Investigation of the current situation of nipple-sparing mastectomy: a large multicenter study in China (CSBrs-003)

Li Zhu1, Yang Yan2, Lin Tian1,3, Li Yang1,4, Bao-Shi Bao1, Hua Kang5, Jian-Dong Wang1

1Department of General Surgery, The First Medical Center of Chinese PLA General Hospital, Beijing 100853, China; 2Department of General Surgery, Hainan Hospital of Chinese PLA General Hospital, Sanya, Hainan 572013, China; 3Department of Thyroid and Breast Surgery, The First Peoples Hospital of Zunyi, Zunyi, Guizhou 563000, China; 4Department of General Surgery, Beijing Shunyi Hospital, Beijing 101300, China; 5Department of General Surgery, Xuanwu Hospital, Capital Medical University, Beijing 100053, China.

Abstract

Background: Mastectomy techniques have been extended to nipple-sparing mastectomy (NSM). This study aimed to assess the actual application of NSM in China and identify the factors influencing postoperative complications.

Methods: The clinical data of 615 patients (641 surgeries) undergoing NSM from January 1st, 2018 to December 31st, 2018 at 28 centers nationwide were retrospectively analyzed to obtain the rate of NSM and investigate factors related to NSM surgery.

Results: The proportion of NSM surgery performed in this study was 2.67% (17/641). Malignant breast tumors accounted for the majority of NSM surgery (559/641, 87.2%). A total of 475 (77.3%) patients underwent NSM combined with reconstructive surgery. The rate of reconstruction decreased with age in our study, and implants were the most common option (344/641, 53.7%) in reconstruction. Radial incision was the most selected method regardless of reconstruction. However, for those who underwent reconstruction surgery, 18.4% (85/462) of cases also chose curvilinear incision, while in the simple NSM surgery group, more patients chose circumareolar incision (26/136, 19.1%). The tumor-to-nipple distance (TND) influenced postoperative complications (P = 0.004). There were no relationships between postoperative complications and tumor size, tumor location, histologic grade, molecular subtype, nipple discharge, and axillary lymph nodes.

Conclusions: NSM surgery is feasible and only TND influenced postoperative complications of NSM surgery. But the proportion of NSM surgery performed is still low in nationwide centers of China. The selection criteria for appropriate surgical methods are important for NSM in clinical practice. To optimize clinical applications of NSM, further multicenter prospective randomized controlled studies are needed.

Trial Registration: ChiCTR.org.cn, ChiCTR1900027423; http://www.chictr.org.cn/showprojen.aspx?proj=38739

Keywords: Breast; Nipple-sparing mastectomy; Reconstruction; Tumor-to-nipple distance

Introduction

Breast tumors are common diseases that endanger women’s health. Comprehensive treatment based on mastectomy has gained broad approval for treatment of breast tumors. The nipple and areola complex (NAC), an essential part of breast tissue, plays a vital role in breast reconstruction, medical aesthetics, and maintaining patient quality of life.[1] In the 1960s, scholars proposed the concept of nipple-sparing mastectomy (NSM)[2] and gradually applied it to breast tumor surgery. However, some studies documented that the risk of tumor recurrence and metastasis increases with preservation of the NAC during surgery because it is a part of the mammary duct.[3,4] Controversy remains concerning whether to retain the NAC after surgery.[5-7] To explore the development, feasibility, and clinical significance of NSM in breast surgery in China, a retrospective observational research was carried out at 28 centers of the Chinese Society of Breast Surgery from January 1st, 2018 to December 31st, 2018. The complications and tumor safety-related factors of NSM were analyzed to provide a basis for further prospective studies.

Methods

Ethical approval

This study was approved by the Ethics Committee of the Chinese People’s Liberation Army General Hospital.

Li Zhu and Yang Yan contributed equally to this work.

Correspondence to: Prof. Jian-Dong Wang, Department of General Surgery, The First Medical Center of Chinese PLA General Hospital, Beijing 100853, China E-Mail: wangjiandong@301hospital.com.cn; Prof. Hua Kang, Department of General Surgery, Xuanwu Hospital, Capital Medical University, Beijing 100053, China E-Mail: kanghua@xwh.ccmu.edu.cn

Copyright © 2021 The Chinese Medical Association, produced by Wolters Kluwer, Inc. under the CC-BY-NC-ND license. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Chinese Medical Journal 2021;134(7)

Received: 20-09-2020 Edited by: Yan-Jie Yin and Xiu-Yuan Hao
(S2019-152-01). The Ethics Committee of the PLA General Hospital approved the immunity of informed consent because the research data would be obtained from the previous medical records but patients have the right to know this research.

