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Autologous Breast Reconstruction after Mastectomy for Breast Cancer: A Systematic Review

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Background: Women undergoing autologous reconstruction (AR) after mastectomy for breast cancer and their surgeons must make decisions regarding timing of the AR and choose among various flap types. We conducted a systematic review to evaluate the comparative benefits and harms of (1) timing of AR relative to chemotherapy and radiation therapy, and (2) various flap types for AR.
Methods: We searched Medline, Embase, Cochrane CENTRAL, CINAHL, and ClinicalTrials.gov for studies, from inception to March 23, 2021, without language restriction. We assessed risk of bias of individual studies and strength of evidence (SoE) of our findings using standard methods.
Results: We screened 15,936 citations. Twelve mostly high risk of bias studies, including three randomized controlled trials and nine nonrandomized comparative studies met criteria (total N = 31,833 patients). No studies addressed timing of AR relative to chemotherapy or radiation therapy. Six flap types were compared, but conclusions were feasible for only the comparison between transverse rectus abdominus myocutaneous (TRAM) and deep inferior epigastric perforator (DIEP) flaps. The choice of either flap may result in comparable patient satisfaction with breasts and comparable risk of necrosis (low SoE for both outcomes), but TRAM flaps probably pose a greater risk of harm to the area of flap harvest (abdominal bulge/hernia and need for surgical repair) (moderate SoE).
Conclusions: Evidence regarding details for AR is mostly of low SoE. New high-quality research among diverse populations of women is needed for the issue of timing of AR and for comparisons among flap types. *(Plast Reconstr Surg Glob Open 2022;10:e4181; doi: 10.1097/GOX.0000000000004181; Published online 14 March 2022.)*

INTRODUCTION

More than 40% of women in the United States who undergo mastectomy for breast cancer have breast reconstruction,[1] amounting to about 107,000 women in 2019.[2] Approximately one in five (19%) reconstruction procedures in the United States involve autologous reconstruction (AR).[2] Once the decision to undergo AR is made, two main considerations are involved: the timing of the procedure relative to chemotherapy and radiation therapy, and the choice of flap. Flap types are generally described by the anatomic region from which the flap tissue is sourced, including the deep inferior epigastric perforator (DIEP; 52% of ARs), latissimus dorsi (LD; 22%), transverse rectus abdominis myocutaneous (TRAM; 21%), and other flaps (5%).[2] The options regarding source of the AR flap may be limited by the patient's body habitus, prior surgery, medical comorbidities, and preference. Each consideration regarding AR (timing and flap type) can have implications on aesthetics, complications, and cost.

Objectives

We conducted a systematic review (SR)[3] for the Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center Program to support the American Society of Plastic Surgeons in its effort to develop a new

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clinical practice guideline on breast reconstruction after mastectomy. Here, we focus on the SR's research questions concerning AR. Companion articles focus on implant-based reconstruction[4] and the comparison between implant-based reconstruction and AR.[5] All reports focus on women undergoing (or who have undergone) mastectomy for breast cancer treatment or prophylaxis. Here, we evaluate the comparative benefits and harms of (1) timing of AR relative to chemotherapy and radiation therapy, and (2) various flap types for AR. For (2), we compare different flap types (eg, DIEP versus TRAM flaps) and not within flap types (eg, free versus pedicled TRAM flaps). We also evaluate whether outcomes varied by age, stage of breast cancer, first versus recurrent occurrence, timing of reconstruction (immediate versus delayed), and laterality (unilateral versus bilateral).

METHODS

This report is part of a larger SR,[6] funded by AHRQ, addressing a range of research questions related to breast reconstruction after mastectomy. The SR followed Evidence-based Practice Center Program methodology for SRs of comparative effectiveness research.[7] The SR protocol was registered in PROSPERO (registration no. CRD42020193183).

The full details of the SR methodology are provided in a companion article[4] and in the full AHRQ report for the project.[6] Briefly, based on discussions with panels of stakeholders and experts, we developed eligibility criteria for the SR. We considered any comparative study [randomized controlled trials (RCTs), or nonrandomized comparative studies (NRCSs) with adequate statistical adjustment analyses) that evaluated timing of AR relative to chemotherapy and radiation therapy or compared any flap types [eg, DIEP, LD, TRAM, superficial inferior epigastric artery perforator (SIEA), lateral thoracodorsal (LTD), thoracodorsal artery perforator (TAP)]. Examples of benefit outcomes included psychosocial well-being, sexual well-being, and satisfaction with breasts. Examples of surgical complications included necrosis, thromboembolic events, and seroma.

