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SURGICAL SYMPOSIUM CONTRIBUTION

Oncological Safety and Technical Feasibility of Nipple-Sparing Mastectomy for Breast Cancer: The Hong Kong Experience

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Abstract

Background Nipple-sparing mastectomy (NSM) has gained widespread popularity in recent years. Nonetheless, patient selection, technical consideration and oncological safety of its extension to breast cancer treatment remain uncertain. Few publications have reviewed the application of NSM in Asian populations.

Methods We retrospectively reviewed 91 women with malignant breast tumours, who underwent 97 NSM in Hong Kong Sanatorium and Hospital from 2009 to 2015. Breast cancer patients who required mastectomy and opted for immediate reconstruction were considered for NSM if they showed no obvious nipple involvement clinically. All breast specimens were subjected to intraoperative pathological examination of the retroareolar tissue to exclude occult tumour infiltration before the final decision of nipple–areola complex (NAC) preservation. Clinical parameters, tumour characteristics and oncological outcomes were analyzed.

Results Carcinoma of the breast accounts for 99.0% of our indications for therapeutic NSM. Almost all NSM were accompanied with immediate reconstruction. Abnormal pathology was shown in retroareolar tissue of ten patients (10.3%), and seven of these NAC were excised due to tumour involvement detected by intraoperative frozen section. Six (6.2%) NSM were complicated with superficial epidermolysis. Yet, there was no delayed NAC excision because of nipple necrosis. Overall NAC preservation rate reached 92.8%. Local and/or distant recurrences occurred in four patients (4.1%) after a mean follow-up of 20.6 months. One NAC recurrence was documented.

Conclusion Our series support the oncological safety of NSM after exclusion of neoplastic NAC involvement preliminarily by intraoperative frozen section and definitively by final pathology. Its technical feasibility is well proven by the low nipple necrosis rate.

Introduction

The nipple–areolar complex (NAC) is a vital component and focal point of the breast. With the ever-improving surgical therapy in managing breast cancer, it is not surprising that one of the long-held dogmas of mastectomy surgery, sacrifice of the NAC, would be challenged as necessary for all women undergoing mastectomy. A presumed advantage of nipple-sparing mastectomy (NSM) compared with the standard mastectomy or skin-sparing mastectomy (SSM) is its typically superior cosmetic result,

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as well as the consequent positive impact on patients' psychosocial and sexual well-being [1].

The debate over NSM, which used to be accepted predominately, if not only, in the setting of risk-reducing surgery, continues to evolve. The primary concerns raised about the preservation of NAC in breast cancer patients are: (1) missing occult tumours in the nipple and/or areola; (2) having an increased risk of subsequent new or recurrent cancers in the retained NAC; and (3) partial or complete necrosis of the NAC, i.e. the technical safety [2]. Numerous studies have analyzed data on patient selection, technical consideration and oncological safety of extending the use of NSM to breast cancer treatment. Nevertheless, there is still a current lack of universally agreed upon conclusion. And few publications have appraised the application of NSM in Asian populations.

The purpose of this study was to evaluate our practice of NSM with immediate reconstruction at a single large-volume centre. As experience was gained since the institution began performing NSM in 2007, we sought to review NSM outcomes over time as the eligibility criteria are broadened. This is also the very first report to document an institutional analysis of NSM among Chinese women.

Materials and methods

We retrospectively reviewed the charts of all women who underwent NSM in Hong Kong Sanatorium and Hospital from 2009 to 2015. Clinical (age, menopausal status, body habitus, nodal involvement), radiological (tumour-to-nipple distance, tumour size, multifocality/multicentricity) and pathological (tumour biology, histological grade, in-situ component, nodal status) data were recorded and analyzed.

Patient selection

Candidates for NSM included women affected by in-situ ductal or invasive carcinoma without evident clinical involvement of the NAC, not amenable to breast-conserving surgery, and willing to undergo immediate reconstruction. Exclusion criteria were those with inflammatory breast cancer or Paget's disease of the nipple; however, the presence of nipple discharge was not considered equivalent to NAC involvement [3]. Patients with bilateral malignancy were also included. Neither prior irradiation nor neoadjuvant chemotherapy was regarded as an absolute contraindication to NSM in our study.

