Comparative Effectiveness Review
Number 245

Breast Reconstruction After Mastectomy: A Systematic Review and Meta-Analysis

Evidence Summary

Main Points

- **Implant-Based Reconstruction (IBR) Versus Autologous Reconstruction (AR)**
  - Compared with IBR, AR is probably associated with clinically better sexual well-being and patient satisfaction with breasts, but comparable general quality of life and psychosocial well-being (Moderate strength of evidence [SoE], all outcomes).
  - Compared with IBR, AR probably poses a greater risk of deep vein thrombosis or pulmonary embolism but comparable risk of unplanned repeat hospitalization (both Moderate SoE).
  - Compared with AR, although results in the short term (1 to 1.3 months) are inconsistent, IBR probably poses greater risk of reconstructive failure in the long term (1.5 to 4 years) (Moderate SoE). IBR may also pose a greater risk of breast seroma (Low SoE).
- **Timing of IBR and AR in Relation to Chemotherapy and Radiation Therapy**
  - Conducting IBR either before or after radiation therapy may result in comparable physical well-being, psychosocial well-being, sexual well-being, and patient satisfaction with breasts (Low SoE for all).
  - Conducting IBR either before or after radiation therapy probably results in comparable risk of implant failure/loss or need for explant surgery (Moderate SoE).
  - We found no evidence comparing timing of IBR or AR before or after chemotherapy or timing of AR before or after radiation therapy.

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- **Comparisons of Implant Materials for IBR**
  - Silicone or saline implants may result in clinically comparable patient satisfaction with breasts (Low SoE).
  - There is insufficient evidence to make conclusions about surgical complications when comparing silicone and saline implants.
  - There is insufficient evidence regarding double lumen implants.
- **Comparisons of Anatomic Planes of Implant Placement During IBR**
  - Whether the implant is placed in the prepectoral or total submuscular plane may not impact the risk of infections that are not explicitly implant-related (Low SoE).
  - There is insufficient evidence for all outcomes comparing prepectoral versus partial submuscular planes and partial versus total submuscular planes.
- **Use Versus Nonuse of Acellular Dermal Matrices (ADMs) During IBR**
  - The evidence is inconsistent regarding whether human ADM use during IBR impacts patient physical well-being, psychosocial well-being, or satisfaction with breasts.
  - ADM use probably increases the risk of implant failure/loss or need for explant surgery (Moderate SoE) and may increase the risk of infections not explicitly related to the implants or ADM (Low SoE). The risks of seroma or of unplanned repeat surgery for revision probably are comparable with or without ADM use (Moderate SoE); the risk of necrosis may be comparable (Low SoE).
- **Comparisons of Flap Types for AR**
  - AR with either transverse rectus abdominis (TRAM) or deep inferior epigastric perforator (DIEP) flaps may result in comparable patient satisfaction with breasts (Low SoE); however, TRAM flaps probably increase the risk of harms to the area of flap harvest (Moderate SoE).
  - AR with either DIEP or latissimus dorsi (LD) flaps may result in comparable patient satisfaction with breasts (Low SoE), but we found no evidence comparing risk of surgical complications.
  - There is insufficient evidence regarding other flap types.

Background and Purpose

Breast cancer is the most common new cancer diagnosis among women in the United States and the second most common cause of cancer death. For women who choose to undergo breast reconstruction surgery (more than 40% of women in the United States who undergo mastectomy), various decisions must be made related to the timing and type of reconstruction. Based on the type of procedure and composition of the newly reconstructed breast, reconstruction is categorized into IBR and AR. Implants are prosthetic devices that replace the surgically removed breast tissue. With AR, breast reconstruction is done with the patient's own tissue, thereby obviating the need for implants (except for LD flaps, which usually require an implant).

This systematic review (SR) aims to inform plastic surgeons, breast surgical oncologists, medical oncologists, radiation oncologists, other care providers, patients, policymakers, and developers of clinical guidance about surgical breast reconstruction options after mastectomy for breast cancer (or breast cancer prophylaxis). The SR addresses six Key Questions (KQs): (1) IBR versus AR, (2) timing of IBR and AR in relation to chemotherapy and radiation therapy, (3) comparisons of implant materials for IBR, (4) comparisons of anatomic planes of implant placement during IBR, (5) use versus nonuse of human ADMs during IBR, and (6) comparisons of flap types for AR.

Methods

We used methods consistent with those outlined in the Agency for Healthcare Research and Quality Evidence-based Practice Center Program Methods Guidance (https://effectivehealthcare.ahrq.gov/topics/cer-methods-guide/overview). Our searches targeted comparative studies and single group studies (i.e., studies without a comparison group) from database inception to March 23, 2021. We extracted study data into the Systematic Review Data Repository Plus (SRDR+). Our conclusions about comparative effectiveness and harms are based solely on the comparative studies. Single group studies provided additional information about incidence of surgical complications. Where there was sufficient evidence with an acceptable amount of heterogeneity, we conducted pairwise meta-analyses. In the Results section of this Evidence Summary, we provide numeric estimates of summary treatment effects only where meta-analyses were feasible for prioritized outcomes. We assessed the risk of bias and evaluated the SoE using standard methods. The PROSPERO protocol registration number is CRD42020193183. This Evidence Summary incorporates SoE ratings into the Main Points through qualifying language to communicate SoE of conclusions: “probably” for Moderate SoE and “may” for Low SoE.

