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Local Recurrence in the Nipple-Areola-Complex After Nipple-Sparing Mastectomy and Skin-Sparing Mastectomy With Immediate Breast Reconstruction

Wan Yu Huang*, Shin Cheh Chen, Jun Han Chen, Cheng Zhi Zhang and Zi Hao Huang

Department of Surgery, CGMH (Chang Gung Memorial Hospital), Taiwan

***Corresponding author:** Wan Yu Huang, Department of Surgery, CGMH (Chang Gung Memorial Hospital), Taiwan

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Abbreviations: NSM: Nipple-Sparing Mastectomy; SSM: Skin-Sparing Mastectomy; NAC: Nipple-Areola-Complex; DIEP: Deep Inferior Epigastric Perforator; SIEA: Superficial Inferior Epigastric Artery Flap

Abstract

Objective: The most important problem associated with Nipple-Sparing Mastectomy (NSM) and Skin-Sparing Mastectomy (SSM) for breast cancer patients is the risk of local recurrence. Local recurrence is associated with concurrent or following distant metastasis and mortality. Patients also suffer from second operation and worse quality of life if local recurrence or distant metastasis occurs. Long-term follow-up data regarding the oncologic safety of NSM and SSM with cancer recurrence at the Nipple-Areola-Complex (NAC) and survival are limited. This is a single center retrospective review and reported as an observational result.

Methods: A retrospective review of 168 female breast cancer patients who had undergone SSM or NSM with immediate breast reconstruction in Chang Gung Memorial Hospital, Linkou, from January 1, 2014 to November 2, 2018, was performed. The focus of this review is simply to determine the local recurrence rate after SSM or NSM in breast cancer patients with immediate reconstruction.

Results: Overall, 172 mastectomies (59 SSM and 113 NSM) of 168 female breast cancer patients were performed. Among these 172 mastectomies, 150 were immediate reconstruction with autologous flap or one-stage prosthesis implantation, 22 were two-stage tissue expander breast reconstructions followed by prosthesis implantation months later. Median follow-up duration was 51 months, ranged from 24 months to 78 months. Local recurrence was found in only one patient. The recurrence location was below NAC (Nipple-Areola-Complex) and it was 45 months after first surgery. There were two patients with distant metastasis during the follow-up period. However, these two patients with distant metastasis had no evidence of local recurrence.

Conclusion: SSM and NSM with immediate reconstruction are both safe surgical intervention methods compared with traditional simple mastectomy and breast-conserving surgery for breast cancer patients regarding to local recurrence rate and long-term overall survival.

Introduction

It is breast cancer that has the highest incidence among all female cancer types in Taiwan. The age at cancer diagnosis in Taiwan female breast cancer patients is much earlier than that in European and American countries. The range of age at diagnosis is between 45 and 64 years old. Young female patients care much about their appearance after therapeutic surgery. With the advancement of radiotherapy and anti-cancer drugs, the proportion of breast-conserving surgery is increasing. Breast preservation surgery accounts for two thirds of all breast cancer surgery in Taiwan. Meanwhile, the issue of oncologic safety, local recurrence, and distant metastasis in the long following life also bother these young female patients. Both SSM and NSM offer these young female patients another choice in surgical options. In 1991, SSM was first described by Toth and Lappert [1] with removing all the breast tissue and nipple-areola-complex while preserving the skin envelope [2]. The first Nipple-Sparing Mastectomy(NSM) report

was from Hinton et al. [3], who mentioned that NSM achieved the same local recurrence rates and survival rates compared to radical mastectomy [1]. Many prospective and retrospective studies [4-6] of NSM have shown the oncologic and surgical safety of NSM as well as the superior aesthetic outcomes and improved quality of life achieved when NSM is with immediate breast reconstruction. Present National Comprehensive Cancer Network guidelines state that NSM is an acceptable surgical option for carefully selected patients with breast cancer [7].