We searched for published studies in Medline (via PubMed), Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), and CINAHL, and for unpublished studies in ClinicalTrials.gov, from database inception through March 23, 2021. We screened each identified record in duplicate using Abstrackr (http://abstrackr.cebm.brown.edu/). We extracted data from included studies into the Systematic Review Data Repository Plus (SRDR+) (http://srdrplus.ahrq.gov/). Data were extracted, and risk of bias was assessed by one researcher and confirmed by a second, independent researcher. We assessed strength of evidence (SoE) using AHRQ methodology.[8] When feasible, for continuous outcomes, we made conclusions based on published estimates of minimal clinically important differences (MCIDs).

RESULTS

For the full SR, our searches yielded 15,936 citations (Fig. 1). We screened 1352 full-text articles, of which 14 articles described 12 eligible studies for the current article.[9–22]

Takeaways

Question: What are comparative benefits and surgical complications of (1) timing of autologous (AR) relative to chemotherapy/radiation, and (2) various flap types for AR.

Findings: In a systematic review, 12 studies met criteria. No studies addressed timing. Six flap types were compared, but conclusions were feasible for only transverse rectus abdominus myocutaneous (TRAM) versus deep inferior epigastric perforator (DIEP). They may result in comparable patient satisfaction with breasts and comparable risk of necrosis, but TRAM probably increases risk of harm to area of flap harvest (abdominal bulge/hernia and need for surgical repair).

Meaning: Most evidence regarding AR options is of low strength.

Characteristics of Included Evidence

Published between 2000 and 2020, the 12 included studies comprised three RCTs[10–12,19] and nine NRCSs with adequate statistical adjustment analyses (Table 1).[9,13–18,20–22] The studies included a total of 31,833 women. Four studies were conducted in the United States, three in Canada, two in Sweden, one each in Denmark and the UK, and one in both the United States and Canada.

Most studies (67%–82%) did not report data about participant age, race, or body mass index (BMI) for the entire population. Where reported, average patient age ranged from 50.0 to 51.8 years (three studies), and average BMI ranged from 25.9 to 28.6 kg per m^2 (four studies). In the two studies that reported data, 70% and 82% of patients were White, and 12% and 13% were Black.[14,17,22] In the one study that reported data, all patients were being treated for their first occurrence of breast cancer, and all mastectomies were reported to be therapeutic.[10,11]

Risk of Bias

Two of the three RCTs had a high risk of bias and one had moderate risk. (**See tables, Supplemental Digital Content 1**, which display the risk of bias assessments. **http://links.lww.com/PRSGO/B961**.)

The primary concerns about bias in the RCTs were lack of blinding of participants and care providers and incompleteness of outcome data. Among the nine NRCSs, eight had a high risk of bias and one had a moderate risk (**Supplemental Digital Content 1**, **http://links.lww.com/PRSGO/B961**). The primary concerns about bias in the NRCSs were evidence of serious or critical risk of confounding and lack of blinding.

Timing of AR Relative to Chemotherapy and Radiation Therapy

No eligible studies evaluated timing of AR relative to timing of chemotherapy or radiation therapy.

TRAM versus DIEP Flaps

Eight NRCSs compared TRAM and DIEP flaps in a total of 27,076 patients (between 241 and 15,836 patients each) (Table 1). Seven NRCSs had a high risk of bias and one had a moderate risk.

