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Breast

Nipple Sparing Mastectomy: Does Breast Morphological Factor Related to Necrotic Complications?

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Background: Nipple sparing mastectomy (NSM) can be performed for prophylactic mastectomy and the treatment of selected breast cancer with oncologic safety. The risk of skin and nipple necrosis is a frequent complication of NSM procedure, and it is usually related to surgical technique. However, the role of the breast morphology should be also investigated.
Method: We prospectively performed an analysis of 124 NSM from September 2012 to January 2013 at the European Institute of Oncology, Milan, Italy, focusing on necrotic complications. We analyzed the association between the risks of skin necrosis and the breast morphology of the patients.
Results: Among 124 NSM in 113 patients, NSM procedures were associated with necrosis in 22 mastectomies (17.7%) among which included partial necrosis of nipple-areolar complex (NAC) in 15 of 124 NSM (12.1%) and total necrosis in 4 cases (3.5%). The NAC was removed in 5 NSM cases (4%). The volume of breast removed was the only significant factor increasing the risk of skin necrosis. The degree of ptosis was not significantly related to the necrosis risk.
Conclusions: Large glandular specimen increases the risk of NAC necrosis. The degree of ptosis and the distance between the sternal notch and the NAC have no significant impact on necrotic complications in NSM. To reduce the necrotic complications in large breast after NSM, reconstruction should better be performed with autologous flap or slow skin expansion using the expander technique. *(Plast Reconstr Surg Glob Open 2014;2:e99; doi: 10.1097/GOX.0000000000000038; Published online 23 January 2014.)*

As compared with the skin sparing mastectomy, nipple sparing mastectomy (NSM) preserves the skin of the nipple-areolar complex (NAC). The risk of loco regional recurrence after preserving the skin envelope and NAC is the major concern in NSM. In 2012, Petit et al[1] reported that the rate of local recurrence in the breast and the NAC was 3.6% and 0.8%, respectively. Several other publications confirmed the safety of the NSM in selected patients.[2–5] The skin envelope and the NAC after removing the gland under the dermis, the NAC, and the peripheral skin are poorly vascularized by the subdermal vessel network.[6,7] The size and the degree of ptosis increase the length of the skin flap between the thoracic wall and the NAC and increase the risk of poor blood supply of the tip of the breast. Therefore, the volume of the breast and the degree of pto-

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sis are hypothesized as a risk factor of necrosis of the NAC area. Moreover, the pressure on the vessels by the tension due to the prosthesis also increases the risk of skin necrosis in the NAC area. Petit et al[8] reported 3.5% of complete nipple loss and partial NAC necrosis in 5.5%. Several recent studies showed that the rate of nipple necrosis ranged from 0% to 29% but most series showed less than 10%.[9–18] Algaithy et al[19] analyzed the correlation between surgical factors and NAC necrosis. Several publications of NSM were concerned with oncologic safety, surgical technique, and cosmetic results and other sequelae.[1,6,8] Few studies focus the factors predisposing to necrotic complications. Age, skin incision, flap thickness, reconstruction type, and smoking have been reported as the risk factors for NAC necrosis and NAC removal.[14,17,19] Lohsiriwat et al[20] demonstrated that clinicopathological features had no significant impact on necrotic complications. No study reported the correlation between breast morphology and necrotic complications. Our prospective study aims at identifying the patient and the breast morphology factors that might increase necrotic complications after performing NSM with immediate reconstruction.

PATIENTS AND METHODS

From September 2012 to January 2013, 113 patients who underwent 124 NSM procedures for prophylactic mastectomy (n = 11) or breast carcinoma (n = 113) were included in our database at European Institute of Oncology. Patients' age, weight, height, body mass index (BMI), smoking history, and associated comorbidities (diabetes mellitus, hypertension, and dyslipidemia) were recorded as patient factors. Specimen weight, volume of breast removed, degree of ptosis (grade 0, 1, 2, 3, pseudoptosis) (Table 1), mammographic breast density, and sternal notch to nipple distance were recorded as breast morphological factors. We recorded the volume of breast removed by measurement length, width, and thickness of specimen after finishing NSM procedure and reported as cubic centimeter. Surgical factors included skin incision types, mode of reconstruction, and duration of operation and were recorded. The selection criteria for NSM were primary tumors located outside the areola margins, no nipple retraction or bloody discharge from the nipple, no retroareolar microcalcifications, no inflammatory signs, and no retroareolar tumor infiltration at the frozen section. Multifocality of lesion was not a contraindication. In our series, patients with previous radiotherapy or neoadjuvant chemotherapy, tumors centrally located area, inflammatory breast cancer, and Paget's disease of nipple were not included. The patients were excluded during the operative procedure if the intraoperative retroareolar frozen examination was positive for malignancy. All patients signed an informed consent for NSM and immediate breast reconstruction before the operation. NSM was performed by the breast surgery team and immediate breast reconstruction by the plastic surgery team.

