Original Study

Nipple Discharge After Nipple-Sparing Mastectomy With and Without Associated Pregnancy

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Abstract

Despite extensive subareolar tissue resection, 22% of women who became pregnant after nipple-sparing mastectomy (NSM) experienced postpartum multiduct nipple discharge. Spontaneous and watery discharge occurred in 0.25% of nonpregnant NSM patients. Discharge resolved without intervention in all patients. No infections or local-regional recurrences occurred in patients with discharge.

Background: Nipple-sparing mastectomies (NSMs) preserve the intact nipple, including nipple duct orifices. Retained orifices might remain patent and communicate with the underlying reconstruction. We report the incidence and outcomes of nipple discharge after NSM in pregnant and nonpregnant women. **Patients and Methods:** Retrospective review of all NSMs at our institution from June 2007 to June 2018 was performed. Subsequent pregnancies and nipple discharge were documented. Patient demographic, operative, histopathology, and cancer treatment data were collected. Descriptive analysis was performed for patients who developed nipple discharge. **Results:** From June 2007 to June 2018, 2778 NSM procedures were performed in 1620 patients, with a mean age of 48 (range, 20-80) years. Fifteen hundred sixty-eight NSMs were therapeutic and 1210 were for risk reduction. Thirty-three subsequent pregnancies were observed in 27 patients, with a mean age of 33 (range, 26-42) years at NSM. Bilateral or unilateral discharge occurred in 6 of 27 (22%) postpartum patients and resolved spontaneously. At 54 months mean follow-up after NSM (range, 16-98 months) and 23 (range, 1-61) months after delivery, no local-regional recurrences were observed. In 1593 patients without subsequent pregnancy, there were 4 patients (0.25%) treated with bilateral NSM with subsequent unilateral watery nipple discharge. There was no evidence of associated malignancy on physical exam, imaging, or cytology, and with 55 to 110 months follow-up, no new or recurrent cancers have been observed. **Conclusion:** Despite extensive removal of nipple and subareolar duct tissue during NSM, milky nipple discharge is possible postpartum. Watery, acellular discharge occurs rarely in nonpregnant patients. To date, no patient with discharge has developed a local recurrence or new breast cancer.

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Introduction

Breast cancer is the most commonly diagnosed malignancy in women of reproductive age.[1] An increasing number of women postpone pregnancy until their 30s or 40s, and some might not have finished childbearing at the time of their breast cancer diagnosis. Ruddy et al[2] reported that 37% of women diagnosed with breast cancer at age 40 years or younger wanted to have 1 or more children in the future.

Many young women with breast cancer choose mastectomy, even if they are eligible for breast-conserving surgery, possibly because of fear of recurrence, and often opt for bilateral mastectomies.[3,4] Some require mastectomy for tumors that are large relative to breast size. Other young women undergo risk-reducing mastectomy for risk gene mutations or a strong family history of breast cancer.[5]

An increasing proportion of women who require mastectomy are eligible for nipple-sparing.[6] There is increasing evidence of the

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oncologic safety of nipple-sparing mastectomy (NSM) for therapeutic and prophylactic mastectomies,[7-13] and NSMs are increasingly performed because of their cosmetic advantage. Previous or postoperative radiation, obesity, and previous breast surgery are no longer absolute contraindications to NSM.[14,15] Recent studies of NSM have shown that there is no significant association between nipple areola complex (NAC) involvement and tumor size, tumor distance from the nipple, multicentricity/multifocality, or patient age.[6,16-18]

There are few data on nipple changes during and after pregnancy in women who have undergone NSM. Although there are several discussion boards and blogs where women who become pregnant or experience nipple discharge after NSM look for advice from others, we identified only a case report of a single patient with discharge after NSM in the medical literature.[19] To our knowledge, our study is the first to examine nipple discharge after NSM in pregnant and nonpregnant women using a large, single-institution NSM cohort.

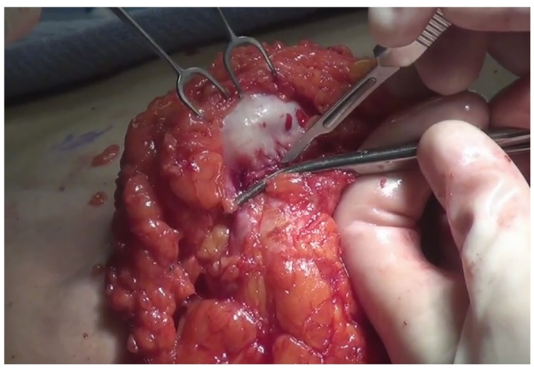
Patients and Methods

An institutional review board-approved retrospective analysis was performed of all patients who underwent NSM and immediate reconstruction at Massachusetts General Hospital from June 2007 to June 2018. Patients who became pregnant after NSM and reconstruction were identified, including patients pregnant at the time of NSM. Any self-reported nipple discharge in pregnant and nonpregnant patients was documented.

