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Initial oncological outcomes of nipple- and areola-sparing mastectomy in patients with breast cancer with nipple discharge

Hong Hou[1,2,3,4,5], Jing Xia[1,2,3,4,5], Lin Tan[6], Yue Yu[1,2,3,4] and Xin Wang[1,2,3,4*]

Abstract

Objective This study aimed to assess the oncological safety of nipple- and areola-sparing mastectomy (NSM) compared to mastectomy without preservation of the nipple-areola complex (NAC) in patients with breast cancer presenting with nipple discharge.

Methods Clinical data were retrospectively reviewed for 93 patients who underwent NSM and 133 patients who underwent mastectomy without NAC preservation for non-metastatic breast cancer between March 2015 and August 2023 at two hospitals. All patients presented with bloody or serous nipple discharge. Clinicopathological characteristics of both groups were assessed to evaluate the oncological safety of NSM and identify prognostic factors.

Results Local recurrence rates and disease-free survival rates at 3 and 5 years did not differ significantly between the groups ($p > 0.05$). Univariate analysis identified tumor T stage, lymph node metastasis count, and histological grade as independent risk factors influencing disease-free survival and overall survival ($p < 0.05$). Tumors larger than 2 cm, lymph node positivity, and grade III histology were associated with an elevated risk of recurrence. Multivariate analysis further confirmed tumor T stage and lymph node metastasis count as significant risk factors for both disease-free survival and overall survival, with larger tumors and positive lymph node status linked to an increased risk of mortality.

Conclusion NSM demonstrated oncological safety in this patient population. Prognostic factors significantly affecting survival outcomes included tumor T stage, lymph node metastasis count, and histological grade.

Keywords Breast cancer, Breast-conserving surgery, Modified radical mastectomy, Nipple-areolar complex nipple- and areola-sparing mastectomy, Skin-sparing mastectomy

*Correspondence:
Xin Wang
wangxinwxmed@163.com
[1]The First Department of Breast Cancer, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, No.1 Huanhuxi Road, Hexi District, Tianjin 300060, China
[2]Tianjin's Clinical Research Center for Cancer, Tianjin 300060, China
[3]Key Laboratory of Breast Cancer Prevention and Therapy, Tianjin Medical university, Ministry of Education, Tianjin 300060, China
[4]Key Laboratory of Cancer Prevention and Therapy, Tianjin 300060, China
[5]Department of Breast Surgery, Qingdao Central Hospital, University of Health and Rehabilitation Sciences (Qingdao Central Hospital), Qingdao 266042, China
[6]Department of Thoracic Surgery, Qingdao Hospital, University of Health and Rehabilitation Sciences (Qingdao Municipal Hospital), Qingdao 266000, China

Introduction

Nipple-areola complex (NAC)-sparing modified radical surgery, commonly referred to as nipple-areola complex-sparing mastectomy (NSM), is a widely used surgical approach for early-stage breast cancer. Unlike traditional mastectomy, this technique preserves the NAC, providing significant advantages in terms of aesthetic outcomes and quality of life for patients. NSM also facilitates immediate breast reconstruction (IBR), making the combination of NSM and IBR a preferred surgical option.

Nipple discharge is a common clinical manifestation of breast disease, with studies indicating a strong relationship between bloody nipple discharge and breast cancer. Early medical evaluation is crucial for patients presenting with bloody discharge to enable timely diagnosis and intervention. According to the *Expert Consensus and Controversies on Nipple-Areola Complex-Preserving Mastectomy* bloody nipple discharge is not an absolute contraindication for NAC preservation [1]. In clinical settings, approximately 34.9% of physicians report that nipple discharge does not necessarily indicate NAC invasion and may recommend NSM for suitable candidates.

However, concerns remain regarding the potential dissemination of cancer cells through mammary ducts associated with nipple discharge, raising questions about the oncological safety of NAC preservation. This underscores the importance of evaluating the oncological safety of NSM in comparison to traditional mastectomy without NAC preservation, which forms the basis of this study.