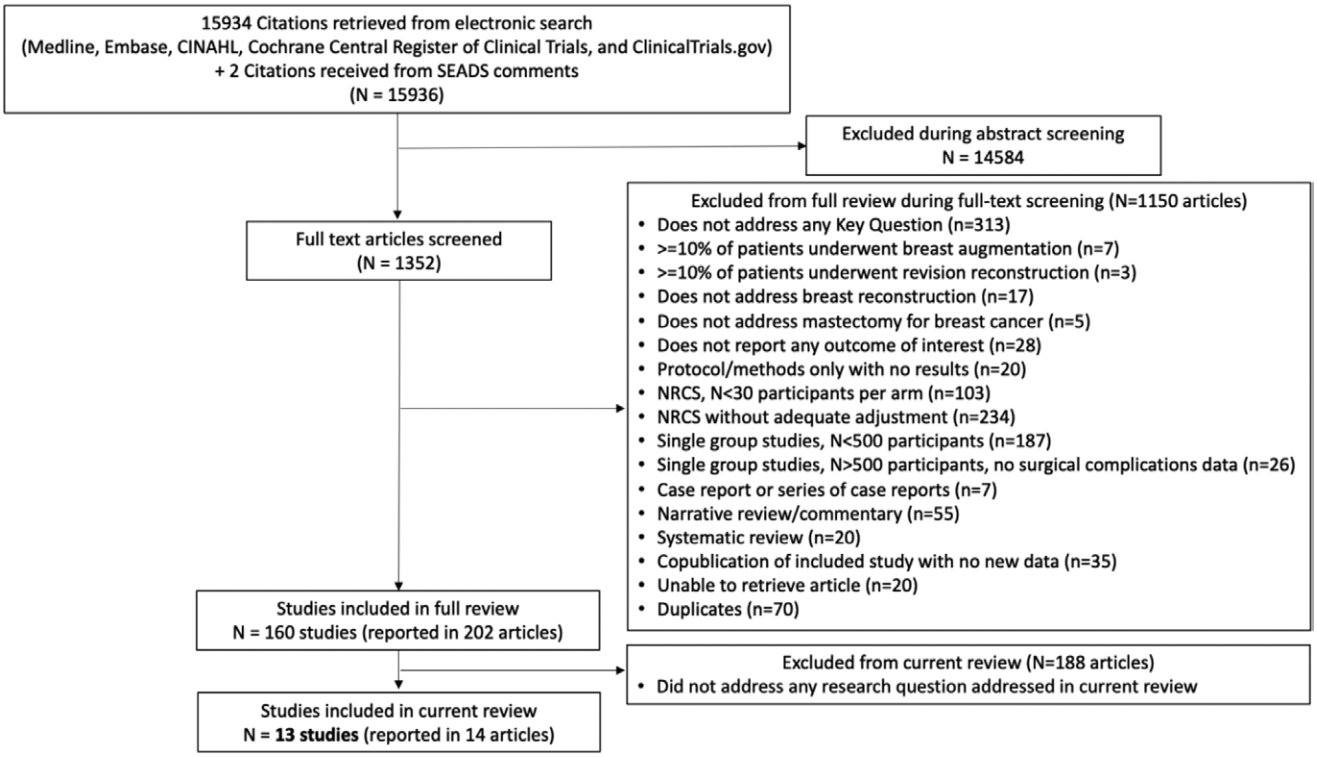

Fig. 1. PRISMA diagram depicting identification of studies in this systematic review.

Clinical/Benefit Outcomes: One NRCS (Erdmann-Sager et al[13]) reported data for physical well-being using the BREAST-Q (0–100; higher is better; MCID 3[23]) (**See tables, Supplemental Digital Content 2**, which displays summary tables for all outcomes. **http://links.lww.com/PRSGO/B962**.) Patients with DIEP flaps experienced clinically significant better abdominal physical function at 1 year than patients with TRAM flaps, whether free [adjusted mean difference (adjMD) 4.16, 95% confidence interval (CI) 0.02–8.33] or pedicled (adjMD 4.01, 95% CI 0.45–8.48). Similar results were observed at 2 years. However, chest and upper body physical function scores were comparable among flap groups at both time-points. The study also reported physical functioning and pain interference using the Patient-Reported Outcome Measurement Information System (PROMIS; 0–100; higher is worse; MCID 6[24]). Scores were comparable among flap groups at both 1 and 2 years.

Erdmann-Sager et al[13] also used the BREAST-Q to evaluate psychosocial well-being (MCID 4[23]) and sexual well-being (MCID 5[23]) (**Supplemental Digital Content 2-2**, **http://links.lww.com/PRSGO/B962**). For both outcomes, scores were comparable among flap groups at both 1 and 2 years.

Two NRCSs reported on patient satisfaction with breasts. Using the BREAST-Q (MCID 5[23]), Erdmann-Sager et al[13] reported that scores were comparable among flap groups at 1 and 2 years (**Supplemental Digital Content 2-2**, **http://links.lww.com/PRSGO/B962**). Yueh et al[20] reported categorical data on whether patients were satisfied with their breasts. The proportions of satisfied patients were comparable between DIEP and TRAM groups [adjusted odds ratio (adjOR) 0.67, 95% CI 0.37–1.23] (**Supplemental Digital Content 2-3 and 2-4**, **http://links.lww.com/PRSGO/B962**).

One NRCS (Yueh et al[20]) also reported that the proportions of patients satisfied with the surgical outcome were comparable (adjOR 0.82, 95% CI 0.33–2.01) (**Supplemental Digital Content 2-4**, **http://links.lww.com/PRSGO/B962**).