Operative technique

All mastectomies in this single-institutional series were performed by one experienced breast surgeon. The technique of NSM used involves the creation of an intact skin envelope through an incision made at the discretion of the surgeon, after considering tumour location, previous scars and method of reconstruction. The choices ranged from omega incision around areolar margin, radial incision over tumour site, or inframammary approach as deemed appropriate. Skin flaps of 5 mm in thickness were raised in a subcutaneous plane to include the Scarpa's fascia, similar to that for an SSM, using electrocautery. Subareolar dissection removed the maximum amount of glandular tissue while raising the NAC as a full-thickness skin flap. After elevating the NAC and exposing the duct bundle, a 5-mm thick disc of tissue containing the ducts deep to the nipple (a specimen labelled "*nipple base*") was sampled from the breast side for frozen section. The NAC was resected at the time of mastectomy if the frozen section revealed malignancy. Axillary staging procedure was also performed if indicated by cancer stage and established treatment guidelines. Patients underwent immediate reconstruction with autologous tissue, expanders/implants or a combination of modalities. Reconstructive options differed based upon body habitus, desired size of reconstructed breast, as well as state of health.

Pathological assessment of the NAC

The nipple base tissue was subjected to additional formal sectioning with haematoxylin and eosin (H&E) staining. If invasive cancer or ductal carcinoma in-situ (DCIS) was noted on either intraoperative frozen section or definitive histology, the nipple was deemed pathologically involved and the NAC would be removed. The presence of lobular carcinoma in-situ (LCIS), atypical lobular hyperplasia (ALH) or atypical ductal hyperplasia (ADH) alone was not reckoned as positive result but further nipple margin might be obtained based on individual consideration.

Definitions

Magnetic resonance imaging (MRI) of the breasts was not routinely performed preoperatively in the institution during the study period. Radiological assessment represented information reported from mammography (MMG) and ultrasonography (USG) with or without MRI. The longest tumour diameter and the shortest distance from the tumour to the nipple were taken, respectively, as "*tumour size on imaging*" and "*tumour-to-nipple distance*" if measurements were available from more than one modalities of imaging.

We defined "*multifocality*" in breast cancer as the presence of two or more tumour foci (at least 5 mm apart) within a single quadrant of the breast, while "*multicentricity*" referred to breast cancer occurring in multiple quadrants of a breast.

Regarding histopathology, "*invasive size*" was defined as the longest diameter (in mm) of the invasive component of formalin-fixed tumour specimens. It determines the pathological T staging of the disease. Hence, it should be "zero" in pure DCIS lesions. Because DCIS lesions frequently manifest near invasive tumours, "*histopathological aggregate size of tumour*" defined as the longest diameter of DCIS or invasive lesions, or the combination of the two if applicable, was calculated to prevent the underestimation of the actual size of the breast cancer lesions [4].

For postoperative complications, "*superficial epidermolysis*" referred to necrosis limited to the layer of epidermis, which might slough off but would leave a pinkish appearance without affecting the nipple projection. We defined "*total nipple necrosis*" as necrosis resulting in loss of nipple projection, or that requiring NAC excision.

Statistical analysis

Descriptive statistics were used to describe patient demographics and clinical characteristics. Means, standard deviations and ranges were used to summarize continuous variables, while categorical variables were reported by frequencies and percentages. Means between groups of interest were compared using an independent sample t test. The data collected were analyzed using the PASW (SPSS) 18.0 software package (IBM Corporation, New York, NY). All p-values were derived from two-sided statistical tests and p-values of less than 0.05 were considered statistically significant.

Results

Indications

From July 2009 through December 2015, NSM was performed on 103 breasts in 91 women. Twelve patients had bilateral NSM and 79 patients had unilateral NSM. Each breast was considered separately for bilateral cases. The vast majority of NSM in our series were of therapeutic indications ($n = 97$, 94.2%). The other six (5.8%) NSM were performed as contralateral prophylactic mastectomy of patient choice in the same operative setting as the diseased side, and thus, excluded from analysis in this retrospective study. The indications for the 97 therapeutic NSM include primary breast cancer ($n = 91$, 93.8%), ipsilateral breast recurrence following breast-conserving surgery

($n = 5$, 5.2%), as well as malignant phyllodes tumour ($n = 1$, 1.0%).

