Oncologic Safety of Immediate Breast Reconstruction

A Single-Center Retrospective Review of 138 Patients

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Objective: The purpose of this study was to assess the oncologic safety of mastectomies associated with immediate breast reconstruction (IBR) in terms of recurrence and survival.

Methods: A retrospective review was conducted at a single center (CHU UCL Namur, Belgium). We analyzed the oncologic safety of IBR for patients with invasive and in situ breast cancer who underwent mastectomy associated with IBR. Patients who underwent palliative surgery and those with a diagnosis of breast sarcoma were excluded.

Results: We retrospectively analyzed 138 patients who underwent mastectomy and IBR between January 2012 and December 2019. Most reconstruction procedures used deep inferior epigastric perforator free flaps (55.1%). The reconstructive failure rate was 8.7%. Among the patients included, 5 cases of local cancer recurrence, 1 case of local cancer recurrence associated with distant metastasis, and 2 cases of systemic recurrence were identified during a mean follow-up of 49.3 months (range, 8–104 months) after surgery. Overall survival was 97.8%, and disease-free survival was 94.2%.

Conclusions: Patients had a low incidence of cancer recurrence in this review. Immediate breast reconstruction after mastectomy had no negative impact on recurrence or patient survival, even in patients with advanced disease. The study findings suggest that mastectomy associated with IBR can be a safe surgical option for patients with invasive and noninvasive breast cancers. Longer follow-ups are needed to confirm these preliminary results.

Key Words: breast cancer, immediate breast reconstruction, autologous reconstruction, implant-based reconstruction, recurrence rates, overall survival, disease-free survival

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Breast-conserving surgery and mastectomy are the criterion standard surgical procedures for breast cancer. To obtain better cosmetic results, skin-preserving surgical techniques, such as skin-sparing mastectomy (SSM) that consists in preservation of the breast skin envelope and nipple-sparing mastectomy (NSM) that consists in preservation of the breast skin envelope and the nipple-areola complex (NAC), are preferred when immediate breast reconstruction (IBR) is performed.[1]

Indications for SSM are extensive ductal carcinoma in situ (DCIS), stages I to II infiltrating carcinomas, multifocal and multicentric tumor not involving the skin, unicentric tumor unsuited to quadrantectomy for anatomic reasons, small-sized breast, margins involvement or local recurrence (LR) after previous breast-conserving treatment, patient's refusal conservative surgery, patient's refusal or impossibility to radiotherapy, and patients at high genetic risk of breast cancer who request mastectomy.[2,3]

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The indications for NSM are the same as for SSM, except that the tumor-nipple distance should be more than 2 cm, without nipple retraction or discharge and without radiological alterations close to the nipple. A large ptotic breast is, however, unsuitable for NSM, because of a risk of mastectomy flap and NAC necrosis.[2–5] An analysis of the National Cancer Database showed increasing rates of NSM from 1.7% of reconstructed mastectomy cases in 2005 to 14.3% in 2015.[6]

Immediate breast reconstruction has become a common and widely used procedure and results in superior aesthetic outcomes. It improved psychosocial, sexual function and quality of life of the patients.[7–11] Nevertheless, we have limited available data concerning safety of immediate reconstruction compared with delayed reconstruction. Because of the increasing numbers of patients with breast cancer benefiting from IBR, it is important to identify the incidence of cancer recurrence and the prognosis for these patients.

MATERIAL AND METHODS

Population Characteristics

All patients who underwent mastectomy and IBR between January 2012 and December 2019 at the CHU UCL Namur (Namur, Belgium) were retrospectively reviewed. All surgical procedures were performed in patients 18 years or older, for primary or recurrent invasive or in situ breast cancer. Patients who underwent palliative surgery and those with a diagnosis of breast sarcoma were excluded from the study, as patients were undergoing bilateral prophylactic mastectomy with no cancer diagnosis.

Data on clinicopathologic characteristics, treatment, and follow-up evaluation were obtained from the CHU UCL Namur database. The age at mastectomy, genetic testing if performed, tumor characteristics (histological type, estrogen receptor status, progesterone receptor status, human epidermal growth factor receptor 2 [HER2], Ki-67 proliferation index), pathologic T and N stage, type of mastectomy, treatment characteristics (chemotherapy, radiation therapy, hormonal therapy, or anti-HER2), type of surgical reconstruction, and among other variables were carefully reviewed. Tumor and node staging were obtained according to the seventh edition of the American Joint Committee on Cancer's "*Cancer Staging Manual*."[12]

Mastectomies (total, skin-sparing, or nipple-sparing) and immediate reconstruction were performed by 1 of 3 senior breast surgeons (P. F., A.B., M.S.). Sentinel lymph node biopsy (SLNB) and/or axillary lymph node dissection were performed if recommended. Reconstructive procedures were performed through autologous (deep inferior epigastric perforator [DIEP] flap, profunda artery perforator [PAP] flap, transverse upper gracilis [TUG] flap, latissimus dorsi flap) or prosthetic methods. Patients were offered all reconstructive options as appropriate. Neoadjuvant and/or adjuvant therapy was administrated after multidisciplinary discussion.

