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Impact of Surgical Techniques, Biomaterials, and Patient Variables on Rate of Nipple Necrosis after Nipple-Sparing Mastectomy

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Abstract

Background—Nipple-sparing mastectomy (NSM) is appropriate for selected patients with early-stage breast cancer or high breast cancer risk. However, the rate of nipple necrosis after NSM is relatively high (10% to 30%). No study has specifically evaluated whether clinical and technical factors contribute to nipple necrosis after NSM. The objectives of this study were to determine the impact of clinicopathologic and surgical variables on rates of partial and total nipple necrosis after NSM and to compare overall complication rates between NSM and skin-sparing mastectomy (SSM).

Methods—The study included 233 cases, 113 had NSM and immediate breast reconstruction and 120 matched (for disease stage, comorbidities, and age) cases of SSM and immediate reconstruction performed at our institution from September 2003 through May 2011. Complications were analyzed using the Fisher's exact test, and in the NSM group, clinicopathologic and surgical variables were analyzed using Rao-Scott chi-squared tests for relationship with partial or total nipple necrosis.

Results—The overall complication rate was 28% for NSM and 27% for SSM ($p>0.99$). In patients who did not have axillary surgery (those undergoing risk-reducing mastectomy), the overall rate of complications was significantly higher in the NSM group than in the SSM group (26% versus 9%; $p=0.06$). However, in patients who had axillary surgery (either sentinel lymph node biopsy or axillary lymphadenectomy), the overall complication rate did not differ between the two groups. For NSM, the overall incidence of any (partial or total) nipple necrosis was 20%. There were only 2 cases (2%) with total necrosis. Larger breasts (C cup or larger) were associated with a higher rate of nipple necrosis (34% for C cup; 6% for A and B cup; $p=0.003$). Smoking ($p=0.08$) and vascular comorbidities ($p=0.09$) did not reach statistical significance as predictors of nipple necrosis. The other factors analyzed were not predictors of nipple necrosis.

Conclusions—We found no significant difference in the overall incidence of complications in patients who have NSM compared to those who have SSM. Interestingly, the exclusion of axillary lymphatic surgery in patients undergoing risk-reducing NSM for high breast cancer risk did not

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decrease the incidence of complications, probably because of the inherent technical complexity of performing NSM in and of itself. Although partial nipple necrosis did occur quite frequently (19%), total nipple necrosis after NSM occurred infrequently (2%). Importantly, patients with breast size of C cup or larger had an increased risk for nipple necrosis after NSM and immediate breast reconstruction.

Clinical Level of Evidence—Therapeutic, III.

INTRODUCTION

Nipple-sparing mastectomy (NSM) is feasible for treatment of selected patients with early-stage breast cancer and for risk-reducing mastectomy in patients at high risk for breast cancer.¹⁻⁴ NSM has increased in popularity as oncologic studies have reported its safety in terms of local recurrence.⁴⁻⁹ An important consideration in the decision to perform NSM is the potential for recurrence of cancer or development of a new primary cancer in the retained nipple-areolar complex (NAC).^{6, 7} Currently, many surgeons offer NSM only to patients who have a peripheral tumor less than 3 cm in diameter with no nodal disease, and some studies recommend that NSM be performed only in patients who have tumors no closer than 5 cm from the NAC.^{1, 7, 10-12} However, it is likely that the indications for NSM will be broadened in the near future as more long-term data on the risk of recurrence after NSM become available.³ However, despite the obvious aesthetic advantages of NSM, the relatively high rate of nipple necrosis after NSM has slowed the incorporation of this approach into routine clinical practice.^{1, 3, 13}

NSM includes removal of the tissue located behind the NAC in order to decrease the risk of recurrence in the NAC, reported rates of which range from 12% to 48%.^{2, 3, 6, 8, 14, 15} The removal of the tissue behind the NAC puts the nipple at risk for ischemic necrosis because it is stripped of local perforators, leaving it dependent on the dermal microvasculature. The decreased perfusion to the NAC may be exacerbated by technical aspects of the mastectomy and reconstruction that may further decrease the regional blood supply.^{13, 16, 17, 18}

The objectives of this study were to determine the impact of clinicopathologic and surgical variables on rates of nipple and areolar necrosis (hereafter referred to as nipple necrosis) after NSM and to compare overall complication rates between NSM and skin-sparing mastectomy (SSM).

