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Original Article

Strategies to avoid mastectomy skin-flap necrosis during nipple-sparing mastectomy

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Abstract

Background: Nipple-sparing mastectomy is associated with a higher risk of mastectomy skin-flap necrosis than conventional skin-sparing mastectomy. There are limited prospective data examining modifiable intraoperative factors that contribute to skin-flap necrosis after nipple-sparing mastectomy.

Methods: Data on consecutive patients undergoing nipple-sparing mastectomy between April 2018 and December 2020 were recorded prospectively. Relevant intraoperative variables were documented by both breast and plastic surgeons at the time of surgery. The presence and extent of nipple and/or skin-flap necrosis was documented at the first postoperative visit. Necrosis treatment and outcome was documented at 8–10 weeks after surgery. The association of clinical and intraoperative variables with nipple and skin-flap necrosis was analysed, and significant variables were included in a multivariable logistic regression analysis with backward selection.

Results: Some 299 patients underwent 515 nipple-sparing mastectomies (54.8 per cent (282 of 515) prophylactic, 45.2 per cent therapeutic). Overall, 23.3 per cent of breasts (120 of 515) developed nipple or skin-flap necrosis; 45.8 per cent of these (55 of 120) had nipple necrosis only. Among 120 breasts with necrosis, 22.5 per cent had superficial, 60.8 per cent had partial, and 16.7 per cent had full-thickness necrosis. On multivariable logistic regression analysis, significant modifiable intraoperative predictors of necrosis included sacrificing the second intercostal perforator ($P = 0.006$), greater tissue expander fill volume ($P < 0.001$), and non-lateral inframammary fold incision placement ($P = 0.003$).

Conclusion: Modifiable intraoperative factors that may decrease the likelihood of necrosis after nipple-sparing mastectomy include incision placement in the lateral inframammary fold, preserving the second intercostal perforating vessel, and minimizing tissue expander fill volume.

Introduction

Nipple-sparing mastectomy (NSM) is increasingly being performed with the intent of obtaining superior cosmetic outcomes[1–3], but it is associated with a higher risk of mastectomy skin-flap necrosis[4]. Patients who undergo NSM have a significantly higher risk of this complication compared with those having skin-sparing mastectomy (SSM), as shown in a previous study with prospectively collected data[5]. Although most cases of mastectomy skin-flap necrosis are classified as superficial and will heal uneventfully, some patients develop more serious complications. In the short term, these include wound infections requiring hospital admission or reoperation, and may ultimately result in implant loss. In the long term, skin-flap necrosis can cause skin contracture and asymmetry of the reconstructed breast. Few studies[6,7] have prospectively examined predictors of skin-flap necrosis after NSM. Retrospective reports[8,9] have consistently suggested that patient-related factors affect the risk, among these size and ptosis of the breasts, as well as previous radiation therapy. Reports on modifiable intraoperative variables, such as incision placement and dissection technique, are heterogeneous, making practice improvement difficult. Identification of predictors of necrosis allows implementation of strategies to mitigate the risk of complications. In the present study, intraoperative practices that have been suggested to contribute to mastectomy skin-flap necrosis in the literature were documented prospectively, and their association with the development of necrosis after NSM analysed.

Methods

In 2018, the breast surgical oncology, and plastic and reconstructive services at Memorial Sloan Kettering Cancer Center (MSKCC) implemented a collaborative quality improvement initiative aiming to identify modifiable intraoperative risk factors for mastectomy skin-flap necrosis after NSM. A list of variables presumed to affect skin-flap necrosis was constructed based on published literature and clinical experience. This included dissection technique, use of tumescence solution for nipple–areolar complex or skin-flap

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dissection, blue dye injection technique, use of nipple-delay procedure, incision location and length (*Fig. 1*), use of separate axillary incisions, visualization and preservation of the second intercostal perforators, breast specimen weight, tissue expander position and saline fill volume, and assessment of nipple–areolar complex and overall skin perfusion at the end of the breast surgery portion of the procedure. The plastic surgeons also documented their assessment of skin perfusion at the beginning of their portion of the procedure as well as their assessment of the presence and location of areas of exposed dermis. At MSKCC, use of indocyanine green and laser-assisted fluorescence angiography (SPY) for assessment of mastectomy skin perfusion is at the discretion of the plastic surgeon. As the practice is variable across the plastic surgery service, it was not assessed in the present study.