We reviewed also the surgical complications, including wound dehiscence, skin desquamation (defined as partial thickness skin loss not requiring surgical debridement), skin necrosis (defined as full-thickness skin loss requiring surgical debridement), infection, seroma, hematoma, implant or tissue expander exposure, and autologous flap necrosis.

Follow-up

The patients were regularly followed postoperatively by the plastic surgeon and the oncologist. Recurrence was identified based on the results of clinical examination, radiology (mammography, computed tomography scanner, or positron emission tomography scan), and tumor marker (cancer antigen 15-3) measurements. The primary end point of this study was LR as the first event, defined as ipsilateral cancerous recurrence in the anterior chest wall (NAC, skin, subcutaneous tissue, or muscle), or systemic recurrence. The time to recurrence was measured from the date of surgery to the date of first LR or metastasis. The secondary end points were overall survival, which was determined from the date of surgery to the date of death or last outpatient clinic visit, and disease-free survival.

RESULTS

Patient, Tumor, and Treatment Characteristics

From January 2012 to December 2019, a total of 138 patients with invasive or in situ breast cancer underwent mastectomy associated with IBR at the CHU UCL Namur, Belgium. The median age of patients at mastectomy was 54 years (range, 29–75 years). The mean follow-up duration after surgery was 49.3 months (range, 8–104 months).

The clinicopathologic characteristics of the patients and their treatments are shown in Table 1. The most common histological type was invasive ductal carcinoma (55.1%), followed by DCIS (34.8%). Most invasive tumors (75%) were ER and PR positive. Nodal disease was present in 13.7% of the patients. The most common pathologic stage was stage 1, followed by stage 0, with subsequent stages decreasing in incidence. There was no stage IV disease. Locally advanced disease (stage IIB or higher) was present in 12 patients (8.7%). Genetic testing was performed in 46 patients (33.3%); 16 were positive for a deleterious BRCA1 mutation, 5 were positive for the BRCA2 mutation, and 3 were positive for the CHEK2 mutation.

Thirty-four patients (24.6%) had a history of prior radiation therapy after previous breast-conserving surgery. Neoadjuvant chemotherapy was provided in 29 patients (21%). Four patients (2.9%) underwent conventional total mastectomy, 83 (60.1%) underwent SSM, and 51 (36.9%) underwent NSM (Table 2). Sentinel lymph node biopsy was the only axillary procedure performed in 77 cases (55.8%), and axillary lymph node dissection was performed in 37 cases (26.8%). Twenty-two patients (15.9%) received postmastectomy radiation therapy (PMRT) because of positive lymph nodes (9.4%), tumor size of greater than 5 cm on histological examination (5.1%), resection margins closer than 1 mm (5.1%), and/or high histological grade (2.2%). Three patients (2.2%) had both a previous radiation and PMRT. Adjuvant chemotherapy was given to 16 patients (11.6%). Seventy patients (50.7%) had hormonal therapy, whereas 13 (9.4%) had anti-HER2–targeted therapy.

Most reconstruction procedures used DIEP free flaps (55.1%). The others included implant or tissue expander reconstructions (26.1%), latissimus dorsi flaps (10.1%), PAP flaps (7.9%), and TUG flaps (0.7%;Table 2).

Complications

Mastectomy flap desquamation (n = 25) was the most common complication, treated with local wound care only. Others complications included seroma (n = 11), wound dehiscence (n = 8), and cellulitis (n = 3). Thirty-two patients (23.2%) had a complication that required a reoperation, including hematoma drainage (n = 14), implant removal (n = 7), skin or NAC debridement (n = 6), and second flap procedure (n = 5). Of the 53 patients who received radiation, 24 had at least 1 complication (45.3%). The reconstructive failure rate (including implant removal for complication or flap necrosis) was 8.7% (Table 2).