Patient characteristics

Patient age ranged from 27 to 68 years with a mean of 44.7. Mean body mass index (BMI) was 21.0 kg/m^2 (range 16.6–28.9 kg/m^2). More than half of the patients had a bra cup size of B or smaller. Few were current smokers ($n = 9$, 9.9%). Although more than 90% of the cases were presented at an early stage, nine (9.9%) patients had gone through neoadjuvant chemotherapy because of more advanced disease at presentation. The mean tumour size measured on imaging was 27.1 mm (range 2.8–65.0 mm). The mean tumour-to-nipple distance assessed radiologically was 32.8 mm (range 5.0–70.0 mm). A considerable proportion (40.2%) had multifocal or multicentric disease, which reflects the patient selection for mastectomy. The median time of follow-up from surgery was 20.6 months (range 1–70 months). Patient characteristics and preoperative details are summarized in Table 1.

Table 1 Patient demographics and preoperative details

	Number (%)
Number of patients	91
Mean age, years (range)	44.7 (27–68)
Mean body mass index, kg/m^2 (range)	21.0 (16.6–28.9)
Current smokers	9 (9.9)
Received neoadjuvant chemotherapy	9 (9.9)
Bra cup size	
A	23 (25.3)
B	28 (30.8)
C	18 (19.8)
D	17 (18.7)
Number of breasts	97
Previous ipsilateral breast surgery	36 (37.1)
Previous ipsilateral radiotherapy	4 (4.1)
Mean tumour size on imaging[a], mm (range)	27.1 (2.8–65.0)
Mean tumour-to-nipple distance on imaging[b], mm (range)	32.8 (5.0–70.0)
Extent of tumour on imaging	
Unifocal	58 (59.8)
Multifocal/Multicentric	39 (40.2)
Clinical stage	
0	33 (34.0)
I	23 (23.7)
II	33 (34.0)
III	3 (3.1)
IV	2 (2.1)

Calculation based on [a] 68 and [b] 51 available data from radiological reports

Operative details

Table 2 describes the operative details. Almost all of the 97 therapeutic NSM were followed by immediate reconstruction. Transverse rectus abdominus myocutaneous (TRAM) flap was used in 53 cases (54.6%), whereas the rest were mostly implant-based reconstruction ($n = 41$, 42.3%). Only two (2.1%) had a combined use of implant and latissimus dorsi flap. One patient (1.0%) opted for NAC preservation without breast reconstruction. Approximately, 60% of all reconstructions were performed together with a plastic surgeon. All except four of these 97 therapeutic NSM were accompanied with a simultaneous staging procedure of the axilla in terms of sentinel lymph node biopsy ($n = 87$, 89.7%) and/or axillary dissection ($n = 26$, 26.8%). Axillary surgery was skipped in four NSM which were completion mastectomy post excision of known DCIS. Excluding the six patients who had bilateral NSM for synchronous bilateral disease, 21 (24.7%) out of the remaining 85 patients with unilateral disease underwent immediate contralateral surgery to improve breast symmetry or for risk reduction.

NAC involvement

Seven NSM were converted to SSM after intraoperative frozen section evaluation of the retroareolar tissue. Overall,

Table 2 Operative details of therapeutic NSM ($n = 97$)

	Number (%)
Mean breast specimen weight, gram (range)	342.0 (48–1324)
Immediate reconstruction	
TRAM flap	53 (54.6)
Implant	41 (42.3)
Latissimus dorsi flap + Implant	2 (2.1)
Nil	1 (1.0)
Mean implant volume, ml (range)	242.3 (100–390)
Axillary procedure	
Sentinel lymph node biopsy	87 (89.7)
Axillary dissection (immediate or delayed)	26 (26.8)
Nil	4 (4.1)
NAC excision	
Immediate	7 (7.2)
Delayed	0 (0)
Concomitant contralateral breast surgery (number of patients, $n = 91$)	
Mastopexy/Reduction	11 (12.1)
Augmentation	4 (4.4)
Mastectomy[c]	12 (13.2)
Nil	64 (70.3)

n number

[c] Six patients had bilateral breast cancers and another six had contralateral prophylactic mastectomy

six (6.2%) of the NSM had NAC involvement confirmed on definitive pathology, which were all correctly identified by frozen section analysis (false-negative rate = 0%). Therefore, no completed NSM procedure was followed by NAC removal as a separate operation because of falsely negative frozen section result. The nipple base specimens of three additional patients showed abnormal intraoperative frozen section findings not to the extent of invasive tumours nor DCIS (papilloma, atypia or atypical ductal hyperplasia). Their NAC were finally preserved after excision of further margin from the nipple side, which were all revealed to be benign on final pathological assessment. One nipple involved by ALH necessitated NAC excision. Overall NAC preservation rate reaches 92.8%. Patient and tumour characteristics of these ten mastectomies are detailed in Table 3.