The collaborative group also developed postoperative forms to capture the presence and extent of skin-flap necrosis (including necrosis of the nipple–areolar complex) occurring by the first postoperative visit approximately 2 weeks after surgery. The severity of skin-flap necrosis was assessed using elements of the Skin Ischaemia and Necrosis (SKIN) score, a validated tool developed by Lemaine *et al.*[4]. The SKIN score captures the depth as well as surface area of mastectomy skin-flap necrosis. SKIN score is based on the following observations: category A, no evidence of necrosis; category B, colour change of skin flap suggesting impaired perfusion or ischaemic injury; category C, partial-thickness skin-flap necrosis resulting in at least epidermal sloughing; and category D, full-thickness necrosis. Each category also includes an assessment of extent of necrosis ranging from 0, 1–10, 11–30, and over 30 per cent of the nipple–areolar complex or skin surface area.

This study was approved by the MSKCC Institutional Review Board. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee, and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consecutive prospectively identified patients who underwent NSM for both prophylactic and therapeutic indications between April 2018 and December 2020 were included. Both breast and plastic surgery teams completed intraoperative forms on the day of surgery. The plastic surgery team completed the postoperative form documenting extent and degree of skin-flap necrosis at the first postoperative visit, as well as treatment and outcomes of necrosis at the 8–10-week postoperative visit. Preoperative patient factors were collected by chart review.

Analyses were carried out on a per-breast or per-patient basis depending on the variable. Patient characteristics were summarized using frequency and percentage for categorical variables. Clinical and intraoperative variables associated with skin-flap necrosis were identified by univariate analysis, using χ^2 test or Fisher's test for categorical variables, and the Wilcoxon rank sum test for continuous variables. Intraoperative variables significant at the type I error rate of 0.05 were then included in a multivariable logistic regression analysis, with the final model chosen by backward selection. Statistical analysis was conducted using R 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

During the study interval, 299 patients underwent 515 NSM procedures (*Table 1*). Of these, 54.8 per cent (282 of 515) were prophylactic and 45.2 per cent were therapeutic procedures. Median patient age was 43 (range 22–73) years, and median BMI was 22.3 (i.q.r. 20.6–24.7) kg/m^2. Some 98.0 per cent of patients were non-smokers, 26.4 per cent had a history of breast surgery, and 3.3 per cent had undergone radiation therapy for breast cancer. The majority (85.4 per cent) underwent tissue expander