**Subjects**

This study included a total of 615 patients who underwent NSM between January 1st, 2018 and December 31st, 2018, at 28 centers of the Chinese Society of Breast Surgery. A total of 641 NSM operations were performed. Clinical data were collected, including gender, age at visit, family history, tumor location, histologic diagnosis, tumor size, the tumor-node-metastasis (TNM) staging (according to American Joint Committee on Cancer (AJCC) version 8), molecular subtype, nipple discharge, tumor-to-nipple distance (TND), pathologic reports of surgical margin in deep nipple and areola, surgical type, incision type, postoperative complications, adjuvant treatment, and postoperative follow-up.

**Definition**

The TNM staging and molecular subtype of breast cancer were classified following AJCC cancer staging[8] and St. Gallen consensus,[9] respectively. Tumor diameter was calculated as maximum tumor diameter at the time of discovery. Multiple breast tumors were divided into multifocal breast cancer and multicentric breast cancer depending on the distance between tumors and whether the tumors were in the same quadrant. The TND refers to the closest distance from the edge of the tumor to the NAC. Surgical incision options include circumareolar incision, circumareolar incision + radial incision, radial incision, curvilinear incision, and inframammary incision. Surgery methods include NSM and NSM + breast reconstruction (expander/implant/autologous tissue with or without patch). Postoperative complications include all/partial nipple necrosis, flap necrosis, and poor wound healing. Follow-up was performed every three months after the surgery until May 1, 2019.

**Surgical procedure**

Surgical incisions were selected based on surgical objective or tumor characteristics such as tumor location (including puncturing needles). The distance between the incision and tumor edge should be more than 2 cm for malignant tumors. For benign tumors, prophylactic resections, or gynecomastia, decisions regarding incisions should be considered to aesthetics and surgical convenience. The operation methods of electric knife freeing skin flap were the same as those of radical mastectomy. The NAC area was separated with sharp tools as much as possible to avoid burns from the electric knife. The entire NAC was saved, and all visible breast tissue, pectoralis fascia, and subcutaneous fat were removed. Sentinel lymph node biopsy or axillary lymph node dissection were performed according to axillary lymph node status, and breast reconstruction surgery was performed if needed.

**Statistical analysis**

Data were processed using SPSS 22.0 (IBM Corporation, Somers, NY, USA). Normally distributed continuous variables were presented as mean ± standard deviation, and non-normally distributed continuous variables were presented as median (range or interquartile range). Data between groups were compared using Student’s t test or one-way analysis of variance (if ≥3 groups) for normally distributed data and Mann-Whitney U test for non-normally distributed data. Categorical data were presented as number and percentage (%) and compared by Pearson Chi-square test or Fisher exact test (if expected value was < 5). All analyses were two-tailed, and \( P < 0.05 \) was considered statistically significant.

**Results**

In this study, 615 patients were included and 641 NSM surgeries were performed. The rate of NSM operations among all breast tumor surgeries in China was 2.67%. Among all 28 branches from which data were collected, the hospital with the highest annual rate of NSM was 14.21%, and the lowest was 0.22% [Figure 1].

The median age of 615 patients was 43 years (range 22–79 years), and 74.2% of patients were 31–50 years. There were 612 females and three males (including 2 cases with male gynecomastia and one case of male breast cancer) [Table 1]. Invasive ductal carcinoma accounted for the majority of tumors (63.2%). There were also six cases of prophylactic mastectomy (two patients underwent simple bilateral prophylactic mastectomy, one patient underwent bilateral NSM due to prior breast augmentation), four cases of mucinous carcinoma, three cases of phyllodes tumors, three cases of gynecomastia (one patient with bilateral mammary gland gynecomastia and two patients with left mammary gland development only), two cases of plasma cell mastitis, two cases of sclerosing adenosis, one case of angiosarcoma, and 20 cases of unknown pathologic type [Table 2].

Eighteen patients had surgery-related complications, including four cases of partial necrosis of the areola, one case of skin flap necrosis, nine cases of poor incision healing, one case of hematoma, and three cases of effusion. Nipple discharge accounted for 3.9% of clinical manifestations. Of these, 12 cases were bloody discharge, including six cases of ductal carcinoma in situ and four cases of invasive ductal carcinoma. There were no reports of surgical-related complications and recurrence or metastasis in those patients.