Pathological findings

Of the 97 NSM in therapeutic setting, there were 64 cases (66.0%) of invasive cancer and 31 cases (32.0%) of DCIS. One (1.0%) was performed for malignant phyllodes tumour. One (1.0%) breast cancer patient had no residual tumour in her mastectomy specimen after neoadjuvant chemotherapy. Two other patients also showed pathological complete response with residual DCIS only. A summary of the histopathology results is listed in Table 4. Mean tumour sizes of invasive carcinoma and DCIS were 23.1 mm (range 0.3–65 mm) and 39.4 mm (range 2–95 mm) respectively. Forty (41.2% out of 97) breasts showed multifocal/multicentric disease on final pathological evaluation ($n = 32$, 50.0% of invasive cancer; $n = 8$, 25.8% of DCIS). Twenty-nine (29.9%) cases had positive axillary lymph nodes. Fifteen of the 87 NSM with nipple base showing negative result on frozen section had the pathological tumour-to-nipple distance reported. The mean was 22.5 mm (range 2.5–60.0 mm). None of the six contralateral prophylactic NSM had notable pathological findings.

Adjuvant therapy

Fifty-seven out of the 64 cases (89.1%) treated for invasive carcinoma received some sort of adjuvant therapy. Post-mastectomy loco-regional radiotherapy was performed on 15 patients (23.4%). Forty-one (64.1%) underwent adjuvant chemotherapy. Forty-eight (75.0%) and 15 (23.4%) received adjuvant hormonal and targeted therapy respectively.

Table 3 Preoperative findings and final histology of the ten patients with abnormal NAC pathological reports

No.	Patient age, year	Presenting symptom	Tumour size[d], mm	Tumour-to-nipple distance[e], mm (measuring means)	Type of cells involving NAC	NAC excision
1	44	Screening	34	30 (USG)	Papilloma	No
2	53	Mass	21	40 (USG)	Atypia	No
3	50	Screening	36	30 (USG)	Invasive carcinoma	Yes
4	41	Screening	10	30 (clinical)	Atypical ductal hyperplasia	No
5	48	Mass	12	20 (clinical)	DCIS	Yes
6	41	Mass	N/A	Not documented	DCIS	Yes
7	52	Mass	34	30 (USG)	Tumour emboli	Yes
8	43	Mass	25	50 (USG)	Invasive lobular carcinoma	Yes
9	35	Mass	58	Not documented	DCIS	Yes
10	50	Mass	26	40 (USG)	Atypical lobular hyperplasia	Yes

[d] The longest diameter of tumour measured by MMG and USG with or without MRI

[e] The shortest distance measured by MMG and USG with or without MRI; clinical measurement if radiological distance not reported

Recurrences

Four patients (4.1%) developed local and/or distant recurrent disease with a mean time to recurrence from surgery of 24.8 months (range 12–40 months). All of them had multifocal/multicentric invasive ductal carcinoma with positive axillary nodal status to start with, and all required axillary dissection. NAC recurrence occurred in one patient (1.0%), which was associated with local skin flap recurrence. She was a 46-year-old woman with Stage IB HER2 type microinvasive carcinoma and 70 mm of high-grade DCIS. No adjuvant therapy was contemplated. She noticed skin nodules and thickened NAC 15 months after NSM. Refusing biopsy or further treatment, she developed extensive metastases in distant lymph nodes, bone and pericardium one year later, and finally succumbed.

Another 53-year-old patient with Stage IIIA 51-mm grade 3 luminal B HER-2 positive invasive ductal carcinoma and 8/21 metastatic axillary lymph nodes developed chest wall recurrence and bone metastases 17 months postoperatively despite complying to the whole course of adjuvant chemotherapy, loco-regional radiotherapy, targeted and hormonal therapy. The nipple base tissue initially showed atypia on frozen section but her NAC was preserved after clearance was confirmed on further excision of nipple margin.

