Impact of Oncoplastic Breast Surgery on Rate of Complications, Time to Adjuvant Treatment, and Risk of Recurrence

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Keywords

Breast cancer · Oncoplastic breast surgery · Delay of treatment · Complications of breast cancer surgery · Recurrence of breast cancer

Abstract

Background: The aim of this study was to compare the risk of complications and recurrence between oncoplastic and conventional breast surgery. **Methods:** This is a retrospective analysis of a consecutive series of 436 patients with stage I–III breast cancer who underwent surgery at the University Hospital of Basel between 2011 and 2018. **Results:** The nipple/skin-sparing mastectomy (NSM/SSM) group showed significantly more delayed wound healing (32.7 vs. 5.8%, $p < 0.001$) and skin necrosis (13.9 vs. 1.9%, $p = 0.020$) compared to conventional mastectomy (CM), which corresponded to significantly higher odds of short-term complications (OR 2.34, 95% CI 1.02–5.35, $p = 0.044$). The incidence rate of long-term morbidity in oncoplastic breast-conserving surgery (OBCS) was significantly higher compared to conventional breast-conserving surgery (CBCS; 25.5 vs. 11.3 per 100 patient years [PY], $p < 0.001$), in particular concerning chronic pain (13.3 vs. 6.6, $p = 0.011$) and lymphedema (4.1 vs. 0.4, $p = 0.003$). Seroma as

a long-term morbidity occurred more often in the CM group compared to the NSM/SSM group (5.8 vs. 0.5 per 100 PY, $p = 0.004$). Patients received adjuvant treatment earlier after CM compared to NSM/SSM (HR 1.83, 95% CI 1.05–3.19, $p = 0.034$). There were no significant differences in the incidence of positive margins nor in the odds of recurrence after OBCS versus CBCS and after NSM/SSM versus CM. **Conclusions:** Even though the present study confirmed expected differences in complications and morbidity, it suggested that oncoplastic surgery is oncologically safe. Patients undergoing NSM/SSM should be followed closely to allow early detection and treatment of frequently associated complications and ensure timely start of adjuvant therapy.

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Introduction

The most common cancer among women worldwide is breast cancer, which causes 14% of all cancer-related deaths [1, 2]. Major treatment progress has been achieved

I.O., J.Z., and M.R. contributed equally to this study.