METHODS

Selection of Cases

After the Institutional Review Board approved the study, we reviewed the records of patients who underwent NSM and immediate breast reconstruction at The University of Texas MD Anderson Cancer Center during the period from September 2003 through May 2011. Cases of NSM performed for breast cancer and cases of NSM performed for risk reduction in high-risk patients were included. During that period, 73 patients underwent NSM and immediate breast reconstruction, and 40 of these patients had bilateral NSM, for a total number of 113 NSM cases. The median age of the patients in the NSM group was 47 years (standard deviation, 9 years). We compared these 113 cases of NSM to 120 cases of SSM that were performed during the same time period and randomly matched them with the NSM cases for stage of disease, comorbidities, and patient age. The median age of the patients in the SSM group was 50 years (standard deviation, 8 years).

Definition of Complications

Overall complications were defined as hematoma (necessitating either open or percutaneous drainage), infection (erythema and inflammation necessitating treatment with antibiotics), breast skin flap necrosis (full-thickness flap loss), delayed wound healing (requiring more than 2 weeks to heal), implant loss, microvasculature thrombosis of free tissue flap, and partial or total nipple necrosis (NSM cases only). For statistical comparison, the presence of multiple complications or one complication in the same reconstructed breast was considered one complication.

Data Collection

Patient medical records and data from prospectively maintained databases from the Departments of Plastic Surgery and Surgical Oncology were retrospectively reviewed to obtain information regarding body mass index, vascular comorbidities, smoking, bra cup size, breast ptosis, breast pathology, distance of the lesion to the NAC, and use of neoadjuvant chemotherapy or radiation therapy. Operative notes were reviewed to obtain data regarding the incision type, extent of nodal surgery, breast surgeon, breast surgeon experience, type of reconstruction, tissue expander type and volume, volume of the breast implant for patients with one-stage reconstruction, and application of a bioprosthetic sling.

Statistical Methods

Categorical variables, including but not limited to the clinicopathologic and surgical variables, are reported in terms of frequency and percentage. Fisher's exact test was used to evaluate differences in overall complication rates between the NSM and SSM groups. The clinicopathologic and surgical variables were analyzed to identify specific correlations with partial or total nipple necrosis. Rao-Scott chi-square tests (adjusted for clustering) were used to perform univariate analyses on nipple necrosis rate for categorical variables. We combined the partial and total nipple necrosis cases to increase the power of the analysis since there were only 2 cases with total necrosis. A forest plot was used to visualize differences in the nipple necrosis rate among multiple subgroups. All tests were two-sided. A p value of <0.05 was considered significant. Statistical software packages SAS, version 9.2 (SAS, Inc., Cary, NC), and R (the R Foundation for Statistical Computing) were used to perform the analyses.

RESULTS

Overall Complication Rates: Nipple-Sparing Mastectomy versus Skin-Sparing Mastectomy

The overall rate of complications did not differ significantly between the NSM group (28%) and the SSM group (27%) ($p=0.99$; Table 1). In patients who did not have axillary surgery (those undergoing risk-reducing mastectomy), the overall rate of complications was significantly higher in the NSM group than in the SSM group (26% versus 9%; $p=0.06$). However, in patients who had axillary surgery (either sentinel lymph node biopsy or axillary lymphadenectomy), the overall complication rate did not differ between the two groups. In the NSM group, there was no difference in overall complication rates between patients with and without axillary surgery. In contrast, in the SSM group, the overall rate of complications was higher with axillary surgery (34% versus 9%, $p<0.01$). The type of axillary surgery performed did not significantly affect the rate of complications with either NSM or SSM.

Impact of Clinicopathologic Variables on Rate of Nipple Necrosis

Table 2 shows clinicopathologic variables that were evaluated to determine their effect on nipple necrosis. The nipple necrosis rate of patients with a C-cup or larger breast was 34%, which was significantly higher than the rate in patients with A- or B-cup breasts (6%)

($p=0.003$). There were some differences in rates of nipple necrosis associated with other clinicopathologic characteristics, although these differences were not statistically significant. Specifically, patients with hypertension or diabetes mellitus had a higher rate of nipple necrosis than those without vascular comorbidities (58% versus 16%; $p=0.09$); smokers had a higher rate of nipple necrosis than nonsmokers (44% vs. 15%; $p=0.08$); and patients with high body mass index had a higher rate of nipple necrosis than those with lower body mass index (43% versus 19%; $p=0.35$). Interestingly, patients with ptotic-shaped breasts, large tumors, tumors located less than 5 cm from the nipple, and prior radiation therapy to the involved breast did not have a significantly higher risk of nipple necrosis compared to patients without these characteristics.