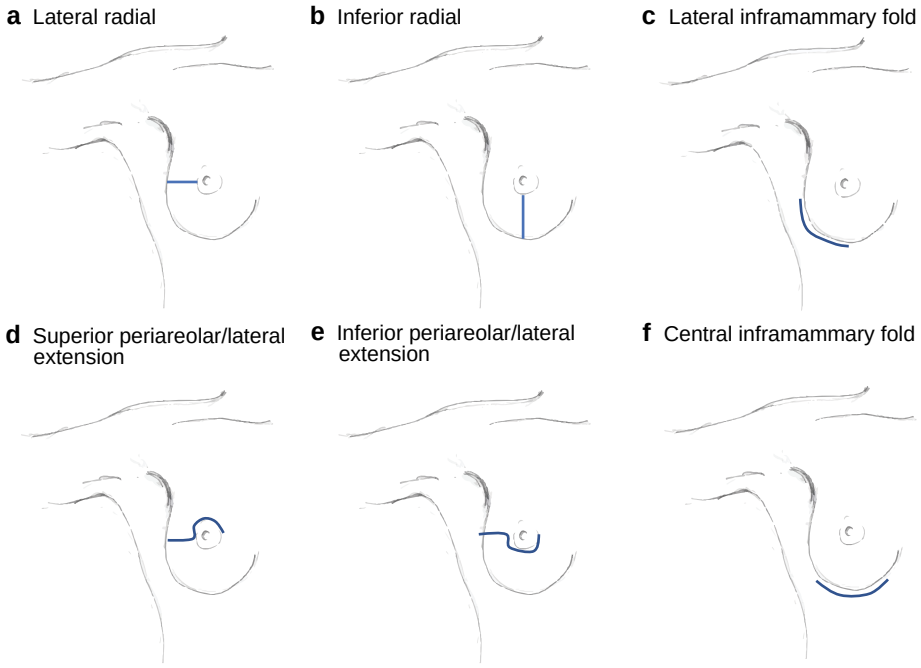

Fig. 1 Nipple-sparing mastectomy incision placement

a Lateral radial, **b** inferior radial, **c** lateral inframammary fold, **d** superior periareolar/lateral extension, **e** inferior periareolar/lateral extension, and **f** central inframammary fold. Reproduced with permission from N. Kinoti-Metz (Studio Parallel, Brooklyn, NY, USA).

Table 1 Clinical characteristics of patients with and without mastectomy skin-flap necrosis after nipple-sparing mastectomy

	All patients ($n = 299$)	Necrosis absent ($n = 228$)	Necrosis present ($n = 71$)	P†
Age (years), median (range)	43 (22–73)	43 (22–3)	42 (22–68)	0.800‡
BMI (kg/m^2)				0.130
< 25	234 (78.3)	183 (80.3)	51 (72)	
≥ 25	65 (21.7)	45 (19.7)	20 (28)	
Smoking status				0.600
Non-smoker	293 (98.0)	224 (97.8)	69 (97)	
Smoker	6 (2.0)	4 (2.2)	2 (3)	
Hypertension	14 (4.7)	6 (2.6)	8 (11)	0.006
Diabetes	2 (0.7)	2 (0.9)	0 (0)	> 0.900
Steroid use	42 (14.0)	36 (15.8)	6 (8)	0.120
Previous radiation for breast cancer	10 (3.3)	5 (2.2)	5 (7)	0.060
Previous breast surgery	79 (26.4)	64 (28.1)	14 (20)	0.140
Previous cosmetic breast surgery*	22 (7.4)	16 (7.0)	6 (8)	0.700
Neoadjuvant chemotherapy	51 (17.1)	39 (17.1)	12 (17)	> 0.900
Ptosis				0.300
None	38 (14.8)	30 (15.3)	8 (13)	
Grade 1	98 (38.1)	79 (40.3)	19 (31)	
Grade 2	106 (41.2)	78 (39.8)	28 (46)	
Grade 3	15 (5.9)	9 (4.6)	6 (10)	
Unknown	42	32	10	

Values are *n* (%) unless otherwise indicated. *A total of 21 augmentations and one reduction. †χ^2 test or Fisher's exact test, except ‡Wilcoxon rank sum test; unknowns were not included in calculation.

reconstruction, 5.2 per cent of reconstructions were direct to implant, and 8.3 per cent underwent autologous flap reconstruction. Fifteen breast surgeons and 10 plastic surgeons participated in the study.

By 2 weeks after operation, 23.3 per cent of breasts (120 of 515) had developed mastectomy skin-flap necrosis, of which 45.8 per cent (55 of 120) had nipple necrosis only. Among breasts with necrosis, 27 of 120 (22.5 per cent) were classified as having SKIN score category B (superficial necrosis), 73 (60.8 per cent) as having SKIN score category C (partial necrosis), and 20 (16.7 per cent) as having SKIN score category D (full-thickness necrosis) (*Table 2*). The extent of necrosis was variable; most cases of category B necrosis involved 1–10 per cent of the surface area of the mastectomy skin flap. Although the majority healed without intervention, 10.0 per cent (12 of 120) required debridement in the operating room, 6.7 per cent (8 of 120) experienced nipple loss, and 7.5 per cent (9 of 120) resulted in implant loss that occurred between 1 and 22 weeks after surgery (*Table 3*). Among the nine cases of implant loss, eight were attributed to wound-healing complications resulting from skin-flap necrosis. By 8–10 weeks, 84.2 per cent of breasts with necrosis (101 of 120) had healed completely; one patient with bilateral superficial necrosis was lost to follow-up. Thirteen breasts with the most severe category of necrosis, SKIN score category D4, were examined further. Clinical and intraoperative variables are shown in *Supplementary Table S1*. Compared with other categories of necrosis, breasts with D4 necrosis showed higher rates of in-office and operating room debridement, infection, and implant loss. At 8 weeks, only 46 per cent of breasts with D4 necrosis had healed completely (*Table 3*).