Table 1. Patient, tumor, and treatment characteristics by group of surgery

	Breast conserving surgery (<i>n</i> = 283)			Mastectomy (<i>n</i> = 153)		
	CBCS (<i>n</i> = 95)	OBCS (<i>n</i> = 188)	<i>p</i> value	CM (<i>n</i> = 52)	NSM/SSM (<i>n</i> = 101)	<i>p</i> value
Median patient age (Q1–Q3), years	62.0 (51.0–72.0)	61.0 (50.0–70.0)	0.633	69.0 (59.5–80)	51.0 (44.0–61.0)	<0.001
T stage, <i>n</i> (%) ^a						
pTis	11 (11.6)	24 (12.8)	0.419	6 (11.5)	20 (19.8)	0.003
pT0	6 (6.3)	8 (4.3)		1 (1.9)	6 (5.9)	
pT1	60 (63.2)	109 (58.0)		11 (21.2)	41 (40.6)	
pT2	18 (18.9)	40 (21.3)		24 (46.2)	26 (25.7)	
pT3	0 (0.0)	6 (3.2)		7 (13.5)	8 (7.9)	
pT4	0 (0.0)	0 (0.0)		3 (5.8)	0 (0.0)	
N stage, <i>n</i> (%) ^a						
pNX	11 (11.6)	12 (6.4)	0.056	8 (15.4)	4 (4.0)	0.008
pN0	64 (67.4)	138 (73.4)		19 (36.5)	64 (63.4)	
pN1	17 (17.9)	27 (14.4)		15 (28.8)	22 (21.8)	
pN2	3 (3.2)	2 (1.1)		5 (9.6)	7 (6.9)	
pN3	0 (0.0)	8 (4.3)		5 (9.6)	4 (4.0)	
Tumor grade, <i>n</i> (%) ^b						
I	24 (25.3)	46 (24.5)	0.460	5 (9.6)	20 (19.8)	0.184
II	44 (46.3)	81 (43.1)		26 (50.0)	38 (37.6)	
III	21 (22.1)	57 (30.3)		20 (38.5)	39 (38.6)	
Cancer biology, <i>n</i> (%) ^c						
Pure DCIS	11 (11.6)	23 (12.2)	0.920	5 (9.6)	19 (18.8)	0.180
Luminal A-like	50 (52.6)	91 (48.4)		19 (36.5)	37 (36.6)	
Luminal B-like (Her2-negative)	21 (22.1)	40 (21.3)		17 (32.7)	23 (22.8)	
Luminal B-like (Her2-positive)	6 (6.3)	15 (8.0)		5 (9.6)	7 (6.9)	
Her2-positive (nonluminal)	2 (2.1)	9 (4.8)		3 (5.8)	2 (2.0)	
Basal like	4 (4.2)	9 (4.8)		2 (3.8)	12 (11.9)	
Margin after initial surgery, <i>n</i> (%)						
Negative	85 (89.5)	162 (86.2)	0.571	50 (96.2)	94 (93.1)	0.719
Positive	10 (10.5)	26 (13.8)		2 (3.8)	7 (6.9)	
Lymph node surgery, <i>n</i> (%) ^a						
None	14 (14.7)	17 (9.0)	0.521	9 (17.3)	5 (5.0)	0.001
Sentinel lymph node biopsy	68 (71.6)	142 (75.5)		19 (36.5)	68 (67.3)	
Tailored axillary surgery ^d	6 (6.3)	11 (5.9)		3 (5.8)	6 (5.9)	
Axillary lymph node dissection	7 (7.4)	17 (9.0)		21 (40.4)	22 (21.8)	
Chemotherapy, <i>n</i> (%)						
No chemotherapy	76 (80.0)	140 (74.5)	0.590	35 (67.3)	64 (63.4)	0.388
Adjuvant chemotherapy	10 (10.5)	31 (16.5)		14 (26.9)	22 (21.8)	
Neoadjuvant chemotherapy	8 (8.4)	15 (8.0)		3 (5.8)	14 (13.9)	
Both	1 (1.1)	2 (1.1)		0 (0.0)	1 (1.0)	
Adjuvant radiotherapy, <i>n</i> (%)	74 (77.9)	161 (85.6)	0.130	19 (36.5)	34 (33.7)	0.724
Median time of follow-up (Q1–Q3), months	34.46 (9.10–55.69)	21.13 (6.37–35.42)	0.004	18.15 (11.22–47.08)	22.93 (8.71–40.48)	0.731

DCIS, ductal carcinoma in situ. Missing: ^a 1, ^b 15, ^c 4. ^d Tailored axillary surgery as surgical intervention in the TAXIS trial [30].

over the past 30 years, leading to improved survival [3, 4]. Systemic and radiation therapies have experienced dramatic paradigm changes in the past 2 decades, and surgical techniques have been refined as well [3, 5, 6].

Oncoplastic breast surgery (OPS) has been developed to improve cosmetic outcomes after breast cancer surgery [7–9]. The term is often used to describe all types of breast surgery that involve immediate reconstruction by displacing or replacing volume of the ipsilateral breast, either with or without surgery of the contralateral breast [6,

10, 11]. As such, nipple- as well as skin-sparing mastectomy (NSM/SSM) with immediate reconstruction are often included in the OPS category [12]. A more restricted definition of OPS refers to oncoplastic breast-conserving surgery (OBCS), which differs from conventional breast-conserving surgery (CBCS) by the use of more extensive partial breast reconstruction techniques [7, 13, 14]. OBCS often involves nononcological skin resection and high-volume tumorectomy [13]. Therefore, OPS is an escalation of surgery compared to conventional breast surgery.