TABLE 1. Clinicopathologic and Treatment Characteristics

Characteristic	n (%)
Age, y	
<35	2 (1.4)
35–49	45 (32.6)
50–64	66 (47.8)
>64	25 (18.1)
pT	
pTis	49 (35.5)
pT1	66 (47.8)
pT2	17 (12.3)
pT3	4 (2.9)
pT4	2 (1.4)
Lymph node status	
N0	119 (86.2)
N1	13 (9.4)
N2	4 (2.9)
N3	2 (1.4)
Breast cancer stage	
0	50 (36.2)
I	55 (39.8)
IIA	21 (15.2)
IIB	4 (2.9)
III	8 (5.8)
IV	0 (0)
Histological type	
Invasive ductal carcinoma	76 (55.1)
Invasive lobular carcinoma	12 (8.7)
DCIS	48 (34.8)
LCIS	2 (1.4)
Receptor status	
ER positive	70 (50.7)
PR positive	57 (41.3)
HER2/neu (c-erbB-2) positive	13 (9.4)
Ki-67 ≥ 10%	63 (45.6)
Genetic testing	46 (33.3)
BRCA1	16 (34.8)
BRCA2	5 (10.9)
CHEK2	3 (6.5)
Axillary procedure	
SLNB	77 (55.8)
Axillary lymph node dissection	37 (26.8)
Prior radiation therapy	34 (24.6)
PMRT	22 (15.9)
Neoadjuvant chemotherapy	29 (21)
Adjuvant chemotherapy	16 (11.6)
Hormonal therapy	70 (50.7)
Anti-HER2–targeted therapy	13 (9.4)

LCIS, lobular carcinoma in situ.

Recurrence Outcomes and Survival

The mean follow-up duration was 49.3 months (range, 8–104 months). Five patients had LR only, 1 patient had LR associated with distant metastasis, and 2 patients had isolated distant metastasis (IDM) as the first event (Table 3). The average time from surgery to cancer recurrence was 34.6 months (range, 10–55 months). These

TABLE 2. Type of Mastectomy, Reconstruction, and Complications

Outcomes	n (%)
Mastectomy	
Conventional total mastectomy	4 (2.9)
SSM	83 (60.1)
NSM	51 (36.9)
Reconstruction	
DIEP flap	76 (55.1)
Implant or tissue expander	36 (26.1)
Latissimus dorsi flap	14 (10.1)
PAP flap	11 (7.9)
TUG flap	1 (0.7)
Complications	
Wound dehiscence	8 (5.8)
Mastectomy flap desquamation	25 (18.1)
Skin necrosis	6 (4.3)
Cellulitis	3 (2.2)
Seroma	11 (7.9)
Hematoma	14 (10.1)
Reconstruction failure	12 (8.7)
Implant/expander extrusion	7 (5.1)
Autologous flap necrosis	5 (3.6)
Venous insufficiency	4 (2.9)
Late flap failure	1 (0.7)
Reoperation for complication	32 (23.2)
Complications in patient with radiation	24 (45.3)
Complications in patient without radiation	31 (36.5)

TABLE 3. Recurrence Outcomes and Survival

Outcomes	n/N	%
LR	5/138	3.6
IDM	2/138	1.4
Concurrent local and systemic recurrence	1/138	0.7
Recurrence in patients aged ≤45 y	5/29	17.2
Recurrence in patients aged>45 y	3/109	2.7
Recurrence at ≤36 mo of follow-up	4/8	50
Recurrence at >36 mo of follow-up	4/8	50
Recurrent tumor histological features		
Invasive ductal carcinoma	5/76	6.6
Invasive lobular carcinoma	0/12	0
DCIS	3/48	6.2
LCIS	0/2	0
Recurrence by type of mastectomy		
Conventional total mastectomy	1/4 (IDM)	25 (IDM)
SSM	5/83*	6*
NSM	2/51(LR)	3.9 (LR)
All mastectomies	8/138	5.8
Overall survival	135/138	97.8
Disease-free survival	130/138	94.2
Death	3/138	2.2

*Three isolated LRs (3.6%), 1 LR associated with distant metastasis (1.2%), and 1 IDM (1.2%).

LCIS, lobular carcinoma in situ.

patients had a mean age of 48.4 years (range, 38–70 years). Recurrent tumor histological features were invasive ductal carcinoma (n = 5) and DCIS (n = 3). Subgroup analyses showed 1 systemic recurrence in patients with conventional total mastectomy (25%), 2 LRs in patients with NSM (3.9%), 3 isolated LRs (3.6%), 1 LR associated with distant metastasis (1.2%), and 1 systemic recurrence (1.2%) in patients with SSM. The global recurrence rate was 5.8%.

The patients with recurrence were treated with completion mastectomy and/or adjuvant treatment according to the biologic disease features. Overall survival was 97.8%, and disease-free survival was 94.2%. All deaths occurred secondary to breast cancer.

DISCUSSION

Since Halsted's radical mastectomy, the surgical management of breast cancer has continued to be ameliorated in decreasing morbidity and increasing quality of life.[13,14] Conservative mastectomies provide a better quality of life for women with breast cancer. The preservation of the NAC allows preservation of the woman body image. Skin-sparing mastectomy was first described by Toth and Lappert[15] and is performed by removing the whole glandular breast parenchyma and preserving the skin without the nipple-areolar complex. Nipple-sparing mastectomy was first described by Freeman[16] and preserves also the nipple-areolar complex. Preserving the skin envelope in either SSM or NSM allows an IBR, using implant or autologous tissue transfer techniques.

