]. The high-dose chemotherapy sample had a 13% rate of infection compared to a 2.9% rate for the conventional chemotherapy group. The differences in these studies may be partially due to the heterogeneity in treatment protocols and makes it difficult to draw strong conclusions. In terms of overall surgical success, the majority of studies indicate that adjuvant chemotherapy is not associated with increased complications or reconstructive failures [44,47,48,50,65,67]. This study has suggested that there are no significant contraindications to breast reconstruction in the setting of adjuvant chemotherapy. Prospective studies with larger sample sizes are needed to more precisely define the impact of adjuvant chemotherapy on breast reconstruction.

The strength of this study is its power and its ability to encompass multiple institutional experiences and various studies. However, there are several limitations, including retrospective study design and the biases within each of the studies included. Inconsistently reported data and scarce reporting of patient comorbidities also limited this study's potential. The majority of current studies report findings from a single institution, many of which differ in relevant factors such as the timing of adjuvant therapy from breast reconstruction and the dosing of adjuvant treatment. Outcomes are often heterogeneously reported precluding a true meta-analysis. Also, lastly some institutions may report similar patients in multiple studies, which could heavily bias our data in the direction of well-published authors (a form of publication bias). A benefit of this manuscript is that it gives a general perspective of outcomes to be expected when breast reconstruction is performed in the setting of adjuvant therapy. Admittedly, this study does not include all of the outcomes that deem breast reconstructions successful, including aesthetic outcome, and patient satisfaction. Rather, it reports the surgical success and long-term feasibility of breast reconstruction when PMRT or adjuvant chemotherapy is required. The authors acknowledge that there are many factors that contribute to a patient's decision when assessing methods of reconstruction. Based on this data, autologous reconstruction has a favorable profile with regards to complication and reconstructive failure; however, the importance of operative time, technical feasibility, patient comorbidities, and quality of life are important factors to consider. This systematic review identifies the complications related to the reconstructive approach thus stressing the importance of proper patient selection when contemplating breast reconstruction in the setting of adjuvant therapy.

CONCLUSIONS

Adjuvant therapy can impact the quality of breast reconstruction following mastectomy. PMRT is associated with a higher incidence of

adverse events compared to chemotherapy. Autologous reconstruction appears to better tolerate the effects of PMRT as compared to implant-based reconstruction. The timing of reconstruction in relation to PMRT may play a role in determining outcomes and may help to better achieve success with implant-based options. Future prospective studies are needed to more precisely define the impact of these adjuvant therapies on breast reconstruction.

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