With a median follow-up time of six months, seven patients experienced local recurrence or distant metastases. Of these, two patients had local recurrence of the chest wall and five patients had distant metastases, including two cases of visceral metastases. All seven patients were diagnosed with invasive ductal carcinoma without nipple discharge. The median age was 39 years (range 31–49 years), mean tumor size was 3.58 cm (range 2–8 cm), and mean TND was 2.85 cm (range 1.8–4.0 cm). All seven patients underwent standard endocrine therapy, Herceptin
targeted therapy, and neo/chemotherapy. Only 1 patient received radiotherapy to the chest wall and lymphatic drainage area, but this patient eventually developed cervical lymph node metastasis. The deep areolar resection margin was negative for carcinoma in five of the seven patients, while it was positive in two patients who both had distant metastasis (including lung, liver, and bone).

Most patients were treated with NSM + implant with or without patch (344/641, 53.7%), 143 patients were treated with single NSM, 78 patients were treated with NSM + expander ± patch, and 56 patients were treated with NSM + autologous tissue reconstruction [Table 2].

The rate of reconstruction decreased with age, which was statistically significant ($P < 0.001$). NSM combined with reconstructive surgery was the preferred strategy for most patients, regardless of having benign or malignant tumors. Radial incision was the most selected method regardless of reconstruction [Table 3].

The mean tumor diameter was 2.4 cm (range 0.2–15.0 cm). The TND of most cases who underwent NSM was greater than 2 cm. Compared with TND > 2 cm, TND ≤ 2 cm had a higher rate of surgical complications (8.8% vs. 1.8%, $P = 0.004$), but the recurrence and metastasis rates (2.5% vs. 1.2%, $P = 0.412$) were not statistically different. The recurrence rate and postoperative complication rate of patients with multicentric breast cancer was 5.6% and 5.0%, respectively, which were significantly higher ($P < 0.01, P < 0.01$) than those of patients with multifocal breast cancer (1.4%, 4.2%) and unifocal breast cancer (0.8%, 2.7%). Recurrence and metastasis in patients with positive axillary lymph nodes (2.2%) were higher ($P < 0.01$) than those in patients with negative axillary nodes (0.1%).

The incidence of postoperative complications was 3.2% in patients who had not received radiotherapy, 13.3% in patients who received nipple areola radiotherapy, and 3.1% in patients treated with chest wall radiotherapy ($P = 0.161$). Although the differences were not statistically significant, the complication rate of radiotherapy in the areolar region was much higher than that in other regions [Table 4].

The rate of negative surgical margins in the deep areola was 90.9%. Fourteen patients had atypical hyperplasia in the surgical margin by pathology report. Among these, six

Table 1: Demographic characteristics of patients undergoing nipple-sparing mastectomy ($n = 615$).

| Characteristics | Values |
|-----------------|--------|
| Age (years)     | 43.1 ± 9.4 |
| ≤40 years       | 242 (39.3) |
| >40 years       | 373 (60.7) |
| Gender          |         |
| Female          | 612 (99.5) |
| Male            | 3 (0.5)   |
| Family history  |         |
| None            | 548 (89.1) |
| Yes             | 39 (6.3)  |
| NA              | 28 (4.6)  |

Data are presented as mean ± standard deviation or n (%). NA: Not available.
patients had the NAC removed directly, three patients underwent resection to obtain a negative resection margin (1 had partial nipple necrosis), one patient underwent localized radiation therapy in the areola area without NAC resection, and four patients received neither NAC removal nor radiotherapy without reports of local recurrence and distant metastases at the end of follow-up. Cancer cells were present in the surgical margin of 19 patients by pathology reports. Among these, 11 patients had NAC resection directly, two patients had resection to obtain a negative surgical margin, one patient had no resection of NAC after local radiotherapy of the areola area, and five patients had neither NAC resection nor radiotherapy. There were no reports of local recurrence and distant metastasis in 4 patients, and one patient had distant metastasis. Pathologic biopsy (frozen + paraffin) of the deep incision of the nipple and areola was not performed in 18 patients, but no surgical-related complications occurred, and no local recurrence and distant metastasis were reported.

