Original Article

DOI: 10.4274/ejbh.galenos.2021.2021-6-4

Can skin sparing mastectomy and immediate submuscular implant-based reconstruction be a better choice in treatment of early-stage breast cancer?

Munire Kayahan. Skin Sparing Mastectomy in Early-Stage Breast Cancer

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Received: 29.06.2021
Accepted: 05.10.2021

ABSTRACT

Objective: To discuss if skin sparing mastectomy (SSM) with immediate submuscular implant-based reconstruction (IBR) can be the preferred treatment in early-stage breast cancer.

Materials and Methods: Patients treated for clinical in situ or early-stage invasive breast cancer with SSM and immediate submuscular IBR between October 2016 and October 2018 were retrospectively evaluated.

Results: 18 patients had two-stage and 3 had one-stage IBR. Median follow-up period of 21 patients was 42mo (rage, 32mo- 61mo). 5 had axillary dissection and 1-2 metastatic nodes were found in 3 (60%). 8 patients (38.09%) with two-stage IBR had radiotherapy because of upstaging. 3 (37.5%) had radiotherapy-linked complications. Rate of complications and mean number of events recorded per patient were higher with radiotherapy. 4 patients (44%) had unwanted events after secondary surgeries. Mean number of surgeries was higher after two-stage IBR. Mean duration increased in those with chemo-radiotherapy. 6 patients with two-stage and 2 with one-stage IBR discontinued secondary surgeries.

Conclusion: It cannot be preferred in all patients with early-breast cancer. It is a long way to have good-appearing symmetrical breasts after primary operation because of additional corrective/matching surgeries. Radiotherapy can still be required because of upstaging. Expectation and tolerability of the patient to the process should be evaluated as well as tumor biology and the status of the axilla.

Key Words: breast cancer surgery, immediate breast reconstruction, implant-based reconstruction, direct-to-implant reconstruction, two-stage implant-based reconstructions, breast-conserving therapy

Key Points:

1.In early-stage invasive breast cancer, mastectomy protects the patient from radiotherapy and its unwanted effects, if upstaging after surgery is not detected.

2.SSM with immediate submuscular IBR is oncologically safe, but minor and major complications requiring medical and surgical therapies may result. Two-stage IBR is safer but requires at least 2 operations and several hospital visits for expander inflations.

3.To have good-appearing, soft and symmetrical breasts, several ipsilateral and contralateral secondary surgeries are required, which may also cause unwanted events.

4.The long duration to reach a satisfying result, extra payments for surgeries and devices, extra operations and multiple hospital visits together with the stress of main disease can disturb. Expectations and tolerability of the patient to the process should be evaluated.

INTRODUCTION

In early-stage breast cancer, breast-conserving therapy (BCT), which includes breast-conserving surgery (BCS) and adjuvant radiotherapy, has been preferred to mastectomy as local recurrence rate and overall survival are equivalent. Most patients are pleased to have retained their own breasts but the esthetic outcome is not always satisfying, even after oncoplastic surgery. Fear of recurrence disturbs the psychology and exposure of normal tissues to radiation sometimes results in morbidities.

Mastectomy decision has increased in patients with in situ and early-stage breast cancer due to increased use of magnetic resonance imaging (MRI) and genetic testing. Skin sparing mastectomy (SSM) with immediate submuscular implant-based reconstruction (IBR) is an oncologically safe alternative (1).

In this study, among our patients indicated to have mastectomy because of disease- or patient-characteristics for clinical in situ and early-stage breast cancer, the outcome of those who were treated with SSM and immediate submuscular IBR were retrospectively evaluated. The target was to see if SSM with immediate submuscular IBR could be superior to BCT in treatment of early stage breast cancer by providing psychosocial and esthetic benefits and by protecting the patient from having radiotherapy for a small mass.

MATERIALS AND METHODS

21 patients operated for clinical in situ and early-stage invasive breast cancer by the author between October 2016 and October 2018 met the inclusion criteria:

1. Clinical in situ or early-stage invasive breast cancer with preoperative stages of 0 (TisN0), I (T1N0) and IIA (T0N1, T1N1, T2N0)
2. Treatment with SSM, sentinel lymph node biopsy with or without completion axillary lymph node dissection (ALND) and immediate submuscular IBR through one-stage or two-stage technique.
3. No systemic metastasis, no neoadjuvant therapy.

