A Systematic Review and Head-to-Head Meta-Analysis of Outcomes following Direct-to-Implant versus Conventional Two-Stage Implant Reconstruction

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Background: Innovative approaches to reconstruction have ushered in an era of breast reconstruction in which direct-to-implant procedures can provide an immediately reconstructed breast. Balancing the benefits against its technical challenges is vital. The authors evaluated the safety and efficacy of using direct-to-implant versus conventional two-stage reconstruction through a systematic meta-analysis.

Methods: A literature search identified all articles published after 1999 involving prosthetic-based breast reconstruction as a two-stage tissue expander/implant or direct-to-implant technique. The primary outcomes of interest, including implant loss, capsular contracture, reoperation, and infection, were analyzed by means of head-to-head meta-analysis.

Results: Thirteen studies involving 5216 breast reconstructions were included. The average patient age was 47.2 ± 1.0 years, the average body mass index was 24.9 ± 0.8 mg/k^2, and the average follow-up was 40.8 months. Wound infection, seroma, and capsular contracture risk were similar between groups. However, direct-to-implant reconstruction was associated with a higher risk for skin flap necrosis (OR, 1.43; p = 0.01; I^2 = 51 percent) and reoperation (OR, 1.25; p = 0.04; I^2 = 43 percent). Ultimately, the risk for implant loss was nearly two-fold higher with direct-to-implant reconstruction compared with tissue expander/implant reconstruction (OR, 1.87; p = 0.04; I^2 = 33 percent).

Conclusions: Although direct-to-implant and two-stage tissue expander/implant reconstruction are successful approaches, this meta-analysis demonstrates significantly greater risk of flap necrosis and implant failure with direct-to-implant reconstruction. The authors' findings suggest that the critical component of patient selection is judgment of mastectomy flap tissue quality. These findings can enhance the risk counseling process and highlight the need for additional investigations to optimize outcomes. (*Plast. Reconstr. Surg.* 136: 1135, 2015.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, III.

Breast reconstruction affords patients significant psychosocial and aesthetic benefits following mastectomy.[1–4] Changing patterns of mastectomy, along with a notable increase in immediate breast reconstructions, have solidified the role of implant-based breast reconstruction in the United States.[5–7] Complications following prosthetic reconstruction, although infrequent, can powerfully impact patient satisfaction and aesthetic outcomes and increase health care costs.[1,8]

Conventional two-stage submuscular implant reconstruction using a tissue expander and implant has been shown to be a safe, reliable, and efficacious modality for reconstructing the breast.[9–11] Skin- and nipple-sparing mastectomy

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techniques, which preserve native soft-tissue structures, have provided the unique opportunity to recreate the breast mound, with little manipulation of surrounding tissues. Emerging reconstructive approaches, technologic advances in implant design, and the advent of acellular dermal matrix have ushered in an era of breast reconstruction in which direct-to-implant procedures can expedite the reconstructive course and optimize quality of life by avoiding a second operation.[12–17] Several landmark studies have demonstrated the efficacy of direct-to-implant–based reconstruction,[12,13,17] but there are few comparative analyses that provide a critical evaluation of the risk versus benefit of each type of prosthetic reconstruction. Furthermore, some studies report higher rates of complications[18,19] and device failure[20,21] with direct-to-implant reconstruction compared with tissue expander/implant–based reconstruction.

With inherent advantages and disadvantages to each reconstructive technique and conflicting reports of complications in the published literature, there is a need to critically appraise the available data to assess the likelihood of successful reconstruction using each technique to provide a foundation for evidence-based practice. In this analysis, the authors report the first head-to-head meta-analysis assessing the relative safety and efficacy of direct-to-implant versus two-stage implant reconstruction.

PATIENTS AND METHODS

Literature Search

This study was performed according to guidelines set forth in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement,[22] and was reviewed and exempted by the Hospital of the University of Pennsylvania Institutional Review Board. A literature search was conducted to identify all articles involving prosthetic-based breast reconstruction either as a two-stage tissue expander/implant or as a direct-to-implant technique. The Ovid MEDLINE and Embase databases were searched using the following headings and keyword terms: “breast reconstruction,” “breast implant,” “breast prosthesis,” “tissue expander,” AND “mastectomy.” In addition, selected study references and review articles were examined for further article sources.

Assessment of Methodologic Quality

After identifying relevant studies through title and abstract information, studies were selected for inclusion based on the following inclusion criteria: (1) the study involved the use of a prosthesis in immediate breast reconstruction for cancer management, and specified that both single-stage direct-to-implant reconstruction and two-stage tissue expander/implant reconstruction were used; (2) prostheses were not placed in conjunction with an autologous tissue flap (e.g., pedicle latissimus or microvascular free flap); (3) reconstructive techniques were similar for direct-to-implant and tissue expander/implant groups, and the study reported relevant outcomes for each group; (4) the study was published between 2000 and 2015; (5) the study was not limited to single case reports or review of the literature; and (6) the study was published in the English language.

Studies were excluded if they did not meet the above criteria. In addition, if multiple publications were from the same group, only studies that reported data from nonoverlapping periods were included. Articles were excluded if they did not report sufficient data for both direct-to-implant and tissue expander/implant cohorts. Studies were then rated on methodologic quality based on the American Society of Plastic Surgeons level of evidence rating scale.[23]

Data Extraction

Data were extracted independently by three members of the study team (P.A.G., M.N.B., and J.P.F.) and subsequently reviewed by the study team together to ensure data accuracy. Patient characteristics included age (in years), body mass index (in kilograms per square meter), smoking history, and need for chemotherapy or irradiation. For tissue expander/implant reconstructions, the average time interval between expander placement and implant exchange was noted when available. Operative characteristics recorded were reconstructive timing (immediate or delayed), laterality of breast reconstructions, final implant volume (in milliliters), and whether reconstruction was assisted with acellular dermal matrix. Outcomes of interest included device loss, wound infection, reoperation, and severe capsular contracture. Implant loss was defined as removal or exchange of implant, or need for subsequent autologous reconstruction for any reason except undesirable aesthetic outcome. Similarly, reoperation was considered when the indication was a complication, and revisions to improve aesthetics were considered separately from this outcome and recorded when available. Finally, severe capsular contracture was defined as Baker grade III or IV if reported, or as contracture requiring

implant removal because of pain/discomfort.[24] The average length of follow-up for each study was also noted.