Table 2. Short-term complications by group of surgery

	Breast conserving surgery (<i>n</i> = 283)			Mastectomy (<i>n</i> = 153)		
	CBCS (<i>n</i> = 95)	OBCS (<i>n</i> = 188)	<i>p</i> value	CM (<i>n</i> = 52)	NSM/SSM (<i>n</i> = 101)	<i>p</i> value
Short-term complications, <i>n</i> (%)	14 (14.7)	30 (16.0)	0.863	16 (30.8)	43 (42.6)	0.166
Relevant seroma ^{a, b}	3 (3.2)	14 (7.4)	0.191	11 (21.2)	12 (11.9)	0.154
Delayed wound healing	2 (2.1)	14 (7.4)	0.099	3 (5.8)	33 (32.7)	<0.001
Infection	4 (4.2)	8 (4.3)	1.000	5 (9.6)	12 (11.9)	0.790
Relevant hematoma ^a	6 (6.3)	6 (3.2)	0.226	1 (1.9)	12 (11.9)	0.062
Skin necrosis	1 (1.1)	2 (1.1)	1.000	1 (1.9)	14 (13.9)	0.020
Flap loss	0 (0.0)	0 (0.0)	1.000	0 (0.0)	5 (5.0)	0.167
Nipple necrosis	0 (0.0)	1 (0.5)	1.000	0 (0.0)	2 (2.0)	0.548

^a Seroma or hematoma requiring intervention and/or causing discomfort. ^b Drainages were removed as soon as a flow rate of <20 mL over 24 h was reached.

It is unclear if this affects safety in terms of short- and long-term morbidity and oncologic outcomes [10, 15].

The aim of this study was to compare the rate of complications, time to adjuvant treatment, and risk of recurrence between OPS and conventional breast surgery.

Materials and Methods

Study Design and Patients

We performed a retrospective analysis of a consecutive cohort of patients with breast cancer, who were operated by 3 breast surgeons (W.P.W., S.D.S., and R.M.) at the University Hospital of Basel, a tertiary referral center in Switzerland, between 2011 and 2018. Women with American Joint Committee on Cancer (AJCC) stage I–III breast cancer were included. Patient, tumor, treatment, and outcome variables were recorded via the online good clinical practice conform clinical data management system secuTrial®, which is maintained by the Clinical Trial Unit Basel. The classification of the 2013 St. Gallen Consensus Conference was used to define luminal A, luminal B/HER2 negative, luminal B/HER2 positive, HER2 positive, and triple negative subtypes [16]. Adverse events were divided into short-term complications (within 30 days after surgery) and long-term morbidity (>30 days after surgery). Time to adjuvant treatment was defined as the time period between first surgery and start of first adjuvant therapy, either radio- or chemotherapy. Tumor-free margins were defined as ≥2 mm for ductal carcinoma in situ and no ink on tumor for invasive cancer. Surgical categories followed the previously described standardized nomenclature of OPS [17]. In short, oncoplastic tumorectomy differed from conventional tumorectomy by use of glandular flaps or volume replacement techniques, while oncoplastic mastopexy was defined by use of nononcologic skin excision. Reduction mammo-plasty was defined by use of glandular flaps as well as nononcologic skin and tissue resection. SSM referred to the conservation of the skin envelope without nipple, while NSM consisted of both skin and nipple preservation.

Statistical Analysis

All analyses were performed on the 436 first consecutive patients recorded in the secuTrial® database. Demographics, baseline characteristics, disease characteristics, and response to thera-

py were summarized descriptively by the occurrence of surgery-related adverse events (short-term complications and long-term morbidity), of recurrences, of adjuvant therapies, and by type of surgical procedure. Categorical variables were summarized by absolute frequencies and percentages. Continuous variables were summarized by median values and interquartile ranges (IQR). Occurrences were compared using Fisher's exact tests. Median values were compared using Wilcoxon test. Generated *p* values were not corrected for multiple testing. Exposure-adjusted incidence rates were calculated per 100 patient years (PY) regarding long-term morbidity and recurrence. Incidence rates were compared using Fisher's exact test.

Logistic regression models were generated in order to identify potential predictors for the occurrence of surgery-related adverse events or recurrence. Type of surgery was included into each model as covariate. Additional covariates (age at baseline, diabetes status, smoking status, nodal stage, T stage, and margin, partly duration of follow-up) were entered based on stepwise selection. Odds ratios (OR) and corresponding 95% confidence intervals (CI) for significant parameters were entered into a forest plot. A Cox model regression was generated in order to identify potential predictors for time to adjuvant therapy. Type of surgery was included into the model as covariate. Additional covariates (age at baseline, diabetes status, smoking status, nodal stage, T stage, and margin) were entered based on stepwise selection. Hazard ratios (HR) and corresponding 95% CIs for significant parameters were entered into a forest plot.

