Risk Factors for Complications Differ Between Stages of Tissue-Expander Breast Reconstruction

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Background: Tissue-expander (TE) placement followed by implant exchange is currently the most popular method of breast reconstruction. There is a relative paucity of data demonstrating patient factors that predict complications specifically by stage of surgery. The present study attempts to determine what complications are most likely to occur at each stage and how the risk factors for complications vary by stage of reconstruction.

Methods: A retrospective chart review was performed on all 1275 patients who had TEs placed by the 2 senior authors between 2004 and 2013. Complication rates were determined at each stage of reconstruction, and these rates were further compared between patients who had pre-stage I radiation, post-stage I radiation, and no radiation exposure. Multivariate logistic regression was used to identify independent predictors of complications at each stage of reconstruction.

Results: A total of 1639 consecutive TEs were placed by the senior authors during the study period. The overall rate for experiencing a complication at any stage of surgery was 17%. Complications occurred at uniformly higher rates during stage I for all complications (92% stage I vs 7% stage II vs 1% stage III, $P < 0.001$). Predictors of stage I complications included increased body mass index [odds ratio (OR), 1.04; 95% confidence interval (CI), 1.01–1.07], current smoking status (OR, 3.0; 95% CI, 1.7–4.8), and higher intraoperative percent fill (OR, 3.3; 95% CI, 1.7–6.3). Post-stage I radiation was the only independent risk factor for a stage II complication (OR, 4.5; 95% CI, 1.4–15.2).

Conclusions: Complications occur at higher rates after stage I than after stage II, and as expected, stage III complications are exceedingly rare. Risk factors for stage I complications are different from risk factors for stage II complications. Body mass index and smoking are associated with complications at stage I, but do not predict complications at stage II surgery. The stratification of risk factors by stage of surgery will help surgeons and patients better manage both risk and expectations.

Key Words: breast reconstruction, complications, tissue expander, risk factors, implant, immediate reconstruction, breast cancer

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Breast cancer is increasing morbidity and mortality for women around the world.[1] The complexity of the choice between breast conservation with follow-up treatment and mastectomy has many women opting for mastectomy. In recent years, more women are electing to undergo mastectomy rather than breast conservation therapy. Currently, tissue-expander (TE) placement followed by implant exchange is the most popular method of postmastectomy reconstruction.[2,3] The completion of reconstruction and avoidance of complications is paramount in ensuring patient satisfaction.[4–6] We will focus on complications, which may occur at any stage of the reconstructive process.

Tissue-expander reconstruction can be divided into 3 stages. Stage I involves placement of the TE, stage II consists of exchanging the TE for a permanent implant, and stage III entails the nipple-areolar complex (NAC) reconstruction. Complication rates differ at each stage,[7] and it has been shown that the timing of adjuvant radiation therapy (ART) affects how complications are distributed among reconstruction stages.[8–15] These trends suggest that predictors of complications vary at each stage of reconstruction. To date, no study has analyzed how risk factors for complications may differ depending on the reconstructive stage; rather, studies have focused on determining risk factors for complications at any point in the reconstruction.[16,17] Although these findings are helpful, the multiphasic nature of TE reconstruction demands a longitudinal stage-by-stage analysis. Surgeons and patients alike will benefit from knowing what complications are most expected at each stage of surgery, and how patient and treatment risk factors may differ at each stage.

By reviewing TE reconstructions performed by 2 surgeons who have been practicing together at the same center for 9 years, we have attempted to fill this gap in the literature. The primary objectives of this study were to (1) determine complication rates after each of the 3 stages of implant-based breast reconstruction and (2) compare and contrast risk factors for complications at each stage.

PATIENTS AND METHODS

A retrospective review of all consecutive TE-based breast reconstructions conducted by the 2 senior authors (J.Y.S.K. and N.A.F.) between 2004 and 2013 was performed with institutional review board approval. Patients whose records had large amounts of missing data were excluded from the review, leaving 1275 patients eligible for chart review during this period.