Radiosurgical Technique

Subcutaneous mastectomy was performed through a cutaneous incision located above the tumor site. Skin incisions for NSM use included superolateral radial, inferolateral radial, superior circum areolar, periareolar, inframammary fold incisions, and others (designed to incorporate prior breast surgery scar) (Fig. 1). The glandular breast tissue was dissected very

Table 1. Degree of Ptosis Classification

Degree of Ptosis	Definition
First degree	Nipple at the level of inframammary fold
Second degree	Nipple below the level of inframammary fold but still higher that the majority of the breast contour
Third degree	Nipple below the level of inframammary fold and sitting at the most dependent, inferior part of the breast contour
Pseudoptosis	A loose breast that looks ptotic from a distance, but the nipple remains above the level of the inframammary fold

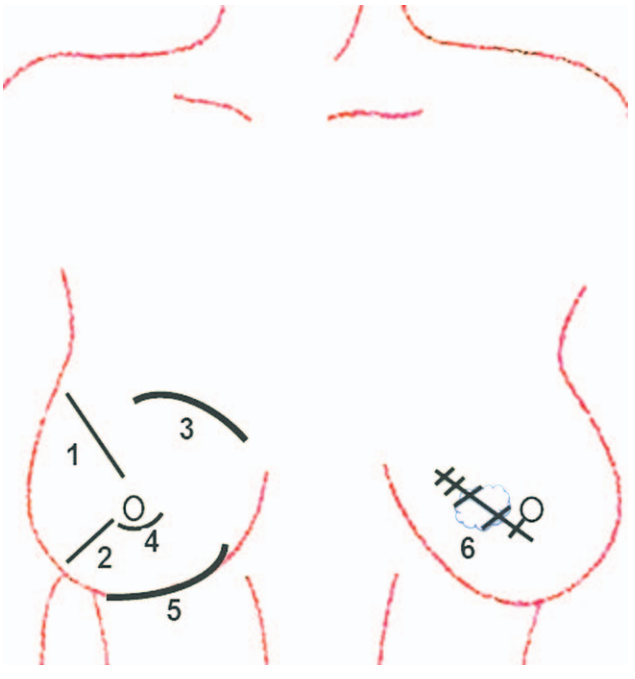

Fig. 1. Skin incision types (1 = superolateral radial incision, 2 = inferolateral radial incision, 3 = superior circumareolar incision, 4 = periareolar incision, 5 = inframammary fold incisions, 6 = other incision) (designed to incorporate prior breast surgery scar).

close to the dermis and from the pectoral fascia.[21] A thin tissue beneath the retroareolar area was removed separately for immediate frozen section examination. If the frozen result was positive, the NAC should be removed and the patient was excluded. In our institute, 16 Gy (at the point of maximum dose) single-shot electron beam radiotherapy is delivered to NAC except for the prophylactic mastectomy in a single fraction with disk protection of the pectoralis muscle and chest wall. The electron intraoperative treatment (ELIOT) technique for the biologic equivalence dose of 16 Gy is calculated to be 1.5–2.5 higher than a dose delivered with conventional fractionated radiotherapy, and this technique has already been described.[22–26] NAC irradiation was delayed if the blood perfusion after NSM was poor. The immediate breast reconstruction was performed by the plastic team using different technique (submuscular implants, tissue expanders, or musculocutaneous flap). Generally, we performed inflation of expander volume postoperatively at least 3 weeks after NSM procedure and then continued inflation every 2–6 weeks. If there was wound problem, the inflation was delayed. The total volume depended on the definitive volume of the tissue expander and the patient's comfort. Almost all of our patients had immediate reconstruction with prosthesis or tissue expanders, only 7 cases had autologous tissue (latissimus dorsi flaps, transverse rectus abdominis myocutaneous flaps) breast reconstructions. All patients were followed up by oncologic or plastic surgeons for at least 1 month postoperatively. NAC necrosis or mastectomy skin flap necrosis with mode of treatment was recorded accordingly.