All patients were re-examined in the breast clinic in May, 2021.

The clinical staging was made through physical examination, mammography and ultrasonography. Preoperative MRI for contralateral breast and positron emission tomography scan were performed in all. Tissue diagnoses were performed through core biopsy, fine needle aspiration biopsy or excisional biopsy in cases with a mass and through stereotactic excision in cases with microcalcifications or occult masses.

The choice of mastectomy instead of BCT had been made together with the patient because of the lesion characteristics, presence of family or personal history, patient's fear for recurrences or in order to escape from radiotherapy. None of the patients had preoperative genetic test. SSM was performed with removal of the nipple-areolar complex (NAC). Removal of the NAC was decided by the patient to eliminate the risk of recurrence and the need for adjuvant radiotherapy. Nipple-sparing mastectomy (NSM) was performed in prophylactic removal of the contralateral breast unexpected to have malignancy or to receive radiotherapy.

Mastectomy was conducted with the pectoral fascia through the subcutaneous adipose tissue. In NSM, the NAC was spared with a thickness of about 2cm. Sentinel node biopsy was performed through subareolar injection of methylene blue dye. The sentinel nodes were removed through an axillary incision and examined by both intraoperative imprint and postoperative immunohistochemistry. Levels 1-2 completion ALND was added in all cases with any macrometastasis in sentinel nodes and a suction drain was positioned in the axilla. Thoracodorsal vessels were tried to be spared.

IBR and all the esthetic surgeries were performed by the reconstructive surgeon. Two-stage reconstruction was preferred when the surface area was insufficient or when postoperative radiotherapy was expected. A subpectoral pocket was prepared in the avascular plane between the pectoralis major and minor muscles. The lower pole was covered by the elevated serratus anterior muscle or its lower slips. In patients with ptotic breasts, skin reduction was added and inferior dermal-adipose flap was also prepared by deepithelization of the inferior skin. Non-autologous materials for coverage of the prosthesis were not used in the diseased side, which might cause complications delaying adjuvant therapies. The costs of the initial reconstruction and the prosthetic devices were paid for by the Social Insurance Institution (SGK).

Two suction drains were placed, one in the surgical pocket and the other above the muscle, which were removed when the drainage decreased to less than 30ml/24hr. In-patient follow-up for 3-5 days was in the plastic surgery department. Antibiotic prophylaxis was started half an hour before the induction of anesthesia and was continued up to the removal of the drains. Supportive brassieres were worn in the operation room and continued through the postoperative 2mo.The tissue expander (TE) was filled with saline once a week after the first fill in the operation room. Inflations were carried on during chemotherapy. Exchange to a permanent implant (PI) was performed at the time the adequate size was reached by multiple inflations. It was postponed to completion of chemotherapy and, when radiotherapy was planned, 4-6 months after completion of radiotherapy.

The necessity and timing of the other esthetic procedures were decided on a patient-basis by the reconstructive surgeon. Autologous fat grafting was performed under general anesthesia (UGA) to the subcutaneous plane to correct the contour and deformities. NAC reconstruction included C-V flap for the nipple and tattooing to the nipple/areola. Contralateral matching surgeries were performed to correct asymmetry. In contralateral NSM, the PI was placed into the subcutaneous area and covered with biological matrix which was derived from acellular bovine pericardium.

Adjuvant therapies were determined by our oncology council. Postmastectomy radiotherapy (PMRT) was applied as intensity-modulated radiotherapy (IMRT) after completion of chemotherapy. Hormone therapy was given when estrogen and/or progesterone receptors were positive. Patients were followed by oncologist every 3mo, by

the surgeon every 6mo and, when on hormone therapy, by the gynecologist every 6mo. The reconstructive surgeon determined the intervals of her follow-ups.
This study was approved by the institutional Ethical Committee for Clinical Researches (HNEAH-KAEK 2020/168).