One NRCS (Zoghbi et al[22]) reported on duration of initial hospitalization. Women with TRAM flaps had statistically significant longer stays than women with DIEP flaps ($P < 0.001$; adjusted effect size not reported) (**Supplemental Digital Content 2-3**, **http://links.lww.com/PRSGO/B962**). Zoghbi et al[22] also reported that women with TRAM flaps had higher odds of an increased length of stay (adjOR 1.59, 95% CI 1.45–1.72) (**Supplemental Digital Content 2-4**, **http://links.lww.com/PRSGO/B962**).

Surgical complications (**Supplemental Digital Content 2-5**, **http://links.lww.com/PRSGO/B962**): Two NRCSs reported on necrosis. Abedi et al[9] reported that risks of mastectomy flap necrosis at 1.6–1.9 years were comparable between DIEP and TRAM groups ($P = 0.61$; adjusted effect size not reported). However, Kroll[16] reported that the risk of fat necrosis at 3 months was higher with DIEP flaps (adjOR 2.10, 95% CI 0.87–5.10), but this was not statistically significant.

Four NRCSs reported on harm to the area of flap harvest. Erdmann-Sager et al[13] reported that, at 2 years, compared with patients who underwent AR with DIEP flaps, patients who received free TRAM flaps had a lower risk of donor site complications (adjOR 0.52, 95% CI 0.27–1.02).

Table 1. Summary of Design, Arm, and Sample Details

Study, Publication Year, PMID, Country	Design (Funding) (Study Years)	Risk of Bias	Eligibility Criteria	Arm	Reconstruction Details (%)	N	Age (y), Mean (SD) or As Specified	Race (%)	Breast Cancer Occurrence %	Cancer Stage or Mastectomy Purpose (%)
Abedi et al,[9] 25003437, Canada	NRCS (none) (2003–2011)	High	I: BR	DIEP	NR	NR	NR	NR	NR	NR
				TRAM	Timing: imm (100)	NR	NR	NR	NR	NR
				Total	N/A	314	50 (8.2)	NR	NR	NR
Brandberg et al,[10] 10626972, Sweden	RCT (non-industry) (1994–1996)	High	I: age ≤79; free of recurrenceE: poorly controlled diabetes and secondary complications, immunosuppressive treatment, family history, or previous rheumatic disease	TRAM	Laterality: uni (100)Timing: del (100)Stages: >1 (100) Radio: timing NR (48)	29	52 (9.2)	NR	1st: 100	Ther (100)
				LD	Laterality: uni (100)Timing: del (100)Stages: >1 (100) Radio: timing NR (47)	30	54 (8.9)	NR	1st: 100	Ther (100)
				LTD	Laterality: uni (100)Timing: del (100)Stages: >1 (100) Radio: no (100)	16	52 (8.5)	NR	1st: 100	Ther (100)
				Total	N/A	75	NR	NR	1st: 100	Ther (100)
Brorson et al,[12] 32807615, Sweden	RCT (non-industry) (2008–2020)	High	I: age 18–60; unilateral mastectomy E: current smoker; BMI >30	DIEP	Laterality: uni (100) Timing: del (100) Stages: 1 (100) Chemo: before (91.2)	44	49.3 (6.4)	NR	NR	Stage 1 (6.5) Stage 2 (45.2) Stage 3 (48.4)
				LD	Laterality: uni (100) Timing: del (100)Stages: 1 (100) Chemo: before (75.0)	39	51.9 (8.3)	NR	NR	Stage 1 (2.9) Stage 2 (32.4) Stage 3 (64.7)
				Total	N/A	83	NR	NR	NR	NR
Erdmann-Sager et al,[13] 29019862, USA, Canada	NRCS (non-industry) (2012–2015)	Moderate	I: first-time, unilateral or bilateral BR	DIEP	Laterality: uni (57.8)/bi (42.2) Timing: imm (84)/del (16) Chemo: after (28.3)/no chemotherapy (71.7)Radio: before (22.5)/after (19.1)/none (58.4)	445	51.1 (8.8)	NR	NR	Ther (88.5), proph (11.5)
				TRAM	Laterality: uni (63.5)/bi (36.5) Timing: imm (76.5)/del (23.5) Chemo: after (46.5)/no chemotherapy (53.5)Radio: before (15.5)/after (36.6)/none (47.9)	115	52.2 (8.6)	NR	NR	Ther (91.3), proph (8.7)
				TRAM	Laterality: uni (80.9)/bi (19.1) Timing: imm (88.8)/del (11.2) Chemo: after (22.5)/no chemotherapy (77.5)Radio: before (30.3)/after (14.6)/none (55.1)	89	53.6 (8.5)	NR	NR	Ther (95.5), proph (4.5)
				SIEA	Laterality: uni (66.2)/bi (33.8) Timing: imm (91.5)/del (8.5) Chemo: after (11.3)/no chemotherapy (88.7)Radio: before (40)/after (1.7)/none (58.3)	71	53.3 (8.2)	NR	NR	Ther (91.5), proph (8.5)
				Total	N/A	791	NR	NR	NR	NR