Variables associated with the development of skin-flap necrosis were examined. In univariate analysis, intraoperative variables associated with a higher likelihood of necrosis included non-lateral inframammary fold placement of the incision ($P < 0.001$), having a nipple-delay procedure ($P = 0.026$), sacrificing (*versus* sparing or not visualizing) the second intercostal perforator ($P = 0.038$), specimen weight over 400 g ($P < 0.001$), erythematous appearance of skin flaps at start of plastic surgery procedure ($P = 0.030$), increasing tissue expander fill volume ($P < 0.001$), subpectoral tissue expander placement ($P = 0.01$), number of procedures performed by surgeon ($P = 0.006$), and exposed dermis in the upper or lower outer quadrant of the skin flap ($P < 0.05$).

Table 2 Severity of necrosis based on SKIN score

SKIN score*	Breasts with necrosis ($n = 120$)
B1	1 (0.8)
B2	23 (19.2)
B3	3 (2.5)
C2	50 (41.7)
C3	17 (14.2)
C4	6 (5.0)
D2	5 (4.2)
D3	2 (1.7)
D4	13 (10.8)

Values are *n* (%). *Highest score for necrosis involving skin flap or nipple–areolar complex. Skin Ischaemia and Necrosis (SKIN) score: A, no evidence of necrosis; B, colour change of skin flap suggesting impaired perfusion or ischaemic injury; C, partial-thickness necrosis resulting in at least epidermal sloughing; D, full-thickness necrosis. Extent of necrosis (% surface area covered): 1, < 1%; 2, 1–10%; 3, 11–30%; 4, > 30%.

In multivariable regression analysis, significant intraoperative variables that predicted necrosis included nipple-delay procedure ($P = 0.033$), sacrificing the second intercostal perforator (*versus* not visualizing or sparing it) ($P = 0.006$), larger tissue expander fill volume ($P < 0.001$), erythematous appearance of skin flaps at start of plastic surgery procedure ($P = 0.007$), exposed dermis in the lower outer quadrant ($P = 0.005$), and non-lateral inframammary fold incision placement ($P = 0.003$) (*Table 4*).

The relationship between incision placement and incision length was examined further, with the hypothesis that incisions placed in the inframammary fold would be wider. It was found that, compared with radial or periareolar incisions, inframammary fold incisions had a median length of 11 cm compared with 8 cm for those in non-inframammary fold positions ($P < 0.001$). As breasts with necrosis had significantly greater fill volumes than those without necrosis (median 240 (i.q.r. 180–300) *versus* 200 (150–250 ml; $P < 0.001$), an analysis

Table 3 Mastectomy skin-flap necrosis management

	All breasts with necrosis (*n* = 120)	SKIN score B1–D3 (*n* = 107)	SKIN score D4 (*n* = 13)
Topical agents (bacitracin, betadine, Xeroform®)	25 (20.8)	22 (20.6)	3 (23)
Hyperbaric oxygen	33 (27.5)	29 (27.1)	4 (31)
Infection	17 (14.2)	12 (11.2)	5 (38)
Antibiotics only	10 (8.3)	8 (7.5)	2 (15)
Debridement and antibiotics	6 (5.0)	3 (2.8)	3 (23)
Debridement in office	9 (7.5)	5 (4.7)	4 (31)
Debridement in operating room	12 (10.0)	6 (5.6)	6 (46)
Implant loss	9 (7.5)	6 (5.6)	3 (23)
Nipple loss	8 (6.7)	5 (4.7)	3 (23)
Nipple depigmentation	3 (2.5)	3 (2.8)	0
Necrosis completely healed at 8 weeks after surgery	101 (84.2)	94 (87.9)	6 (46)

Values are *n* (%). Xeroform® (Cardinal Health, Dublin, OH, USA).