Eligibility criteria for NSM at our institution are quite inclusive and have been previously described.[6,14,15] We only exclude women with clinical or imaging evidence of NAC involvement, locally advanced breast cancer with skin involvement, inflammatory breast cancer, or bloody nipple discharge. Patients with marked ptosis are excluded for cosmetic reasons. We do not exclude patients on the basis of tumor-to-nipple distance or tumor size.

Mastectomy flaps are raised in the Cooper ligament plane, which leaves flaps with less than 1 cm of subcutaneous fat in most patients. There are no Cooper ligaments under the areola and nipple, so no subcutaneous fat is left under the areola (Figure 1). Our approach for obtaining nipple margin specimens for pathologic evaluation has been reported and involves taking a nipple/subareolar margin specimen that contains superficial retroareolar tissue as well as the ductal tissue from within the nipple papilla.[20-23] This specimen is sent separately for permanent pathology. After taking this margin, only the dermis and epidermis of the nipple and areola remain.

Figure 1 No Subcutaneous Fat Is Left Under the Areola, and Ductal Tissue Within the Nipple Papilla Is Removed



Retrospective chart review was performed and demographic, operative, histopathology, treatment, and recurrence-related information was collected. A descriptive summary and analysis were performed of reported episodes of nipple discharge, and breast and nipple changes during pregnancy and the postpartum period.

Results

From June 2007 to June 2018, there were 2778 NSM procedures performed in 1620 patients. Mean age at the time of surgery was 48 (range, 20-80) years. Among these, 570 (35%) patients were younger than the age of 45 years. Indications for mastectomy were malignancy in 1568 NSM and risk reduction in 1210 for risk reduction. Immediate reconstruction techniques included 1859 (67%) breasts reconstructed with a single-stage implant, 852 (30%) with a 2-stage tissue expander to implant reconstruction, 55 (2%) with an autologous flap reconstruction, and 12 (1%) breasts had no reconstruction surgery performed.

Thirty-three subsequent pregnancies were observed in 27 patients with a mean age of 33 (range, 26-42) years at time of NSM and mean age of 36 (range, 27-47) years at delivery (Table 1). Eleven of 27 patients (41%) had a documented *BRCA1,* a breast cancer risk gene, mutation, 1 had a *BRCA2* mutation, 1 had a variant of uncertain significance in *BRCA2*, and 1 had a *TP53* mutation. Twenty-three patients had bilateral NSM, and 4 had unilateral NSM, for a total of 50 NSM procedures. Sixteen NSMs were therapeutic (8 for invasive ductal cancer [IDC], 1 for invasive lobular carcinoma, and 7 for ductal carcinoma in situ [DCIS]), and the remaining 34 were prophylactic. One of 18 (5.6%) prophylactic NSMs in a *BRCA1* mutation carrier revealed unexpected IDC in the NSM specimen. One patient who underwent therapeutic NSM had a positive nipple/areola margin and the NAC on this side was removed before pregnancy. Twelve patients (44%) had tissue expanders placed at the time of NSM, whereas the other 15 patients (56%) had immediate implant placement at the time of NSM. All 27 patients received subpectoral implants. Twenty-three patients (85.2%) had acellular dermal matrix used as sling material, 2 patients (7.4%) had absorbable mesh slings, and 2 patients (7.4%) had no sling material used in reconstruction. Seven patients received postoperative chemotherapy; all 8 patients with IDC and 1 patient with DCIS received endocrine therapy. No patient in this cohort received neoadjuvant chemotherapy or postmastectomy radiation.