Demographic variables collected included patient age, body mass index (BMI), and comorbidities, specifically diabetes mellitus, smoking status, hypertension, and peripheral vascular disease/coronary artery disease (PVD/CAD). Other comorbidities, for example, hypothyroidism, hyperlipidemia, bleeding disorders, were captured as a catchall variable. Oncologic variables included preoperative radiation, postoperative radiation, and adjuvant chemotherapy. Surgical variables included type of mastectomy, bilateral or unilateral reconstruction, sentinel lymph node biopsy, axillary lymph node dissection, use of acellular dermal matrix, type of TE or implant, size of TE or implant, and intraoperative fill volume of TE or implant. Complications included wound dehiscence/necrosis, hematoma, seroma, major infection requiring intravenous antibiotics, and failed reconstruction, defined as a TE removal or conversion to autologous reconstruction. Capsular contracture was not recorded due to subjective reporting in chart reviews and the difficulty of consistently reporting outcomes.[18] Rather, complaints of tightness or discomfort that eventually resulted

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in TE removal or conversion to autologous reconstruction were recorded as "failed reconstructions."

Surgical Technique

All reconstructive procedures were performed by the 2 senior authors (J.Y.S.K. and N.A.F.).

Stage I

The mastectomy was performed by the oncologic surgeon, usually through an incision encompassing the NAC with a lateral extension for skin-sparing mastectomy, or through a lateral inframammary fold incision for nipple-sparing mastectomy. Tissue expanders were placed in a submuscular position with serratus fascia or acellular dermal matrix used for lateral and/or inferior support. The expander was filled to the point at which the skin laxity was taken up, but the skin was not stretched. Two closed suction drains were placed, and the skin was closed.

Postoperatively, the closed suction drains remained in place until output was less than 30 mL over 24 hours. Oral antibiotic prophylaxis was prescribed until removal of drains. Once the incisions had healed (yet not longer than 3 weeks), serial expansions were performed with intervals and fill volumes determined on a per-patient basis. Expansions were delayed if patients were to undergo ART. Patients proceeded with stage II after completion of tissue expansion and adjuvant therapy.

Stage II

Preoperatively, with the patient in an upright sitting position, areas requiring capsule modification or fat grafting were identified and marked. Under general anesthesia or conscious sedation, the lateral mastectomy scar was opened, and the expander was removed. Linear or multiplanar capsulotomy or capsular plication was performed as necessary. The pocket was copiously irrigated with antibiotic solution, and the permanent implant was inserted using a minimal touch technique.

Stage III

Nipple-areolar complex reconstruction was performed under local anesthesia with or without sedation using a C-V flap followed by medical tattooing.

Statistical Analysis

Independent categorical variables were compared using Pearson χ^2 and Fisher exact test when appropriate, whereas paired categorical data were compared using McNemar test. Continuous variables were compared using Wilcoxon rank sum tests and reported as medians with associated interquartile ranges. To determine independent risk factors for complications at stages I and II of reconstruction, logistic regression models were generated. Each outcome of interest was screened for a univariate association with all patient demographics, comorbidities, oncologic characteristics, and surgical variables. Additionally, the occurrence of a stage I complication and the interval between stages I and II were screened for possible inclusion into the regression model for a stage II complication. Factors with a univariate association of $P \leq 0.20$ and an event occurrence of at least 10 for the stage I complication model and at least 5 for the stage II complication model were included as covariates in the multivariate model.[19,20] Hosmer-Lemeshow and C-statistics were computed to assess goodness-of-fit and discriminatory capacity of the model.[21] All statistical analyses were performed using SPSS for Windows (Version 21.0; IBM Corp, Armonk, NY).

RESULTS

A total of 1639 TEs were placed in 1275 patients during the 9-year period covered by this review. Demographic data are displayed in Table 1. Seventy-eight percent of TEs (1271 of 1639) went on to undergo implant exchange, whereas the remaining 22% (368 expanders) were lost to follow-up, underwent explantation, or converted to autologous reconstruction. Excluding 187 nipple-sparing mastectomy cases, 41% of stage I patients (599 of 1452) went on to receive NAC reconstruction. Average follow-up time was 26.8 months from the original surgery.