Table 1 Clinical pathological features of the mastectomy and NSM groups

Characteristics	Mastectomy $n=133$	NSM $n=93$	*P* value
T.stage, n (%)			0.888
Tis + T1	94	64	
T2	36	26	
T3	3	3	
N.stage, n (%)			0.732
N0	112	76	
N1	17	15	
N2 + N3	4	2	
ER, n (%)			0.245
> 10	91	73	
0	35	17	
≥ 1; < 10	7	3	
PR, n (%)			0.131
Positive	83	67	
Negative	50	26	
Age, n (%)			0.355
≥ 35	113	64	
< 35	20	29	
Histological grade, n (%)			0.551
I+II	110	74	
III	23	19	
HER-2+, n (%)			0.445
Negative	97	72	
Positive	36	21	
ki-67%, n (%)			0.532
≥ 20	98	65	
< 20	35	28	
Location (central area/No), n (%)			0.379
Yes	49	29	
No	84	64	
Sentinel lymph node/axillary lymph node dissection, n (%)			0.274
Sentinel lymph node	56	46	
Axillary lymph node dissection	77	47	
Nipple discharge			0.320
Bloody	51	62	
Non-bloody	42	71	

Materials and methods

Clinical data and methods

Clinical data were obtained from individuals diagnosed with non-metastatic breast cancer treated at Tianjin Medical University Cancer Institute & Hospital and Qingdao Central Hospital of Health Sciences University between January 2014 and August 2023. Inclusion criteria encompassed female patients aged 20 to 60 years presenting with unilateral bloody or serous nipple discharge, a pathological diagnosis of invasive breast carcinoma or ductal carcinoma in situ, and staging of I–IIIC based on the 2010 American Joint Committee on Cancer (AJCC) staging guidelines. All included patients had undergone surgical treatment. Patients were excluded if they had bilateral breast cancer, received neoadjuvant chemotherapy, lacked standard nipple pathological examinations, had incomplete clinicopathological data, or exhibited abnormal nipple conditions such as inversion or eczematous changes.

Basic information

In the NSM group, patient ages ranged from 21 to 60 years, with a mean age of 42.0 years. Among these patients, 53 cases involved left breast lesions, and 40 cases involved right breast lesions, with no cases of bilateral lesions. In the mastectomy group, patient ages ranged from 28 to 60 years, with a mean age of 46.9 years. This group included 77 cases with left breast lesions and 56 cases with right breast lesions, with no bilateral cases. No significant differences in clinicopathological characteristics were identified between the two groups (all $p > 0.05$, Table 1).

Treatment methods

1. Imaging examination: 40 patients presented with only nipple discharge, 186 patients presented with

both nipple discharge and breast mass detected by ultrasound or mammography. All patients underwent imaging examinations. Patients with intraductal space-occupying lesions as indicated by ductography and those with suspicious malignant lesions as suggested by color Doppler ultrasound/MRI/X-ray underwent surgical excision biopsy or core needle biopsy. During the surgery, methylene blue was injected into the nipple discharge ducts to mark the discharge ducts and breast glandular tissue through staining, the related ducts and surrounding tissues were removed. If the lesion can be detected by color Doppler ultrasound/MRI/X-ray, it should undergo core needle biopsy.

2. NSM Group: A total of 93 patients with pathologically confirmed malignancy, identified through preoperative core needle biopsy and intraoperative frozen section pathology, underwent NSM. Two surgical approaches were used: selective excision of mammary ducts within the nipple while preserving the nipple and areolar skin tissue, or complete preservation of the NAC. Intraoperative frozen section pathology confirmed the absence of cancer at the nipple base. Nipple involvement was defined as the presence of carcinoma in situ, invasive carcinoma, lymphovascular invasion, or Paget's disease in the nipple skin or underlying tissue. Of the patients in this group, 87 (93.5%) underwent breast reconstruction using either autologous tissue or implant-based methods (Table 2).
3. Mastectomy Group: A total of 133 patients with pathologically confirmed malignancy, determined through preoperative core needle biopsy and intraoperative frozen section pathology, underwent mastectomy. In this group, 18 patients initially planned for NSM were converted to traditional mastectomy due to positive intraoperative frozen section results (12 cases) or atypical hyperplasia/ADH (6 cases). The management of these cases fully considered the potential risks of postoperative paraffin pathology and was communicated thoroughly with the patients' families.
4. Adjuvant Therapy: Postoperative adjuvant therapy was administered to all patients in accordance with the Chinese Society of Clinical Oncology (CSCO) guidelines. Treatment decisions were guided by tumor size, lymph node status, and molecular subtyping to assess recurrence risk. Adjuvant therapies included chemotherapy, radiotherapy, endocrine therapy, and anti-HER-2 targeted therapy.
5. Follow-up: Patients were monitored through outpatient visits and telephone interviews, with follow-up concluding on August 1, 2024. Complete follow-up data were obtained for all patients.