Statistical Analysis

Patients were classified according to reconstructive modality as either direct-to-implant or tissue expander/implant. Outcomes of interest were analyzed by means of head-to-head meta-analysis. Continuous variables, such as age, were reported by means of standard summary statistics. Dichotomous data, such as incidence of complications, were summarized with Fisher's exact test or chi-square test, with significance set to $p < 0.05$. Meta-analyses of continuous outcomes were reported as weighted mean differences and dichotomous outcomes were reported as odds ratios with 95 percent confidence intervals. A random-effects analytic model was applied, using the method of DerSimonian and Laird, and estimation of heterogeneity was derived from the Mantel-Haenszel model.[25] The I^2 statistic, an estimate of heterogeneity, was judged low for I^2 less than 50 percent, borderline heterogeneous for I^2 of 50 to 75 percent, and unacceptable for I^2 greater than 75 percent. Publication bias was inspected routinely by means of funnel plots and the Egger et al. regression asymmetry test for publication bias. All analyses were conducted in Stata IC 13.1 (Stata Statistical Software, Release 13; StataCorp LP, College Station, Texas) and figures were generated with RevMan 5.2 (The Cochrane Collaboration, Copenhagen, Denmark).[26]

RESULTS

Literature Search

The initial literature search, after removal of duplicate results, yielded 380 unique articles (Fig. 1). Title and abstract search identified 85 articles of potential interest that underwent full manuscript review. A total of 13 studies met inclusion criteria with adequate reporting of head-to-head outcomes.

Study Quality and Patient Characteristics

Overall, 13 studies involving 5216 breast reconstructions were included (Table 1).[18,21,27–37] Ten studies were retrospective cohort studies providing Level III evidence; two studies were prospective cohorts offering Level II evidence; and one study was a prospective, randomized, controlled trial offering Level I evidence. All but one study involved only immediate reconstructions, and

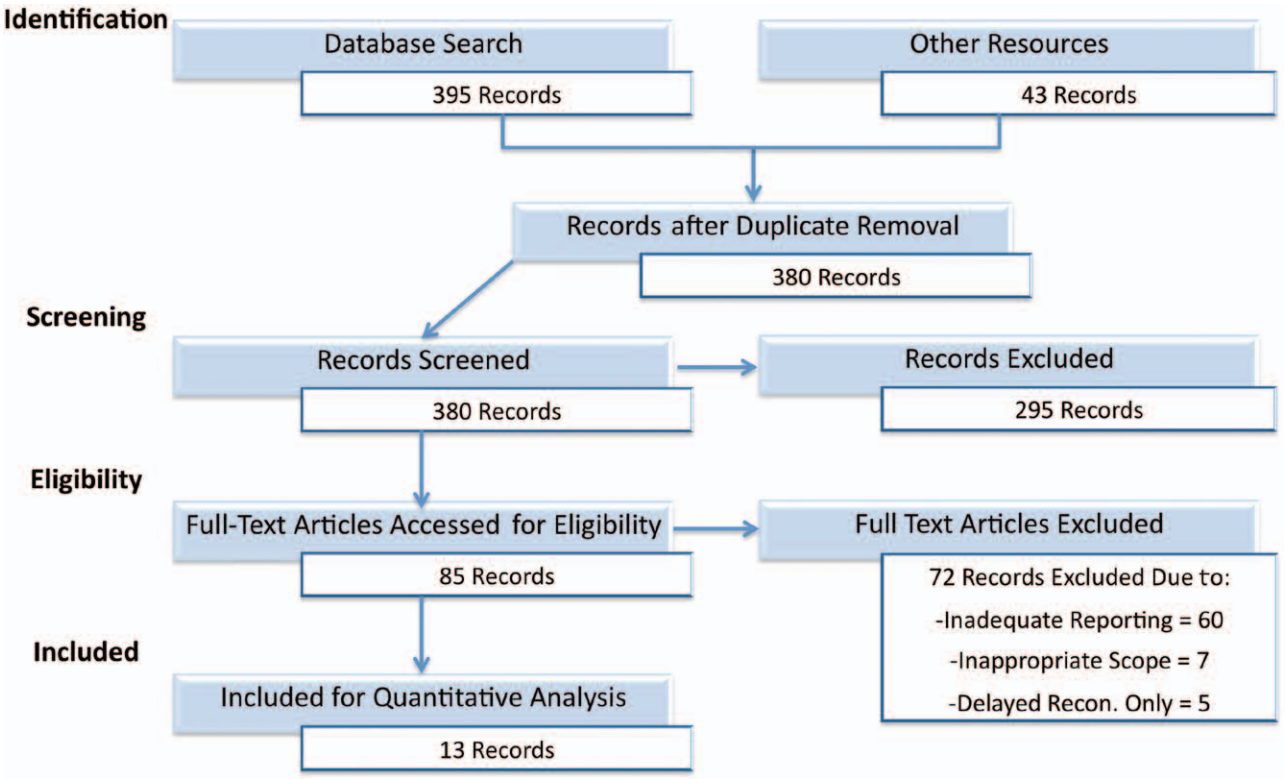


Fig. 1. Flow diagram of study selection and inclusion.