(*Continued*)

Table 1. (*Continued*)

Study, Publication Year, PMID, Country	Design (Funding) (Study Years)	Risk of Bias	Eligibility Criteria	Arm	Reconstruction Details (%)	N	Age (y), Mean (SD) or As Specified	Race (%)	Breast Cancer Occurrence %	Cancer Stage or Mastectomy Purpose (%)
Knox et al,[15] 26267400, Canada	NRCS (NR) (2002–2013)	High	I: unilateral or bilateral AR with DIEP or pedicled TRAM flapE: history of abdominal hernia or bulge	DIEP	Laterality: uni (59.3)/bi (49.8) Timing: imm (63.1)/del (33.9)/mixed (3.1)Stages: 1 (100)Chemo: before (51.5)/after (9.2)/no chemotherapy (39.3)Radio: before (47.7)/after (7.7)/none (44.6)	130	49 (8.4); range 16, 72	NR	NR	Stage 0 (16.2), stage NR (77.7), proph (5.4)
				TRAM	Laterality: uni (82.2)/bi (17.8) Timing: imm (74.5)/del (24.9)/mixed (0.5)Stages: 1 (100)Chemo: before (48)/after (11.9)/no chemotherapy (40.1)Radio: before (45.6)/after (11.9)/none (42.5)	377	50.2 (8); range 29, 71	NR	NR	Stage 0 (28.7), stage NR (58.1), proph (1.3)
				Total	N/A	507	NR	NR	NR	NR
Kroll,[16] 10987463, USA	NRCS (NR) (1989–2000)	High	I: AR with DIEP/free TRAM flap	DIEP	NR	NR	NR	NR	NR	NR
				TRAM	NR	NR	NR	NR	NR	NR
				Total	N/A	241	NR	NR	NR	NR
Massenburg,[17] 26487657, USA	NRCS (NR) (2005–2012)	High	I: AR	TRAM	NR	2464	52 (9)	W (82.3), B (12.4), A (3.3), H (1.4), others (0.6)	NR	NR
				LD	NR	2085	52.8 (10.9)	W (83.8), B (12.2), A (2.6), H (0.4), others (0.7)	NR	NR
				Total	N/A	4549	51.8 (9.7)	W (82.3), B (13), A (3.4), H (0.7), others (0.6)	NR	NR
Mennie et al,[18] 25839173, UK	NRCS (industry; non-industry) (2006–2012)	High	I: ARE: other types of immediate or delayed BR	DIEP	Laterality: uni (87.6)/bi (12.4)Stages: 1 (100)	5144	NR	NR	NR	NR
				TRAM	Laterality: uni (91.9)/bi (8.1)Stages: 1 (100)	1963	NR	NR	NR	NR
				TRAM	Laterality: uni (91.3)/bi (8.7)Stages: 1 (100)	922	NR	NR	NR	NR
				Total	N/A	7929	16–45 y (29.2%), 46–50 y (23.4%), 51–55 y (20.5%), 56–60 y (13.9%), ≥60 y (13%)	NR	NR	NR
Rindom et al,[19] 31515191, Denmark	RCT (industry) (2013–2015)	Moderate	I: age ≥18, unilateral, delayed BR	LD	Laterality: uni (100)Timing: del (100)Stages: 1 (100) Chemo: timing NR (77.78)Radio: timing NR (50)	25	54.2; range 41, 71	NR	NR	Ther (94.45), proph (5.55)
				TAP	Laterality: uni (100)Timing: del (100)Stages: >1 (13.64) Chemo: timing NR (68.18)Radio: timing NR (77.27)	25	55.8; range 35, 70	NR	NR	Ther (100)
				Total	N/A	50	NR	NR	NR	

(*Continued*)

Table 1. (*Continued*)