Table 2 Selection of surgical techniques in NSM and mastectomy groups

Surgical approach	NSM group (93 cases)	Mastectomy group (133 cases)
Major ducts within nipple		
Removed	21(22.6%)	-
Preserved	72(77.4%)	-
Breast surgery method		
Implant/expander breast reconstruction	74	25
Autologous flap breast reconstruction	14	12
No breast reconstruction	5	96

Statistical methods

Statistical analysis was conducted using SPSS version 22.0. The chi-squared (χ^2) test was used to compare clinicopathological characteristics between the groups. The Kaplan–Meier method was used to estimate the 3-year local recurrence rate (LRR), 3-year disease-free survival rate, and 5-year overall survival rate, with survival differences between the groups assessed using the log-rank test. Logistic regression models were used to conduct univariate and multivariate analyses to identify risk factors associated with recurrence and death. The significance level was $\alpha = 0.05$.

Results

Prognosis of patients in the NSM and mastectomy groups

In the NSM group, follow-up durations ranged from 12 to 130 months, with a median follow-up period of 77 months. During the first 3 years post-surgery, 6 cases of local recurrence were observed, 3 on the chest wall and 3 in axillary lymph nodes. Additionally, 5 cases of distant metastasis were identified, with 2 to bone and 3 to the liver or lung. A total of 9 deaths occurred within 5 years, resulting in a 5-year overall survival rate of 90.3%.

In the mastectomy group, follow-up durations ranged from 12 to 150 months, with a median follow-up period of 77 months. Within 3 years post-surgery, 5 cases of local recurrence were reported, comprising 3 in the chest wall and 2 in the axillary lymph nodes. Distant metastasis was noted in 3 cases, with 2 to bone and 1 to the brain. A total of 8 deaths were recorded within 5 years.

The NSM group demonstrated a 3-year LRR of 5.4%, a 3-year DFS rate of 88.1%, and a 5-year OS rate of 90.3%. In comparison, the mastectomy group indicated a 3-year LRR of 3.8%, a 3-year DFS rate of 94.0%, and a 5-year OS rate of 91.5%. No statistically significant differences were identified between the two groups ($p > 0.05$).

Univariate and multivariate analysis of disease-free survival factors

Univariate analysis indicated that tumor size, histological grade, and the number of lymph node metastases were significantly associated with 3-year DFS (all $p < 0.05$, Table 3). Patients with T3 tumors, positive lymph nodes, and histological grade III exhibited a higher risk of recurrence. Preservation of the NAC, patient age, and hormone receptor status did not influence prognosis.

Multivariate analysis further identified tumor T stage, lymph node metastases count, and histological grade as independent risk factors for DFS. Tumors larger than 2 cm (T > 2) and positive lymph node involvement were associated with a significantly increased risk of recurrence (Table 3).

Univariate and multivariate analysis of overall survival factors

Univariate analysis indicated that tumor size, histological grade, and the number of lymph node metastases were significantly associated with 3-year DFS (all $p < 0.05$, Table 4). Patients with T > 2, positive lymph node involvement, and histological grade III demonstrated a higher risk of mortality. Preservation of the NAC, patient age, and hormone receptor status did not have a significant impact on prognosis.

Multivariate analysis confirmed tumor T stage, lymph node metastases count, and histological grade as independent risk factors influencing OS. T > 2 and positive lymph nodes status were associated with a significantly higher risk of mortality (Table 4).