Table 4 Intraoperative variables associated with nipple and skin-flap necrosis after nipple-sparing mastectomy

	Overall (*n* = 515)	Necrosis absent (*n* = 395)	Necrosis present (*n* = 120)	Univariable *P*†	Multivariable regression analysis	
					OR*	*P*
Nipple delay performed#	11 (2.2)	5 (1.3)	6 (5.0)	0.026	9.03 (1.28, 87.7)	0.033
Unknown	11	11	0			
Nipple tumescence	287 (57.2)	225 (58.9)	62 (51.7)	0.200		
Unknown	13	13	0			
Skin-flap tumescence	8 (1.6)	6 (1.6)	2 (1.7)	> 0.900		
Unknown	11	11	0			
Skin-flap dissection technique				> 0.900		
Electrocautery	487 (96.6)	371 (96.6)	116 (96.7)			
Sharp	17 (3.4)	13 (3.4)	4 (3.3)			
Unknown	11	11	0			
Nipple–areolar complex dissection technique				0.800		
Electrocautery	113 (23.1)	85 (22.8)	28 (23.7)			
Sharp	377 (76.9)	287 (77.2)	90 (76.3)			
Unknown	25	23	2			
Blue dye injection				0.140		
Intraparenchymal	213 (44.3)	166 (46.0)	47 (39.2)			
Superficial subareaolar	61 (12.7)	40 (11.1)	21 (17.5)			
Not injected	207 (43.0)	155 (42.9)	52 (43.3)			
Unknown	34	34	0			
Incision location				< 0.001		
Lateral radial	94 (19.9)	66 (18.3)	28 (25.0)		1.00 (reference)	
Inferior radial	13 (2.7)	5 (1.4)	8 (7.1)		0.56 (0.03, 5.16)	0.600
Lateral IMF	206 (43.6)	181 (50.1)	25 (22.3)		0.35 (0.17, 0.7)	0.003
Superior periareolar/lateral extension	51 (10.8)	30 (8.2)	21 (18.8)		1.59 (0.65, 3.92)	0.300
Inferior periareolar/lateral extension	51 (10.8)	32 (8.9)	19 (17.0)		1.24 (0.52, 2.93)	0.600
Central IMF	58 (12.3)	47 (13.0)	11 (9.8)		0.54 (0.19, 1.39)	0.200
Unknown	42	34	8			
Incision length (cm), median (i.q.r.)	10 (8–12)	10 (8–12)	10 (8–12)	0.800‡		
Unknown	7	7	0			
Axillary incision for SLNB	123 (26.1)	98 (27.1)	25 (22.7)	0.400		
Unknown	43	33	10			
Second intercostal perforator				0.04		
Not visualized	215 (44.1)	168 (45.0)	47 (40.9)		1.00 (reference)	
Preserved	233 (47.7)	181 (48.5)	52 (45.2)		1.73 (0.99, 3.08)	0.059
Sacrificed	40 (8.2)	24 (6.4)	16 (13.9)		3.57 (1.44, 8.88)	0.006
Unknown	27	22	5			
Specimen weight (g)				< 0.001		
< 300	227 (48.2)	181 (50.1)	46 (41.8)			
300–400	116 (24.6)	97 (26.9)	19 (17.3)			
> 400	128 (27.2)	83 (23.0)	45 (40.9)			
Unknown	44	34	10			
Skin-flap perfusion at start of plastic surgery procedure				0.030		
Erythematous	34 (7.6)	19 (5.7)	15 (13.2)		1.00 (reference)	
Slightly dusky	22 (4.9)	16 (4.8)	6 (5.3)		0.31 (0.07, 1.21)	0.100
Good	394 (87.6)	301 (89.6)	93 (81.6)		0.31 (0.13, 0.73)	0.007
Unknown	65	59	6			

(continued)

Table 4 (continued)