Study, Publication Year, PMID, Country	Design (Funding) (Study Years)	Risk of Bias	Eligibility Criteria	Arm	Reconstruction Details (%)	N	Age (y), Mean (SD) or As Specified	Race (%)	Breast Cancer Occurrence %	Cancer Stage or Mastectomy Purpose (%)
Yueh et al,[20] 19228537, USA	NRCS (non-industry) (1996–2006)	High	I: therapeutic or prophylactic mastectomyE: BR for breast augmentation only	DIEP TRAM LD Total	Stages: 1 (100) Stages: 1 (100) Stages: 1 (100) N/A	420 143 112 675	NR NR NR NR	NR NR NR NR	NR NR NR NR	NR NR NR NR
Zhong et al,[21] 24675183, Canada	NRCS (non-industry) (2009–2012)	High	I: AR with DIEP or free TRAM flaps	DIEP TRAM Total	Stages: 1 (100) Stages: 1 (100) N/A	244 48 292	NR NR 50.1 (8.6)	NR NR NR	NR NR NR	NR NR NR
Zoghbi et al,[22] 28052051, US	NRCS (none) (2010–2011)	High	I: AR with DIEP or free TRAM flaps	DIEP TRAM Total	NR NR N/A	9699 6137 15836	50 (13) 50 (13) 50 (13); median 50	W (70.8), B (11.2), A (3.6), H (10.9), others (3.5) W (67.2), B (13.8), A (3.7), H (11.3), others (3.6) W (69.5), B (12.2), A (3.6), H (11.1), others (3.6)	NR NR NR	NR NR NR

Laterality: whether the reconstruction was unilateral ("uni") or bilateral ("bi"). Stages: Whether the reconstruction was completed in 1 stage or >1 stages. Timing: timing of reconstruction relative to mastectomy, ie, immediate ("imm") or delayed ("del"). Chemo: timing of chemotherapy relative to reconstruction.
A, Asian; B, Black; BR, breast reconstruction; E, exclusion criteria; H, Hispanic; I, inclusion criteria; IQR, interquartile range; N/A, not applicable; NR, not reported; PMID, PubMed identifier; proph, prophylactic; ther, therapeutic; W, White.

However, DIEP and pedicled TRAM flaps were associated with comparable risks. The other three NRCSs reported greater risks with TRAM flaps: abdominal bulge/hernia (Knox et al[15]: adjOR 5.2, 95% CI 1.3–20.9; and Zhong et al[21]: adjOR 2.73, 95% CI 1.01–7.07) and needing hernia repair surgery (Mennie et al[18]: free TRAM versus DIEP: adjOR 1.81, 95% CI 1.24–2.64; pedicled TRAM versus DIEP: adjOR 2.89, 95% CI 1.91–4.37).

One NRCS (Zoghbi et al[22]) reported that, compared with DIEP flaps, TRAM flaps were associated with greater risks of wound infections (adjOR 1.67, 95% CI 1.23–2.27) and wound dehiscence (adjOR 4.3; CI not reported; $P < 0.001$).

DIEP versus LD Flaps

One RCT and one NRCS compared DIEP and LD flaps in a total of 845 patients (RCT: 83 patients and NRCS: 762 patients) (Table 1). Both studies had a high risk of bias.

Clinical/Benefit Outcomes: The NRCS (Yueh et al[20]) reported that comparable proportions of DIEP and LD flap recipients were satisfied with their breasts (adjOR 0.90, 95% CI 0.60–1.34) or satisfied with their surgical outcome (adjOR 1.05, 95% CI 0.70–1.57) (**Supplemental Digital Content 2-4**, **http://links.lww.com/PRSGO/B962**).

Surgical Complications: The RCT (Brorson et al[12]) reported on thromboembolic events (**Supplemental Digital Content 2-5**, **http://links.lww.com/PRSGO/B962**). Neither group experienced any deep venous thrombosis or pulmonary embolism events by 1 month of follow-up.

SIEA versus DIEP Flaps

One moderate risk of bias NRCS (Erdmann-Sager et al[13]) compared SIEA and DIEP flaps in 791 patients (Table 1).

Clinical Outcomes: Data for physical well-being were evaluated using the BREAST-Q (**Supplemental Digital Content 2-1**, **http://links.lww.com/PRSGO/B962**). Patients with SIEA flaps experienced clinically significant better abdominal physical function at 1 year (adjMD 4.72, 95% CI −0.07 to 9.52) but not at 2 years (adjMD 0.58, 95% CI −4.79 to 5.95). A similar pattern was observed for chest and upper body physical function. However, scores were comparable among flap groups at both time-points for the PROMIS physical functioning and pain interference components.