Skin-sparing mastectomy and NSM, followed by IBR, has gained popularity, with improving aesthetic outcomes and psychological well-being.[8,9,17–22] However, concerns have been raised about their oncologic safety because these procedures may compromise the completeness of the mastectomy.[23] Previous studies have reported that the remaining skin after SSM or NSM can contain residual breast parenchyma.[24,25] On the other hand, many previous studies showed no difference between SSM or NSM and conventional mastectomies concerning oncological safety.[26–30]

A second concern was that IBR could interfere with LR detection.[7,31] However, most LRs occur at the skin level, allowing detection by clinical examination or radiology in its early presentation.[25,32–35] Numerous series have reported comparable or even better survival rates in patients who underwent IBR compared with those who underwent conventional mastectomy alone.[7,24,36–39]

Our series reviewed retrospectively 138 mastectomies associated with IBR performed for invasive or in situ breast cancer. The unplanned reoperation rate was 23.2%, which is relatively high. However, our series includes a large proportion of patients who benefited from previous radiation (24.6%) and PMRT (15.9%). In the same way, a previous study reported an association between radiotherapy and an increased risk of wound breakdown, skin necrosis, infection, expander/implant loss, and unplanned reoperation.[40] In our center, IBR is not proposed for patients requiring PMRT. The decision of PMRT in this series was based on histopathological criteria (tumor size, pathologic nodal status, histological grade, and resection margins) after postoperative multidisciplinary discussion. An alternative to delayed reconstruction for patients requiring PMRT could be a delayed-immediate reconstruction, limiting the adverse events of radiotherapy on the definitive reconstruction (capsular contracture, implant exposure, infection, or wound breakdown for implant-based reconstruction; fat necrosis, volume loss, or wound contracture for autologous procedure).[41] Lastly, our reconstructive failure rate was acceptable with a rate of 8.7%.

We observed an LR rate of 4.8% and a systemic recurrence rate of 2.4% for patients benefiting from SSM. These recurrence rates are consistent with several recent studies reviewing the oncologic safety of SSM, finding LR rates ranging from 0% to 6.6% and systemic recurrence rates ranging from 0% to 5% after a mean follow-up of 28 to

73 months.[36,42–45] Concerning NSM, the LR rate was 3.9% and the systemic recurrence rate was 0% in our series, which is concordant with rates reported in previous studies ranging from 0% to 7.9% and from 0% to 3.4% respectively, after a mean follow-up of 18 to 60 months.[17,38,46–54] Otherwise, a number of series reported that the recurrence rates with SSM and NSM are comparable with recurrence rates seen with traditional mastectomy in selected patients on long-term follow-up.[20,27,47,55,56] Our series, however, includes too few cases of total mastectomies (n = 4) to draw the same conclusions.

Twelve patients had stage IIB or higher disease and only 2 of these patients had cancer recurrence. Of the 19 patients with node-positive disease, only 3 had tumor recurrence. Studies have showed that most breast cancer recurrences occur within 24 to 36 months after surgery[57,58]; the annual recurrence rate curve displays a double-peaked distribution, with the highest peak in the first 2 years and a low flat peak at 5 years after mastectomy.[59–62] Therefore, our follow-up period does not highlight the second peak at 5 years of follow-up but is adequate to identify the majority of tumor recurrences in this series. Overall survival was 97.8%, and disease-free survival was 94.2%. Our findings are concordant with previous literature analyzing the safety of mastectomies associated with IBR.[48,63,64]

Our study has a number of limitations, including its retrospective nature, a small sample size, and a medium follow-up; longer follow-ups are needed to value the second tumor recurrence peak and confirm our preliminary results. This review was conducted in a single center, and the surgical interventions were realized by one surgical team only. These limitations may result in failure to detect statistically significant associations between patients or tumor characteristics and oncologic outcomes. Moreover, we analyzed the short-term surgical complications rather than the long-term complications (capsular contracture, implant rotation, chronic pain, late seroma, revision rates, or long-term patient dissatisfaction).

CONCLUSIONS

Our study revealed an acceptable low incidence of short-term recurrence after mastectomy and IBR. We demonstrated that this procedure had no negative impact on patient survival, regardless of the type of mastectomy or cancer stage. It is oncologically safe and is an acceptable surgical option that has to be proposed to selected patients, in discussion with the plastic surgeon. However, longer follow-ups are needed to evaluate the incidence of delayed recurrences and surgical complications.

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