Impact of Surgical Factors on Rate of Nipple Necrosis

The surgical technique and biomaterials used for reconstruction did not significantly impact the rate of nipple necrosis (Table 3). However, some factors (axillary surgery, use of a separate axillary incision for the axillary lymphadenectomy, use of a flap rather than an expander or implant for immediate reconstruction, a larger intraoperative saline fill volume in the expander, and the absence of a bioprosthetic sling) may have been associated with an adverse effect on nipple necrosis but we were unable to assess these due to small sample size.

Different incision types were grouped according to their potential effect on the blood supply to the nipple. These groups were not shown to be associated with significantly different rates of nipple loss. The complete description of surgical incisions and the rates of nipple necrosis for each incision type are shown in Figure 1. The experience of the surgeon in terms of number of previous cases of NSM also did not correlate with the rate of nipple necrosis.

Figure 2 is a forest plot showing the impact of various types of breast reconstruction and types of incision on the nipple necrosis rate.

DISCUSSION

NSM is being used more frequently as a result of studies reporting its oncologic safety.⁹ More patients undergoing NSM are currently being treated off protocol using quadrant biopsies of the retroareolar tissue⁹ or intraoperative irradiation of the nipple¹⁹ to reduce recurrence rates. The benefits of NSM include preservation of the three-dimensional breast skin envelope, which allows for a one-stage implant-based reconstruction. In addition, often the mastectomy incisions for NSM can be camouflaged within a breast crease, which can decrease the stigma of breast cancer surgery. However, high rates of nipple necrosis have hampered incorporation of NSM into routine clinical practice.

In this study, clinicopathologic and surgical variables were analyzed to determine their effects on the rate of nipple necrosis after NSM and immediate breast reconstruction, and overall complication rates were compared between NSM and SSM. Among the key findings was that the overall rate of any (partial or total) nipple necrosis for NSM was 20%. There were only 2 cases (2%) with total necrosis. Larger breasts (C cup or larger) were associated with a significantly higher rate of nipple necrosis. Smoking and vascular comorbidities showed a trend as predictors of nipple necrosis but did not reach statistical significance. However, pathologic and surgical factors, including surgeon experience with performing NSM were not significant predictors of nipple necrosis. Other key findings were that the overall complication rate did not differ significantly between NSM and SSM and that the addition of axillary nodal surgery increased the complication rates for SSM but not NSM.

Our finding that the addition of axillary surgery increased the incidence of complications with SSM (9% versus 34%; $p<0.01$) but not NSM (26% versus 31%; $p=0.69$) was contrary to the expected outcome. We expected that the decrease in vascular supply to the breast skin envelope and nipple in the case of NSM would be further compromised by the addition of axillary surgery because disrupting the perforators and subdermal vascular plexus in the axillary compartment may jeopardize collateral flow to the nipple. Our findings suggest that the impact of NSM on the blood supply to the nipple must outweigh the impact of axillary surgery on this blood supply.

Also unexpected was our finding that for both NSM and SSM, there was no significant difference in the overall rate of complications between patients who had sentinel lymph node biopsy and those who had axillary lymphadenectomy. We expected that the increased extent of surgical resection associated with axillary lymphadenectomy would be associated with a significantly increased rate of complications.

Importantly, our findings regarding overall complication rates with NSM and SSM support the use of NSM because it does not result in a higher rate of complications than SSM, the current standard of care in breast cancer surgery. These findings endorse the continued use of NSM in the treatment of breast cancer, at least in the context of immediate reconstruction and its associated perioperative complication rates.

Several of our findings with respect to the impact of clinicopathologic variables on nipple necrosis also deserve mention. Our finding that large breast size was associated with higher risk of nipple necrosis ($p=0.003$) probably relates to the longer distance between the nipple and the surrounding blood supply from the chest wall in larger breasts. In addition, NSM in large-breasted patients is associated with an increased potential to decrease vascular perfusion to regions of the breast skin envelope during the dissection which can endanger the blood supply to the delicate subdermal nipple plexus. Finally, the increased manipulation of the breast skin envelope usually required when NSM is performed in large-breasted patients may also contribute to their increased rate of nipple necrosis.