Discussion

With the development of breast reconstruction technology, more patients with breast cancer can preserve the integrity of their bodies after surgery. NAC removal with conventional mastectomy requires breast reconstruction surgery. However, according to the literature,[10,11] nearly 40% of patients who underwent breast reconstruction were not satisfied with the effect of nipple reconstruction. Thus, NSM brought hope to these patients. However, there is a lack of large-scale clinical trials associated with NSM in China and abroad. This single-arm, cross-sectional, retrospective study was designed to provide data regarding Chinese NSM surgery and was supported by the Chinese Society of Breast Surgery.

According to our findings, the overall rate of NSM surgery in China is low, but it is well accepted in young patients. More young patients choose NSM combined with reconstructive surgery to obtain good aesthetic results. In addition, radial incision was the first choice for both NSM and NSM combined with reconstructive surgery, and this incision did not produce more surgical complications. Surprisingly, patients with benign tumors had a lower rate of NSM combined with reconstruction than patients with malignant tumors. Among 66 non-malignant tumor cases, the average age of patients who underwent NSM combined with reconstructive surgery (40.9 years) was significantly lower than patients who underwent NSM alone (47.6 years), indicating that age is an important factor influencing the choice of surgical methods.

One of the most common complications after NSM is skin or nipple necrosis. In the current study, the necrosis rate was between 0 and 7%.[12-14] The incidence of flap necrosis and wound healing was 1.56%, and the rate of partial or full nipple necrosis was 0.62%, similar to data reported in the previous literature.

Strict selection of patients undergoing NSM surgery is the key to ensure a successful surgery. Although there is no consensus for guidelines concerning NSM surgery, the National Comprehensive Cancer Network (NCCN) and many studies recommend that at least 2 cm between tumors and NAC is visualized on imaging before surgery to reduce the possibility of tumors invading the NAC.[13,15-17]
Existing studies had a low rate of local recurrence due to careful selection of suitable patients, and tumors less than 2 cm from the NAC are considered a relative contraindication for NSM surgery. In the current study, there were more postoperative complications in patients with tumors close to the nipple. Many studies have shown that smaller TND is associated with higher probability that the NAC will be involved by tumor. The optimal threshold for TND remains controversial. With a threshold of 2 cm, this study found that larger TND was associated with lower surgical complication rate (8.8% vs. 1.8%, \( P = 0.004 \)), indicating that patients with TND greater than 2 cm had a higher success rate of NSM surgery. In terms of oncologic safety, no relationship was found between TND and tumor recurrence and metastasis. In this study, the recurrence and metastasis rates of TND > 2 cm were 2.5% and 1.2%, respectively (\( P = 0.412 \)), with no statistical differences.

Tumor size is also important to consider when performing NSM surgery. Most studies have shown that the incidence of NAC involvement was significantly associated with tumor size.\(^7,18\) Some studies suggested that NSM can be performed safely regardless of tumor size, as long as the deep nipple and areola area had negative surgical margins.\(^19\) With a threshold tumor diameter of 2 cm, tumor size did not significantly relate to the rates of postoperative complications, recurrence, and metastasis after NSM. This may be because most patients in the study had early stage breast cancer (21 cases with tumor diameter > 5 cm, including 14 cases of invasive ductal carcinoma, four cases of carcinoma in situ, and three cases of invasive lobular carcinoma).

A previous study reported that among patients with abnormal NAC manifestations on physical breast examination (such as nipple depression, nipple area lumps, nipple discharge, or nipple bleeding, etc.), 61% had NAC involvement.\(^{20}\) These findings are considered contraindications to NSM in most literature. Although no patients with nipple discharge had recurrence and metastasis in this study, the relationship between nipple discharge and NSM surgery could not be obtained due to the short follow-up time.

Pathologic biopsy of the surgical margin of the deep nipple and areola is a key step in NSM that determines further treatment of the NAC. In this study, 19 patients had positive surgical margins, and only 5 of them had neither NAC resection nor radiation therapy. One of them had distant metastases after surgery. These results suggest that as long as the surgical margin behind the nipple has no evidence of malignancy by pathologic report, patients can still receive NSM. A retrospective study conducted by Tang et al.\(^{21}\) described their experiences treating positive surgical margins in the deep nipple, including removing only the nipple and preserving the areola. During a median follow-up of 36 months, there was no NAC recurrence, which may support expanding the indications for NSM in the future.