	Overall (*n* = 515)	Necrosis absent (*n* = 395)	Necrosis present (*n* = 120)	Univariable *P*†	Multivariable regression analysis	
					OR*	*P*
Reconstruction type				0.056		
Autologous flap	43 (8.4)	27 (6.9)	16 (13.3)			
Direct implant	27 (5.3)	23 (5.9)	4 (3.3)			
Tissue expander	440 (86.3)	340 (87.2)	100 (83.3)			
Unknown	5	5	0			
Expander fill volume (ml), median (i.q.r.)	200 (150–300)	200 (150–250)	240 (180–300)	< 0.001‡		
Expander fill volume (ml)				< 0.001		
≤ 100	63 (13.4)	52 (14.2)	11 (10.6)		1.00 (reference)	
101–200	175 (37.2)	151 (41.1)	24 (23.1)		1.23 (0.46, 3.69)	0.700
201–300	189 (40.1)	130 (35.4)	59 (56.7)		4.23 (1.69, 12.1)	0.004
> 300	44 (9.3)	34 (9.3)	10 (9.6)		1.97 (0.55, 7.18)	0.300
Unknown	44	28	16			
Expander location				0.010		
Prepectoral	215 (48.4)	177 (51.8)	38 (37.3)			
Subpectoral	229 (51.6)	165 (48.2)	64 (62.7)			
Axillary procedure				0.900		
None	171 (33.2)	129 (32.7)	42 (35.0)			
SLNB	293 (56.9)	226 (57.2)	67 (55.8)			
SLNB/ALND	47 (9.1)	36 (9.1)	11 (9.2)			
ALND	4 (0.8)	4 (1.0)	0			
Duration of operation (min), median (i.q.r.)	189 (162–220)	188 (165–212)	198 (158–252)	0.070		
Breast surgeon experience (no. of procedures performed)**				0.006		
≤ 25	94 (18.3)	61 (15.4)	33 (28.5)			
26–48	117 (22.7)	97 (24.6)	20 (16.7)			
49–120	304 (59.0)	237 (60.0)	67 (55.8)			
Exposed dermis present	99 (22.0)	72 (21.4)	27 (23.5)	0.600		
Unknown	64	59	5			
Location exposed dermis						
UIQ	6 (1.2)	3 (0.8)	3 (2.5)	0.200		
LIQ	16 (3.1)	13 (3.3)	3 (2.5)	0.800		
UOQ	19 (3.7)	10 (2.5)	9 (7.5)	0.033		
LOQ	18 (3.5)	9 (2.3)	9 (7.5)	0.024	5.76 (1.75, 20.3)	0.005**
Central	49 (9.5)	42 (10.6)	7 (5.8)	0.056		

Values are *n* (%) unless otherwise indicated; *values in parentheses are 95% confidence intervals. Clinical variables are not shown; #analysis limited by small number of patients undergoing nipple delay; **location exposed dermis LOQ was used as binary variable in MVA. IMF, intramammary fold; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; UIQ, upper inner quadrant; LIQ, lower inner quadrant; UOQ, upper outer quadrant; LOQ, lower outer quadrant. †χ^2 test or Fisher's exact test, except ‡Wilcoxon rank sum test.

of tissue expander fill volume was also conducted. Tissue expander fill volume was categorized based on a 100-ml incremental increase. Breasts with a fill volume of 201–300 ml had four times the odds of skin-flap necrosis compared with those with 100 ml or less (OR 4.23, 95 per cent c.i. 1.69 to 12.1; $P = 0.004$).

Discussion

The rate of mastectomy skin-flap necrosis was 23.3 per cent after NSM in this prospective study, with 45.8 per cent of instances being nipple-only necrosis. In 83.3 per cent of patients, the necrosis was classified as superficial or partial thickness, and few cases resulted in reoperation or nipple loss (10.0 and 6.7 per cent respectively). Implant loss occurred in nine breasts, eight of which had experienced skin-flap necrosis. Modifiable intraoperative factors significantly associated with nipple and skin-flap necrosis were non-lateral inframammary fold incisions, sacrificing the second intercostal perforator vessels, and large tissue expander fill volumes.