Although ptotic breasts were not found to be a significant predictor of nipple necrosis, patients with no or grade 1 ptosis (12%) did have a lower rate of nipple loss than patients with grade 2 or 3 ptosis (18%).

Not surprising was our finding that patients with vascular comorbidities (diabetes or hypertension) had higher rates of nipple necrosis than patients without these conditions (58% versus 16%; $p=0.09$). This probably relates to the high prevalence of small-vessel vascular disease in patients with these risk factors. Not unlike vessels in other regions of the body, small and medium-sized blood vessels in the breast are also prone to atherosclerotic disease and vasospasm, which can adversely affect the blood supply not only to the nipple but also to the preserved breast skin. Similarly, smokers had a higher rate of nipple necrosis than nonsmokers (44% versus 15%; $p=0.08$), which may also be related to the association of smoking with atherosclerosis and vasospasm. Although relatively large differences in rates of nipple necrosis were observed in patients with higher body mass index and in patients with larger tumors, these differences were not statistically significant, most likely because of the small sample size.

When we examined the impact of surgical factors on nipple necrosis, there were no significant findings. However, there were some differences in rates of nipple necrosis that might have been statistically significant with a larger sample size (Table 3). These include axillary nodal surgery (sentinel lymph node biopsy or axillary lymphadenectomy) (nipple necrosis rate 27% for patients with versus 12% for patients without axillary surgery) and use of a separate axillary incision to perform the axillary nodal surgery (nipple necrosis rate

44% versus 18% for patients without a separate incision). Both of these factors result in decreased blood supply to the preserved breast skin envelope and nipple with undermining of the lateral blood supply (axillary surgery) and disruption of the subdermal vascular plexus (separate incision). The use of a flap instead of an expander or implant for immediate reconstruction resulted in higher rates of nipple necrosis (40%, 16%, and 13%, respectively). Although it could be presumed that an implant-based reconstruction would apply more direct pressure on the underlying blood supply to the nipple, our findings must be interpreted in light of the fact that the recipient vessels for the microvascular flaps used in these reconstructions were supplied by the internal mammary blood vessels. The internal mammary blood vessels are usually the dominant blood supply to the breast skin and nipple, and when these vessels are disrupted for use as recipient blood vessels for microvascular breast reconstruction, the blood supply to the nipple may be decreased. Higher rates of nipple necrosis were also observed when larger implants were used for one-stage implant reconstruction and with larger intraoperative saline fill volumes instilled into tissue expanders. Both of these variables probably relate to increased pressure on the underlying blood supply to the nipple with subsequent decreased perfusion of the nipple. The impact of the surgeon on the outcome should always be considered in the success of a surgical procedure. Our findings suggest that surgeons with less experience in performing NSM do not have less success in preserving the viability of the nipple.

Another important finding was a lower rate of nipple necrosis when a bioprosthetic mesh sling was used in the reconstruction (13% with a sling compared to 23% without a sling; $p=0.27$). Bioprosthetic slings tend to support the underlying expander or implant, thereby decreasing the biomechanical stress placed on the blood supply to the breast skin and nipple. This decreased biomechanical stress during the early phases following reconstruction may account for the lower rate of nipple necrosis in patients with bioprosthetic slings.

In this study, the mastectomy incision types were grouped according to their potential adverse effect on the blood supply to the nipple. Except for a radial incision not abutting the nipple, which was associated with no cases of nipple necrosis, there were no significant differences in the rate of nipple necrosis among the different incision groups. We expected periareolar incisions to be associated with a significantly higher rate of nipple necrosis than the other incision types. The lack of difference was probably related to the fact that the periareolar incisions used in this study never extended more than 90 degrees around the nipple, to help maintain the subdermal vascular supply (Figure 1).