Results

Patient, Tumor, and Treatment Characteristics by Type of Surgery

In total, 436 patients were included in this study. Median follow-up was 22.8 months (IQR 8.0–40.9). Patient, tumor, and treatment characteristics by group of surgery are demonstrated in Table 1. Detailed surgical procedures are listed in online supplementary Table 1 (see www.karger.com/doi/10.1159/000511728 for all online suppl. material).

Fig. 1. Multivariate analysis for short-term complications. Type of surgery was included in the model as covariate. Additional covariates, including age at baseline, diabetes (yes/no), smoking (yes/no/prior), nodal stage (pNx/pN0/pN1/pN2/pN3), T stage (pTis/pT0/pT1/pT2/pT3/pT4), and margin (+/-), were entered into the model based on the stepwise selection. Twenty-nine observations were deleted due to missing values.

Patients undergoing NSM/SSM were significantly younger ($p < 0.001$) and had lower tumor stages ($p = 0.003$ for T stage and $p = 0.008$ for N stage) compared to patients in the conventional mastectomy (CM) group without immediate reconstruction. Accordingly, axillary dissection was more frequently performed in the CM group ($p = 0.001$). The groups of OBCS and CBCS were comparable at baseline and differed only in time of follow-up (median follow-up time 34.5 vs. 21.1 months, $p = 0.004$).

Short-Term Complications

Table 2 shows the occurrence of surgical short-term complications by type of surgery. There was no significant difference between OBCS and CBCS in terms of overall short-term complications ($p = 0.863$) or within the individual types of complications. Even though the NSM/SSM group did not show significantly more overall short-term complications compared to CM ($p = 0.166$), delayed wound healing ($p < 0.001$) and skin necrosis ($p = 0.002$) occurred significantly more often after NSM/SSM.

Multivariate analysis (Fig. 1) did not show a significant difference in short-term complications between OBCS and CBCS (OR 1.38, 95% CI 0.62–3.05, $p = 0.431$). However, there was a significant difference between NSM/SSM and CM (OR 2.34, 95% CI 1.02–5.35, $p = 0.044$). Furthermore, there were significant associations between increasing nodal stage and the occurrence of short-term complications (pN1 vs. pN0: OR 2.84, 95% CI 1.56–5.17, $p = 0.001$; pN2 vs. pN0: OR 2.44, 95% CI 0.78–7.65, $p = 0.127$; pN3 vs. pN0: OR 7.55, 95% CI 2.44–23.36, $p < 0.001$).

Long-Term Morbidity

There was a significantly higher exposure-adjusted incidence rate per 100 PY for long-term morbidity (Table 3) in the OBCS versus CBCS group (25.5 vs. 11.3 per 100 PY, $p < 0.001$), in particular concerning chronic pain (13.3 vs. 6.6 per 100 PY, $p = 0.011$) and lymphedema (4.1 vs. 0.4 per 100 PY, $p = 0.003$). When comparing CM and NSM/SSM, overall long-term morbidity did not differ (29.6 vs. 27.9 per 100 PY, $p = 0.832$), but the CM group had a significantly higher incidence rate of relevant seroma (5.8 vs. 0.5 per 100 PY, $p = 0.004$).

Multivariate analysis for long-term morbidity (online suppl. Fig. 1) showed no significant differences between the surgical groups. Significant associations were found concerning increasing nodal stage and younger age. There was no significant association found concerning duration of follow-up.

Online supplementary Table 2 shows patient, tumor, and treatment characteristics by adverse events related to surgery.

Time to Adjuvant Treatment

Time to adjuvant treatment overall and time to adjuvant radiotherapy in particular did not differ significantly in CBCS versus OBCS and in NSM/SSM versus CM (Table 4). However, time to adjuvant chemotherapy was significantly prolonged in the NSM/SSM group compared to the CM group (42.5 days, IQR 32.0–54.0 vs. 30.0 days, IQR 27.0–34.0, $p = 0.023$).