The remaining two patients, aged 33 and 62 years, both with Stage IIIA pT2N2 disease of luminal A subtype, suffered from distant metastases without local recurrence 13 and 40 months after NSM, respectively.

Association between clinicopathological factors and NAC involvement

Six of the 97 therapeutic mastectomy specimens (6.2%) were found to have occult neoplastic involvement of the nipple. All of these six NSM were performed for invasive carcinoma of the breast. Table 5 demonstrates the association between clinicopathological characteristics and NAC involvement. No significant difference in age was observed between patients with NAC involvement and those without (mean age 44.8 years vs 45.1 years, $p = 0.935$). The mean histopathological aggregate size of tumour in the group with NAC involvement was 45.2 mm, and that of the unaffected group was 33.7 mm ($p = 0.189$). There was also no statistically significant difference between the two groups in the mean tumour size measured from preoperative imaging reports (33.0 mm vs 26.6 mm, $p = 0.337$). However, statistically significant difference was observed in the mean invasive size (39.8 mm for NAC involved group vs 21.4 mm for NAC uninvolved group, $p = 0.003$), which also reflects the pathological T staging of the disease. Other factors such as menopausal status, histological grade, multifocal/multicentric disease, lymphovascular invasion, hormonal receptor status or proliferation markers (Ki-67) did not show significant difference between the two.

Surgical complications

Superficial epidermolysis of the nipple occurred as early postoperative complications in six (6.2%) of our 97 NSM.

Table 4 Histopathology results of 97 therapeutic NSM

	Number (%)
Histopathological type	
Invasive ductal carcinoma	57 (58.8)
Invasive lobular carcinoma	7 (7.2)
DCIS	31 (32.0)
Others	2 (2.1)
Tumour grade	
Grade 1 invasive cancer	13 (13.4)
Grade 2 invasive cancer	33 (34.0)
Grade 3 invasive cancer	18 (18.6)
Low-grade DCIS	5 (5.2)
Intermediate-grade DCIS	10 (10.3)
High-grade DCIS	16 (16.5)
Mean histopathological aggregate size of tumour, mm (range)	
Invasive	23.1 (0.3–65)
DCIS	39.4 (2–95)
Pathological T stage	
T0	1 (1.0)
Tis	31 (32.0)
T1	32 (33.0)
T2	28 (28.9)
T3	4 (4.1)
Pathological N stage	
Nx	4 (4.1)
N0	64 (66.0)
N1	22 (22.7)
N2	6 (6.2)
N3	1 (1.0)
Pathological stage (AJCC grouping)	
0	31[f] (32.0)
I	30[f] (30.9)
II	26 (26.8)
III	8 (8.2)
IV	1 (1.0)

[f] Including three (Stage 0) and two (Stage I) patients down-staged after neoadjuvant chemotherapy

None of these patients were current smokers, and they all were healed with conservative treatment without major sequelae. There was no documented incident of more serious complications like full-thickness skin loss or total nipple necrosis. No NAC was excised in a second surgical procedure for complication. Wound infection occurred in ten NSM (10.3%), which is slightly higher but comparable to the 7–9% incidence of postoperative infection in published studies [5, 6]. These infections were not related to any of the superficial epidermolysis of NAC, and were