Out of all TEs placed, 283 breasts experienced 1 or more complications at any time during the reconstruction, for an overall complication rate of 17.3%. Patients uniformly experienced more complications after stage I compared to both of the other stages (15.9% complication rate in stage I vs 1.5% stage II vs 1% stage III, $P < 0.001$). Additionally, failed reconstructions occurred at a higher rate after stage I than after stage II or III (7.2% stage I vs 1.7% stage II vs 0.3% stage III, $P < 0.001$; Table 2). The distribution of complication type was similar at both stages I and II (Fig. 1), with exposure/dehiscence representing the bulk of complications (52% vs 46%, $P = 0.335$).

TABLE 1. Case Series Characteristics [n = 1639 Breasts (1275 Patients)]

Demographics	
Age,* y	47 (41–56)
BMI,* kg/m^2	24 (22–29)
Diabetes	72 (4.4)
Smoker	
Current	139 (8.5)
Past	287 (17.5)
Hypertension	271 (16.5)
PVD/CAD	65 (4.0)
Other comorbidity	396 (24.2)
Oncologic variables	
Radiation	
Pre-stage I	164 (10.0)
Post-stage I	327 (20.0)
Chemotherapy	849 (51.8)
Surgical variables	
Axillary dissection	417 (25.4)
Sentinel node biopsy	830 (50.6)
Prophylactic mastectomy	539 (32.9)
Bilateral mastectomy	958 (58.5)
Nipple-sparing mastectomy	187 (11.4)
Use of ADM	318 (19.4)
Average intraoperative fill,* %	50 (31–75)

Values are number (percentage) unless otherwise indicated.
*Continuous variables are reported as median with interquartile range.
ADM indicates acellular dermal matrix; PVD/CAD indicates peripheral vascular disease/coronary artery disease.

TABLE 2. Complication by Stage of Surgery

	Stage I (n = 1639)		Stage II (n = 1271)		Stage III (n = 599)		
	n	%	n	%	n	%	Total
Any complication (≥1)*	261	15.9	21	1.5	3	0.5	283
Dehiscence/necrosis	159	9.7	11	0.9	2	0.3	172
Infection requiring intravenous antibiotics	67	4.1	9	0.7	1	0.2	77
Hematoma	33	2.0	3	0.2	0	0.0	36
Seroma	46	2.8	1	0.1	0	0.0	47
Failed reconstruction*	118	7.2	21	1.7	2	0.3	141

*McNemar test for paired data or Pearson χ^2 shows significance of $P < 0.001$.

Effect of Radiation on Complication Rates

Figure 2 presents overall complication rates among patients who received radiation at different times of treatment. Stage I complication rates were comparable between patients who received pre-stage I radiation and those who had not (19.3% treated vs 14.4% untreated, $P = 0.136$). On the other hand, patients who received radiation after placement of the TE had higher rates of stage II complications (8.1% vs 0.6%, $P < 0.001$). Out of the 3 patients who experienced a stage III complication, 2 had post-stage I radiation.

Independent Predictors of Complications at Each Stage

After controlling for confounders, various factors were found to increase the odds of experiencing a stage I complication (Table 3). Each unit increase in BMI and each 10% increase in intraoperative percent fill conferred a higher odds of experiencing a stage I complication [odds ratio (OR), 1.04; 95% confidence interval (CI), 1.01–1.07; OR, 3.3; 95% CI, 1.7–6.3, respectively]. Additionally, patients who were current smokers were 3 times as likely to experience a complication (OR, 3.0; 95% CI, 1.8–4.9). The model had a C-statistic of 0.673, indicative of decent discriminatory capacity.

Risk factors for stage II complications differed from risk factors for stage I complications (Table 4). Smoking, BMI, and high intraoperative fill volume were not predictive of stage II complications. Post-stage I radiation served as a strong independent predictor of experiencing a stage II complication (OR, 4.5; 95% CI, 1.4–15.2). The regression model demonstrated a high discriminatory capacity, indicated by a C-statistic of 0.818.

Finally, the limited number of stage III complications prevented the generation of a logistic regression model.