Table 1. Summary of Included Study Characteristics

Reference	Design	LOE	Two-Stage	DTI	Total	Timing	Follow-Up (mo)
Pinsolle et al., 2006[21]	R-COH	III	27	38	65	Immediate	84.0
Breuing and Colwell, 2007[27]	R-COH	III	14	30	44	Immediate*	18.9
Mitchem et al., 2008[28]	P-COH	II	34	5	39	Immediate	NR
Plant et al., 2009[29]	R-COH	III	10	14	24	Immediate	NR
Hvilsom et al., 2011[18]	P-COH	II	149	40	189	Immediate	46.8
Petersen et al., 2012[31]	R-COH	III	81	127	208	Immediate	44.4
Roostaeian et al., 2012[32]	R-COH	III	87	62	149	Immediate	14.0
Kim et al. (in press)[34]	R-COH	III	40	23	63	Immediate	22.4
Lardi et al., 2014[35]	R-COH	III	90	110	200	Immediate	22.2
Susarla et al., 2015[37]	R-COH	III	416	166	582	Immediate	NR
Eriksen et al., 2012[30]	P-RCT	I	20	20	40	Immediate	42
Colwell et al., 2014[33]	R-COH	III	185	286	471	Immediate	26.0
Gfrerer et al., 2015[36]	R-COH	III	1264	1878	3142	Immediate	86.9
Total	—	—	2417	2799	5216	—	40.8 (SD, 26.8)

LOE, level of evidence; DTI, direct to implant; R-COH, retrospective cohort; P-COH, prospective cohort; P-RCT, prospective, randomized, controlled trial; NR, not reported.
*Four delayed reconstructions excluded from analysis.

delayed reconstruction data were excluded for the one study with both delayed and immediate reconstruction. The average age of the sample was 47.2 years, and nine studies reported an average incidence of smoking in 7 percent of the population (Table 2). Radiation therapy was documented in nine studies and, overall, 14 percent of those patients had either premastectomy or postmastectomy chest wall irradiation, and chemotherapy history was present in 31 percent of patients overall. The final volume of tissue expander/implant reconstruction was slightly higher than that for direct-to-implant reconstruction (416 ml versus 389 ml). The average time to tissue expander exchange for permanent implant was 9.0 months, and the average follow-up was 40.8 months.

Wound Complications and Reconstructive Failure

Head-to-head comparison of direct-to-implant versus tissue expander/implant reconstructions demonstrated no difference in infection, seroma, hematoma, or contracture rates (Table 3). The incidence of flap necrosis was higher for direct-to-implant reconstructions (OR, 1.43; 95 percent CI, 1.09 to 1.86; $p = 0.01$; $I^2 = 51$ percent) (Fig. 2). Similarly, reoperation for a complication was significantly more common for direct-to-implant reconstructions (OR, 1.25; 95 percent CI, 1.02 to 1.53; $p = 0.04$; $I^2 = 43$ percent). Eleven studies reported implant loss rates for both cohorts, demonstrating a significant increase in implant loss with direct-to-implant reconstructions versus tissue expander/implant reconstructions (OR, 1.87; $p = 0.04$; $I^2 = 33$ percent) (Fig. 3). The pooled absolute incidence of implant loss was calculated for each cohort, which also reflected the nearly two-fold greater risk of implant loss with which direct-to-implant reconstructions were associated compared with tissue expander/implant reconstructions (14.4 percent versus 8.7 percent).

DISCUSSION

This systematic review and meta-analysis compares outcomes following breast reconstruction using direct-to-implant versus conventional two-stage tissue expander/implant reconstruction. Among 13 studies involving 5216 breast reconstructions, skin flap necrosis, unplanned reoperation, and, ultimately, implant loss were more common after direct-to-implant reconstruction. With the growing emphasis on less invasive and more cost-effective surgical care today, careful evaluation of the relative safety and efficacy of different implant-based reconstructive techniques is necessary. Several findings presented here merit further consideration.

Assessment of the Quality of Included Studies

Although prospective cohort studies and a randomized trial were included in this review, the majority of studies were retrospective cohort studies offering Level III evidence. Baseline patient characteristics were variably reported as illustrated in Table 2, with some studies providing detailed comparison of demographics and comorbidities between the two reconstructive modalities and other studies not reporting characteristics for either group. When assessing two interventions for the same disease process, it is critical to identify any baseline differences that may be sources of confounding and selection bias. The decision to choose single- versus two-stage

Table 2. Summary of Patient and Operative Characteristics

Reference	Age (yr)	BMI (kg/m²)	Smoker (%)	Radiation Therapy (%)	Chemotherapy (%)	ADM (%)	Volume (ml)		Time to Implant (mo)
							DTI	TE/I*	
Pinsolle et al., 2006[21]	48	—	14	—	—	—	—	—	—
Breuing and Colwell, 2007[27]	46	—	2	23	20	100	—	—	—
Mitchem et al., 2008[28]	—	—	—	—	100	—	—	—	—
Plant et al., 2009[29]	44.1	—	13	—	—	—	586	613	—
Hvilsom et al., 2011[18]	47.7	—	—	0	—	—	—	—	7.6
Petersen et al., 2012[31]	44	23	13	6	—	—	—	—	—
Roostaeian et al., 2012[32]	46.2	22.4	3	9	15	98	395	386	10.8
Kim et al. (in press)[34]	44.1	—	—	16	62	—	—	—	—
Lardi et al., 2014[35]	48	24.9	13	31	43	100	387	—	—
Susarla et al., 2015[37]	47.5	25.2	8	26	54	64	—	—	—
Eriksen et al., 2012[30]	50.1	23.4	—	—	—	—	409	410	—
Colwell et al., 2014[33]	45.7	23.7	6	16	—	84	376	—	—
Gfrerer et al., 2015[36]	47.6	25.3	6	11	25	38	—	—	—
Total, mean (SD)	47.2 (1.0)	24.9 (0.8)	7 (2)	14 (7)	31 (13)	45 (27)	389 (34)	416 (70)	9.0 (1.6)

BMI, body mass index; ADM, acellular dermal matrix; DTI, direct-to-implant; TE/I, tissue expander/implant.
*Tissue expander/implant volume only recorded if final volume was reported.