As the use of NSM has increased[1,2], particular attention has been paid to ischaemic complications at the nipple–areolar complex. Necrosis occurring elsewhere on the mastectomy flap may, however, also cause wound-healing complications, scarring, and eventual distortion of the reconstructed breast. These complications adversely affect cosmetic outcomes and patient satisfaction[10]. An even more concerning result is the progression to infection or exposure of the underlying implant, which can lead to reoperations and may delay adjuvant therapy. In this study, the overall rate of mastectomy skin-flap necrosis was 23.3 per cent after NSM. This is higher than reported for SSM[5], and also higher than the rates of 9–13 per cent reported in previous retrospective studies[9,11–13] of skin-flap necrosis after NSM. This difference in reported outcomes may be explained by variation in mastectomy technique and skin-flap thickness, but also by the differences inherent to prospective *versus* retrospective data collection. Among published retrospective reports, there is no consistent definition of skin-flap necrosis, and documentation is also variable, particularly in cases of superficial necrosis that heal without intervention. These limitations make accurate comparison across studies challenging. Two other studies have examined nipple and skin-flap necrosis in prospective NSM cohorts, and also reported higher rates of mastectomy skin-flap necrosis. A prospective study by Odom *et al.*[14], which examined skin perfusion patterns and complications in 79 patients who underwent NSM, reported necrosis complications in 26 per cent of patients, in line with the present findings. The French multi-institutional prospective

MAPAM trial[7] included 59 women who underwent NSM, and reported nipple–areolar complex necrosis in nine patients, a rate of 15 per cent. Necrosis elsewhere in the breast was not reported and would presumably increase this rate. Given these relatively high rates of necrosis compared with those for SSM, it is important to identify and implement strategies to mitigate this complication.

Three technical aspects of the NSM procedure were identified that can be modified to reduce the risk of nipple and skin-flap necrosis: incision placement in the lateral inframammary fold, sparing the second intercostal perforator, and limiting tissue expander fill volume. The present findings also provide insight into incision location and length, and its impact on nipple and skin-flap necrosis. Patients with incisions placed in the lateral inframammary region of the breast (*Fig. 1f*) had significantly lower rates of skin-flap necrosis. The inframammary fold position also correlated with longer incisions, with a median length of 11 cm compared with 8 cm in non-inframammary fold placement ($P < 0.001$). This may explain the association with lower rates of flap necrosis, as there is likely to be less tension placed on the skin flap during dissection through a longer incision owing to improved exposure, particularly as the dissection approaches the boundaries of the breast. Although the literature on this topic is heterogeneous, the findings of this study are consistent with a number of previously published retrospective studies[9,15,16] showing that incision placement in the inframammary fold is associated with a lower risk of skin necrosis. In a retrospective evaluation of 500 breasts after NSM, Colwell *et al.*[9] found that inferolateral inframammary fold placement of the incision was significantly associated with a lower risk of complications, including the nipple–areolar complex and skin-flap necrosis. Other studies examining isolated necrosis of the nipple–areolar complex reported a similar association with the inframammary fold approach, with a decreased risk of necrosis. When thinking in terms of necrosis limited to the nipple–areolar complex, there is further support for inframammary fold incision placement. Daar and colleagues[16] undertook a meta-analysis examining incision placement and its association with necrosis at the nipple–areolar complex; among 4645 NSMs, periareolar incisions were associated with a higher rate of nipple–areolar complex necrosis than inframammary fold incision placement. Carlson *et al.*[17] examined risk factors for nipple ischaemia after NSM in 71 consecutive procedures, and found that partial nipple necrosis occurred in 28 per cent and was associated with periareolar incisions (OR 9.69, 95 per cent c.i. 1.57 to 59.77; $P = 0.014$). These results endorse consideration of the inframammary fold approach when feasible from the perspective of both the breast surgical oncologist and plastic surgeon.

The impact of preservation of the second intercostal perforator on incidence of skin-flap necrosis after NSM is unclear. The breast is perfused by arteries originating from the lateral thoracic and internal mammary vessels. The dominant blood supply to the breast comes from the internal mammary perforating vessels in 68–74 per cent of breasts[18]. Based on cadaveric and chest wall perfusion studies, there is evidence supporting the concept of a principal perforating vessel usually located in the second or third intercostal space[18]. This vessel courses obliquely toward the nipple–areolar complex, where it joins radiating tributaries of the lateral thoracic artery around the nipple. In the context of NSM, active preservation of this vessel to reduce nipple–areolar complex necrosis has been suggested[19]. For the purposes of the present study, this dominant vessel was referred to as the 'second intercostal perforator'. There was a significantly lower rate of nipple and skin-flap necrosis in the breasts when the second intercostal perforator was visualized and spared, or not visualized, than when this vessel was sacrificed. This finding also highlights the importance of preservation of the subcutaneous blood supply during mastectomy flap dissection.