RESULTS

21 cases were included. The median age and the median follow-up period were 48yr (range, 37yr- 67yr) and 42mo (rage, 32mo- 61mo), respectively. 6 patients (28.57%) had history for breast cancer. One had personal history for contralateral breast cancer. Contralateral mastectomy was added in 2, one for contralateral widespread microcalcifications and the other for contralateral fibroadenomatosis with ipsilaretal invasive lobular carcinoma (table 1).
Completion ALND was performed in 5 cases. Total numbers of metastatic lymph nodes found were 5/13, 3/15, 2/17, 1/11 and 1/16 (table 2). Upstaging after surgery was observed in 8 cases (38.09%), 4 in nodal stage, 1 in tumor stage and 3 in both (table 3).
All had SSM for the tumor side with submuscular IBR (18 two-stage, 3 one-stage). 2 contralateral mastectomies were SSM in case 1 and NSM in case 7 with submuscular two-stage IBR.
13 patients with TE had adjuvant chemotherapy (61.90%) and 8 of them had also adjuvant radiotherapy (38.09%). Hormone therapy was given to 19 patients (90.47%). 1 patient was hormone-negative and 1 had received anti-estrogen therapy before. All 21 patients are alive and disease free. Adjuvant chemotherapies were not delayed beyond 1.5 months after the tumor operation (table 4).
Mean implant size was 346.66 ml (between 300ml and 390ml) in one-stage and 519.70 ml (between 375ml and 700ml) in two-stage cases. Mean intraoperative fill volume was 141.76 ml (between 20ml and 350ml) and mean number of fills to complete expansion was 7.85 (between 3 and 14). Replacement of the TE with a PI was performed successfully in 14 out of 18 cases. Case 4 is scheduled to have a third PI after removal of the last two. 2 had removal of the TE because of rupture and 1 refused the exchange of the inflated TE to a PI.
Complications after primary and secondary surgeries are presented in table 5.
7 events were detected in 3 (37.5%) out of 8 patients who had adjuvant radiotherapy over the subpectoral TE. Case 2 had placement of a new TE and scoring of the capsule. Case 13 had capsulotomy. In case 4, exposure of the PI was detected four months after placement and fat grafting. The latissimus dorsi muscle was atrophic and a new PI was placed, which was removed 1mo later due to wound dehiscence, infection and abscess.
In 6 (33.3%) of the 18 patients with two-stage reconstruction, complications unrelated to radiation were observed. Dermatitis intermingled to cellulitis was treated with long-term medical therapies. Skin flap ischemia was treated by excision. Ruptured TE was exchanged with a PI in one and removed in 2. Capsulotomy was performed for capsular contracture.
Among 3 patients with one-stage reconstruction, 2 (66.6%) had skin flap ischemia and one (33.3%) progressed to wound dehiscence. None of the patients had grade IV capsular contracture. Mild to moderate contractures were managed during operations performed for other reasons.
Ipsilateral fat grafting was performed in 12 patients, more than once in 3. Dermatitis detected after nipple reconstruction in case 5 lasted 1mo and skin biopsy revealed no malignancy.

Matching surgeries were required in 19 cases with unilateral operation. Contralateral NSM and subcutaneous one-stage IBR with acellular matrix was performed 10 months after mastopexy in case 2 to eliminate the deformities produced by macrocysts, and in case 16, to relieve the patient's anxiety for contralateral recurrences. Postoperative infection was managed by medical therapy and debridement for three times in one. But in the other, removal of the PI was required followed by placement of a TE. Capsulorrhaphy was performed for exposition of contralateral implant placed in augmentation mammoplasty.
6 (33.3%) out of 18 patients who had two-stage reconstruction gave up having the complementary and/or corrective surgeries. Among 3 patients who refused the second stage, 1 remained with the expanded TE, and the other 2, with no prosthesis. 2 (66.6%) of the 3 patients with one-stage reconstruction refused all secondary surgeries (table 6).
In patients who completed all the surgeries, the mean number of operations UGA and the mean duration were as follows: 1 patient with one-stage IBR had 4 operations UGA within 19 mos. The mean number of operations UGA in 9 patients with two-stage procedure was 3.5 (range, 2-8). The mean duration in those were 17.5mo (11- 24) in 2 patients who did not receive chemo-radiotherapy, 18mo (12- 23) in 4 patients who had chemotherapy and 29.3mo (24-39) in 3 patients who had chemo-radiotherapy. The mean number of operations performed UGA in 3 patients who have not yet completed because of complications is 4.6 (between 3 and 7).