Multivariate analysis (Fig. 2) showed that patients of the CM group received adjuvant treatment earlier than

Table 3. Exposure-adjusted incidence rate per 100 patient years for long-term morbidity by group of surgery

	Breast conserving surgery (<i>n</i> = 283)						
	CBCS (<i>n</i> = 95), exposure (d) = 94,048			OBCS (<i>n</i> = 188), exposure (d) = 126,068			<i>p</i> value
	patients with events, <i>n</i> (%)	number of events	rate per 100 PYs	patients with events, <i>n</i> (%)	number of events	rate per 100 PYs	
Long-term morbidity	25 (26.3)	29	11.3	56 (29.8)	88	25.5	<0.001
Atrophy	0 (0.0)	0	0.0	1 (0.5)	1	0.3	1.000
Axillary web syndrome	0 (0.0)	0	0.0	3 (1.6)	4	1.2	0.141
Chronic pain	15 (15.8)	17	6.6	40 (21.3)	46	13.3	0.011
Fat necrosis	1 (1.1)	1	0.4	2 (1.1)	4	1.2	0.401
Fibrosis	0 (0.0)	0	0.0	4 (2.1)	4	1.2	0.141
Impairment of shoulder mobility	9 (9.5)	9	3.5	10 (5.3)	11	3.2	0.826
Lymphedema	1 (1.1)	1	0.4	11 (5.9)	14	4.1	0.003
Relevant seroma ^a	1 (1.1)	1	0.4	4 (2.1)	4	1.2	0.401

	Mastectomy (<i>n</i> = 153)						
	CM (<i>n</i> = 52), exposure (d) = 44,421			NSM/SSM (<i>n</i> = 101), exposure (d) = 78,605			<i>p</i> value
	patients with events, <i>n</i> (%)	number of events	rate per 100 PYs	patients with events, <i>n</i> (%)	number of events	rate per 100 PYs	
Long-term morbidity	18 (34.6)	36	29.6	37 (36.6)	60	27.9	0.832
Abdominal hernia	0 (0.0)	0	0.0	1 (1.0)	1	0.5	1.000
Atrophy	0 (0.0)	0	0.0	1 (1.0)	1	0.5	1.000
Axillary web syndrome	1 (1.9)	2	1.6	6 (5.9)	6	2.8	0.719
Chronic pain	7 (13.5)	10	8.2	23 (22.8)	25	11.6	0.385
Fat necrosis	0 (0.0)	0	0.0	2 (2.0)	2	0.9	0.539
Fibrosis	0 (0.0)	0	0.0	1 (1.0)	1	0.5	1.000
Impairment of shoulder mobility	7 (13.5)	8	6.6	14 (13.9)	15	7.0	1.000
Lymphedema	7 (13.5)	9	7.4	5 (5.0)	6	2.8	0.063
Relaxatio	0 (0.0)	0	0.0	1 (1.0)	2	0.9	0.539
Relevant seroma ^a	6 (11.5)	7	5.8	1 (1.0)	1	0.5	0.004

^a Seroma or hematoma requiring intervention and/or causing discomfort.

Table 4. Time to first adjuvant treatment by group of surgery

	Breast conserving surgery (<i>n</i> = 283)			Mastectomy (<i>n</i> = 153)		
	CBCS (<i>n</i> = 95)	OBCS (<i>n</i> = 188)	<i>p</i> value	CM (<i>n</i> = 52)	NSM/SSM (<i>n</i> = 101)	<i>p</i> value
Time to adjuvant chemotherapy						
Number	7	32		13	22	
Median (Q1–Q3), days	34.0 (27.0–60.0)	41.0 (32.5–61.0)	0.537	30.0 (27.0–34.0)	42.5 (32.0–54.0)	0.023
Time to adjuvant radiotherapy						
Number	54	114		10	14	
Median (Q1–Q3), days	46.5 (37.0–60.0)	47.0 (39.0–60.0)	0.447	60.0 (43.0–63.0)	50.5 (40.0–68.0)	0.908
Time to adjuvant treatment ^a						
Number	61	146		23	36	
Median (Q1–Q3), days	46.0 (34.0–60.0)	47.0 (39.0–61.0)	0.501	39.0 (30.0–60.0)	45.5 (37.0–60.0)	0.172

^a Either chemotherapy or radiotherapy.