Intuitively, greater tissue expander fill volume contributes directly to pressure on mastectomy skin flaps and affects flap perfusion. Odom *et al.*[14] examined perfusion of the mastectomy flap before and after placement of tissue expanders or implants after NSM, and found a decrease in perfusion by 36 per cent compared with before prosthesis placement, indicating that expander fill volume can immediately affect skin perfusion and likely the development of necrosis.[14] Here, higher rates of nipple and skin-flap necrosis were observed in breasts with larger tissue expander fill volumes. Breasts with a fill volume of 201–300 ml had four times the odds of skin-flap necrosis than those with a fill volume below 100 ml ($P = 0.004$). In reality, the decision regarding how much to fill expanders initially, or whether to place immediate implants, is multifactorial and should take into consideration mastectomy skin-flap perfusion and nipple position. In this study, larger fill volumes also correlated with larger mastectomy weights in univariate analysis. In these instances, the skin envelope usually requires a greater fill volume to appropriately position the nipple. If the fill is low and the nipple is malpositioned, subsequent revision can be challenging. Plastic surgeons at MSKCC carefully assess the fill during NSM, balancing fill volume with risk of necrosis, and appropriate nipple position.

This study found that clinical assessment of skin-flap perfusion by the plastic surgeon at the start of the reconstructive procedure was associated with the risk of developing necrosis. Rates of necrosis were significantly lower in patients with good *versus* erythematous flaps, suggesting that the visual impression of flap perfusion is likely to provide a reliable estimation of flap perfusion, which should be considered when determining the tissue expander fill volume. Whether this assessment is improved further by use of intraoperative SPY was not captured in this data set owing to significant variability in its use.

Nipple delay is thought to increase the blood supply to the nipple–areolar complex; however, in a meta-analysis[20] including 101 patients undergoing nipple delay, rates of necrosis in the nipple–areolar complex or mastectomy skin flap ranged from 0 to 16 per cent, comparable to those reported in the literature for procedures in which no nipple delay was performed. There were very few nipple-delay procedures in the present series (2 per cent) and, although breasts undergoing the nipple-delay procedure were significantly more likely to experience skin-flap necrosis, these results are likely biased, as the procedure would have been done in higher-risk patients. Given the small numbers, meaningful conclusions regarding its efficacy cannot be drawn.

Several parameters thought to affect mastectomy skin-flap necrosis were not found to be significant in this study. Rates of necrosis did not differ significantly based on injection of blue dye in the subareolar space or intraparenchymally. Similarly, use of tumescence solution, sharp dissection *versus* use of electrocautery, or use of a separate axillary incision for the sentinel lymph node biopsy procedure were not significant factors contributing to skin-flap necrosis. Breast surgeon volume was also examined, and a small but not statistically significantly lower risk of skin necrosis for surgeons with larger NSM volumes was found in the multivariable analysis.

Strengths of this study include its large size, prospective data collection, and use of a validated tool to document the presence and extent of necrosis. Currently, comparison of necrosis rates in the literature is difficult because of a lack of standardized definitions of skin necrosis. Use of the SKIN score should allow more accurate comparisons of severity of necrosis in future studies. A limitation of this study is that NSM was performed by a number of different breast surgeons (15) and plastic surgeons (10) with variable procedure volumes. All participants, however, undertake a high volume of breast surgery and breast reconstruction respectively, and these results may not reflect the outcomes of lower-volume surgeons. Additionally, analyses of some variables found to be significant, such as hypertension, exposed dermis location, and nipple delay, were based on small numbers of patients, limiting conclusions regarding the impact on necrosis.

In a prospective cohort of patients having NSM with comprehensive documentation of intraoperative technique, 23.3 per cent of breasts had mastectomy skin-flap necrosis, with approximately half of cases being nipple-only necrosis. Modifiable intraoperative factors that decreased the likelihood of necrosis included incision placement in the lateral inframammary fold, preservation of the second intercostal perforating vessels, and minimizing tissue expander fill volume.

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Supplementary material

Supplementary material is available at *BJS* online.

Data availability

The data and methods used in the analysis, and materials used to conduct the research, will be made available upon request to the authors.

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