Statistical Analysis

The statistical analysis of data was performed using the *t* test, Wilcoxon rank-sum test, and Fisher's exact test as appropriate. NAC necrosis can be partial complete necrosis. All tests were 2 sided. The level of significant was set at $P < 0.05$.

RESULTS

Postoperative Complications

Rates of postoperative complications and type of necrosis are shown in Table 2 (Figs. 2 and 3), whereas management of necrotic complications is shown in Table 3.

Necrosis Types and Management

Postoperative hematoma was seen in 7 NSM cases (5.6%) and all cases required reoperation. Three infections (2.4%) were observed in the postoperative period and 2 prostheses were removed. Mastectomy skin flap necrosis occurred in 10 mastectomies (8.1%). Nipple necrosis occurred in 19 NSM cases (15.3%), with only 4 cases (3.5%) of complete NAC necrosis. The NAC was removed in 5 NSM cases (4%) one of which was partial NAC necrosis with mastectomy skin flap necrosis around NAC which required NAC removal with the necrotic skin.

Table 2. Complications of NSM

Complication NSM	Number (%) (n = 124 Mastectomies)
Hematoma	7 (5.6)
Skin necrosis	10 (8.1)
Infection	3 (2.4)
NAC necrosis	19 (15.3)

Fig. 2. Total NAC necrosis after left NSM. The incision is superolateral radial incision.

Fig. 3. Mastectomy skin necrosis after right NSM. The necrosis occupied mostly in the superior outer quadrant, and incision is superior circumareolar incision.

Patient Risk Factors

As shown in Table 4, there was no clear association between NAC necrosis and age, weight, height, BMI,

Table 3. Description of Necrosis Type and Management

Necrotic Complications	Number (n = 22)
Necrosis type	
Total NAC necrosis with skin flap necrosis	2
Total NAC necrosis without skin flap necrosis	2
Partial NAC necrosis with skin flap necrosis	5
Partial NAC necrosis without skin flap necrosis	10
Skin flap necrosis without NAC necrosis	3
Necrosis mode of treatment	
Conservative dressing NAC	12
Surgical debridement NAC	2
Remove NAC	4
Remove NAC + debridement skin flap	1
Surgical debridement skin flap	3

smoking history, and comorbid disease (diabetes mellitus, hypertension, and dyslipidemia).

Breast Morphological Factors

Breast morphological factors including specimen weight, volume of breast removed, degree of ptosis, mammographic breast density, and nipple distance from sternal notch were analyzed for association with the necrotic complications after performing NSM. The analysis showed (Table 5) no clear association between NAC necrosis and mammographic breast density and nipple distance from sternal notch. Focusing on the breast specimen weight showed the median weight was 308 g (range, 102–856 g) and 339 g (range, 200–550 g) in no NAC necrosis group and NAC necrosis group, respectively. There seemed to be a slight but nonsignificant tendency (P = 0.13) for patients with NAC necrosis to have greater weight specimen. Significant association could be seen between NAC necrosis and volume of breast removed (P = 0.04). The median volume of breast removed was 784 cm^3 (range, 60–4410 cm^3) and 920 cm^3 (range, 302.5–1870 cm^3) in no NAC necrosis group and NAC necrosis group, respectively. We found that 37% of mastectomy skin flap necrosis had the NAC necrosis. Significantly more patients with NAC necrosis had associated mastectomy skin flap necrosis (P < 0.01). We examined the cutoff volume of breast removed and proportions of NAC necrosis (Table 6). Patients with volume of breast removed greater than 750 cm^3 that had 23% of NAC necrosis were compared with patients with volume of breast removed less than 750 cm^3 that had 6% of NAC necrosis (P < 0.01).

There seemed to be some tendency for patients with NAC necrosis to have higher degree of ptosis in evaluating the association between necrotic complications and degree of ptosis. We additionally focused

Table 4. Comparison of Patient Risk Factors and Outcomes

Patients Characteristics	No NAC Necrosis (n = 105)	NAC Necrosis (n = 19)	P
Age (y), mean (SD)	47.9 (9.3)	48.8 (9.8)	0.67*
Weight (kg), mean (SD)	58.6 (9.3)	59.5 (7.0)	0.70*
Height (m), mean (SD)	1.64 (0.07)	1.65 (0.05)	0.60*
BMI (kg/m^2), mean (SD)	21.7 (3.0)	21.7 (2.0)	0.92*
Comorbidity (DM, HT, dyslipidemia), n (%)	14 (13)	4 (21)	0.38†
Smoker, n (%)	31 (29)	3 (16)	0.22†

DM, Diabetes Mellitus; HT, Hypertension
*P value by unpaired t test;
†P value by Fisher's exact test.