Fig. 2. Multivariate analysis for time to adjuvant therapy (radiation or chemotherapy). Type of surgery was included in the model as covariate. Additional covariates, including age at baseline, diabetes (yes/no), smoking (yes/no/prior), nodal stage (pNx/pN0/pN1/pN2/pN3), T stage (pTis/pT0/pT1/pT2/pT3/pT4), and margin (+/-), were entered into the model based on the stepwise selection. Sixty-three observations were deleted due to missing values.

patients of the NSM/SSM group (HR 1.83, 95% CI 1.05–3.19, $p = 0.034$). Significant associations were also found for nodal stage and age.

Oncologic Outcomes

There was no significant difference in the incidence of positive margins after OBCS versus CBCS ($p = 0.571$) or after NSM/SSM versus CM ($p = 0.719$; Table 1). Overall, there were no significant differences in the exposure-adjusted incidence of recurrence between CBCS and OBCS and between CM and NSM/SSM (Table 5). Multivariate analysis confirmed the absence of significant differences between those groups (online suppl. Fig. 2). Longer follow-up, increasing nodal stage and age were associated with higher odds of recurrence.

Discussion

The present study compared OPS with conventional techniques in terms of short-term complications, long-term morbidity, time to adjuvant treatment, rate of positive margins, and risk of recurrence. Rate of positive margins and risk of recurrence did not differ significantly or relevantly between the groups.

However, patients undergoing NSM/SSM experienced a longer time to adjuvant chemotherapy than CM patients, presumably caused by increased risk of ischemic complications. In the individual patient, this delay may become relevant. Therefore, patients undergoing NSM/

SSM should be followed closely and complications treated promptly to ensure oncologic safety. Other studies did not show a delay of treatment in NSM/SSM in comparison with CM [18, 19]. In 2018, the Oncoplastic Breast Consortium consensus expert panel was asked about risk factors for severe mastectomy skin flap necrosis. The panel considered the location of the incision, the amount and duration of pressure applied by retractors during surgery, the thickness of the skin flaps, and insufficient surgeon experience as relevant risk factors [12, 20, 21], all of which are at least partially modifiable. In the present study, the main predictor of surgical complications besides NSM/SSM was increasing axillary nodal stage. While the latter is explained by more radical surgery, the former is mainly driven by preservation of the skin envelope with associated necrosis. The rate of nipple or skin necrosis (2.0 or 13.9%, respectively) in this study is well in line with findings from other studies [21].

OBCS showed a higher incidence rate of long-term morbidity than CBCS. This might be explained by the inclusion of complications attributed to axillary surgery, such as lymphedema and chronic pain in the arm or axilla. Previous studies mostly showed similar complication rates in OBCS versus CBCS, with the exception of delayed wound healing, which, however, did not differ in our study population [22, 23]. Despite the higher complication rate, OBCS did not cause any delay of treatment when compared to CBCS, which is in accordance with prior studies [22]. All patients in this study were operated by the same team of breast surgeons who have specialized

Table 5. Exposure-adjusted incidence rate per 100 patient years for recurrence by group of surgery

	Breast conserving surgery (<i>n</i> = 283)						
	CBCS (<i>n</i> = 95), exposure (d) = 94,048			OBCS (<i>n</i> = 188), exposure (d) = 126,068			<i>p</i> value
	patients with events, <i>n</i> (%)	number of events	rate per 100 PYs	patients with events, <i>n</i> (%)	number of events	rate per 100 PYs	
Recurrence	6 (6.3)	6	2.3	9 (4.8)	9	2.6	1.000
Local	4 (4.2)	4	1.6	4 (2.1)	4	1.2	0.731
Distant	1 (1.1)	1	0.4	5 (2.7)	5	1.4	0.248
Combined	1 (1.1)	1	0.4	0 (0.0)	0	0.0	0.427
	Mastectomy (<i>n</i> = 153)						
	CM (<i>n</i> = 52), exposure (d) = 44,421			NSM/SSM (<i>n</i> = 101), exposure (d) = 78,605			<i>p</i> value
	patients with events, <i>n</i> (%)	number of events	rate per 100 PYs	patients with events, <i>n</i> (%)	number of events	rate per 100 PYs	
Recurrence	8 (15.4)	9	7.4	6 (5.9)	6	2.8	0.063
Local	1 (1.9)	1	0.8	2 (2.0)	2	0.9	1.000
Loco-regional	2 (3.8)	2	1.6	0 (0.0)	0	0.0	0.130
Regional	0 (0.0)	0	0.0	2 (2.0)	2	0.9	0.539
Distant	2 (3.8)	2	1.6	0 (0.0)	0	0.0	0.130
Combined	4 (7.7)	4	3.3	2 (2.0)	2	0.9	0.198