Table 3 Univariate and multivariate examination of the factors influencing Disease-Free survival rate

Characteristics	Total(*N*)	Univariate analysis		Multivariate analysis	
		Odds Ratio (95% CI)	*P* value	Odds Ratio (95% CI)	*P* value
T.stage	226				
Tis + T1	158	Reference		Reference	
T2	62	3.753 (1.245–11.310)	0.019	3.094 (0.973–9.836)	0.056
T3	6	126.667 (12.740–1259.353)	< 0.001	64.816 (5.296–793.188)	0.001
N.stage	226				
N0	188	Reference		Reference	
N1	32	37.000 (9.624–142.246)	< 0.001	31.455 (6.868–144.067)	< 0.001
N2 + N3	6	123.333 (15.956–953.337)	< 0.001	72.314 (7.596–688.451)	< 0.001
ER	226				
> 10	164	Reference			
0	52	0.968 (0.301–3.109)	0.956		
≥ 1; < 10	10	2.904 (0.558–15.117)	0.205		
PR	226				
Positive	150	Reference			
Negative	76	1.167 (0.440–3.096)	0.757		
Age	226				
≥ 35	170	Reference			
< 35	56	1.881 (0.702–5.040)	0.209		
Histological grade	226				
I+II	184	Reference		Reference	
III	42	6.076 (2.289–16.128)	< 0.001	2.180 (0.641–7.411)	0.212
Sentinel lymph node/axillary lymph node dissection	226				
Sentinel lymph node	102	Reference			
Axillary lymph node dissection	124	1.454 (0.550–3.841)	0.450		
HER-2+	226				
Negative	169	Reference			
Positive	57	1.412 (0.510–3.906)	0.507		
ki-67%	226				
≥ 20	163	Reference			
< 20	63	0.669 (0.213–2.099)	0.491		
Location (central area/no)	226				
Yes	78	Reference			
No	148	1.525 (0.528–4.404)	0.435		
group	226				
Mastectomy	133	Reference			
NSM	93	2.096 (0.809–5.433)	0.128		

Table 4 Univariate and multivariate analysis of the factors influencing overall survival

Characteristics	Total(*N*)	Univariate analysis		Multivariate analysis	
		Odds Ratio (95% CI)	*P* value	Odds Ratio (95% CI)	*P* value
T.stage	226				
Tis + T1	158	Reference		Reference	
T2	62	4.302 (1.462–12.658)	0.008	3.714 (1.205–11.449)	0.022
T3	6	126.667 (12.740–1259.353)	< 0.001	74.443 (6.058–914.759)	< 0.001
N.stage	226				
N0	188	Reference		Reference	
N1	32	42.193 (11.034–161.337)	< 0.001	34.149 (7.612–153.202)	< 0.001
N2 + N3	6	123.333 (15.956–953.337)	< 0.001	69.638 (7.375–657.530)	< 0.001
ER	226				
> 10	164	Reference			
≥ 1; < 10	10	2.679 (0.518–13.856)	0.240		
0	52	0.893 (0.281–2.842)	0.848		
PR	226				
Positive	150	Reference			
Negative	76	1.069 (0.408–2.802)	0.892		
Age	226				
≥ 35	170	Reference			
< 35	56	1.725 (0.652–4.566)	0.272		
Histological grade	226				
I+II	184	Reference		Reference	
III	42	5.437 (2.094–14.118)	< 0.001	1.843 (0.552–6.155)	0.320
Sentinel lymph node/axillary lymph node dissection	226				
Sentinel lymph node	102	Reference			
Axillary lymph node dissection	124	1.589 (0.609–4.146)	0.344		
HER-2+	226				
Negative	169	Reference			
Positive	57	1.303 (0.476–3.567)	0.607		
ki-67%	226				
≥ 20	163	Reference			
< 20	63	0.623 (0.200–1.941)	0.414		
Location (central area/no)	226				
Yes	78	Reference			
No	148	1.254 (0.462–3.402)	0.657		
group	226				
Mastectomy	133	Reference			
NSM	93	2.315 (0.907–5.910)	0.079		

Discussion

Traditional breast cancer surgery has typically involved the removal of the NAC due to concerns over the potential risk of occult malignancy involvement [1]. The oncological safety of NSM remains a subject of debate, primarily due to concerns regarding the potential for malignant transformation of residual glandular and ductal tissue beneath the NAC, which may increase the likelihood of local recurrence. However, increasing evidence challenges these concerns.

Early studies by Turner-Warwick in 1959 and Handley in 1964 demonstrated that breast lymphatics not only drain into the subareolar lymphatic plexus but extend to the deep pectoral lymphatic plexus. These findings provide theoretical support and novel insights into the safety of preserving the NAC. Furthermore, Wellings and Jensen analyzed 196 breast specimens and observed that mammary dysplasia, metaplasia, hyperplasia, and neoplastic lesions predominantly occur within the terminal duct lobular unit (TDLU) [2, 3]. While some authors [4, 5] have argued that TDLUs are absent within the nipple, subsequent studies detected TDLUs in approximately 9% of nipple base samples obtained from mastectomy specimens [6]. Notably, TDLUs were not identified at the nipple tip.