In a previous study, there was no significant difference in incidence of NAC involvement in multifocal and unifocal breast cancer, while involvement of NAC was as high as 29.6% in multicentric breast cancer.\(^{22}\) This study also demonstrated that for multicenter breast cancer, the rates of recurrence and metastasis and the probability of surgical complications were higher than those of unifocal and multifocal breast cancer. However, in central breast cancer (seven cases) with more NAC involvement, no recurrence and metastasis were found during the follow-up.

Histologic grade, TNM stage, and molecular subtypes are also associated with the NAC involvement rate. Based on
previous reports, the NAC involvement rate of histologic Grade III was 17.2%, while that of Grade I was only 8.7%.\[^{23}\] In addition, HER-2 positive breast cancer has a higher NAC involvement rate than HER-2 negative breast cancer. However, the association between estrogen receptor and progesterone receptor expression and the NAC involvement rate remains controversial.\[^{7,13,22,24,25}\] In this study, patients were grouped based on oncologic grade. There were no differences in postoperative complications and recurrence and metastasis rates among each group, which may have resulted from a short follow-up time.

Other studies have documented that patients with positive axillary lymph nodes had an increased potential NAC involvement rate, and the correlation between number of positive axillary lymph nodes and NAC involvement has been controversial.\[^{13,25}\] The results of this study suggest that the recurrence and metastasis rates in patients with positive lymph nodes were higher than those in patients with negative axillary lymph nodes. However, due to the short follow-up of this retrospective study, correlation between the number of axillary lymph nodes and the safety of surgery was not assessed.

| Items | Without complications (n = 585) | With complications (n = 18) | \(\chi^2\) or \(Z\) | \(P\) |
|-------|-------------------------------|-----------------------------|-----------------|-----|
| Surgical types | | | | |
| NSM | 129 (22.1) | 1 (5.6) | | 0.154* |
| NSM + reconstruction | 440 (75.2) | 16 (88.9) | | |
| Others or NA | 16 (2.7) | 1 (5.6) | | |
| Options for incision | | | | 0.098* |
| Circumareolar incision | 75 (12.8) | 0 | | |
| Circumareolar incision + radial incision | 89 (15.2) | 6 (33.3) | | |
| Radial incision | 194 (33.2) | 6 (33.3) | | |
| Curvilinear incision | 94 (16.1) | 4 (22.2) | | |
| Inframammary incision | 74 (12.6) | 0 | | |
| Others or NA | 59 (10.1) | 2 (11.1) | | |
| Radiation therapy | | | | 0.161* |
| None | 398 (68.0) | 13 (72.2) | | |
| Areola radiation | 13 (2.2) | 2 (11.1) | | |
| Chest wall radiation | 95 (16.2) | 3 (16.7) | | |
| NA | 79 (13.6) | 0 | | |
| Chemotherapy | | | | 0.939* |
| None | 209 (35.7) | 7 (38.9) | | |
| Neoadjuvant chemotherapy | 89 (15.2) | 3 (16.7) | | |
| Adjuvant chemotherapy | 271 (46.3) | 8 (44.4) | | |
| Neo + Adjuvant | 4 (0.7) | 0 | | |
| NA | 12 (2.1) | 0 | | |
| Tumor size | | | | |
| \(\leq 2\) cm | 307 (52.5) | 7 (38.9) | | |
| >2 and \(\leq 5\) cm | 201 (34.4) | 10 (55.6) | | |
| >5 cm | 29 (5.0) | 1 (5.6) | | |
| NA | 48 (8.2) | 0 | | |
| Tumor-to-nipple distance | | | | 10.860* |
| \(\leq 2\) cm | 73 (12.5) | 7 (38.9) | | |
| >2 cm | 326 (55.7) | 6 (33.3) | | |
| NA | 186 (31.8) | 5 (27.8) | | |
| Tumor location | | | | 0.669* |
| Central quadrant | 21 (3.6) | 0 | | |
| Other quadrants | 564 (96.4) | 18 (100) | | |
| Lymph node status | | | | 1.000* |
| None metastases | 397 (67.9) | 13 (72.2) | | |
| Metastases | 136 (23.2) | 4 (22.2) | | |
| NA | 52 (8.9) | 1 (5.6) | | |
| Classification of breast cancer | | | | 0.476* |
| Unifocal breast cancer | 469 (80.2) | 13 (72.2) | | |
| Multifocal breast cancer | 72 (12.3) | 3 (16.7) | | |
| Multicentric breast cancer | 43 (7.4) | 2 (11.1) | | |
| NA | 1 (0.2) | 0 | | |