Twenty-one patients each had 1 uneventful pregnancy and delivery, 4 patients had 2 normal deliveries, and 2 patients had 1 normal pregnancy followed by a miscarriage, totaling 33 pregnancies and 31 deliveries. The mean time from NSM to delivery was 31 (range, 6-75) months. Five of 27 (18.5%) patients who had a term pregnancy experienced multiduct milky nipple discharge soon after delivery, and 1 patient (3.7%) experienced bilateral multiduct watery discharge soon after delivery (Table 1). Among these, patient 3 had no spontaneous discharge but could express discharge with nipple pressure for 30 months after delivery. Patient 5 had milky

Table 1 Characteristics of Patients Who Became Pregnant After NSM

Patient ID	Age at Delivery, Years	Risk Gene Mutation	Laterality	NSM Indication		Sling Material Used	Time of Delivery, Months After NSM	Nipple Discharge	Length of Follow-Up, Months After NSM
				L	R				
1	31	*BRCA 1*	BL	RR	RR	None	43	No	77
2	35	*BRCA2* VUS	BL	RR	IDC	None	54	No	98
3	39	*BRCA 1*	BL	RR	RR	Acellular dermal matrix	50	Yes, BL milky	80
4	34	*BRCA1*	BL	RR	RR	Acellular dermal matrix	23	No	83
5	34	*BRCA 1*	BL	RR	RR	Acellular dermal matrix	25	Yes, BL milky	84
6	35	None	BL	IDC	RR	Absorbable mesh	39	No	63
7	27	*BRCA 2*	BL	RR	RR	Acellular dermal matrix	17	No	54
8	29	*BRCA 1*	BL	RR	RR	Acellular dermal matrix	12	No	73
9	33	*BRCA 1*	BL	RR	RR	Acellular dermal matrix	22	No	70
10	42	None	Left	DCIS	—	Absorbable mesh	13	No	17
11	34	*BRCA 1*	BL	RR	RR	Acellular dermal matrix	29	Yes, R milky	56
12	36	*BRCA 1*	BL	IDC	RR	Acellular dermal matrix	65	No	77
13	37	None	BL	IDC	RR	Acellular dermal matrix	72	Yes, BL clear	78
14	37	None	BL	RR	RR	Acellular dermal matrix	40	No	41
15	40	None	BL	RR	DCIS	Acellular dermal matrix	32	No	48
16	38	None	BL	RR	ILC, DCIS	Acellular dermal matrix	18	No	35
17	34	*BRCA 1*	BL	RR	DCIS	Acellular dermal matrix	11	No	19
18	36	None	BL	RR	DCIS	Acellular dermal matrix	16	No	43
19	34	None	R	—	IDC, DCIS	Acellular dermal matrix	30	Yes, milky	35
20	40	None	R	—	DCIS	Acellular dermal matrix	6	No	44
21	35	*BRCA 1*	BL	RR	DCIS	Acellular dermal matrix	13	No	18
22	43	None	BL	RR	RR	Acellular dermal matrix	17	No	33
23	37	None	BL	RR	RR	Acellular dermal matrix	14	No	46
24	42	None	BL	IDC	RR	Acellular dermal matrix	34	No	50
25	39	*TP53*	BL	IDC	RR	Acellular dermal matrix	50	No	53
26	31	None	L	DCIS	—	Acellular dermal matrix	21	Yes, milky	24
27	47	*BRCA 1*	BL	RR	IDC, DCIS	Acellular dermal matrix	75	No	77

Abbreviations: BL = bilateral; DCIS = ductal carcinoma in situ; IDC = invasive ductal carcinoma; ILC = invasive lobular carcinoma; L = left; NSM = nipple-sparing mastectomy; R = right; RR = risk-reducing; VUS = variant of uncertain significance.

Table 2 Characteristics of Nonpregnant Patients Who Developed Nipple Discharge After NSM

Patient ID	Age at NSM, Years	Risk Gene Mutation	Laterality	NSM Indication		Sling Material Used	Nipple Discharge Side	Start of Discharge, Months After NSM	Frequency of Nipple Discharge	Follow-Up, Months After NSM
				L	R					
28	50	*BRCA 2*	BL	IDC, DCIS	RR	Acellular dermal matrix	R, watery	70	Persistent	110
29	60	*BRCA 2*	BL	RR	DCIS	Absorbable mesh	L, watery	21	Episodic	67
30	52	No	BL	RR	DCIS	Acellular dermal matrix	L, watery	23	Persistent	102
31	54	No	BL	IDC	IDC	Absorbable mesh	R, watery	12	Episodic	55

Abbreviations: BL = bilateral; DCIS = ductal carcinoma in situ; IDC = invasive ductal carcinoma; L = left; NSM = nipple-sparing mastectomy; R = right; RR = risk-reducing.