BREAST-Q data were also reported for psychosocial well-being, sexual well-being, and satisfaction with breasts at 1 and 2 years of follow-up (**Supplemental Digital Contents 2-2 and 2-3**, **http://links.lww.com/PRSGO/B962**). For all three outcomes, scores were clinically comparable between flap groups at both time-points.

Surgical Complications: At 2 years of follow-up, SIEA flaps were associated with a greater risk of harm to the area of flap harvest (donor site complications: adjOR 2.73, 95% CI 1.51–4.96).

TAP versus LD Flaps

One moderate risk of bias RCT (Rindom et al[19]) compared TAP and LD flaps in 40 patients (Table 1).

Clinical/Benefit Outcomes: Overall and subscale data for the Constant Murley Score evaluating physical function of

the shoulder were reported at 1 year (**Supplemental Digital Content 2-1**, **http://links.lww.com/PRSGO/B962**). The overall score ranges from 0 to 100 (higher is better; MCID 10[25]), with subscale scores ranging from 0 to 15 (pain), 0 to 20 (activity in daily life), 0 to 40 (range of motion), and 0 to 25 (strength) (MCIDs for subscale scores not available). Both overall and across the subscales, TAP and LD groups had comparable scores.

LD and TAP groups had similar durations of initial hospitalization (adjMD 0.9 days, 95% CI −1.4 to 3.2) (**Supplemental Digital Content 2-3**, **http://links.lww.com/PRSGO/B962**).

Surgical Complications: Patients with TAP flaps were considerably less likely than patients with LD flaps to experience shoulder-related pain at 1 year (OR 0.05, 95% CI 0.005–0.51) (**Supplemental Digital Content 2-5**, **http://links.lww.com/PRSGO/B962**). Between-flap comparison data for major necrosis (necrosis necessitating repeat surgery), minor necrosis (epidermolysis or small necrosis of the most distal part of the flap), infections, and seroma were all highly imprecise.

TRAM versus LD Flaps

One RCT and two NRCSs compared TRAM and LD flaps in a total of 5386 patients (between 75 and 4549 patients each) (Table 1). All three studies were at a high risk of bias.

Clinical/Benefit Outcomes: The RCT (Brandberg et al[10]) constructed its own questionnaire for patient satisfaction with breasts. Questionnaire items included cosmesis, shape, size, breast scars, donor site scars, and similarity with contralateral breast (each item was scored from 1 to 6 points; MCIDs not available) (**Supplemental Digital Content 2-4**, **http://links.lww.com/PRSGO/B962**). At 1 year, between-group differences for each item were less than one point. One NRCS (Yueh et al[20]) reported that comparable proportions of LD and TRAM recipients were satisfied with their breasts (adjOR 0.78, 95% CI 0.54–1.14) or satisfied with their surgical outcome (adjOR 0.77, 95% CI 0.53–1.11) (**Supplemental Digital Content 2-4**, **http://links.lww.com/PRSGO/B962**).

The RCT (Brandberg et al[10]) reported low rates of mortality at 1 year in both groups (**Supplemental Digital Content 2-5**, **http://links.lww.com/PRSGO/B962**). Data for between-flap comparisons were highly imprecise.

Surgical Complications: One NRCS (Massenburg et al[17]) reported that women with pedicled TRAM flaps were more likely than women with LD flaps to have an unplanned repeat surgery for revision within 1 month (adjOR 1.71, 95% CI 1.25–2.33) (**Supplemental Digital Content 2-5**, **http://links.lww.com/PRSGO/B962**).

Comparisons between TRAM and LTD Flaps, and between LD and LTD Flaps

One high risk of bias RCT (Brandberg[10]) made comparisons between TRAM and LTD flaps and between LD and LTD flaps in 75 patients (Table 1).

Clinical/Benefit Outcomes: Based on their own questionnaire, the authors reported that all between-group differences in patient satisfaction with breasts at 1 year were within one point (**Supplemental Digital Content 2-4**, **http://links.lww.com/PRSGO/B962**). All groups had low rates of mortality at 1 year, and all between-group mortality comparisons were highly imprecise (**Supplemental Digital Content 2-5**, **http://links.lww.com/PRSGO/B962**).

Surgical Complications: Not reported.