Table 3. Comparison of Pooled Outcome Incidence and Head-to-Head Odds Ratios for Direct-to-Implant versus Two-Stage Implant Reconstructions

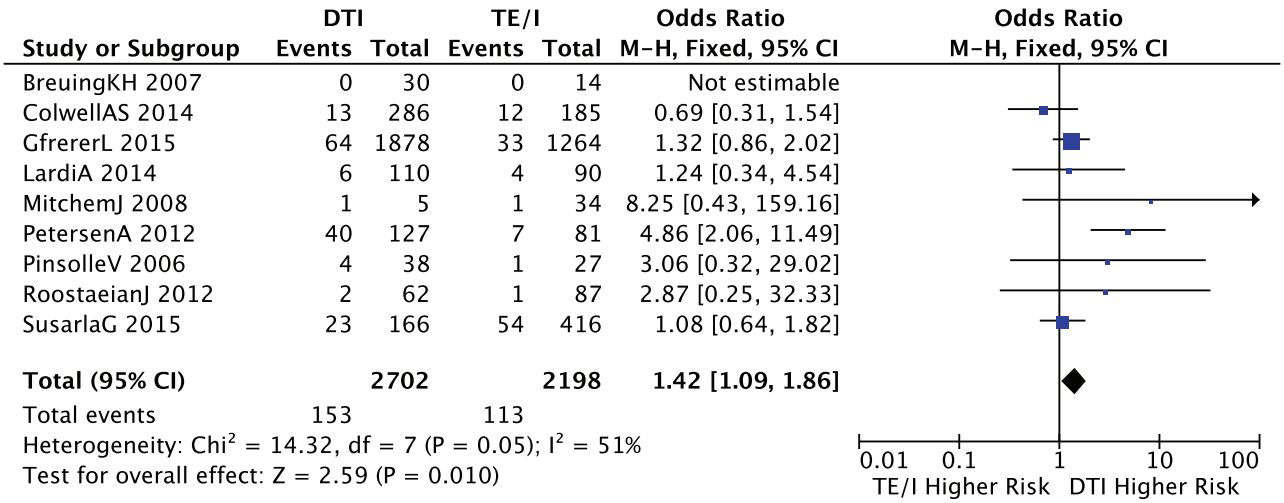
Outcome	*n* (*N*)	Incidence (%)		OR (95% CI)	*p*	I^2 (%)
		DTI (95% CI)	Two-Stage (95% CI)			
Implant infection	11 (5129)	7.8 (3.7–12.0)	7.4 (2.7–12.1)	1.08 (0.68–1.72)	0.74	38
Seroma	7 (1675)	6.8 (2.5–11.0)	7.1 (3.1–11.1)	0.95 (0.57–1.60)	0.85	0
Hematoma	7 (1700)	4.3 (0.3–8.3)	5.2 (−1.0–12.4)	0.96 (0.49–1.89)	0.90	0
Flap necrosis	9 (4900)	8.6 (1.9–15.4)	6.7 (2.7–10.6)	1.43 (1.09–1.86)	0.01	51
Contracture	5 (647)	13.5 (−5.1–32.3)	13.8 (0.3–27.2)	0.90 (0.44–1.85)	0.77	0
Reoperation	9 (4432)	17.9 (5.0–30.8)	14.1 (6.2–22.1)	1.25 (1.02–1.53)	0.04	43
Implant loss	11 (1683)	14.4 (7.3–21.4)	8.7 (2.0–15.4)	1.87 (1.05–3.34)	0.04	33

n (*N*), no. of studies (no. of patients) for each outcome; DTI, direct-to-implant; I^2, interstudy heterogeneity.

implant reconstruction, however, relies more on operative characteristics and tissue quality than on general patient health.[38–41] The use of acellular dermal matrix during reconstruction is one such operative factor requiring closer evaluation. Seven studies did not report using acellular dermal matrix for either direct-to-implant or tissue expander/implant modalities, and although two studies used acellular dermal matrix in less than 65 percent of patients, the remaining four studies incorporated acellular dermal matrix in 85 to 100 percent of breast reconstructions. Based on these findings, a reasonable assertion is that acellular dermal matrix was generally used in a comparable fashion between the two reconstructive modalities and did not likely contribute to differences in outcomes in this review. Other characteristics, including radiation therapy, implant size, and premastectomy cup size, were difficult to assess because of relatively poor reporting.

Outcomes and Complications

There are a number of potential advantages to single-stage direct-to-implant as opposed to conventional two-stage implant reconstruction. One benefit is avoiding a second operation and the expansion period necessary for tissue expander/implant reconstruction. Doing so allows a shorter time to final reconstruction, which improves patient quality of life and mitigates the inconvenience of frequent clinical visits.[32] With expander manipulation, increased risk for infection and seroma must be considered as well.[15,16,42] Although only two studies reported the time to final implant placement in this review, the average was 9 months after initial expander insertion, which represents a considerable burden for patients. However, short-term wound complications, including implant infection, seroma, and hematoma, were no more likely for tissue expander/implant reconstruction. In contrast, although a single-stage procedure may reduce certain complication risks, the immediate placement of a large implant in the mastectomy pocket may necessitate increased tension on the closure.[15,16] As a result, skin flap necrosis remains a considerable wound issue following direct-to-implant reconstruction. Of the nine studies reporting flap necrosis, only one found a lower complication incidence