Data are presented as \(n\) (%). None-radiation therapy included cases with malignant tumors who did not receive radiation therapy and patients with benign breast disease; None-chemotherapy included patients with malignant tumors who did not receive chemotherapy and patients with benign breast disease; Neo + Adjuvant: Received neoadjuvant chemotherapy and adjuvant chemotherapy. NA: Not available. *Fisher exact probability. **Z values. ***\(\chi^2\) values.
Surgical incision options and surgical types should be evaluated based on the tumor situation and patient needs. This study showed that different surgical types (P = 0.154) and surgical incisions (P = 0.098) did not relate to the postoperative complication rate. Restricted by strict indications, NSM is recommended more to patients with a poor expected outcome of breast-conserving surgery (smaller breasts, negative surgical margins cannot be achieved by breast-conserving surgery).

Currently, there was no large trial data to support intraoperative or postoperative radiation therapy during NSM. In this study, fewer complications occurred in patients using combined radiation therapy. Compared with cases using combined radiation therapy and non-radiotherapy, local recurrence rates were similar after NSM. Patient selection and surgical quality control are the keys to treatment with NSM. Different patients with different recurrence risks require use of different combinations of radiation therapy.

Some studies reported that smoking increases the incidence of breast surgery complications. In a prospective study published by Matsen et al., flap necrosis occurred in 14% of patients after mastectomy, and smoking was an important factor in flap necrosis by univariate analysis. In a study published in 2014 in which 6% of patients undergoing NSM had a history of smoking, the complication rate was 3.3% compared to patients without a history of smoking. Because this study was retrospective and has limited data, the smoking history of patients was not assessed. Smoking history will be planned as an observation index in further prospective experiments to investigate the relationship between smoking history and NSM complications.

In conclusion, NSM surgery is feasible and only TND influenced postoperative complications of NSM surgery. Due to the retrospective nature of this study, some information is limited. A prospective study will be planned to assess smoking history, breast size, and other related factors in the context of NSM surgery. The long-term effects of NSM in treating breast disease also require further study.

Acknowledgements

The authors thank the Chinese Society of Breast Surgery, especially the following 28 doctors and the hospitals:

Hua Kang, Xuanwu Hospital, Capital Medical University; Xiang Qu, Beijing Friendship Hospital affiliated to Capital Medical University; Rui Ling, Xijing Hospital, Fourth Military Medical University; Hong-Chuan Jiang, Beijing Chaoyang Hospital, Capital Medical University; Jun Jiang, The First Hospital Affiliated to Army Medical University/Southwest Hospital; Zhi-Gang Yu, The Second Hospital of Shandong University; Jian-Dong Wang, The First Medical Center of Chinese PLA General Hospital; Zhen-zhen Liu, Henan Tumor Hospital; Da-Hua Mao, Affiliated Wudang Hospital of Guizhou Medical University; Zuo-Wei Zhao, The Second Affiliated Hospital of Dalian Medical University; Yi Zhao, Shengjing Hospital of China Medical University; Shu Wang, Peking University People’s Hospital; Xing-Song Tian, Shandong Provincial Hospital; Jing-Hua Zhang, Tang Shan People’s Hospital; Jian-Guo Zhang, The Second Affiliated Hospital of Harbin Medical University; Ke-Jin Wu, Obstetrics and Gynecology Hospital of Fudan University; Jian Huang, The Second Affiliated Hospital of Zhejiang University; Pei-Fen Fu, The First Affiliated Hospital of Zhejiang University; Zhong-Wei Cao, Inner Mongolia Autonomous Region People’s Hospital; Yin-Hua Liu, Peking University First Hospital; Rong Ma, Qili Hospital of Shandong University; Zhi-Min Fan, The First Hospital of Jilin University; Feng Jin, The First Hospital of China Medical University; Ai-Ling Song, Lanzhou University Second Hospital; Wei Zhu, Zhongsan Hospital, Fudan University; Yong-Hui Luo, The Second Affiliated Hospital of Nanchang University; Yun-Jiang Liu, The Fourth Hospital of Hebei Medical University; Li-Li Tang, Xiangya Hospital, Central South University.

Conflicts of interest

None.