Nevertheless, the application of NSM for breast cancer remains controversial because of the limited long-term follow-up data, such as the rate of local recurrence rate and distant metastasis, and mortality rate after local recurrence or distant metastasis [8]. Because increasing numbers of patients with breast cancer are selecting NSM [9,10], it is important to identify the incidence of cancer recurrence at the NAC after NSM, describe the associated factors, and determine its association with prognosis. Previous studies [11-15] have reported cancer recurrence incidence at the NAC from 0% to 3.7% after NSM. This study is to review the local recurrence rate after Nipple-Sparing Mastectomy(NSM) and Skin-Sparing Mastectomy(SSM) with immediate breast reconstruction.

Methods

A retrospective data was collected including all patients who underwent SSM and NSM followed by immediate or immediate 2-stage tissue expander breast reconstruction in our hospital from January 1, 2014 to November 2, 2018. If breast reconstruction was applied with implant, silicone Style 410 implants by Allergan (Parsippany-Troy Hills, NJ, USA) were used for subpectoral augmentation. The first choice of autologous tissue reconstruction was Deep Inferior Epigastric Perforator (DIEP) flap. If DIEP flap was not suitable, Perfundus Artery Perforator (PAP) flap would be harvested. The third flap choice was Superficial Inferior Epigastric Artery Flap (SIEA). The age at diagnosis, type of surgery, tumor stage, node stage, histologic grade, subtype, and tumor histologic type were reviewed. Tumor and node staging were conducted according to the 8th edition of the American Joint Committee on Cancer Cancer Staging Manual [16]. These 168 patients all have regular follow-ups. The patients were regularly followed up postoperatively every 3 to 6 months for the first 5 years and 6 to 12 months 5 years after surgery if no recurrence or metastasis occurs. Local recurrence or distant metastasis was identified by clinical physical examination, breast ultrasonography, mammography, or chest radiography. Abnormal clinical findings were evaluated through further studies, including computed tomography of the chest, bone scan, and liver ultrasonography. Core needle biopsy was performed to evaluate suspicious lesion below the NAC.

Results

Overall, 172 mastectomies (59 SSM and 113 NSM) of 168 female breast cancer patients were performed. Among these 172 mastectomies, 150 were immediate reconstruction with permanent autologous tissue or one-stage prosthesis implantation, 22 were two-stage tissue expander breast reconstruction followed by prosthesis implantation months after adjuvant chemotherapy and radiation therapy. Median follow-up duration was 51 months, ranged from 24 months to 78 months. Local recurrence was found in only one patient. The recurrence location was below NAC (nipple-areola-complex) and it was 45 months after first surgery. There were two patients who developed distant metastasis during the follow up period. However, these two patients with distant metastasis had no evidence of local recurrence. The basic characteristics of these 168 breast cancer patients are shown in Table 1. The median age of patients at diagnosis was 44 years (range, 27-76 years). One hundred and thirty-six patients were less than fifty years old. Thirty-six patients were older than fifty years old. One hundred and thirty-six patients had invasive carcinoma and thirty-six patients had carcinoma in situ. Among the 136 patients with invasive disease, 101 were node negative, 2 had malignant cells in regional lymph node(s) no greater than 0.2 mm(pN0i+), 5 had micrometastases lymph nodes(N1mic), 19 had pN1a, 9 had more than pN1. As regard to histologic type, among the 136 patients with invasive disease, 121 had invasive ductal carcinoma, 6 had invasive lobular carcinoma. There were 9 patients had other invasive types including invasive tubular carcinoma and invasive mucinous carcinoma. Most of the histologic grade is intermediate grade or grade 2. In all 172 mastectomies, 48 were low grade or grade 1, 86 were intermediate grade or grade 2, 35 were high grade or grade 3, and 3 were unknown Table 2.

Table 1: Characteristics of Patients.