These observations indicate that preserving the NAC does not increase the risk of local recurrence, provided that biopsy samples are free from malignant components. Additionally, retroareolar margin assessment has been shown to provide reliable accuracy in evaluating nipple

involvement, supporting the feasibility of NAC preservation during surgery [7]. These findings offer substantial scientific evidence and a reference framework for managing the NAC in mastectomy procedures, carrying significant clinical implications.

NSM, when combined with immediate breast reconstruction, facilitates tumor removal and preservation of the NAC in a single surgical procedure. This approach maintains the external morphology of the breast, resulting in a more natural postoperative appearance. Additionally, it avoids the need for secondary nipple reconstruction, thereby reducing associated medical costs, psychological stress, and surgical risks. Advances in surgical techniques and systemic therapies have contributed to a significant decline in locoregional recurrence rates following mastectomy, further supporting the feasibility and safety of NSM. As a result, NSM is increasingly regarded as a preferred surgical option for patients with early-stage breast cancer.

Nipple discharge is a common clinical manifestation of breast disease, typically arising from pathological changes in the mammary ducts or acini. These changes lead to epithelial cell proliferation, heightened secretory activity, and structural disruption of the surrounding tissue, often resulting in erosion and bleeding. Bloody nipple discharge, in particular, is strongly associated with breast cancer, emphasizing the importance of timely medical evaluation for early diagnosis and treatment.

Previous clinical studies on NSM have frequently excluded patients with nipple discharge, creating a gap in safety data for this subgroup. *The Expert Consensus and Controversy on Nipple-Areola Complex-Sparing Mastectomy* highlights concerns regarding potential intraductal implantation of cancer cells present in the discharge and the possibility of misdiagnosis due to incomplete pathological sampling of retroareolar tissue [1]. Despite these concerns, 34.9% of physicians in clinical practice maintain that nipple discharge does not necessarily indicate lesion invasion of the nipple. Theoretical evidence indicates that meticulous excision of major ducts within the nipple during NSM can achieve satisfactory oncological safety. Domestic expert consensus aligns with this perspective, asserting that bloody nipple discharge is not an absolute contraindication for NSM.

Chang et al. conducted a study on 60 patients diagnosed with breast cancer presenting with nipple discharge and found that when intraoperative frozen sections confirmed no malignancy at the nipple base, patients in the nipple preservation group experienced no local recurrence during a 27-month follow-up period [8]. They concluded that nipple discharge does not necessarily indicate nipple involvement and that preserving the nipple does not increase prognostic risk, provided the nipple base margin is confirmed as negative.

An analysis of mastectomy specimens from 1,190 patients diagnosed with breast cancer demonstrated a low probability (4.3%) of nipple involvement in patients without clinical abnormalities of the nipple, with no observed correlation between nipple discharge and nipple involvement [9]. This aligns with prior research reporting 2–4% recurrence rates following nipple-preserving surgery. Conversely, another study involving 2,323 mastectomy specimens reported a higher incidence of nipple involvement (14.2%), including 10.7% occult involvement. These findings emphasize the need to carefully weigh the low risk of residual malignancy against tumor recurrence risk and patient preferences when determining the optimal surgical approach [10].

However, NSM has been associated with a higher risk of breast flap necrosis compared to traditional mastectomy procedures [11]. Recommendations from the Memorial Sloan Kettering Cancer Center indicate that strict excision of major ducts within the nipple, while preserving the epidermal and dermal layers, can minimize the risk of NAC necrosis [12]. Despite these recommendations, only 17.4% of experts in China endorse this approach [1].

In the current study, only 22.6% of patients in the NSM group underwent removal of the major nipple ducts during surgery, as excessive dissection of these ducts was considered to potentially compromise the vascular network of the dermal layer, increasing the risk of nipple necrosis. Consequently, a conservative surgical strategy was adopted to balance optimal surgical outcomes with patient safety.