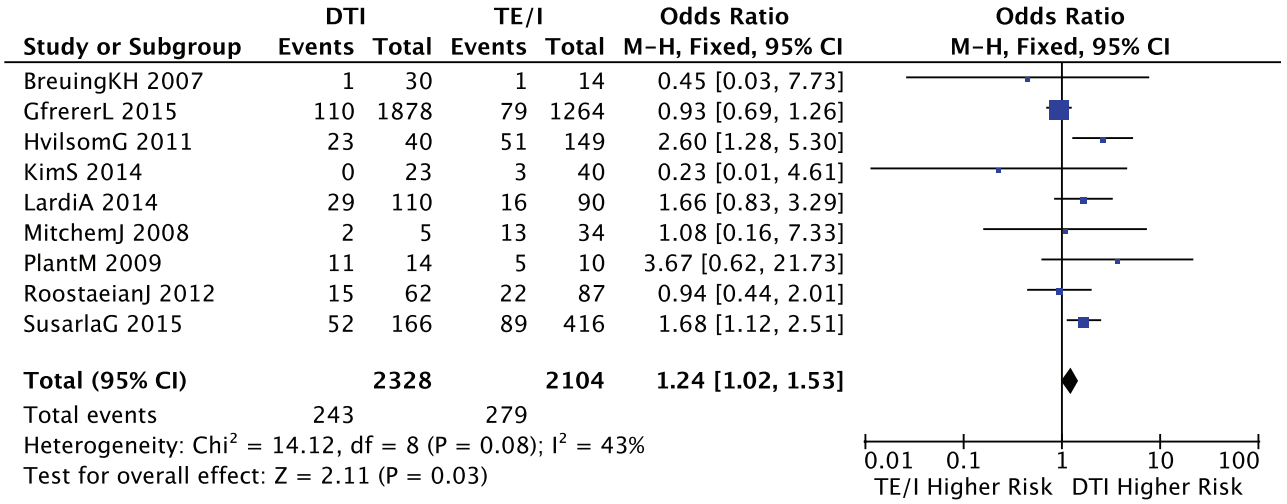


Fig. 2. Head-to-head comparison of outcomes for direct-to-implant versus tissue expander/implant reconstruction. (*Above*) Skin flap necrosis. (*Below*) Need for reoperation.

with direct-to-implant reconstruction, resulting in a significantly higher risk for flap necrosis with direct-to-implant compared to tissue expander/implant reconstruction (8.6 percent versus 6.7 percent; OR, 1.43). Although many patients may go on to heal with only conservative wound care, a subset of patients are predisposed to further complications after flap necrosis, including those patients requiring postmastectomy radiation therapy or chemotherapy.[11,19,31,43] This risk for compounding complications was most evident when reviewing long-term endpoints, including reoperation attributable to complication and implant loss. Both were significantly more common in patients undergoing direct-to-implant reconstruction compared with conventional two-stage tissue expander/implant reconstruction, which may partially be attributable to more skin flap necrosis with direct-to-implant reconstruction. Moreover, two-stage reconstruction offers flexibility in managing necrosis. If flap necrosis necessitating débridement occurs while an expander is in place, partial deflation may allow primary closure without expander removal. With a permanent implant, however, this may not be possible without implant exchange. Thus, a discussion of postoperative expectations with patients must incorporate not only the possible benefits in quality of life afforded by a shorter reconstructive course but also the distinct possibilities of reoperation and/or initial reconstructive failure following direct-to-implant reconstruction.

Patient Selection

In performing this systematic review, a common theme for reconstructive success emerged; namely, to provide the best chance for optimal

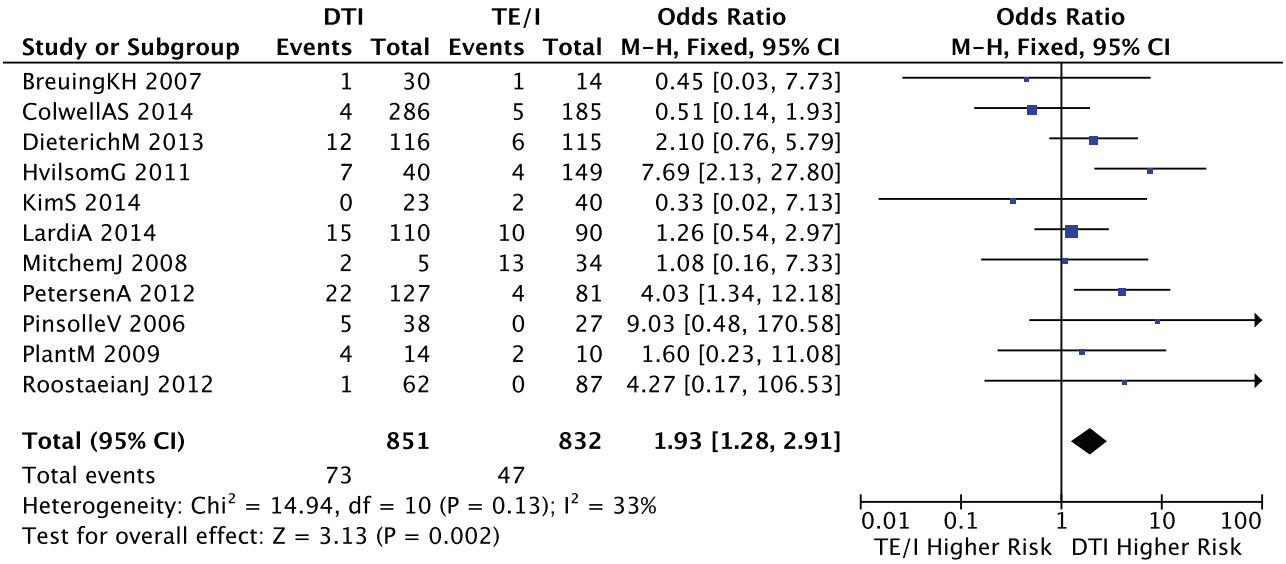


Fig. 3. Rate of implant loss for direct-to-implant versus tissue expander/implant reconstructions.