Results

We found 160 primary studies comprising 478,650 patients in total. These included 8 randomized controlled trials (N = 570 patients), 83 nonrandomized comparative studies (i.e., observational studies that compared 2 or more interventions; N = 202,862), and 69 single group studies (N = 275,218).

IBR versus AR: Compared with IBR, AR is probably associated with clinically significant better sexual well-being (summary adjusted mean difference [adjMD] 5.8, 95% confidence interval [CI] 3.4 to 8.2; 3 studies) and satisfaction with breasts (summary adjMD 8.1, 95% CI 6.1 to 10.1; 3 studies) but comparable psychosocial well-being (summary adjMD 3.1, 95% CI 1.3 to 5.0; 3 studies) and general quality of life (Moderate SoE, all outcomes) (Table A). Compared with IBR, AR may be associated with greater risks of deep vein thrombosis or pulmonary embolism (Moderate SoE) but comparable risk of unplanned repeat hospitalizations (Moderate SoE). On the other hand, IBR may be associated with greater risk of seroma (Low SoE). Results were inconsistent regarding

whether the choice of IBR versus AR impacts physical well-being, satisfaction with surgical outcome, or risks of reconstructive failure, infections that are not explicitly implant-related, pain, analgesic use, or unplanned surgeries for revision or for complications.

Timing of IBR and AR in relation to chemotherapy and radiation therapy: Whether IBR is conducted before or after radiation therapy may result in comparable physical well-being, psychosocial well-being, sexual well-being, and patient satisfaction with breasts (Low SoE for each). We found that IBR probably results in comparable risk of implant failure/loss or need for explant surgery whether conducted before or after radiation therapy (summary adjusted odds ratio [adjOR] 0.87, 95% CI 0.62 to 1.24; 3 studies) (Moderate SoE). We found no evidence addressing timing of AR in relation to radiation therapy. We did not find any studies comparing timing of IBR or AR before or after chemotherapy.

Comparisons of implant materials for IBR: Silicone and saline implants may result in clinically comparable assessments of satisfaction with breasts (Low SoE). We found insufficient evidence addressing surgical complications when comparing silicone and saline implants. We found insufficient evidence addressing double lumen implants.

Comparisons of anatomic planes of implant placement for IBR: Prepectoral and total submuscular placements of implants may result in comparable risks of infections that are not explicitly implant-related (Low SoE). We found insufficient evidence for clinical outcomes for this comparison. We found insufficient evidence for all outcomes when comparing prepectoral versus partial submuscular placements and partial versus total submuscular placements.

Use versus nonuse of human ADMs during IBR: ADM use probably increases the risk of implant failure/loss or need for explant surgery (summary adjOR 1.28, 95% CI 0.97 to 1.70; 6 studies) (Moderate SoE) and may increase the risk of infections not explicitly related to the implants or ADM (summary adjOR 1.56, 95% CI 0.96 to 2.53; 7 studies) (Low SoE). However, ADM use and nonuse groups probably experience comparable risks of seroma (summary adjOR 1.52, 95% CI 0.62 to 3.71; 4 studies) (Moderate SoE) and unplanned repeat surgeries for revision (Moderate SoE). ADM use and nonuse groups may experience comparable risks of necrosis (summary adjOR 0.89, 95% CI 0.63 to 1.25; 4 studies) (Low SoE). The results are inconsistent regarding whether ADM use impacts physical well-being, psychosocial well-being, satisfaction with breasts, pain, or risks of wound dehiscence or capsular contracture.

Comparisons of flap types for AR: *TRAM versus DIEP flaps*: These two flap types may result in clinically comparable patient satisfaction with breasts (Low SoE) and risk of necrosis (Low SoE), but TRAM probably poses greater risk of harms to the area of flap harvest (abdominal bulge/hernia and need for abdominal hernia surgery) (Moderate SoE). *DIEP versus LD flaps*: These two flap types may result in clinically comparable patient satisfaction with breasts (Low SoE). There was insufficient evidence to make conclusions about thromboembolic events, and no studies addressed other surgical complications. (Note that AR with LD flaps often also requires an implant during the reconstruction [i.e., a "hybrid" reconstruction], while AR with DIEP flaps usually does not.) *Other flaps*: We found insufficient evidence addressing lateral thoracodorsal (LTD), superficial inferior epigastric artery (SIEA), and thoracodorsal artery perforator (TAP) flaps.