This retrospective analysis of patients diagnosed with breast cancer and presenting with nipple discharge indicated no significant differences in clinicopathological characteristics between the NSM and total mastectomy groups, with the exception of patient age. Younger patients demonstrated a stronger preference for preserving breast appearance, as supported by real-world data. A comparison of clinical outcomes between NSM and traditional mastectomy indicated that NSM offered comparable oncological safety, with no statistically significant differences observed in local recurrence rates, 3-year DFS rates, or 5-year OS rates between the two groups.

Among the NSM group, six patients experienced local recurrence; however, none of these recurrences involved the nipple-areola complex. This finding indicates that while preoperative nipple discharge may contain cancer cells originating from mammary ducts, the study did not identify any cases of local recurrence linked to cancer cell implantation in the ducts.

Univariate analysis identified tumor size, lymph node status, and histological grade as significant risk factors for recurrence, metastasis, and mortality. Multivariate analysis further confirmed tumor size and lymph node

status as independent risk factors for these outcomes, aligning with established clinical consensus. Importantly, the presence of nipple discharge as a clinical symptom did not emerge as an additional risk factor for recurrence. Furthermore, inclusion of the surgical approach in both univariate and multivariate analyses demonstrated no differences in patient prognosis between the two surgical methods. A more thorough investigation into local and regional recurrences will be conducted in future studies to ascertain the local control effects of the surgical approaches. However, several limitations should be acknowledged. First, this study was retrospective, younger patients with lower risk profiles were more likely to select NSM, potentially introducing selection bias, data bias, and confounding factors. Although the oncological safety of NSM appears promising, the inherent limitations of retrospective research must be acknowledged. Second, the median follow-up duration of 47 months precludes definitive conclusions about long-term oncological safety, particularly regarding the extrapolated 5-year overall survival estimates. To validate these preliminary findings, we will extend the follow-up period to over 10 years in future studies, which will allow us to more accurately assess the long-term oncological outcomes and provide more robust evidence for the safety of NSM in this patient population. Third, our preliminary data showed that the tumor-nipple distance was not statistically significant between patients who experienced local recurrence and those who did not, possible due to the relatively small number of recurrence cases. The follow-up period and the sample size should be increased in future studies to better evaluate the impact of tumor-nipple distance on recurrence. In addition, we did not analyze residual glandular tissues. MRI and mammography should be included in subsequent research to assess the impact of residual glandular tissue on oncological safety. Lastly, the exclusion of stage III patients receiving NAC in this study may have introduced certain limitations to the research outcomes. Patients with stage III are generally more suitable candidates for NAC. In future studies, a dedicated NAC patient cohort should be established. By using the AJCC/CAP Residual Cancer Burden scoring system to quantify post-treatment residual lesions, a more comprehensive analysis of pathological and survival outcomes can be performed.

In this study, patients were excluded if they had received neoadjuvant chemotherapy. Because after neoadjuvant therapy, the primary tumor will show varying degrees of pathological remission. The posterior nipple tissue is the key to the surgical margin. Neoadjuvant therapy may increase the difficulty of pathological diagnosis and raise the risk of false-negative margins. Therefore, this group of patients was not included in the study. Even the III-stage patients included in this study did not receive neoadjuvant chemotherapy. Among all the III-stage patients during these years, a large proportion still received neoadjuvant therapy but were not included in this study.

Conclusion

Our findings indicate that NSM is a safe and effective surgical alternative to traditional mastectomy for patients diagnosed with breast cancer who present with nipple discharge. Preservation of the NAC, a key anatomical structure, contributes to improved cosmetic outcomes in breast reconstruction and enhances the quality of life of patients. NSM is a viable option for cases where breast-conserving surgery is not feasible, a position supported by broad expert consensus. For eligible patients, breast-conserving surgery remains the preferred approach, given its less invasive nature, cost-effectiveness, and potential to maximize treatment outcomes and quality of life.

A significant proportion of patients undergoing NSM opt for simultaneous breast reconstruction, where the technical proficiency of the surgeon and aesthetic considerations play a key role in achieving high levels of post-operative satisfaction. However, this approach may be associated with higher medical costs and an increased risk of complications.

NSM offers the dual benefits of preserving the NAC and improving quality of life while the selection of an appropriate surgical approach for patients with nipple discharge necessitates a comprehensive assessment of pathological findings, clinical presentation, recurrence risk, potential for occult nipple involvement, and the need for long-term surveillance. Currently, the lack of large-scale, randomized controlled prospective studies—partially due to ethical considerations and patient preferences—limits further validation of these findings. Future clinical research is required to more comprehensively assess the oncological safety of NSM for patients with breast cancer and nipple discharge, thereby providing stronger evidence to guide clinical practice.