Table 5. Comparison of Breast Morphological Factors and Outcomes Patients

Patients Characteristics	No NAC Necrosis (n = 105)	NAC Necrosis (n = 19)	P
Degree of ptosis, n (%)			
None	20 (19)	2 (11)	0.42*
1	41 (39)	5 (26)	
2	31 (30)	9 (47)	
3	13 (12)	3(16)	
Specimen weight (g), median (range)	308 (102–856)	339 (200–550)	0.13†
Volume of breast removed (cm^3), median (range)	784 (60–4410)	920 (302.5–1870)	0.04†
Sternal notch to nipple distance (cm), mean (SD)	22.2 (2.2)	22.7 (1.7)	0.37‡
Breast density, n (%)			
Fatty breast	10 (10)	0	0.64*
Scattered fibroglandular	47 (45)	10 (53)	
Heterogeneous	45 (43)	9 (47)	
Extremely dense	3(3)	0	
Flap necrosis, n (%)	3 (3)	7 (37)	<0.01*

*P value by Fisher's exact test;
†P value by Wilcoxon rank-sum test;
‡P value by unpaired t test.

Table 6. Cutoff Volume of Breast Removed and Proportions of NAC Necrosis

Cutoff Values	Cutoff Positive: No. NAC Necrosis (%)	Cutoff Negative: No. NAC Necrosis (%)	*P*
Volume ≥500 cm^3	18/99 (18)	1/25 (4)	0.12
Volume ≥750 cm^3	16/71 (23)	3/53 (6)	0.01
Volume ≥1000 cm^3	8/41 (20)	11/83 (13)	0.43
Volume ≥1250 cm^3	6/24 (25)	13/100 (13)	0.20

All *P* values by Fisher's exact test.

on individual degree of ptosis (Table 5). On statistical analysis, no statistically significant differences between groups could demonstrate association between degree of ptosis and NAC necrosis.

Surgical Risk Factors

Duration of operation, type of surgical incision, and type of reconstruction were not statistically significant (Table 7). Similarly, we could not find the significant correlation between the total expander or prosthesis volume and the risk of necrotic complications.

To evaluate more efficiently the possible association between skin incision types and necrosis, we combined superior circumareolar and periareolar skin incisions for comparing with other skin incisions (Table 8). We found 25% NAC necrosis with superior circumareolar and periareolar incisions as compared with 13% necrosis with other incisions. There was no statistically significant difference between the 2 groups of skin incisions.

DISCUSSION

The objective of our study was to evaluate the relationship between the morphology of the breast and the risk of NAC and skin necrosis. Our study showed a 4% rate of NAC removal consistent with the results of the literature (range, 0.0–29%).[4,9,13,17,19,27] The volume of breast removed was the only factor significantly associated with NAC necrosis. We observed a trend of higher risk of necrosis in ptotic breast, with larger volume of breast removed and larger volume of prosthesis inserted for the reconstruction, which were not significant (Tables 5 and 6). Rusby and Gui[28] described a higher risk of necrosis in patients with large or ptotic breast, but there is no study showing an association between degree of ptosis and the risk of NAC necrosis in the NSM procedure. In our study, patients with ptosis grade 0 had only 9% of NAC necrosis compared with higher percentages of NAC necrosis in higher grade ptosis (11–19%). This finding should be investigated further in larger studies. Because of the risk of local recurrence in the breast parenchyma preserved beneath the NAC for the vascular supply, we performed the NSM with the ELIOT technique. The single application of 16 Gy should be sufficient to sterilize more than 90% of the residual cancer cells. The risk of radiodystrophy is low with ELIOT. A mild pigmentation was reported in 20% of the patients at 1-year follow-up, and no local recurrence was observed on NAC area.[8] Type of reconstruction was not significantly associated with NAC necrosis in our study. This was different from other studies showing a significant impact of reconstructive techniques on necrotic complications.[13,17,19] The lack of association in our study was probably due to selection bias. The choice of reconstructive technique is related to the quality of the blood supply of the skin at the end of mastectomy. We usually preferred to place an expander only moderately inflated but may choose an autologous flap reconstruction in case of poor blood supply of the skin envelope. Skin incision types are not related to necrotic complications in our study. Several studies have shown that incision types are an important risk factor of NAC necrosis.[13,17,29,30] Regolo et al[31] report-