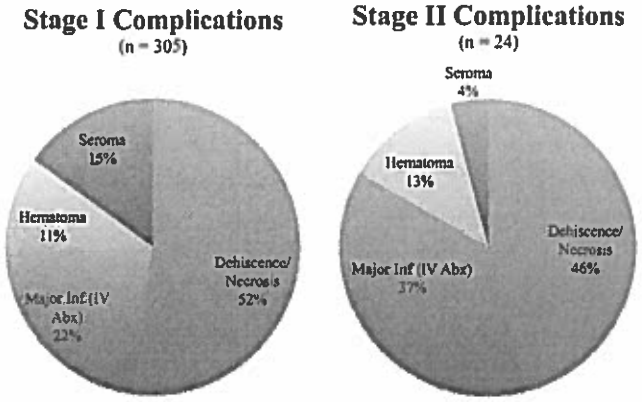

FIGURE 1. The distribution of complications by stage of surgery. Although the distributions of complication type are comparable at each stage ($P = 0.335$), stage I and II complications occur in an approximately 10:1 ratio ($P < 0.001$, McNemar test for paired data, see Table 1).

DISCUSSION

Prosthetic-based reconstruction makes up most of breast reconstructions nationwide.[2,3] Prior studies have identified risk factors for complications during TE/implant surgery,[16,17] but none have stratified the risk factors by stage of reconstruction. Given the multistage nature of TE breast reconstruction, knowing what patient risk factors predict complications at each stage helps surgeons plan how and when surgeries will be performed to ensure completion of the reconstruction. Using a large review of cases performed by 2 surgeons using the same surgical technique and treatment protocol, we have been able to show that risk factors for complications do indeed differ at each stage of reconstruction.

Uniformly, complications occurred in greater rates after TE placement than after implant exchange and NAC reconstruction. From stages I to III, overall complications occurred at about a 100:10:1 ratio. Our findings corroborate recent publications,[7,15] which show that complications occur at higher rates after stage I. Given the high rates of complications after mastectomy alone,[22,23] this pattern is not surprising. Elevation of the mastectomy flap with subsequent TE placement has been cited as a reason for higher complication rates,[7] highlighting the importance of confirming proper flap perfusion. Dehiscence/necrosis was the most common complication, and the one most likely to occur in stage I, findings that further support the need to ensure tissue viability at the time of TE placement.

Differences in Predictors of Complications

Although knowing what complications are most likely to occur at each stage is important in advising patients, the unique contribution of this study is our demonstration that risk factors for complications differ by stage of reconstruction. The risk factors for stage II complications are inherently different from those associated with stage I complications, which we attribute to 2 surgical aspects. Mastectomy and immediate TE placement involves a hypovascular field subject to a larger degree of tissue manipulation compared to the implant exchange procedure. Second, the implant exchange is performed only once the breast tissue has had sufficient time to heal and reestablish perfusion.

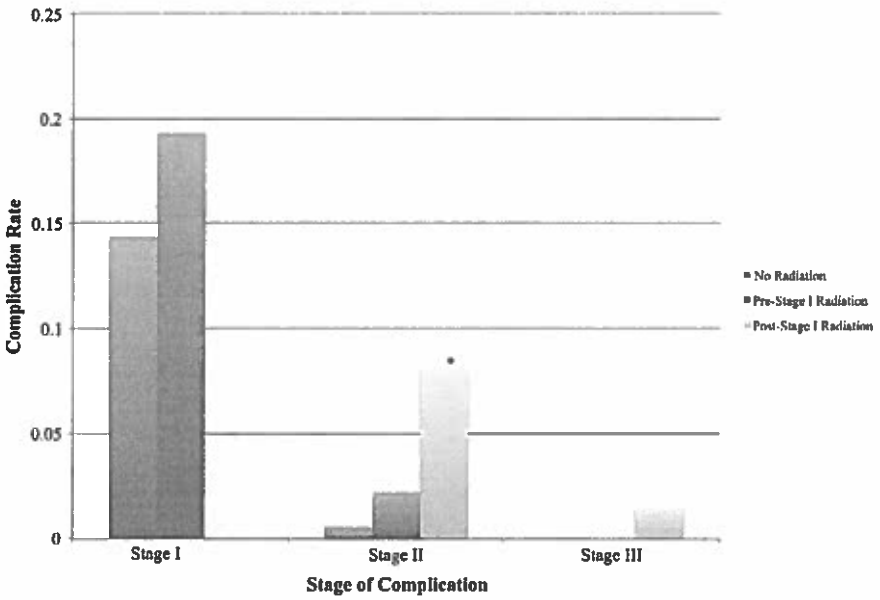

FIGURE 2. Complication rate by stage of surgery, stratified by radiation status. Patients who have radiation between stages I and II experience higher rates of complications after stage II surgery. *Denotes significant difference compared to "No Radiation" cohort.