DISCUSSION AND CONCLUSION

SSM with immediate IBR has local recurrence rate ranging between 0% and 8.3%. Recurrences are in the subcutaneous tissue of the tumor location in 82%. Survival and local recurrence rates are not worse after NSM, although some glandular tissue is left behind the NAC to prevent ischemia (2). Inferolateral pole of the subpectoral implant can be covered with biological matrices or synthetic meshes (3). In our cases, we removed the NAC, performed early excision for the ischemic areas and used autologous tissues instead of external materials for coverage of the prosthesis. Consequently, adjuvant therapies started in time, despite various complications observed, and none had local or systemic recurrences at a mean follow-up period of 43.38 months.
In early-stage invasive and in situ tumors, 65% of immediate reconstructions in mastectomies are IBRs (4). Two-stage reconstruction is preferred when postoperative radiotherapy is probable. One-stage reconstruction is performed in thin women with small-to-medium, nonptotic breasts when radiotherapy is not expected (5). We performed two-stage IBR in 18 patients who might upstage and one-stage procedure in 3 patients unexpected to have radiotherapy. The mean size of the prosthesis in two-stage procedure was larger.
In patients with lumpectomy who will receive whole breast irradiation, completion ALND is indicated only when 3 or more sentinel nodes are metastatic or when there are matted nodes intraoperatively (6). The ongoing SENOMAC trial has been randomizing mastectomy patients to either ALND or no ALND (7). The current approach in patients with mastectomy is completion ALND in presence of any macrometastasis. Our 5 patients had completion ALND, and in 3 (60%) of them, 1 or 2 metastatic nodes were found. If those patients had undergone BCS, they could have escaped from ALND and, if tumor biology was favorable, from axillary irradiation, as well. Postponing the analysis of the sentinel nodes to postoperative period and giving axillary irradiation instead of ALND is another option in patients with mastectomy.

Mastectomy protects the patient from receiving radiotherapy for a small mass with good prognostic features. Radiotherapy makes the resected breast smaller, darker and tough. Exposure of nearby organs can cause rare aggressive tumors, such as angiosarcoma and myeloid neoplasms, pneumonitis and pulmonary fibrosis, cardiac failure, brachial plexopathy and lymphedema (8, 9). Normal tissues can be protected to some extent by intraoperative localization of the tumor bed, giving IMRT and using additional techniques during the procedure (10). In older patients, bypassing radiotherapy or giving partial-breast irradiation is questioned (11).

We saved 13 (61.90%) patients from having radiotherapy and its adverse effects by performing SSM. 8 (38.09%) patients upstaged and received radiotherapy. PMRT protects from recurrences but nearby organs expose to significant amount of radiation (12). A carefully performed axillary ultrasound and a core biopsy giving detailed information of the tumor can prevent upstaging. We had preoparetive ultrasound and positron emission tomography. An additional ultrasound by the surgeon as another pair of eyes can be safe, and now, the author confirms the preoperative staging by performing an additional ultrasound herself.

In patients with reconstruction, complications and implant failure are detected more frequently with radiotherapy. The rate of implant failure is higher when the TE placement is after radiotherapy (13). Getting radiotherapy over the submuscular TE and then replacing it to a PI with or without latissimus dorsi flap will be safe. PMRT was given to our 8 patients who had submuscular TE. 3 (37.5%) of them had unwanted events requiring surgical corrections. Four of the 7 events were detected in one patient and resulted in implant failure. Latissimus dorsi muscle was atrophic. In our patients with two-stage IBR, both the rate of complications requiring surgical corrections and the mean number of events recorded per patient were higher in 8 patients with radiotherapy than in 10 patients without radiotherapy (37.5% vs. 27.7% and 2.3vs. 1.5, respectively).

Even if no radiotherapy was administered, SSM with submuscular IBR may result in unwanted events, such as hematoma, seroma, skin flap necrosis, infection ranging from cellulitis to sepsis, wound dehiscence and exposure. Explantation results from infection in 21% (14). Rupture and deflation of the prosthesis, exposition with asymmetry, capsular contracture, impaired contour, chronic pain and discomfort are the long-term events (15). Besides radiotherapy, obesity, diabetes, smoking, and steroid administration increase complications (3). In patients without radiotherapy, risk for any complication is 52.4% in the first year and 76.4% within 8 years. Reoperation rate increases from 23.3% within the first year to 40.6% within 8 years. Skin-flap necrosis, reoperation and extrusion of the implant were more common after one-stage reconstruction (14, 16). In our cases who did not have radiotherapy, events requiring surgical corrections in 5 two-stage IBR patients were skin flap ischemia, rupture of the TE and capsular contracture, and in 2 one-stage IBR patients were skin flap ischemia and wound dehiscence. We had also skin flap ischemia more commonly in one-stage IBR (66.6% vs. 11.1%, respectively).