green discharge and a palpable nodule in the right breast upper inner quadrant. Ultrasound showed a 5-mm collection of simple cysts at the site of the palpable finding. The palpable finding and discharge resolved 3 months after delivery without intervention. Patient 11 had bilateral NSM but had milky discharge after delivery only on the right and only with nipple manipulation. Patient 13 had clear, nonmilky discharge from both nipples after delivery which lessened, then completely resolved 5 months postdelivery. Patient 19 had copious milky discharge from her unilateral NSM while breastfeeding from her native contralateral breast. The discharge stopped when she discontinued breastfeeding from the opposite breast. Patient 26 had scant milky discharge from her unilateral NSM while breastfeeding from her native contralateral breast. She was still breastfeeding at the time of this review. There was a single patient who reported breast engorgement during pregnancy but had no nipple discharge after delivery. There was no nipple discharge or breast engorgement noted in the 2 patients who had miscarriages after term pregnancies. One patient reported scant nipple discharge during fertility treatments, which stopped when treatment ended without a successful pregnancy.

Among the 1593 NSM patients who did not become pregnant after NSM, there were 4 patients (0.25%) who reported nipple discharge (Table 2). None had nipple discharge before NSM. Three patients had therapeutic NSM for their index breast cancer (1 with IDC and 2 with DCIS) and a prophylactic contralateral NSM; all 3 had discharge only on the prophylactic side. The fourth had bilateral NSM for bilateral cancers with mixed ductal and lobular features and had unilateral discharge. All 4 patients had immediate subpectoral implants placed at the time of mastectomy. Two patients had acellular dermal matrix slings, and 2 had absorbable mesh slings. Two of 4 patients received systemic therapy and none received postmastectomy radiation.

In all nonpregnant patients, discharge was spontaneous and watery. Patient 28 had right nipple discharge after increased physical activity beginning 70 months after surgery. There were no nipple skin changes or palpable findings on physical examination. Breast magnetic resonance imaging showed no evidence of malignancy. Cytology showed foamy histiocytes and proteinaceous debris, no epithelial cells, and no evidence of malignancy. Her discharge persisted at the time of last follow-up (110 months) and fluctuates with physical activity. Partial resection of the nipple's discharging orifices did not stop the discharge, and she has declined complete nipple resection. Patient 29 had 2 isolated episodes of discharge from her left nipple, which began 21 months after surgery, once after a prolonged time in a hot tub and the other during hot weather. Her clinical exam was negative for malignancy. Cytology showed amorphous debris with scattered mixed inflammatory cells and no epithelial cells. Patient 30 developed left nipple discharge 23 months after NSM. Her right nipple had been removed because of a positive nipple/areola margin, and she elected left nipple excision for the discharge. Histopathology of the excised nipple was negative for malignancy. Patient 31 reported scant, clear nipple discharge from the right breast while sleeping 1 year after NSM and 2 months after bilateral implant exchange for right capsular contracture. Nipple discharge stopped without intervention and had not recurred at 55-month follow-up.

Among the 27 patients who became pregnant after NSM, there were no local-regional recurrences observed at mean follow-up of 54 months after surgery (range, 16-98 months) and mean follow-up of 23 months after delivery (range, 1-60 months). For the 4 nonpregnant patients with nipple discharge after NSM there have been no new or recurrent cancers at 55, 67, 102, and 110 months' follow-up after surgery. No patient has had an infection associated with nipple discharge.

Discussion

Nipple-sparing mastectomies are increasingly common procedures for treatment and prevention of breast cancer. Preservation of the NAC and complete breast skin envelope improves cosmetic outcomes and might increase rates of single stage implant reconstruction without oncologic compromise.[6]

Early nipple-sparing approaches intentionally spared a small amount of glandular tissue behind the areola to protect the nipple's blood supply.[7] In contrast, our technique includes extensive retroareolar tissue and nipple duct tissue removal,[24] leaving only full-thickness nipple and areola skin with 1- to 2-mm duct stumps on the underside of the nipple papilla. This approach results in low rates of nipple necrosis,[6,25] and no nipple recurrences to date in our cohort. We believe few if any lobules remain near the areola with our technique. Our approach develops thin skin flaps in the Cooper ligament plane, with an effort to remove all visible breast tissue. Despite this, we observed nipple discharge in approximately 20% of postpartum patients and in rare nonpregnant patients.