Table 7. Comparison of Surgical Risk Factors and Outcomes

Patients Characteristics	No NAC Necrosis (*n* = 105)	NAC Necrosis (*n* = 19)	*P*
Type of incision, *n* (%)			
Superolateral radial	83 (79)	13 (68)	0.26*
Inferolateral radial	1 (1)	1 (5)	
Superior circumareolar	14 (13)	4 (21)	
Periareolar	1 (1)	1 (5)	
Inframammary fold	3 (3)	0	
Others	3 (3)	0	
Duration of operation (min), mean (SD)	165.5 (59.1)	177.5 (80.7)	0.45†
Prosthesis volume (mL), median (range)	302 (100–600); *n* = 60	338 (125–520); *n* = 8	0.66‡
Expander volume (mL), median (range)	200 (90–400); *n* = 38	200 (100–350); *n* = 9	0.91‡
Recon (transverse rectus abdominis myocutaneous, latissimus dorsi), *n* (%)	6 (6)	1 (5)	0.99*
Hematoma/infection, *n* (%)	9 (9)	2 (11)	0.68*

**P* value by Fisher's exact test;
†*P* value by unpaired *t* test;
‡*P* value by Wilcoxon rank-sum test.

Table 8. Comparing Type of Incisions

	Superior Circumareolar + Periareolar Incision	Others Incisions
NAC necrosis, *n* (%)	5 (25)	14 (13)
No NAC necrosis, *n* (%)	15 (75)	90 (87)
Total, *n* (%)	20 (100)	104 (100)

P = 0.19 by Fisher's exact test.

ed of 60% NAC loss with the periareolar incision. As we know, the periareolar incision provides the best cosmetic outcomes. This incision limits the view of operative field and may compromise blood supply to the NAC.[32,33] Lateral or inframammary incisions give a better view in the operative field and does not compromise blood supply to the NAC.[34] Other authors also favor the use of radial or lateral incisions.[13,15] In contrast, Paepke et al[35] reported only a 1% NAC loss with periareolar incision. Algaithy et al[19] recommended maintaining a 5 mm thickness of the areola and periareolar area to prevent from flap necrosis. In our study, the superior circumareolar and periareolar incisions were associated with a NAC necrosis rate of 25% as compared with a rate of 13% with other incisions, but this difference was not statistically significant. It seems likely that the variation in the NAC necrosis rates may relate to the individual surgeon's technique. Smoking history is not related to NAC necrosis in our study, but the literatures have shown that smoking status is an important risk factor for NAC necrosis.[17,19] However, the number of smokers in our study was too small to show a significant association. Diabetes mellitus, hypertension, and dyslipidemia were nonsignificant risk factors for NAC necrosis. Although there was no relation between BMI and NAC necrosis in our study, Davies et al[29] reported higher risk of skin necrosis in women with BMI greater than 25 kg/m^2 and Platt et al[36] also showed higher rate of wound complication for higher BMI women.[30] The nipple sternal notch distance did not influence the risk of skin necrosis in our study as mentioned in different studies.[37–39] There is no study showing the correlation between volume of breast removed and NAC necrosis after performing NSM. The study by Nahabedian et al[40] reported the risk of flap-related complication due to inadequate vascular perfusion in patient with breast volume larger than 1000 cm^3. Our study showed a positive relationship between larger breast volume removed and higher NAC necrosis rate which was most marked for the cutoff of 750 cm^3. This finding may be related to the method of the glandular specimen measurement. The influence of the individual surgeon's technique on NAC necrosis should be investigated further in larger studies.

CONCLUSIONS

Despite a relatively high necrotic complication rate (17.7%) after therapeutic NSM, NSM remains an option for appropriately selected patients. Our study underlined the risk of skin and NAC necrosis in patients with larger breasts and suggests careful consideration of the choice of breast reconstruction in such cases, such as the use of tissue expanders with slow expansion or autologous musculocutaneous flap.

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