CONCLUSION

In conclusion, this study has provided insight into the factors that may affect the risk of nipple necrosis following NSM. Importantly, the overall rate of complications with NSM is similar to that of SSM. Our findings indicate that partial nipple necrosis occurs much more frequently (19%) than total nipple necrosis (2%) and patients who are well suited to NSM include nonsmokers without vascular comorbidities (hypertension or diabetes) with small to medium-sized breasts. In addition, the surgical approach should be designed to minimize the disruption of the blood supply to the nipple. It appears that surgical technique may have a more significant impact on the outcome of NSM than surgical experience. Bioprosthetic slings may serve an integral role in NSM by potentially reducing the risk of nipple necrosis by reducing the pressure on the vascular supply to the nipple. Overall, applying the lessons from this study may help to reduce the rates of nipple necrosis, thus improving the outcomes of NSM in select patient populations.

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Fig. 1.

Impact of location of NSM incision on rate of nipple necrosis. Incisions were grouped on the basis of potential to affect the blood supply to the nipple. Periareolar incisions and incisions on the breast envelope abutting the nipple (groups A and B) might disrupt adjacent subdermal vasculature. Incisions on the breast envelope not abutting the nipple and crease or periphery incisions (groups C and D) have less effect on subdermals but might disrupt the blood supply from distant vessels.

Fig. 2. Forest plot demonstrating the impact of type of surgical incision and type of reconstructive procedure on the rate of nipple necrosis.

Table 1

Overall Complication Rates for Nipple-Sparing Mastectomy (NSM) and Skin-Sparing Mastectomy (SSM)

Patient Group	No. of Patients with Complications/All Patients (%) [*]		p Value
	Nipple-Sparing Mastectomy [†]	Skin-Sparing Mastectomy	
Overall	32/113 (28)	33/120 (27)	0.99
Axillary surgery			
No	15/58 (26)	3/33 (9)	NSM vs. SSM: 0.06
Yes	17/55 (31)	30/87 (34)	NSM vs. SSM: 0.71
Type of axillary surgery			NSM w/ vs. w/o axillary surgery: 0.69 SSM w/ vs. w/o axillary surgery: <0.01
SLNB	17/54 (31)	23/70 (32)	NSM vs. SSM: 0.97
ALND	0/1 (0)	7/17 (41)	NSM vs. SSM: 0.99 NSM SLNB vs. ALND: 0.99 SSM SLNB vs. ALND: 0.71

SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; w/, with; w/o, without.

^{*} Complications included hematoma, infection, flap necrosis, delayed wound healing, implant loss, thrombosis.[†] Complications in this group also included partial or total nipple necrosis.

Table 2
Impact of Clinical and Pathological Factors on Rates of Nipple Necrosis in 113 Cases of Nipple-Sparing Mastectomy*

Factor	No Necrosis	Nipple Necrosis			p Value
		Any Necrosis	Partial Necrosis	Total Necrosis	
Overall	90 (80)	23 (20)	21 (19)	2 (2)	
Body mass index (kg/m ²)					
29	86 (81)	20 (19)	18 (17)	2 (2)	
30	4 (57)	3 (43)	3 (43)	0 (0)	0.35
Vascular comorbidities					
None	85 (84)	16 (16)	15 (15)	1 (1)	
Hypertension/diabetes mellitus [†]	5 (42)	7 (58)	6 (50)	1 (8)	0.09
Smoking					
None	77 (85)	14 (15)	12 (13)	2 (2)	
Current/prior	13 (56)	9 (44)	9 (44)	0 (0)	0.08
Bra cup size [‡]					
A or B	45 (94)	3 (6)	3 (6)	0 (0)	
C or larger	39 (66)	19 (34)	18 (32)	1 (2)	0.003
Breast ptosis					
None/grade 1	64 (88)	16 (12)	16 (12)	0 (0)	
Grade 2/3	26 (84)	7 (18)	5 (16)	2 (25)	0.91
Breast pathology**					
Prophylactic surgery	50 (81)	12 (19)	12 (19)	0 (0)	
Ductal carcinoma <i>in situ</i>	8 (80)	2 (20)	2 (20)	0 (0)	
Invasive disease < 2 cm	18 (82)	4 (18)	4 (18)	0 (0)	
Invasive disease > 2 cm	14 (74)	5 (26)	3 (16)	2 (10)	0.91
Distance from lesion to NAC ^{††}					
< 5 cm	13 (81)	3 (19)	3 (19)	0 (0)	0.86
5 cm	25 (83)	5 (17)	5 (17)	0 (0)	
Neoadjuvant chemotherapy [€]					
Yes	18 (86)	3 (14)	2 (9)	1 (5)	
No	70 (78)	20 (22)	19 (21)	1 (1)	0.42

Factor	Nipple Necrosis				p Value
	No Necrosis	Any Necrosis	Partial Necrosis	Total Necrosis	
Radiation therapy ^{††}					
Yes	1 (100)	0 (0)	0 (0)	0 (0)	
No	87 (79)	23 (21)	21 (19)	2 (2)	--

NAC, nipple-areolar complex.