These issues are manifest when we consider increased BMI, which was found to be a risk factor for stage I complications, but not for stage II complications. Obese patients have more dead space after the mastectomy, predisposing them to a complication.[17,24,25] Additionally, long mastectomy skin flaps are more vulnerable to distal ischemia. However, after expansion, sufficient time is given for perfusion to be reestablished. As a result, obese patients have the same odds of stage II complications as their nonobese counterparts.

A similar effect occurs with smoking. Current smokers were found to have a 3.0 times higher odds of a stage I complication. Our OR closely mirrors that of McCarthy et al,[17] who found that the odds of a complication (from the beginning of the reconstruction up to 6 months after completion) in current smokers is 2.2 times that of a nonsmoker. However, smoking did not predict a stage II complication. Smoking increases complications through a general reduction in wound healing capacity.[26,27] Compared with stage I, there is less tissue manipulation performed during implant exchange, reducing the healing burden after surgery.

Patients who had higher intraoperative fill percentages had a greater likelihood of experiencing a stage I complication. Crosby et al[28] suggested that higher intraoperative fill percentages contributed to complications but were unable to demonstrate percent fill as an independent risk factor, likely due to a small sample size. Our larger patient series was able to show that each 10% increase in percent fill independently predisposed patients toward having a stage I complication. Although surgical judgment is used to avoid placing undue tension on the mastectomy flap by overfilling the expander

TABLE 3. Multivariate Regression Analysis for a Stage I Complication

		95% CI for OR		
	OR	Lower	Upper	*P*
Covariate				
Age,* y	1.02	1.00	1.03	0.110
BMI,*† kg/m^2	1.04	1.01	1.07	0.011
Diabetes	1.53	0.74	3.17	0.250
Current smoker†	2.96	1.79	4.91	<0.001
Past smoker	1.03	0.66	1.59	0.909
Hypertension	0.96	0.58	1.58	0.872
PVD/CAD	1.49	0.73	3.02	0.270
Other comorbidity	1.05	0.70	1.58	0.826
Pre-stage I radiation	1.22	0.73	2.06	0.448
Bilateral mastectomy	0.86	0.60	1.23	0.397
Axillary dissection	1.10	0.72	1.68	0.657
Percent fill (per 10%)†	3.29	1.72	6.29	<0.001

C-statistic of 0.673; Hosmer-Lemeshow statistic of 0.358.
*Continuous variable, ORs represent change in likelihood of outcome per unit increase.
†Denotes significance $P \leq 0.05$.

TABLE 4. Multivariate Regression Analysis for a Stage II Complication

		95% CI for OR		
	OR	Lower	Upper	*P*
Covariate				
BMI,* kg/m^2	1.03	0.95	1.12	0.481
Chemotherapy	1.00	0.28	3.61	1.000
Pre-stage I radiation	3.47	0.91	13.25	0.069
Post-stage I radiation†	4.54	1.36	15.18	0.014
Bilateral mastectomy	0.31	0.09	1.02	0.054
Percent fill (per 10%)	0.90	0.75	1.07	0.226

C-statistic of 0.818; Hosmer-Lemeshow statistic of 0.513.
*Continuous variable, ORs represent increase in likelihood of outcome per unit increase.
†Significance $P \leq 0.05$.

during placement, there is still minimal tension that affects blood perfusion to the healing wound. Additionally, it is hard to fully exclude the impact of longer mastectomy skin flaps being part of the issue with higher fill volumes. In stage II of reconstruction, we have tissue with a stable, intact blood supply, and thus initial intraoperative fill volume was not a risk factor for stage II complications.