Table 5 Association between NAC involvement and clinicopathological parameters

	N	NAC involvement		p value
		Yes (%)	No (%)	
Menopausal status				
Premenopausal	81	4 (66.7)	77 (84.6)	0.257
Postmenopausal	16	2 (33.3)	14 (15.4)	
Clinical stage				
0–II	87	4 (66.7)	83 (92.2)	0.097
III–IV	9	2 (33.3)	7 (7.8)	
Neoadjuvant chemotherapy				
Yes	8	1 (16.7)	7 (7.7)	0.412
No	89	5 (83.3)	84 (92.3)	
Multifocality/Multicentricity on imaging				
Yes	39	1 (16.7)	38 (41.8)	0.396
No	58	5 (83.3)	53 (58.2)	
Tumour type				
In-situ ductal	31	0 (0.0)	31 (34.8)	0.173
Invasive	64	6 (100.0)	58 (65.2)	
Invasive tumour grade				
1	13	1 (16.7)	12 (20.7)	0.946
2	33	3 (50.0)	30 (51.7)	
3	18	2 (33.3)	16 (27.6)	
Presence of DCIS				
Yes	84	4 (66.7)	80 (87.9)	0.183
No	13	2 (33.3)	11 (12.1)	
Multifocality/Multicentricity on pathology				
Yes	40	1 (16.7)	39 (42.9)	0.396
No	57	5 (83.3)	52 (57.1)	
Invasive size (mm)				
<20	32	2 (33.3)	30 (51.7)	0.016
≥20 and <50	28	2 (33.3)	26 (44.8)	
≥50	4	2 (33.3)	2 (3.4)	
Nodal status				
Positive	28	3 (50.0)	25 (28.7)	0.361
Negative	65	3 (50.0)	62 (71.3)	
Pathological stage[g]				
0	31	0 (0.0)	31 (34.1)	0.103
I–II	56	4 (66.7)	52 (57.1)	
III–IV	9	2 (33.3)	7 (7.7)	
Others	1	0 (0.0)	1 (1.1)	
Oestrogen receptor				
Positive	84	5 (83.3)	79 (88.8)	0.532
Negative	11	1 (16.7)	10 (11.2)	
Progesterone receptor				
Positive	69	6 (100.0)	63 (70.8)	0.184
Negative	26	0 (0.0)	26 (29.2)	
Ki67 (%)				
>14	51	3 (50.0)	48 (55.2)	1.000
≤14	42	3 (50.0)	39 (44.8)	

Table 5 continued

	N	NAC involvement		p value
		Yes (%)	No (%)	
HER-2				
Positive	32	1 (16.7)	31 (34.1)	0.660
Negative	65	5 (83.3)	60 (65.9)	
Lymphovascular invasion				
Positive	14	2 (33.3)	12 (32.4)	1.000
Negative	29	4 (66.7)	25 (67.6)	

[g] AJCC grouping

treated conservatively. There was no loss of implant in our series.

Discussion

Surgical treatment of breast cancer has greatly evolved during the past few decades in order to combine oncological safety with cosmetic satisfaction. Skin-sparing mastectomy (SSM) with immediate reconstruction has clearly been an important advancement since the 1990s [7]. Being even more able to offer a natural NAC appearance and retain the original breast contour, much interest has been aroused in defining the role of nipple-sparing mastectomy (NSM) in breast cancer treatment.

Occult NAC tumour involvement

NSM leaves a thin nipple-areola flap with sparse or no ductal component. The risk of cancer developing in the preserved tissue is the major concern [8]. Most published data report NAC tumour involvement rates between 5.6 and 30% in unselected mastectomy specimens of breast cancer patients [9]. The NAC involvement rate in our study was 6.2%; six NAC with close or involved margins were excised. This relatively low incidence echoes with the findings of a recent systemic review of the literature, which showed that only 6.4% of the nipple cores of 2477 NAC-sparing mastectomy were involved with tumour [10]. Such a difference likely reflects a selection bias towards tumours of less advanced stage, and/or not involving the central quadrant of the breast, in patients submitted to NSM as compared to total mastectomy in the first place [11].

Pathological evaluation of the retroareolar breast tissue at surgery is now widely accepted as the crucial decisional criterion for NAC preservation in carefully selected patients [8]. In our series, we adopted an omega incision for most NSM, which was usually 5 or 6 cm in length. This enables a biopsy of the nipple base tissue to be instantly attained and sent for frozen section analysis at the beginning of the operation. Intraoperative frozen section evaluation provides preliminary findings that facilitate excision of the NAC at the initial surgery if indicated; therefore, immediate adjustments in the reconstructive procedure can be made if necessary [7]. On the other hand, and in fact more importantly, it allows additional nipple margin to be excised in case of abnormal results. This helps to avoid sacrificing the whole nipple unnecessarily if a clear resection margin can be achieved with further excision.

Nevertheless, preoperative assessment of the NAC is important as it may help select the best surgical strategy and inform the patient about the likelihood of the NAC being removed. Many clinical factors have been identified to correlate with the risk of occult NAC involvement. They include the proximity of cancer to the nipple, tumour size, axillary nodal status, multifocality, lymphovascular invasion, etc. [12–19]. The more consistently recognized criteria seem to be the breast tumour size and the distance of the tumour from the nipple [20]. Our cohort, however, did not illustrate a statistically significant difference in the mean size of lesion between the NAC involved and uninvolved groups; neither on preoperative radiological assessment nor on final pathological evaluation (as the mean histopathological aggregate size of tumour). Though the difference in mean invasive size on histopathology reached statistical significance, it is not easy to translate this postoperative tumour parameter into a preoperative predicting factor.