DISCUSSION

The current evidence regarding AR after mastectomy for breast cancer is limited. We found no evidence addressing the best timing of AR before or after chemotherapy or radiation therapy. Regarding choice of flap type, we found evidence for six flap types but could draw conclusions only for the comparison between DIEP and TRAM flaps. Most outcomes for any given comparison were reported by only a single study, or studies were underpowered and provided highly imprecise between-flap treatment effect estimates. The only patient-reported clinical outcome for which a conclusion was feasible is patient satisfaction with breasts, which may be comparable between DIEP and TRAM groups (low SoE). The only feasible conclusions regarding surgical complications are that risks of necrosis may be comparable (low SoE), but TRAM flaps are probably associated with a greater risk of harm to the area of flap harvest (abdominal bulge/hernia and needing abdominal hernia repair surgery) (moderate SoE). The evidence for outcomes for all other flap comparisons was either absent or insufficient to merit conclusions.

Implications for Clinical Practice

This SR provides has several implications for clinical practice. Firstly, the findings from our comprehensive evaluation of reconstructive options in AR reveal that, in general, AR is well-tolerated and results in improved quality of life, regardless of which flap is used.

Secondly, the existing literature is lacking as to the optimal timing of performing AR in relation to chemotherapy or radiation therapy. Given the lack of evidence, clinicians should discuss with patients the potential advantages of providing immediate AR in the setting of postmastectomy radiation therapy (eg, faster time to completion of reconstruction, no need for prosthetic device) and weigh them against the potential disadvantages (eg, radiation damage to reconstruction, revisionary surgery).

Thirdly, this report provides a comprehensive summary of donor site morbidity associated with abdominally-based AR. As expected, TRAM flaps likely pose a greater risk of abdominal bulge/hernia requiring abdominal hernia repair. This is worth considering during shared decision-making between the clinicians and patient, especially because the risk of necrosis may be comparable between DIEP and TRAM flaps.

Fourthly, clinicians should emphasize to patients the limitations of existing research. For example, much of the research addressing breast reconstruction has focused largely on patients whose mastectomy was performed for therapeutic (and not prophylactic) purposes. In addition, patients in existing studies have been mostly White, middle-aged, and nonobese women living in high-income countries. For patients in clinical practice who

do not belong to these categories, clinicians and patients will need to consider the appropriateness of extrapolating information about benefits and harms of AR options from the evidence to the decision-making context. The patient's values and preferences and the clinician's expertise and experience are thus highly important.

Strengths and Limitations

We followed contemporary methodological standards for SRs, including state-of-the-art methods for stakeholder engagement, literature searching, screening, assessing risk of bias, extracting and synthesizing data, and assessing SoE. A few limitations to the evidence base are worth noting. Only three of the 12 included studies were RCTs, each small and generally providing imprecise estimates of effect sizes. Most studies were at a high risk of bias, primarily because participants, care providers, and/or outcome assessors were not blinded and because of incomplete outcome data. Studies commonly reported incomplete data regarding adjusted analyses. Furthermore, comparisons of subgroups were limited in that none of the studies reported statistical analyses of differences between subgroups or, what would have been preferable, evidence of treatment effect heterogeneity.

Implications for Research

More high-quality research is needed to address questions related to timing of AR and comparisons of some flap types. The evidence gap related to optimal timing of AR in relation to postmastectomy radiation is a particularly important one. Immediate breast reconstruction has traditionally been thought to be associated with an improved ability to utilize the native mastectomy tissue envelope and lower overall costs. However, it is unclear whether exposing a newly reconstructed autologous breast to radiation is associated with flap necrosis, discoloration, contracture, displacement, volume loss, and/or other complications that often require additional revision procedures and/or hospitalizations.

Future studies should enroll more diverse groups of women, particularly by race, ethnicity, age, and socioeconomic position. It is also important that, when possible, future studies conduct randomization (to avoid selection bias). When randomization is not feasible or practical,[26] studies should fully report between-group estimates of treatment effect that conduct adequate statistical adjustment analyses to account for important confounders, including age, race/ethnicity, weight, and breast cancer stage. Future studies should also evaluate important outcomes that have not been reported sufficiently in the identified evidence, including quality of life, incidence and duration of unplanned repeat hospitalizations and surgeries, and analgesic use.

CONCLUSIONS

The current evidence base allows only a few conclusions, tempered by the low-to-moderate SoE, regarding flap types for women undergoing AR after mastectomy for breast cancer. No evidence was found regarding the best timing of the AR before or after chemotherapy or radiation therapy. The only flap comparison for which conclusions are feasible is TRAM versus DIEP. Although patient satisfaction with breasts and risk of necrosis may be comparable (low SoE for both outcomes), TRAM flaps probably pose a greater risk of harm to the area of flap harvest. Future research is needed to identify effective and safe surgical options related to AR for women who undergo mastectomy for breast cancer.

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