We believe that the mechanism of discharge is different in nonpregnant and postpartum patients. Discharge among nonpregnant patients is rare, seen only in 0.25% of our NSM patients who did not become pregnant. This discharge is watery, acellular, and intermittent. We believe this discharge results from persistently patent nipple duct orifices that allow drainage of fluid present around the implant reconstruction. With extended follow-up, there has been no evidence of tumor or infection associated with this discharge.

In contrast, nipple discharge among postpartum patients is milky, and occurs immediately after delivery when lactation is expected. It resolves spontaneously, usually within weeks or a few months after delivery, but can persist if lactation continues from an intact contralateral breast. This suggests that small amounts of breast tissue with functioning lobules remain on the underside of the mastectomy flaps and produce milk that can track along subcutaneous planes to patent nipple ducts. The volume of milky nipple discharge produced by the postpartum patients in our cohort was small; in some cases a few cubic centimeters per day and in others amounts small enough to be apparent only with nipple manipulation. In comparison, the average volume of milk produced by an intact breast 1 to 6 months postpartum is estimated to be approximately 450 g per day (16 oz per day) for each breast.[26]

It is recognized that some breast tissue remains on skin flaps and at the periphery of the mastectomy cavity after most, if not all, mastectomies, because of the absence of distinct borders between breast tissue, and subcutaneous and peripheral tissues. Torresan et al[27] raised skin-sparing flaps in 42 patients but then performed conventional mastectomies. When the excess skin flaps were examined, residual breast tissue, including terminal ductal lobular units, was identified in 60% of flaps. Studies of prophylactic mastectomies also confirm retention of breast tissue after mastectomy, with breast cancer risk reduced by only 90% to 95% rather than the expected 100% if complete removal of breast tissue was possible.[28-31]

Rates of local recurrence after NSMs are similar to rates after skin-sparing mastectomies.[32] This suggests that similar amounts of breast tissue remain after skin-sparing and nipple-sparing surgeries. It is likely that postpartum milk production occurs under the skin flaps of skin-sparing mastectomies but is not detected because no nipple orifices or skin openings remain.

We performed extensive evaluation of our early patients who presented with discharge in an effort to understand the cause and implications of discharge. No epithelial cells were detected in discharging fluid. A single patient had a 5-mm collection of simple cysts on ultrasound at the site of a palpable finding, but no other patient had abnormal findings on imaging studies. No patient has developed a new or recurrent breast cancer after developing discharge. We no longer perform routine imaging of patients with postpartum milky discharge that is self-limited. We continue to recommend annual physical exams of all NSM patients, with imaging performed only for focal areas of concern on physical exam.

Nipple discharge in the absence of pregnancy must be distinguished from nipple erosion or other signs of tumor recurrence in the nipple. Lohsiriwat et al[33] reported tumor recurrence presenting as Paget disease in 0.8% of their NSM patients where surgery techniques included routine retention of a thin layer of breast tissue under the nipple. None of our patients with discharge had any changes in nipple or areola skin, and no tumor was seen in the 1 patient who had resection of a discharging nipple. We recommend skin biopsy for any visible erosion or masses in nipple or areola skin, but do not recommend biopsy for postpartum milky discharge or for watery discharge from a normal-appearing nipple.

Conclusion

Postpartum milky nipple discharge is observed in approximately 20% of women who become pregnant after NSM. This discharge is self-limited, and in the absence of a palpable finding, does not require biopsy or imaging. Milky nipple discharge does not appear to be associated with a significantly increased risk of new or recurrent breast cancer but does confirm that residual breast tissue remains. Watery nipple discharge in nonpregnant women who have had a NSM is likely benign drainage of fluid from around the reconstruction, but careful physical exam and biopsy of eroded skin or palpable findings is warranted.

Clinical Practice Points

- Postpartum milky nipple discharge is observed in approximately 20% of women who become pregnant after NSM.
- Milky postpartum discharge after NSM is self-limited, and in the absence of a palpable finding, does not require biopsy or imaging.
- Watery nipple discharge after NSM in nonpregnant women is rare and requires careful physical exam and biopsy of eroded skin or palpable findings.
- Skin biopsy is not recommended for postpartum milky discharge or for watery discharge from a normal-appearing nipple.
- Results to date suggest that nipple discharge after NSM reflects patent nipple orifices and underlying fluid but is not associated with a significantly increased risk of new or recurrent breast cancer.

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Disclosure

The authors have stated that they have no conflicts of interest.

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