	Mastectomy numbers(172)	
Age	**172**	
<50	136	79.0%
>=50	36	20.9%
invasive	136	79.0%
DCIS	36	20.9%
Tumor Stage	**172**	
T0(After neoadjuvant chemotherapy)	4	2.3%
Tis	36	20.9%
T1	68	39.5%
T2	56	32.5%
T3	8	4.7%
Number of positive lymph nodes	**136**	
0	101	74.3%
N0i+	2	1.5%
N1mic	5	3.7%
1~3(pN1a)	19	13.9%

>=4(>=pN2)	9	6.6%
Histologic Type	**136**	
ductal	121	88.9%
lobular	6	4.4%
mixed	0	0%
other(invasive)	9	6.6%
Histologic Grade	**172**	
1 or low	48	27.9%
2 or INTERMEDIATE	86	50%
3 or high	35	20.3%
Unknown	3	1.7%
Subtype	**invasive 136 patients**	
HR+/HER2-	97	71.3%
HR-/HER2-	5	3.7%
HR+/HER2+	18	13.2%
HR-/HER2+	16	11.7%
Unknown	0	0%
Subtype	**carcinoma insitu 36 patients**	
HR+/HER2-	22	61.1%
HR-/HER2-	2	5.5%
HR+/HER2+	6	16.7%
HR-/HER2+	5	13.9%
Unknown	1	2.8%

Table 2: Reconstruction Type Analysis.

	Invasive	Carcinoma insitu	Total	Percentage
DIEP	54	14	68	39.53
DIEP+SEIA	0	1	1	0.58
Implant	59	16	75	43.6
PAP flap	3	2	5	2.9
SIEA	1	0	1	0.58
TE	19	3	22	12.79
	136	36	172	99.98

As for reconstruction type, most of patients chose prosthesis implantation. In 172 mastectomies with reconstructions, 75(43.6%) had prosthesis implantation, 68(39.5%) had DIEP flap reconstruction, 5(2.9%) had PAP flap reconstruction, 1(0.58%) had SIEA flap reconstruction, and 1(0.58%) had DIEP plus SIEA flap reconstruction. The only one patient who later developed local recurrence was a 38-year-old lady. In March 2014, she had a diagnosis of DCIS (ductal carcinoma in situ). Following NSM, she had immediate DIEP flap reconstruction. She had a histologic type of negative estrogen receptor, negative progesterone receptor, and positive type 2 Human Epidermal Growth Factor Receptor (HER2). She did not receive anti-HER2 therapy after first mastectomy because the histologic type was DCIS. But later in December 2017, she had a mass right below the NAC. After wide excision, it was proved that she had an invasive ductal carcinoma with pathologic T2 (tumor over than 2 centimeters) status this time. The duration from surgery to cancer recurrence at the NAC was 45 months. Sentinel lymph node excision was negative for metastasis in both frozen section and permanent pathology. This time, she had a histologic type of positive estrogen receptor, negative progesterone receptor, and still positive type 2 human epidermal growth factor receptor (HER2). Therefore, adjuvant therapy for this patient included anti-hormone therapy with Tamoxifen (10mg BID), chemotherapy with twelve times of weekly Paclitaxel, and eighteen times of anti-HER2 target therapy with Trastuzumab. Because she had ductal carcinoma in situ in 2014 when the first time she was diagnosed with breast DCIS, strictly speaking, she had a new cancer instead of recurrence in 2017. There were two distant metastasis patients but there was no evidence of local recurrence.