direct-to-implant reconstruction, patient selection is essential. Criteria for the ideal single-stage reconstructive candidate are numerous and include absence of comorbidities for poor wound-healing, avoiding postmastectomy chemotherapy and irradiation, and favorable mastectomy tissue quality at the time of initial reconstruction.[20,44] In studies reporting relative success with direct-to-implant reconstruction, patients generally had a lower prevalence of smoking. Similarly, poorer outcomes were consistently observed in patients requiring postreconstructive irradiation. Although these modifiable risk factors should be addressed in the preoperative setting if possible, it appears that the single most important criterion for patient candidacy is intraoperative judgment of mastectomy flap quality. Indeed, this is reflected in the recommendations by Colwell et al. on patient selection.[13,33] They present impressive results with direct-to-implant reconstruction, and their approach to implant-based reconstruction emphasizes flap tissue quality, with single-stage reconstruction reserved for only those patients that have both thick and well-vascularized mastectomy skin flaps. This algorithm suggests that the risk for skin flap necrosis and, subsequently, implant loss may decrease with higher quality mastectomy tissue. The advent of real-time perfusion mapping assisted by SPY (Novadaq Technologies, Inc., Bonita Springs, Fla.) and similar technologies represents an important aid for intraoperative planning. Specifically, in addition to perfusion assessment, models predicting the risk for mastectomy flap necrosis with 88 percent sensitivity and 83 percent specificity have surfaced.[45] Although simple in concept, the surgeon's intraoperative judgment may be one of the more challenging aspects of direct-to-implant reconstruction and should be a focus of the perioperative decision-making process.[9,33,46,47]

Given the number of reports demonstrating higher complications with direct-to-implant reconstruction, another important consideration in perioperative decision-making is recognizing the technically demanding nature of a single-stage reconstruction.[18,21,31,32] Several aspects of a single-stage procedure render it more challenging than conventional tissue expander/implant reconstruction. The unpredictable nature of the defect after oncologic resection is a particularly limiting factor, as implant size depends on the available soft-tissue envelope. Thus, the prosthesis placed may not align with the surgeon's or patient's expectations. Similarly, rotation or horizontal displacement of an expander can be readily addressed in the planned second stage of reconstruction, but is viewed as a complication in direct-to-implant procedures. One technical modification aimed at improving both the size and position of the implant with direct-to-implant reconstruction has been the use of an acellular dermal matrix inferolateral sling.[27,41] In this manner, acellular dermal matrix provides structural support of the muscular pocket and allows for insertion of larger prosthetics immediately. Although acellular dermal matrix–assisted reconstruction addresses some of the difficulties encountered with direct-to-implant reconstruction, it may

increase wound complication risks and represents a considerable source of health care costs.[39,48–50] Finally, management of patient expectations and satisfaction is particularly concerning in single-stage reconstruction. Indeed, the basis for choosing direct-to-implant reconstruction is to obtain a breast mound immediately and avoid a second operation at the same time. Although this study excluded implant revision secondary to aesthetic complaints, dissatisfaction with final implant appearance may influence the reconstructive preferences of the surgeon and the patient. Most notably, Eriksen et al. performed a prospective randomized trial comparing outcomes and satisfaction, demonstrating a 70 percent revision rate with direct-to-implant reconstruction because of unacceptable cosmetic appearance compared to only 10 percent of two-stage reconstructions.[30] If revision rates are higher after direct-to-implant reconstruction, as this study suggests, it may be attributable to an increased likelihood of implant malposition or need for contouring or capsule work. These findings further emphasize the importance of perioperative counseling and informed consent before surgery.

Limitations and Future Considerations

There are important limitations to this study that merit discussion. First, there was the potential for significant heterogeneity among patient populations, studies, and reconstructions. For this reason, careful inclusion criteria and analyses were used to critically assess and account for heterogeneity across and within studies. Assessment of outcome heterogeneity using the I^2 statistic demonstrates that only skin flap necrosis had a moderate amount of interstudy heterogeneity (50 to 75 percent), whereas all other outcomes had no to minimal heterogeneity (0 to 50 percent). Thus, it is likely that our findings are representative of the current literature; furthermore, skin flap necrosis has been the most common wound complication unique to direct-to-implant reconstruction in recent experience.[28,31,35] This observation lends further support to the assertion that it appears significantly more likely with direct-to-implant versus tissue expander/implant reconstruction despite borderline heterogeneity. Another consideration is mastectomy technique and incision type. Studies have demonstrated greater wound complication risks with nipple-sparing approaches.[51,52] As nipple-sparing techniques are used more commonly in direct-to-implant reconstruction, this may confound our results. A further limitation is the potential reverse bias. Patients selected for direct-to-implant reconstruction in this meta-analysis already resembled ideal direct-to-implant reconstruction candidates from both comorbidity and physical standpoints but still had higher complication rates. Therefore, direct-to-implant complication rates may have been higher if patient selection had been random. The average follow-up was 40.8 months, which certainly will not capture all long-term prosthesis-related complications. Namely, implant contracture was reported in only five studies, with no modality-specific difference in outcome. Because multiple operations may theoretically increase the risk for capsular contracture, this long-term outcome is of particular interest moving forward. Furthermore, the general underreporting of data in this review underscores the importance of continued research on implant outcomes to clarify performance by reconstructive modality over the long-term.

Finally, perhaps the most significant limitation of this study and an important target for future research was the inability to perform outcome subgroup analyses by patient subpopulations and operative techniques. Specifically, differentiating efficacy by the use of acellular dermal matrix or the presence of perioperative chemotherapy or irradiation is an important area that deserves further investigation. Along similar lines, there are considerations aside from postoperative surgical outcomes that should be explored to provide a more complete picture of the relative safety and efficacy of these two reconstructive modalities. As continuing advancements in technology and bioprosthetic design are realized, different implant characteristics and nonhuman acellular dermal matrix may illustrate improved cost efficacy, which has yet to be explored adequately.[12,42,53,54] Similarly, patient-reported outcomes and quality of life are quickly growing foci in health care outcomes research. Incorporating these aspects in reconstructive modality comparisons is vital to optimizing patient outcomes.

CONCLUSIONS

This head-to-head meta-analysis of 5216 breast reconstructions demonstrates a statistically higher incidence of skin flap necrosis and implant loss when a permanent prosthesis is placed immediately compared with conventional expander-implant reconstruction. These findings serve to aid in the risk-counseling process for patients and highlight the importance of continued investigation to assess outcomes more definitively.