Leaving no breast tissue under the thin skin envelope, removing the pectoral fascia, using a complete muscular coverage without acellular matrices in addition to patient-linked factors might be the reasons for complications. The necessity to remove the pectoral fascia in tumors distant from the fascia can be discussed. Case 1 who developed prolonged infection had diabetes.

Secondary surgeries are required after SSM and immediate submuscular IBR for good-appearing, soft and symmetrical breasts, such as autologous fat grafting, NAC reconstruction, and matching surgeries for the ptotic, larger or smaller contralateral breast (17). We performed ipsilateral fat grafting in 12 patients, NAC reconstruction in 10 and contralateral matching surgeries in 11.

Secondary surgeries may also result in unwanted events. Our 4 patients (44%) had events after contralateral matching surgeries, 2 after reduction and augmentation mammoplasties and 2 after NSM. Acellular matrix derived from bovine pericardium was used for coverage of the subcutaneous PI in those with NSM and both had NAC ischemia and infection, resulting in implant failure in 1. Subcutaneous PI is usually covered with acellular dermal matrix (ADM) which relieves the pressure on the skin flaps and provides more natural pseudo-ptosis and inferior pole projection compared to submuscular pocket (18). It decreases the rate of capsular contracture but causes increased seroma formation, implant failure, partial NAC necrosis and rippling (19).

Unwanted events increase both the number of surgeries UGA and the duration to reach a satisfying result. In patients who completed all the surgeries, the mean number of surgeries UGA was slightly lower in 9 patients with two-stage reconstruction compared to 1 patient with one-stage procedure (3.5 vs. 4.0, respectively). The mean duration for completion of the surgeries was more in two-stage patients who had chemo-radiotherapy compared to those who did not (29.3mo vs. 17.5mo for two-stage and 19mo for one-stage, respectively). In 3 patients with two-stage procedure who have not yet completed because of complications, the mean number of surgeries UGA is already 3.83at a mean time period of 43.33 mos.

Submuscular two-stage reconstruction is safer in cancer patients, but it requires at least 2 operations with several outpatient visits for expander inflation. ADM-coverage of the lower pole provides more rapid filling, and prevents displacement. ADM use increases mean intraoperative fill volume from 130.4ml to 412.5ml and decreases the number of fills from 4.3 to 1.7 (20). We did not use ADM in the diseased side and the mean intraoperative fill volume was 141.7ml and the mean number of fills was 7.85. Rupture of the TE was observed in 16.6%.

SSM and immediate submuscular IBR protect the patient from having radiotherapy for a small mass and relieve the anxiety for recurrences. However, it may result in unnecessary ALND, PMRT because of upstaging, extra hospital visits, and extra surgeries UGA both for complications and to have normal appearance. Too many hospital visits, the discomfort formed by the implants as well as the costs of secondary surgeries and materials result in exhaustion of the patient, which in turn causes discontinuation of secondary surgeries or ignorance of the follow-ups for the main disease. Our 6 (33.3%) out of 18 patients with two-stage procedure discontinued in some step and 2 (66.6%) of the 3 patients with direct-to-implant IBR refused all additional surgeries.

Our number of patients is low, but it can be concluded that SSM and immediate submuscular IBR cannot be preferred in all patients with early-breast cancer. It is important to choose the right patient for the procedure not only with ultrasound and core biopsy but also by evaluating the expectations and tolerability of the patient to the process. Cancer patients are different from patients of reconstructive surgery. It may be better to provide good appearance and early return to normal life than trying to reach the perfect

reconstruction with multiple surgeries, except for those young and tolerant patients with high cosmetic expectations.

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Table 1. Patient characteristics and co-morbidities with breast signs.