References

1. Wellisch DK, Schain WS, Noone RB, Little JW 3rd. The psychological contribution of nipple addition in breast reconstruction. Plast Reconstr Surg 1987;80:699–704. doi: 10.1097/00006534-198711000-00007.
2. Freeman BS. Subcutaneous mastectomy for benign breast lesions with immediate or delayed prosthetic replacement. Plast Reconstr Surg 1980;65:371–372. doi: 10.1097/00006534-198003000-00019.
3. Wellings SR. A hypothesis of the origin of human breast cancer from the terminal duct lobular unit. Patol Res Pract 1980;166:515–535. doi: 10.1016/S0344-0338(80)80248-2.
4. Stoller AJ, Wang J. Terminal duct lobular units are scarce in the nipple: implications for prophylactic nipple-sparing mastectomy: terminal duct lobular units in the nipple. Ann Surg Oncol 2008;15:438–442. doi: 10.1245/s10434-007-9568-4.
5. Hartmann LC, Schaid DJ, Woods JE, Crotty TP, Myers JL, Arnold PG, et al. Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer. N Engl J Med 1999;340:77–84. doi: 10.1056/NEJM199901113400301.
6. Pennisi VR, Capozzi A. Subcutaneous mastectomy data: a final statistical analysis of 1500 patients. Aesthetic Plast Surg 1989;13:15–21. doi: 10.1007/BF01570320.
7. Chan YH, Yau WM, Cheung PS. Oncological safety and technical feasibility of nipple-sparing mastectomy for breast cancer: The Hong Kong Experience. World J Surg 2018;42:1375–1383. doi: 10.1007/s00268-017-4197-y.
8. Kall S, Semme A, Cohen S, Nabzer SP, Makim SS, Bahl M. American joint committee on cancer’s staging system for breast cancer, eighth edition: what the radiologist needs to know. Radiographics 2018;38:1921–1933. doi: 10.1148/rg.2018180036.
9. Burstein HJ, Curgilgano G, Lobl S, Dubsky P, Granet M, Poortmans P, et al. Estimating the benefits of therapy for early-stage breast cancer: the St. Gallen International Consensus Guidelines for the primary therapy of early breast cancer 2019. Ann Oncol 2019;30:1541–1557. doi: 10.1093/annonc/mdz235.
10. Jabor MA, Shavani P, Collins DR Jr, Karas T, Cohen BE. Nipple-areola reconstruction: satisfaction and clinical determinants. Plast Reconstr Surg 2002;110:437–463. discussion 464-455. doi: 10.1097/00006534-200208000-00013.
11. Akintayo RM, Weinstein AL, Olorunmopa OB, Otterburn DM. The price of aesthetics after nipple-sparing mastectomy: a cost minimization analysis of skin banking with deep inferior epigastric perforator flap. Ann Plast Surg 2020;84:300–306. doi: 10.1097/SAP.0000000000002067.
12. Endara M, Chen D, Verma K, Nahabedian MY, Spear SL. Breast reconstruction following nipple-sparing mastectomy: a systematic review of the literature with a pooled analysis. Plast Reconstr Surg 2013;132:1043–1044. doi: 10.1097/PRS.0b013e3182a48b8a.
13. Jensen JA, Orringer JS, Giuliano AE. Nipple-sparing mastectomy in 99 patients with a mean follow-up of 5 years. Ann Surg Oncol 2011;18:1665–1670. doi: 10.1245/s10434-010-1475-4.

14. Colwell AS, Tessler O, Lin AM, Liao E, Winograd J, Cetrulo CL, et al. Breast reconstruction following nipple-sparing mastectomy: predictors of complications, reconstruction outcomes, and 5-year trends. Plast Reconstr Surg 2013;133:496–506. doi: 10.1097/PRS.0b013e3182673755.

15. Vlajcic Z, Zic R, Stanec S, Lambasa S, Petrovecki M, Stanec Z. Nipple-areola complex preservation: predictive factors of neoplastic nipple-areola complex invasion. Ann Plast Surg 2005;55:240–244. doi: 10.1097/01.sap.0000171680.49971.85.

16. Pirozzi PR, Rossetti C, Carelli I, Ruiz CA, Pompei LM, Piato S. Clinical and morphological factors predictive of occult involvement of the nipple-areola complex in mastectomy specimens. Eur J Obstet Gynecol Reprod Biol 2010;148:177–181. doi: 10.1016/j.ejogrb.2009.10.021.

17. Mallon P, Feron JG, Couturaud B, Fitoussi A, Lemasurier P, Guihard C, et al. The role of nipple-sparing mastectomy in breast cancer: a comprehensive review of the literature. Plast Reconstr Surg 2013;131:969–984. doi: 10.1097/PRS.0b013e3182865a3c.