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REFERENCES

1. Alderman AK, Wilkins EG, Lowery JC, Kim M, Davis JA. Determinants of patient satisfaction in postmastectomy breast reconstruction. *Plast Reconstr Surg.* 2000;106:769–776.
2. McCarthy CM, Klassen AF, Cano SJ, et al. Patient satisfaction with postmastectomy breast reconstruction: A comparison of saline and silicone implants. *Cancer* 2010;116:5584–5591.
3. Pusic AL, Klassen AF, Scott AM, Klok JA, Cordeiro PG, Cano SJ. Development of a new patient-reported outcome measure for breast surgery: The BREAST-Q. *Plast Reconstr Surg.* 2009;124:345–353.
4. Zhong T, McCarthy C, Min S, et al. Patient satisfaction and health-related quality of life after autologous tissue breast reconstruction: A prospective analysis of early postoperative outcomes. *Cancer* 2012;118:1701–1709.
5. Gurunluoglu R, Gurunluoglu A, Williams SA, et al. Current trends in breast reconstruction: Survey of American Society of Plastic Surgeons 2010. *Ann Plast Surg.* 2013;70:103–110.
6. Cemal Y, Albornoz CR, Disa JJ, et al. A paradigm shift in U.S. breast reconstruction: Part 2. The influence of changing mastectomy patterns on reconstructive rate and method. *Plast Reconstr Surg.* 2013;131:320e–326e.
7. Albornoz CR, Bach PB, Mehrara BJ, et al. A paradigm shift in U.S. breast reconstruction: Increasing implant rates. *Plast Reconstr Surg.* 2013;131:15–23.
8. Colakoglu S, Khansa I, Curtis MS, et al. Impact of complications on patient satisfaction in breast reconstruction. *Plast Reconstr Surg.* 2011;127:1428–1436.
9. Cordeiro PG, McCarthy CM. A single surgeon's 12-year experience with tissue expander/implant breast reconstruction: Part II. An analysis of long-term complications, aesthetic outcomes, and patient satisfaction. *Plast Reconstr Surg.* 2006;118:832–839.
10. Cordeiro PG, McCarthy CM. A single surgeon's 12-year experience with tissue expander/implant breast reconstruction: Part I. A prospective analysis of early complications. *Plast Reconstr Surg.* 2006;118:825–831.
11. Fischer JP, Nelson JA, Serletti JM, et al. Peri-operative risk factors associated with early tissue expander (TE) loss following immediate breast reconstruction (IBR): A review of 9305 patients from the 2005–2010 ACS-NSQIP datasets. *J Plast Reconstr Aesthet Surg.* 2013;66:1504–1512.
12. Delgado JF, García-Guilarte RF, Palazuelo MR, Mendez JI, Pérez CC. Immediate breast reconstruction with direct, anatomic, gel-cohesive, extra-projection prosthesis: 400 cases. *Plast Reconstr Surg.* 2010;125:1599–1605.
13. Colwell AS, Damjanovic B, Zahedi B, Medford-Davis L, Hertl C, Austen WG Jr. Retrospective review of 331 consecutive immediate single-stage implant reconstructions with acellular dermal matrix: Indications, complications, trends, and costs. *Plast Reconstr Surg.* 2011;128:1170–1178.
14. Glasberg SB, Light D. AlloDerm and Strattice in breast reconstruction: A comparison and techniques for optimizing outcomes. *Plast Reconstr Surg.* 2012;129:1223–1233.
15. Salzberg CA. Focus on technique: One-stage implant-based breast reconstruction. *Plast Reconstr Surg.* 2012;130(Suppl 2): 95S–103S.
16. Salzberg CA. Direct-to-implant breast reconstruction. *Clin Plast Surg.* 2012;39:119–126.
17. Salzberg CA, Ashikari AY, Koch RM, Chabner-Thompson E. An 8-year experience of direct-to-implant immediate breast reconstruction using human acellular dermal matrix (AlloDerm). *Plast Reconstr Surg.* 2011;127:514–524.
18. Hvilsom GB, Friis S, Frederiksen K, et al. The clinical course of immediate breast implant reconstruction after breast cancer. *Acta Oncol.* 2011;50:1045–1052.
19. Bailey MH, Smith JW, Casas L, et al. Immediate breast reconstruction: Reducing the risks. *Plast Reconstr Surg.* 1989;83:845–851.
20. Fischer JP, Wes AM, Tuggle CT III, Serletti JM, Wu LC. Risk analysis of early implant loss after immediate breast reconstruction: A review of 14,585 patients. *J Am Coll Surg.* 2013;217:983–990.
21. Pinsolle V, Grinfeder C, Mathoulin-Pelissier S, Faucher A. Complications analysis of 266 immediate breast reconstructions. *J Plast Reconstr Aesthet Surg.* 2006;59:1017–1024.
22. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: Explanation and elaboration. *BMJ* 2009;339:b2700.
23. Sullivan D, Chung KC, Eaves FF III, Rohrich RJ. The level of evidence pyramid: Indicating levels of evidence in *Plastic and Reconstructive Surgery* articles. *Plast Reconstr Surg.* 2011;128:311–314.
24. Spear SL, Baker JL Jr. Classification of capsular contracture after prosthetic breast reconstruction. *Plast Reconstr Surg.* 1995;95:1119–1123; discussion 1124.
25. Harbord RM, Higgins JPT. Meta-regression in Stata. *Stata J.* 2008;8:493–519.
26. *Review Manager (RevMan) (Computer Program).* Version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration; 2012.
27. Breuing KH, Colwell AS. Inferolateral AlloDerm hammock for implant coverage in breast reconstruction. *Ann Plast Surg.* 2007;59:250–255.
28. Mitchem J, Herrmann D, Margenthaler JA, Aft RL. Impact of neoadjuvant chemotherapy on rate of tissue expander/implant loss and progression to successful breast reconstruction following mastectomy. *Am J Surg.* 2008;196:519–522.
29. Plant MA, Scilley CG, Speechley M. Single-stage immediate breast reconstruction using a skin-sparing incision and definitive saline implants compared with a two-stage reconstruction using tissue expansion plus implants. *Can J Plast Surg.* 2009;17:117–123.
30. Eriksen C, Lindgren EN, Frisell J, Stark B. A prospective randomized study comparing two different expander approaches in implant-based breast reconstruction: One stage versus two stages. *Plast Reconstr Surg.* 2012;130:254e–264e.
31. Petersen A, Eftekhari AL, Damsgaard TE. Immediate breast reconstruction: A retrospective study with emphasis on complications and risk factors. *J Plast Surg Hand Surg.* 2012;46:344–348.
32. Roostaeian J, Sanchez I, Vardanian A, et al. Comparison of immediate implant placement versus the staged tissue