Case Number	Age of diagnosis (yr)	Pre-menopausal	Cancer History	Co-morbidities	Breast Sign
1	62	No	Family	DM	Mass
					Calcifications
2	47	Yes	-	-	Mass
3	65	No	-	-	Mass
4	37	Yes	-	Smoking	Mass
5	46	Yes	-	-	Mass
6	48	Yes	-	-	Calcifications
7	43	Yes	-	-	Mass
					Mass
8	56	No	Personal	-	Calcifications
9	51	Yes	Family	-	Mass
10	43	Yes	-	DM	Mass
11	41	Yes	-	HT	Mass
12	46	Yes	-	Smoking	Mass
13	48	Yes	-	-	Mass

14	67	No	Family	DM, HT, HF	Mass
15	54	No	-	-	Mass
16	48	Yes	-	-	Mass
17	52	No	-	HT	Calcifications
18	45	Yes	-	-	Mass
19	45	No	Family	-	Mass
20	45	Yes	Family	DM	Mass
21	48	Yes	-	-	Mass

DM: diabetes mellitus, HT: hypertension, HF: heart failure.

Table 2. Clinical and pathological stages with tumor characteristics.

Case Number	Clinical Stage	Pathological Stage	Histological Type	Tumor Subtype	Ki67 value (%)
1	IL:T1 N0 M0	IL:T1c N0 Mx	IDC	Luminal A	28.8
	CL:Tis N0 M0	CL:Tis N0 Mx	DCIS	ER/PR+	DCIS
2	T2 N0 M0	T3mf N0i+ Mx	IDC	Luminal A	14.2
3	T2 N0 M0	T2mf N1mi Mx	ILC	Luminal A	40
4	T2 N0 M0	T2 N1a Mx	IDC	Luminal A	20-25
5	T1 N0 M0	T2 N1a Mx	IDC	Luminal A	30-40
6	T1 N0 M0	T1a N0 Mx	ILC+ DCIS	Luminal A	<5
7	IL:T1 N0 M0	IL:T1b N0 Mx	ILC+ LCIS	Luminal A	2-3
	CL:Benign	CL:Benign	Benign	Benign	Benign
8	Tis N0 M0	Tis N0 Mx	DCIS	ER/PR+	DCIS
9	T2 N0 M0	T3 N2a Mx	Mixed	Luminal A	25-30
10	Tis N0 M0	Tis N0 Mx	DCIS	ER/PR+	DCIS
11	T1 N0 M0	T1c N0 Mx	IDC+DCIS	Luminal A	20-25

12	Tis N0 M0	Tis N0 Mx	DCIS	ER/PR-	DCIS
13	T1 N0 M0	T1c N1a Mx	IDC	Luminal A	10
14	T1 N0 M0	T1c N0 Mx	IDC	Luminal A	7-8
15	T2 N0 M0	T2mf N1mi Mx	IDC	Luminal A	30-40
16	T1 N0 M0	T2mf N1a Mx	IDC	Luminal A	10
17	T1 N0 M0	T1a N0 Mx	IDC+DCIS	Luminal A	Unknown
18	T2 N0 M0	T2 N0 Mx	IDC+DCIS	Luminal A	9.4
19	T1 N0 M0	T1c N0i+ Mx	ILC	Luminal A	10-15
20	T1 N0 M0	T1b N0 Mx	IDC	Luminal A	7-8
21	T1 N0 M0	T1b N0 Mx	IDC	Luminal A	10

IL:ipsilateral breast, CL:contralateral breast, IDC:invasive ductal carcinoma, ILC:invasive lobular carcinoma, Mixed: mixed invasive ductal and invasive lobular carcinoma, DCIS: ductal carcinoma in situ, LCIS:lobular carcinima in situ, ER: estrogen receptor, PR: progesterone receptor.

Table 3. Number of patients according to the preoperative clinical and postoperative pathological stages.

Stages	Stage 0 (n)	Stage I (n)	Stage IIA (n)	Stage IIB (n)	Stage IIIA (n)
Clinical	3	12	6	-	-
Pathological	3	9	2	6	1

Table 4: Type of primary cancer surgery, prosthesis used, adjuvant therapies and follow-up period.