Among the ten patients with abnormal NAC pathological reports, most had their breast tumours located at a radiological distance of 20–50 mm from the nipple. Unfortunately, a limitation to this study is that the tumour-to-nipple distance was recorded only in a small number of preoperative imaging. The lack of recording, nonetheless, may be explained by lesions that were not well defined, such as calcifications or architectural distortions. Evaluation of a larger sample size with known tumour-to-nipple distance may elicit a better understanding of the predictive value of this preoperative indicator.

Although selection criteria can be used to identify those at lower risk for occult tumour in the nipple, it should not be inferred that other patients cannot be considered if they so desire. After all, in any case, the final decision to spare the nipple must ultimately await frozen and then definitive pathological section. At this institution, NSM is currently offered when there is no inflammatory breast cancer, Paget's disease of the nipple or clinical gross involvement of the NAC. Challenging the theoretical concern about preserving the nipple in the presence of nipple discharge, the authors do not regard this symptom as an absolute contraindication to NSM [3]. Seven patients in this cohort study presented with nipple discharge, but none of their

nipple base tissues harboured tumour cells. They all went through successful NSM and remained disease-free up to their last follow-up dates. On the contrary, those ten patients with abnormal nipple base pathology did not complain of nipple discharge at all; and seven of them need to have their NAC excised.

Risk of subsequent new or recurrent cancers in the retained NAC

The local recurrence rate without distant metastasis in our series was 1.0% after a mean follow-up of 20.6 months, whereas that for isolated NAC recurrence was 0%. In spite of the relatively short follow-up time, this result is consistent with other published data, which report local recurrence rates between 0 and 12% following NSM after a mean follow-up period of 52.4 months [5, 6, 21–24]. The extremely low rate of local recurrence within the NAC (0.16%) found on a review of 1826 NSM supports the opinion that local failure is a manifestation of tumour biology rather than preservation of the NAC [5].

Technical safety

Nipple necrosis becomes a new entity of perioperative complication emerging with this novel surgical procedure that retains all the surface landmarks of the breast. We did encounter six NAC with postoperative superficial epidermolysis among our 97 NSM (6.2%), which all resolved with wound care without loss of nipple projection. This is comparable to other series, where the rate of partial nipple necrosis varies between 5% and 16% [9]. We had no total nipple necrosis that required excision for treatment, in contrast to the reported 5% to 8% in the published literature [22, 24, 25]. Our high viability rate of the nipple can be attributed to the extreme caution in avoiding excessive thermal injury during dissection at the NAC base. In addition, we did not core out the nipple. Instead, the "nipple base" from the mastectomy specimen was harvested for intraoperative assessment. This might have helped to prevent severe ischaemia of the NAC. A similar technique has been used by Voltura et al. [26], who found that local recurrence rates with NSM showed an equivalency to SSM. Regarding surgical technique, our preferential use of periareolar incision did not seem to adversely affect our nipple necrosis rate, contrasting reports of some studies [9], which advocate lateral or inframammary incision placement to preserve blood supply to the NAC.

In most cases, NSM equates with removing little if any skin, in other words, a total skin-sparing mastectomy. For that reason, the larger or more ptotic the breast, the more likely there will be nipple or flap necrosis, or both [27]. The mean BMI of our patients in this cohort was only 21.0 kg/ m^2. The average weight of the mastectomy specimens was 342 g. The smaller body habitus and breast size of our Chinese population in general may also explain our low rate of necrosis. Our overall NAC preservation rate was 92.8%, which is similar to other published reports [9].

Conclusion

In spite of the relatively small sample size, our results regarding occult NAC tumour involvement, local recurrence and technical safety showed consistency with most literature. This study demonstrated the feasibility of performing NSM in an oncologically rigorous fashion with low perioperative complication rate and good short-term results. Although obvious clinical involvement of the NAC remains an absolute contraindication, the use of intraoperative biopsy results with less stringent preoperative criteria would allow more patients to be considered for NSM with what is likely to be minimal risk.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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