Pre-stage I radiation did not independently change the likelihood of a complication after stage I or II, contrasting a widely believed notion.[13,29] The findings of our study may be attributed to the methodology behind our logistic regression model and the selection of patients who underwent TE reconstruction. For example, Lin et al[13] found that preoperative radiation predisposed a patient to a major complication, but only included covariates that have been historically implicated as confounders. We statistically determined covariates through the use of a univariate screen with strict inclusion criteria, a method that has been used successfully on multicenter databases with the necessary sample sizes to perform such an analysis.[24] Additionally, the selection of patients for TE reconstruction must be considered. Patients at our center only underwent TE reconstruction if their skin quality was deemed viable enough to undergo the procedure. This is the same selection criteria described in McCarthy et al,[17] which also found that irradiation of the chest wall before breast reconstruction was not a predictor of complications.

In contrast, radiation after placement of the TE greatly increases the odds of a complication after stage II (OR, 4.5), a finding consistent with past literature.[12–14] Dehiscence/necrosis was the most common complication seen in patients who received post-stage I ART, supporting the well-known mechanism that damage to the microvasculature leads to tissue fibrosis. After implant exchange, the fibrotic tissue has limited regenerative capacity, making wound dehiscence much more likely.

Complications after nipple reconstruction were exceedingly rare. The completion of nipple reconstruction (stage III) is paramount in ensuring patient satisfaction,[5,6,30] yet few studies have focused on complications and risk factors that may interrupt the reconstructive process.[31–33] Forty-one percent of our series underwent NAC reconstruction, which is similar to the 47% to 51% rate reported by other centers.[30,34] Momoh et al[30] reported that the occurrence of a complication did not affect nipple reconstruction rate. Our series is the largest to date that reports on outcomes after nipple reconstruction. Only 3 complications and 2 failed reconstructions occurred after stage III, demonstrating that the procedure is performed safely. However, post-stage I radiation may affect complication rates after nipple reconstruction, a notion supported by past literature.[32] In our series, 2 of 3 stage III complications occurred in patients who had post-stage I radiation, and 1 of the 2 failed reconstructions also occurred in this cohort (Fig. 2). These trends did not reach significance, likely due to the limited statistical power provided by such a small number of events.

Despite the advantages provided by a large, dual-surgeon, single-center series, including homogeneity of surgical technique and treatment protocol, there were limitations to this analysis. First, patients most likely to have a complication may have experienced a stage I reconstructive failure and not progressed to stage II. Thus, the risk factors that predisposed them to a complication in the first place may have been underrepresented in the regression model for stage II complications. Second, the study was performed in an urban academic hospital, so the patient population, treatment options, and surgical volume may vary from that of other institutions, limiting the general applicability of our findings. The volume of breast reconstruction cases is high at our institution, which has been shown to confer favorable outcomes.[35,36] Third, our logistic regression model was limited in its ability to identify risk factors for stage II complications. There were 21 stage II complications, which did not provide the statistical power necessary to identify all possible covariates. Fourth, our initial goal of identifying risk factors for complications at all stages of surgery was restricted by the small number of nipple reconstruction complications that occurred. More research on complications after nipple reconstruction is needed, especially given the increasing prevalence of radiation therapy given before this stage of reconstruction. Lastly, it is well recognized that delayed expander reconstruction decreases complications[37]—but precludes the advantages of immediate skin-sparing or nipple-sparing reconstruction.

CONCLUSIONS

On the basis of the results of our series, complications in TE breast reconstruction consistently occur at a higher rate after stage I than after stage II or III. Dehiscence/necrosis is the most common complication seen at all stages of reconstruction.

Surgeons and patients must be aware that independent predictors of stage I complications include higher BMI, current smoking status, and higher intraoperative fill volume. Although stage II complications occur at lower rates, post-stage I radiation predisposes patients to experience complications after implant exchange. Lastly, stage III complications occur at a very low rate, but may also be affected by post-stage I radiation. We hope this information will help surgeons, hospitals, and patients alike to ensure patient satisfaction through the full completion of each TE breast reconstruction.

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