Local, reappearance of breast cancer in the ipsilateral breast (after breast-conserving surgery) or the ipsilateral chest wall (after mastectomy); regional, reappearance of breast cancer in the regional lymph nodes; loco-regional, reappearance of breast cancer in both ipsilateral chest wall and regional lymph nodes; distant, distant metastases; combined, combination of (loco-)regional and distant recurrence.

in oncoplastic surgery and the ratio of oncoplastic to conventional surgery seems to be high. Importantly, however, many procedures included nononcological skin resection or nipple recentralization in the absence of large-volume resections or reduction mammoplasty techniques. When comparing the different types of surgery, this study showed no differences in tumor recurrence, suggesting an overall similar safety profile throughout the different surgery groups. However, the median follow-up time of only 22.8 months must be considered. The comparable safety profile of the procedures is further reflected by the similar numbers of positive margins when comparing the different surgery groups, which is supported by some but not all previous studies [24–28].

The most important limitation of this study is the retrospective single-center observational study design. The selection bias inherent in this type of study is caused by both patients and surgeons. Younger patients tend to choose NSM/SSM to achieve better aesthetic results. Surgeons recommend CM without reconstruction in older patients with higher tumor stages to decrease the risk of adverse events related to more extensive surgery [27, 29]. Furthermore, the surgical groups showed varying follow-up times, which may have caused an attrition bias, especially concerning recurrence and long-term morbidity rates. We tried to adjust for differences between groups

by performing multivariate analyses and exposure-adjusted incidence rates but realize that residual confounding is likely. Another limitation of this study is the inclusion of both ductal carcinoma in situ and invasive cancer, which could limit the informative value in terms of oncological safety due to the heterogeneity of the patient population.

Conclusions

While OBCS showed a higher incidence rate of long-term morbidity than CBCS, there were no significant or relevant differences in risk of complications, time to adjuvant treatment, and risk of recurrence. The increased risk of short-term complications after NSM/SSM, while being associated with time to adjuvant therapy, had no significant impact on risk of long-term morbidity or recurrence. We conclude that oncoplastic techniques are overall oncologically safe but recommend that patients undergoing NSM/SSM be followed closely to allow prompt diagnosis and treatment of complications in order to ensure timely adjuvant therapy.

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Statement of Ethics

This research project complies with the guidelines for human studies according to the Declaration of Helsinki as revised in 2013. The study protocol was approved by the Ethics Committee of Northwest and Central Switzerland (Ethikkommission Nordwest- und Zentralschweiz, EKNZ), and all subjects have given their written informed consent.

Conflict of Interest Statement

W.P.W. has received research support from Takeda Pharmaceuticals International via Swiss Group for Clinical Cancer Research (SAKK), honoraria/consultation from Genomic Health, Inc., USA, and support for conferences and meetings from Sandoz, Genomic Health, Medtronic, Novartis Oncology, and Pfizer. J.L. has received personal fees for his work by the Department of Breast Surgery, University Hospital of Basel. C.K. has received research support from Roche, Tessaro, Genomic Health, Pfizer, Astra Zeneca, GSK, and Lilly.

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Author Contributions

Study concepts and design were contributed by Jasmin Zeindler, Savas Deniz Soysal, and Walter Paul Weber. Data was acquired by Ida Oberhauser, Mathilde Ritter, Madleina Maria Müller, Veronica D'Amico, and Giacomo Montagna. Quality control and analysis of data was conducted by Ida Oberhauser, Jasmin Zeindler, Mathilde Ritter, Jeremy Levy, and Walter Paul Weber. Statistical analysis was performed by Jeremy Levy. The manuscript was prepared by Ida Oberhauser, Jasmin Zeindler, Mathilde Ritter, Jeremy Levy, and Walter Paul Weber. All authors helped draft the work, revised it critically for important intellectual content, and read and approved the final version to be published. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy of any part of the work are appropriately investigated and resolved.

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