expander technique in breast reconstruction. *Plast Reconstr Surg.* 2012;129:909e–918e.
33. Colwell AS, Tessler O, Lin AM, et al. Breast reconstruction following nipple-sparing mastectomy: Predictors of complications, reconstruction outcomes, and 5-year trends. *Plast Reconstr Surg.* 2014;133:496–506.
34. Kim SW, Lee HK, Kang SM, et al. Short-term outcomes of immediate breast reconstruction using an implant or tissue expander after mastectomy in breast cancer patients. *Breast Cancer* October 22, 2014 (e-published ahead of print).
35. Lardi AM, Ho-Asjoe M, Mohanna PN, Farhadi J. Immediate breast reconstruction with acellular dermal matrix: Factors affecting outcome. *J Plast Reconstr Aesthet Surg.* 2014;67:1098–1105.
36. Gfrerer L, Mattos D, Mastroianni M, et al. Assessment of patient factors, surgeons, and surgeon teams in immediate implant-based breast reconstruction outcomes. *Plast Reconstr Surg.* 2015;135:245e–252e.
37. Susarla SM, Ganske I, Helliwell L, et al. Comparison of clinical outcomes and patient satisfaction in immediate single-stage versus two-stage implant-based breast reconstruction. *Plast Reconstr Surg.* 2015;135:1e–8e.
38. Becker H. A prospective randomized study comparing two different expander approaches in implant-based breast reconstruction: One stage versus two stages. *Plast Reconstr Surg.* 2013;131:643e–644e.
39. Butterfield JL. 440 Consecutive immediate, implant-based, single-surgeon breast reconstructions in 281 patients: A comparison of early outcomes and costs between SurgiMend fetal bovine and AlloDerm human cadaveric acellular dermal matrices. *Plast Reconstr Surg.* 2013;131:940–951.
40. Francel TJ, Ryan JJ, Manson PN. Breast reconstruction utilizing implants: A local experience and comparison of three techniques. *Plast Reconstr Surg.* 1993;92:786–794.
41. Weichman KE, Wilson SC, Weinstein AL, et al. The use of acellular dermal matrix in immediate two-stage tissue expander breast reconstruction. *Plast Reconstr Surg.* 2012;129:1049–1058.
42. Salzberg CA, Dunavant C, Nocera N. Immediate breast reconstruction using porcine acellular dermal matrix (Strattice): Long-term outcomes and complications. *J Plast Reconstr Aesthet Surg.* 2013;66:323–328.
43. Antony AK, McCarthy C, Disa JJ, Mehrara BJ. Bilateral implant breast reconstruction: Outcomes, predictors, and matched cohort analysis in 730 2-stage breast reconstructions over 10 years. *Ann Plast Surg.* 2014;72:625–630.
44. Momoh AO, Ahmed R, Kelley BP, et al. A systematic review of complications of implant-based breast reconstruction with prereconstruction and postreconstruction radiotherapy. *Ann Surg Oncol.* 2014;21:118–124.
45. Munabi NC, Olorunnipa OB, Goltsman D, Rohde CH, Ascherman JA. The ability of intra-operative perfusion mapping with laser-assisted indocyanine green angiography to predict mastectomy flap necrosis in breast reconstruction: A prospective trial. *J Plast Reconstr Aesthet Surg.* 2014;67:449–455.
46. Cordeiro PG, McCarthy CM. A single surgeon's 12-year experience with tissue expander/implant breast reconstruction: Part I. A prospective analysis of early complications. *Plast Reconstr Surg.* 2006;118:825–831.
47. Wang F, Peled AW, Garwood E, et al. Total skin-sparing mastectomy and immediate breast reconstruction: An evolution of technique and assessment of outcomes. *Ann Surg Oncol.* 2014;21:3223–3230.
48. Jansen LA, Macadam SA. The use of AlloDerm in postmastectomy alloplastic breast reconstruction: Part I. A systematic review. *Plast Reconstr Surg.* 2011;127:2232–2244.
49. Jansen LA, Macadam SA. The use of AlloDerm in postmastectomy alloplastic breast reconstruction: Part II. A cost analysis. *Plast Reconstr Surg.* 2011;127:2245–2254.
50. Ganske I, Verma K, Rosen H, Eriksson E, Chun YS. Minimizing complications with the use of acellular dermal matrix for immediate implant-based breast reconstruction. *Ann Plast Surg.* 2013;71:464–470.
51. Reish RG, Lin A, Phillips NA, et al. Breast reconstruction outcomes after nipple-sparing mastectomy and radiation therapy. *Plast Reconstr Surg.* 2015;135:959–966.
52. Endara M, Chen D, Verma K, Nahabedian MY, Spear SL. Breast reconstruction following nipple-sparing mastectomy: A systematic review of the literature with pooled analysis. *Plast Reconstr Surg.* 2013;132:1043–1054.
53. Dieterich M, Paepke S, Zwiefel K, et al. Implant-based breast reconstruction using a titanium-coated polypropylene mesh (TiLOOP Bra): A multicenter study of 231 cases. *Plast Reconstr Surg.* 2013;132:8e–19e.
54. Liu DZ, Mathes DW, Neligan PC, Said HK, Louie O. Comparison of outcomes using AlloDerm versus FlexHD for implant-based breast reconstruction. *Ann Plast Surg.* 2014;72:503–507.