18. Paprottka FJ, Schlett CL, Luketina R, Paprottka K, Klimas D, Radtke C, et al. Risk factors for complications after skin-sparing and nipple-sparing mastectomy. Breast Care (Basel) 2019;14:289–296. doi: 10.1159/000503218.

19. Coopey SB, Tang R, Lei L, Freer PE, Kansal K, Colwell AS, et al. Increasing eligibility for nipple-sparing mastectomy. Ann Surg Oncol 2019;26:3219–3222. doi: 10.1245/s10434-019-07374-x.

20. Wu ZY, Kim HJ, Lee JW, Chung IY, Kim JS, Lee SB, et al. Breast cancer recurrence in the nipple-areola complex after nipple-sparing mastectomy with immediate breast reconstruction for invasive breast cancer. JAMA Surg 2019;154:1030–1037. doi: 10.1001/jamasurg.2019.2959.

21. Tang R, Coopey SB, Merrill AL, Rai U, Specht MC, Gaidd MA, et al. Positive nipple margins in nipple-sparing mastectomies: rates, management, and oncologic safety. J Am Coll Surg 2016;222:1149–1155. doi: 10.1016/j.amcollsurg.2016.02.016.

22. Huang NS, Wu J. Nipple-sparing mastectomy in breast cancer: from an oncologic safety perspective. Chin Med J (Engl) 2015;128:2256–2261. doi: 10.4103/0366-6999.162500.

23. Orzalesi L, Casella D, Santi C, Cicconi L, Murgo R, Rinaldi S, et al. Nipple sparing mastectomy: Surgical and oncological outcomes from a national multicentric registry with 913 patients (1006 cases) over a six year period. Breast 2016;23:75–81. doi: 10.1016/j.breast.2015.10.010.

24. Wang M, Huang J, Chaggar AB. Is nipple sparing mastectomy associated with increased complications, readmission and length of stay compared to skin sparing mastectomy? Am J Surg 2020;219:1030–1035. doi: 10.1016/j.amjsurg.2019.09.011.

25. Benediktsson KP, Perbeck L. Survival in breast cancer after nipple-sparing subcutaneous mastectomy and immediate reconstruction with implants: a prospective trial with 13 years median follow-up in 216 patients. Eur J Surg Oncol 2008;34:143–148. doi: 10.1016/j.ejso.2007.06.010.

26. Hehr T, Baumann R, Budach W, Duma MN, Dunst J, Feyer P, et al. Radiotherapy after skin-sparing mastectomy with immediate breast reconstruction in intermediate-risk breast cancer: Indication and technical considerations. Strahlenther Onkol 2019;195:949–963. doi: 10.1007/s00066-019-01507-9.

27. Pan L, Ye C, Chen L, Tang W, Zhang X, Gao J, et al. Oncologic outcomes and radiation safety of nipple-sparing mastectomy with intraoperative radiotherapy for breast cancer. Breast Cancer Res Treat 2019;26:618–627. doi: 10.1007/s12282-019-00962-7.

28. Berton D, Nguyen D, Rochlin D, Hernandez-Boussard T, Meyer S, Choy N, et al. Protecting nipple perfusion by devascularization and surgical delay in patients at risk for ischemic complications during skin-sparing mastectomies. Ann Surg Oncol 2016;23:2665–2672. doi: 10.1245/s10434-016-3201-8.

29. Chung CU, Wink JD, Nelson JA, Fischer JP, Serletti JM, Kanchwala SK. Surgical site infections after free flap breast reconstruction: an analysis of 2,899 patients from the ACS-NSQIP datasets. J Reconstr Microsurg 2013;31:434–441. doi: 10.1055/s-0035-1548739.

30. Matsen CB, Mehrara B, Eaton A, Capko D, Berg A, Stempel M, et al. Skin flap necrosis after mastectomy with reconstruction: a prospective study. Ann Surg Oncol 2016;23:257–264. doi: 10.1245/s10434-015-4709-7.

How to cite this article: Zhu L, Yan Y, Tian L, Yang L, Bao BS, Kang H, Wang JD. Investigation of the current situation of nipple-sparing mastectomy: a large multicenter study in China (CSBrs-003). Chin Med J 2021;134:806–813. doi: 10.1097/CM9.000000000001350