Abbreviations

BCS	(Breast-conserving surgery)
SSM	(Skin-sparing mastectomy)
NSM	(Nipple- and areola-sparing mastectomy)
ASM	(Areola-sparing mastectomy)
MRM	(Modified Radical Mastectomy, MRM)
NCCN	(National comprehensive cancer network)
NAC	(Nipple-areola complex)
TDLU	(Terminal duct lobular unit)
ER	(Estrogen receptor)
PR	(Progesterone receptor)
HER-2	(Human epidermal growth factor receptor-2)
FISH	(Fluorescence in situ hybridization)
CSCO	(Chinese society of clinical oncology)
IBR	(Immediate breast reconstruction)

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Author contributions
Conception and design of the research: Hong Hou, Xin Wang, Yue Yu Acquisition of data: Hong Hou, Jing Xia Analysis and interpretation of the data: Hong Hou, Lin Tan, Jing Xia, Xin Wang Statistical analysis: Lin Tan, Yue Yu Writing of the manuscript: Hong Hou Critical revision of the manuscript for intellectual content: Xin Wang All authors read and approved the final draft.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This study was conducted with approval from the Ethics Committee of Tianjin Medical University Cancer Institute and Hospital. This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. Hu Z, Wu L, et al. Expert consensus and controversy on preserving nipple areola complex mastectomy. China Oncology; 2015.
2. WELLINGS S R, JENSEN HM. On the origin and progression of ductal carcinoma in the human breast. J Natl Cancer Inst. 1973;50(5):1111–8.
3. WELLINGS SR. A hypothesis of the origin of human breast cancer from the terminal ductal lobular unit. Pathol Res Pract. 1980;166(4):515–35.
4. ROSEN PP. TENCH W. Lobules in the nipple. Frequency and significance for breast cancer treatment. Pathol Annu, 1985, 20 Pt 2: 317– 22.
5. REYNOLDS C, DAVIDSON J A, LINDOR N M, et al. Prophylactic and therapeutic mastectomy in BRCA mutation carriers: can the nipple be preserved? Ann Surg Oncol. 2011;18(11):3102–9.
6. STOLIER AJ. Terminal duct lobular units are scarce in the nipple: implications for prophylactic Nipple-Sparing mastectomy. Ann Surg Oncol. 2008;15(2):438–42.
7. Munhoz AM, Montag E, Filassi JR, et al. Immediate nipple-areola-sparing mastectomy reconstruction: an update on oncological and reconstruction techniques. World J Clin Oncol. 2014;5(3):478–94. https://doi.org/10.5306/wjco.v5.i3.478. PMID: 25114861; PMCID: PMC4127617.
8. CHANG R Y K, CHEUNG P S Y. Nipple preservation in breast cancer associated with nipple discharge. World J Surg. 2017;41(1):176–83.
9. Yang HP, Wang WQ, Wang S et al. Nipple involvement in early breast cancer: retrospective analysis of 1,190 consecutive mastectomy specimens. Chin J Clin Oncol 2016(2):67–71. https://doi.org/10.3969/j.issn.1000-8179.2016.02.263
10. Li W, Wang S, et al. Nipple involvement in breast cancer: retrospective analysis of 2323 consecutive mastectomy specimens. Int J Surg Pathol. 2011;19(3):328–34. https://doi.org/10.1177/1066896911399279. Epub 2011 Mar 31. PMID: 21454374.
11. Lemaine V, Hoskin TL, Farley DR, et al. Introducing the SKIN score: a validated scoring system to assess severity of mastectomy skin flap necrosis. Ann Surg Oncol. 2015;22(9):2925–32. https://doi.org/10.1245/s10434-015-4409-3. Epub 2015 Jan 30. PMID: 25634782.
12. Chung AP, Sacchini V. Nipple-sparing mastectomy: where are we now? Surg Oncol. 2008;17(4):261-6. https://doi.org/10.1016/j.suronc.2008.03.004. Epub 2008 May 5. Erratum in: Surg Oncol. 2010;19(2):114. PMID: 18456492.

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