Limitations

Although we found a large body of evidence, it included many single group studies and relatively few studies reported the same outcomes pertaining to similar comparisons. Thus, evidence regarding surgical breast reconstruction options is largely insufficient or of only low or moderate SoE. Nonrandomized comparative studies often did not report adjusted effect sizes or omitted confidence intervals and P values. When subgroup data were reported, statistical analyses evaluating heterogeneity of treatment effects were not reported. The included studies were mostly at moderate to high risk of bias. Several prioritized outcomes, including general quality of life and risk of animation deformity, were infrequently reported.

Implications and Conclusions

Our analysis of all surgical choices examined as KQs in this review finds no clear winners when all outcomes are considered. We encourage clinicians to inform patients about the limitations of existing research and to help patients make decisions regarding options for breast reconstruction based on their values and preferences, together with the clinician's expertise and experience. Research is needed to address various questions related to breast reconstruction, particularly the timing of IBR and AR in relation to chemotherapy and radiation therapy, and the choices of implant materials, anatomic planes of implant placement during IBR, and flaps used for AR. Future studies should either randomize patients or adequately account for important confounders and evaluate key outcomes, especially those in the existing core outcome set for breast reconstruction after mastectomy.

Table A. Summary of evidence identified in this systematic review

Category	Outcomes	KQ 1	KQ 2*	KQ 3	KQ 4	KQ 5	KQ 6
Clinical outcomes	General quality of life	~~	nd	?	nd	nd	nd
	Physical well-being	↑↓	~	?	?	↑↓	?
	Psychosocial well-being	~~	~	?	?	↑↓	?
	Sexual well-being	▲▲ AR clinically better	~	?	nd	?	?
	Patient satisfaction with breasts	▲▲ AR clinically better	~	~	?	↑↓	~
	Patient satisfaction with outcome	↑↓	?	?	nd	nd	?
	Planned surgeries for reconstruction	N/P	N/P	nd	nd	nd	nd
	Duration of initial hospitalization	.	.	.	.	.	?
	Mortality	?	nd	?	nd	?	?
Surgical complications	Unplanned repeat hospitalization	~~	nd	nd	nd	nd	nd
	Duration of unplanned repeat hospitalization	nd	nd	nd	nd	nd	nd
	Unplanned repeat surgery for revision	↑↓	?	nd	?	~~	?
	Unplanned repeat surgery for complications	↑↓	nd	nd	nd	?	nd
	Pain	↑↓	?	nd	↑↓	↑↓	?
	Analgesic use	?	nd	nd	?	?	nd
	Necrosis	?	?	nd	?	~	~
	Harms to area of flap harvest	.	.	.	.	.	◆◆ Increased abdominal bulge/hernia, hernia repair surgery with TRAM than DIEP
	Animation deformity	nd	nd	nd	nd	nd	.
	Implant-related infections	.	nd	nd	nd	nd	.
	Implant rupture	.	nd	nd	nd	?	.
	Implant deflation	.	nd	nd	nd	nd	.
	Implant malposition	.	nd	nd	nd	?	.
	Implant failure/loss or needing explant	.	~~	?	?	◆◆ with ADM	.
	Capsular contracture	.	N/P	?	?	↑↓	.
	New neoplasms	.	.	nd	nd	nd	.
	Complications delaying other cancer treatments	nd	nd	nd	nd	nd	nd
	Thromboembolic events	◆◆ DVT or PE with AR	nd	nd	nd	?	?
	Infections not explicitly implant-related	↑↓	N/P	.	~	◆ with ADM	?
	Wound dehiscence	N/P	N/P	N/P	N/P	↑↓	?
	Delayed healing	N/P	N/P	N/P	N/P	?	nd
	Seroma	◆ with IBR	?	nd	?	~~	nd
	Chronic conditions	N/P	N/P	nd	nd	N/P	.
	Reconstructive failure	◆◆ with IBR in the long term	.	.	.	.	.

* KQ 2 data refer only to IBR before versus after radiation [KQ 2b]

Abbreviations: ADM = acellular dermal matrix, AR = autologous reconstruction, DIEP = deep inferior epigastric perforator, DVT = deep vein thrombosis, IBR = implant-based reconstruction, KQ = Key Question, LD = latissimus dorsi, N/P = not prioritized (for strength of evidence assessment), nd = no data (no evidence identified), PE = pulmonary embolism, SoE = strength of evidence, TRAM = transverse rectus abdominis myocutaneous. ▲ = Low SoE of better clinical outcomes, ▲▲ = Moderate SoE of better clinical outcomes, ▲▲▲ = High SoE of better clinical outcomes (no instances in this table)
◆ = Low SoE of increased complications, ◆◆ = Moderate SoE of increased complications, ◆◆◆ = High SoE of increased complications (no instances in this table)
~ = Low SoE of comparable outcomes, ~~ = Moderate SoE of comparable outcomes, ~~~ = High SoE of comparable outcomes (no instances in this table)
? = Insufficient SoE due to sparse evidence, ↑↓ = Insufficient SoE due to inconsistent or conflicting results, . = not applicable (i.e., outcome not applicable to KQ)

Colors: Insufficient SoE, Low SoE, Moderate SoE, High SoE (no instances). The colors do not add unique information.

Full Report

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