Discussion

There is much more acceptance of skin-sparing mastectomy or nipple-sparing mastectomy with immediate breast reconstruction for the surgical treatment of breast cancer. Because skin-sparing mastectomy or nipple-sparing mastectomy with immediate breast reconstruction achieve almost excellent aesthetic outcomes and improved much in quality of life without compromising oncologic safety. However, SSM was first introduced in 1991[1], limited long-term follow-up data are rarely available regarding the oncologic safety. The data of NSM is even less. Patients who have undergone either mastectomy or breast-conserving surgery and Radiation Therapy (RT) are at risk for locoregional recurrence. For women treated for early breast cancer, the recurrence rate ranges from 4 to 7 percent after mastectomy or breast-conserving therapy, respectively [17]. If locoregional recurrence occurs within two years after primary treatment, distant metastatic disease is already present in 25 to 30 percent of cases [18]. Available studies [11-15,19-22] have shown low rates of cancer recurrence at the NAC (0%-3.7%) after NSM. The recurrence rate (4%-7%) after NSM was even lower than that after traditional mastectomy or breast-conserving surgery [17]. Most of these findings were obtained in a heterogeneous population of patients, including those with invasive and noninvasive disease, and reported variable follow-up durations. In a series by Jensen et al. [21], no cancer recurrence at the NAC was reported among 149 patients who underwent NSM during a mean follow-up of 60.2 months; however, 57% of these cases had only noninvasive disease. In a study by Wang et al. [22], no case of cancer recurrence at the NAC was found among 981 patients who underwent NSM; however, the follow-up evaluation was only 29 months, and 52% of the surgeries were performed for in situ disease [20]. During a median follow-up duration of 78

months, Sakurai et al. [13] reported a cancer recurrence rate at the NAC of 3.7% among 788 patients who underwent NSM without radiotherapy between 1985 and 2004. In one study [8], it included patients with invasive breast cancer who underwent NSM and immediate breast reconstruction between 2003 and 2015 and identified a 5-year local recurrence at the NAC of 3.5%.

The indication for adjuvant radiation therapy after breast cancer treatment surgeries in our hospital include breast-conserving surgery, primary tumor larger than 5 centimeters, final pathology showing lymphovascular invasion, and more than two metastatic ipsilateral axillary lymph nodes found. So most of our study populations did not undergo adjuvant radiation therapy after SSM or NSM. It was because the whole breast tissue was removed. Only two studies investigated variables through a multivariate analysis. One of these two studies was published by Petit et al. [22]. There were 934 NSMs performed for invasive and intraepithelial breast cancer with a follow-up duration of 50 months. Eleven cases of local cancer recurrence at the NAC were found. The tumor size, receptor status, ERBB2 status, histologic grade, and Ki-67 proliferation index were associated with the risk of recurrence in a multivariate analysis. Regarding the surgical technique for NSM, Petit et al. [22] mentioned that they leaved a 5-mm-thick layer of glandular tissue below the NAC to avoid malperfusion and for the intraoperative delivery of electron-beam radiotherapy exclusively to the NAC to minimize the risk of local recurrence.

In the other study by Zhen-Yu Wu, et al. [8], in multivariate analysis, multifocality or multicentricity, negative hormonal receptor status, ERBB2-positive status, high histologic grade, and presence of extensive intraductal component were associated with an increased risk of cancer recurrence at the NAC after NSM. This study showed that multifocality or multicentricity and presence of extensive intraductal component has the strongest associations with cancer recurrence at the NAC. The association between tumor-nipple distance and cancer recurrence at the NAC did not show significance. Our data reveal our experience with the treatment and outcomes of cancer recurrence at the NAC after NSM and SSM. The only one patient with cancer recurrence at the NAC underwent wide local excision, and then received multimodal adjuvant treatment according to the biologic disease features, including hormonal therapy, chemotherapy, and target therapy. This patient has no more evidence of local cancer recurrence or distant metastasis after multimodal adjuvant treatment after cancer treatment surgery in 2017.

Conclusion

Nipple-sparing mastectomy and skin-sparing mastectomy are both safe surgical treatment options for breast cancer patients compared with traditional mastectomy and breast-conserving surgery. There is lower local recurrence rate and comparable distant metastatic rate. Nipple-Sparing Mastectomy and skin-sparing mastectomy definitely reveal much better aesthetic outcomes and quality of life in breast cancer patients.

Limitations

The limitation of our data is that it is retrospective review. Our patient numbers are small and populations are heterogeneous.

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Wan Yu Huang. Biomed J Sci & Tech Res

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