* Values in table are number of patients (percentage) unless otherwise indicated.

[†] None of the patients had both hypertension and diabetes.

[‡] In 7 patients, the bra cup size was unknown.

** Pathology was determined from specimens. Tumor size was determined with clinical ultrasonography.

^{††} In 5 patients, information about distance from the tumor to NAC was not available. The distance from the tumor to the NAC was determined with clinical ultrasonography. Some patients did not have a primary tumor and received the NSM for prophylaxis or risk reduction.

[€] In 2 patients, information about chemotherapy was not available.

^{‡‡} In 2 patients, information about radiation therapy was not available. Radiation therapy was administered after mastectomy but prior to reconstruction.

Table 3
Impact of Surgical Technique and Biomaterials on the Rates of Nipple Necrosis in 113 Cases of Nipple-Sparing Mastectomy*

	No Necrosis	Any Necrosis	Nipple Necrosis		p Value
			Partial Necrosis	Total Necrosis	
Overall	90 (80)	23 (20)	32 (19)	2 (2)	
Incision type [†]					
Crease or periphery	23 (79)	6 (21)	6 (21)	0 (0)	
All others	67 (80)	17 (20)	15 (18)	2 (2)	0.96
Nodal surgery					
No	50 (86)	8 (12)	6 (10)	2 (3)	
Yes	40 (73)	15 (27)	15 (27)	0 (0)	0.13
Separate axillary incision for nodal surgery					
Yes	5 (56)	4 (44)	4 (44)	0 (0)	
No	85 (82)	19 (18)	17 (16)	2 (2)	0.25
Breast surgeon experience					
1–2 cases	11 (85)	2 (15)	2 (15)	0 (0)	
3–10 cases	33 (77)	10 (23)	9 (21)	1 (2)	
>10 cases	46 (80)	11 (20)	10 (18)	1 (2)	0.86
Type of breast reconstruction [‡]					
Tissue expander (staged reconstruction)	67 (84)	13 (16)	12 (15)	1 (1)	
Implant (direct Reconstruction to implant)	14 (87)	2 (13)	2 (13)	0 (0)	
Latissimus dorsi flap plus tissue expander or implant	0 (0)	2 (100)	1 (50)	1 (50)	
Autologous tissue flap	9 (60)	6 (40)	6 (40)	0 (0)	0.23
Tissue expander volume (% of manufacturer's suggested fill volume) ^{**}					
20%	16 (94)	2 (6)	2 (6)	0 (0)	
21%–75%	35 (80)	9 (20)	8 (18)	1 (2)	
76%–100%	7 (70)	3 (30)	3 (30)	0 (0)	0.27
Tissue expander height ^{††}					
Low	2 (50)	2 (50)	2 (50)	0 (0)	
Moderate	41 (85)	7 (15)	7 (15)	0 (0)	
Full	3 (50)	3 (50)	2 (33)	1 (17)	0.40

	No Necrosis	Nipple Necrosis			p Value
		Any Necrosis	Partial Necrosis	Total Necrosis	
Direct-to-implant prosthesis volume					
<400 cc	6 (100)	0 (0)	0 (0)	0 (0)	
401 to 600 cc	7 (78)	2 (22)	2 (22)	0 (0)	
>601 cc	1 (100)	0 (0)	0 (0)	0 (0)	0.55
Application of bioprosthetic sling ^{‡‡}					
Yes	27 (87)	4 (13)	3 (10)	1 (3)	
No	63 (77)	19 (23)	18 (22)	1 (1)	0.27

* Values in table are number of patients (percentage) unless otherwise indicated.

[‡] For a complete description of incision types used in this study and numbers of complications associated with each type of incision, see Figure 1.

[‡] Includes only immediate breast reconstruction at the time of nipple sparing mastectomy.

** In 27 cases, the intraoperative saline fill volume was not recorded.

^{‡‡} In 21 cases, the tissue expander height was not recorded.

^{‡‡} Bioprosthetic materials were various types of acellular dermal matrices.