Case No.	Primary Surgery	Adjuvant CT	Adjuvant RT	Adjuvant HT	Follow-up (mo)
1	SSM+ SLNB+TE SSM+ SLNB+TE	No	No	+	61
2	SSM+ SLNB+TE	ST	+	+	48
3	SSM+ SLNB+TE	ST	+	+	47
4	SSM+ ALND+TE	ST	+	+	46
5	SSM+ ALND+TE	ST	+	+	57
6	SSM+ SLNB+PI	No	No	+	33
7	SSM+ SLNB+TE NSM+SLNB+ TE	A	No	+	56
8	SSM+ SLNB+TE	No	No	No	57
9	SSM+ ALND+TE	ST	+	+	44
10	SSM+ SLNB+TE	No	No	+	43

11	SSM+ SLNB+TE	A	No	+	42
12	SSM+ SLNB+TE	No	No	No	42
13	SSM+ ALND+TE	ST	+	+	42
14	SSM+ SLNB+TE	No	No	+	42
15	SSM+ SLNB+TE	ST	+	+	42
16	SSM+ ALND+TE	ST	+	+	38
17	SSM+ SLNB+PI	No	No	+	36
18	SSM+ SLNB+TE	ST	No	+	34
19	SSM+ SLNB+TE	A	No	+	35
20	SSM+ SLNB+PI	No	No	+	34
21	SSM+ SLNB+TE	A	No	+	32

SSM: skin sparing mastectomy, NSM: nipple sparing mastectomy, SLNB: sentinel lymph node biopsy,
ALND: axillary dissection, TE: tissue expander, PI: permanent breast implant, CT: chemotherapy,
RT: radiation therapy, HT: hormone therapy, ST: sequential use of anthracycline and taxane containing regimens, A: antracycline regimen.

Table 5. Unwanted events after primary and secondary surgeries in patients with one-stage reconstruction and in those with two-stage reconstruction with and without radiotherapy, and completion of surgeries.

Status		Case No.	IL events after primary surgery	CL events after matching surgeries	Completion of the surgeries

no CT/RT	One-stage	6	Skin flap necrosis/ dehiscence	-	Discontinued
		17	-	Hematoma	Completed
		20	Skin flap necrosis	-	Discontinued
	Two-stage	1	Cellulitis/dermatitis	-	Completed
		8	Skin flap necrosis/TE rupture	-	Discontinued
		10	TE rupture/ TE removal	-	Discontinued
		12	-	Exposition of PI	Completed
		14	-	-	Discontinued
CT	Two-stage	7	Capsular contracture (BII/III)	-	Completed
		11	-	-	Completed
		18	-	-	Discontinued
		19	-	-	Completed
		21	-	-	Completed
CT+RT	Two-stage	2	TE exposition/capsular contracture (BII/III)	NAC ischemia, infection, Dehiscence	Not yet
		3	-	-	Discontinued
		4	PI exposure/infection/ Dehiscence/ PI removal	-	Not yet
		5	Dermatitis	-	Completed
		9	-	-	Completed
		13	Capsular contracture (BII/III)	-	Completed
		15	TE rupture/ TE removal (beforeRT)	-	Discontinued
		16	Skin flap necrosis (before RT)	NAC ischemia/PI exposure, infection, PI removal	Not yet

CT: chemotherapy, RT: radiotherapy, TE: tissue expander, PI: permanent implant, CL: contralateral breast, NAC: Nipple-areolar complex, Capsular contracture (BII/III): mild to moderate contracture (Baker classification, grade II-III).

Table 6. Performance of primary and secondary surgeries.

Type of surgeries		Two-stage IBR without RT	Two-stage IBR with RT	One-stage IBR
Primary surgery	Number of patients	10	8	3
	Exchange of TE to PI	8	7	-
Secondary surgeries performed	IL fat grafting	6	6	
	IL IMF	2		1
	IL NAC	6	3	1
	CL mastopexy	2	1	
	CL augmentation	1	2	
	CL reduction	2	2	1
	CL NSM with subcutaneous PI		2	
	CL IMF	2		
Other surgeries	Rhinoplasty	1	1	
Surgeries not accepted	Exchange of TE to PI	2	1	-
	NAC	1		
	NAC and CL corrective surgeries	1		
	NAC, IL and CL corrective surgeries			2

IBR: implant-based reconstruction, RT:radiotherapy, TE:tissue expander, PI:permanent implant, IL: ipsilateral, CL:contralateral, NAC:nipple-areolar complex reconstruction, IMF:Inframammary fold repositioning, NSM:nipple-sparing mastectomy, ADM:acellular dermal matrix.