Ann Surg Oncol (2019) 26:2730–2737
https://doi.org/10.1245/s10434-019-07408-6

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – BREAST ONCOLOGY

Neoadjuvant Chemotherapy does not Increase Complications in Oncoplastic Breast-Conserving Surgery

Karri Adamson, MD[1], Mariana Chavez-MacGregor, MD, MSc[2,3], Abigail Caudle, MD, MS, CMQ, FACS[4], Benjamin Smith, MD[5], Donald Baumann, MD, FACS[1], Jun Liu, PhD[1], and Mark Schaverien, MB ChB, MD, MSc, MEd, FRCS(Plast)[1]

[1]Division of Surgery, Department of Plastic Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Department of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; [3]Health Services Research Department, The University of Texas MD Anderson Cancer Center, Houston, TX; [4]Division of Surgery, Department of Breast Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; [5]Department of Radiation Oncology, Division of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

ABSTRACT

Background. Oncoplastic breast-conserving surgery (OBCS) broadens the indications for breast conservation. Neoadjuvant systemic chemotherapy (NAC) is used increasingly in the treatment of patients with early-stage and locally advanced breast cancer. This study aimed to evaluate the outcomes for patients who received NAC followed by OBCS.

Methods. A retrospective chart review was performed for all patients who underwent OBCS involving the mastopexy/breast-reduction technique, including synchronous mastopexy/breast reduction for symmetry, at the University of Texas MD Anderson Cancer Center between January 2010 and January 2016. Patients who had received NAC were compared with those who had undergone surgery first. Demographic, treatment, and outcomes data were collected.

Results. The study included 429 patients, corresponding to 713 breasts. Of these patients, 122, corresponding to 199 breasts, received NAC. The patients who received NAC were younger ($p < 0.001$) and had a more advanced cancer stage ($p < 0.001$). The overall complication rate per patient was 25.9%, with major complications occurring in 9.1% of the patients. After adjustment for risk factors, NAC was not shown to be associated with an increased risk of complications or delayed adjuvant radiation therapy ($p = 0.37$), irrespective of the chemotherapy regimen used or whether the interval between NAC and surgery was 4 weeks or longer.

Conclusions. In a high-volume center, OBCS can be performed safely for carefully selected patients after NAC without an increased risk of complications or delayed adjuvant radiation therapy. An interval of at least 4 weeks between completion of NAC and surgery can be regarded as safe irrespective of the chemotherapy regimen used.

Approximately two thirds of patients with breast cancer receive breast-conserving therapy (BCT).[1] It is safe and effective, with survival similar to that for mastectomy.[1–4] Oncoplastic breast-conserving surgery (OBCS) most commonly incorporates mastopexy/breast-reduction techniques to avoid the often undesirable aesthetic results from BCT,[5–7] and its use is increasing.[8,9] The OBCS option broadens the indications for BCT by enabling resection of larger parenchymal volumes, particularly in cosmetically sensitive areas of the breast.[10–14] Several studies have reported a lower positive margin rate for patients with OBCS than with BCT alone,[9,10,12,15,16] and the local recurrence rate for OBCS is the same as for breast-conserving surgery (BCS) or lower, although the clinical stage

Presented at the American Society for Reconstructive Microsurgery annual meeting, Palm Desert, CA, February 1–5, 2019.

First Received: 11 February 2019;
Published Online: 29 April 2019

M. Schaverien, MB ChB, MD, MSc, MEd, FRCS(Plast)
e-mail: mvschaverien@mdanderson.org

is often more advanced.[9,14] Compared with BCT alone, OBCS is associated with improved self-esteem and quality of life, as well as with improved patient satisfaction, and achieves long-lasting aesthetic results.[10,15,17]

Neoadjuvant systemic chemotherapy (NAC), also known as preoperative chemotherapy, is the standard of care for locally advanced and inoperable tumors and currently is commonly used to treat patients with early-stage breast cancer. The advantages of NAC include its utility for assessment of tumoral response and its associated increase in the rate of breast conservation, with recurrence and survival rates similar to those for adjuvant systemic chemotherapy.[18–22] Although multiple studies have failed to demonstrate increased complications of breast surgery in the setting of NAC,[11,12,23–31] patients who receive NAC are less likely to receive immediate breast reconstruction,[23] partly due to concerns for increased wound-related complications and the consequent possibility of delayed adjuvant radiation therapy. No study, however, has specifically examined the effect of NAC on complications of OBCS.

Although there is no known difference in oncologic outcomes when surgery is performed up to 8 weeks after the completion of NAC,[32] in practice, most patients undergo surgery about 4 weeks after the completion of NAC.[24,33,34] A shorter interval between completion of NAC and surgery often is observed when paclitaxel is administered last due to the faster cell count recovery associated with weekly administration of paclitaxel than with anthracycline- or docetaxel-based chemotherapy. This study aimed to characterize the complications associated with OBCS involving the mastopexy/breast-reduction technique for patients who received NAC, and to determine the rate of such complications according to NAC regimen and timing.

PATIENTS AND METHODS

An institutional review board (IRB)-approved (PA17-0901) retrospective chart review was conducted. All patients with a diagnosis of breast cancer who underwent OBCS involving the mastopexy/breast-reduction technique at The University of Texas MD Anderson Cancer Center from 1 January 2010 through 1 January 2016 were included. Patients who had received NAC were compared with those who had not. All patients had a minimum 24-month follow-up period to capture all complications and treatment delays after the primary surgery. Patient demographics, preoperative white blood cell count (WBC) and absolute neutrophil count (ANC) the day before surgery, procedure details, tumor characteristics, chemotherapy regimen and timing, complications, and follow-up data were recorded. Only complications that occurred as a result of the primary operation were collected. Major complications were defined as those that required hospital readmission, involved a return to the operating room, or resulted in delayed radiation adjuvant therapy, defined as administration more than 8 weeks after surgery and documented to have occurred as a result of a complication.[32,35–39]

The study defined OBCS involving the mastopexy/breast-reduction technique as parenchymal rearrangement, with nipple relocation based on an established vascular pedicle with breast skin envelope resection/reshaping. Patients were excluded from the study if they had undergone local parenchymal tissue rearrangement only or contralateral oncologic breast surgery or were receiving chemotherapy for non-breast primary cancers.

Statistical Analysis

Statistical analysis was performed to compare the two study groups (NAC and no-NAC cohorts). Descriptive statistics including means and standard deviations as well as medians and ranges were used as appropriate. Frequencies and percentages were used to summarize the categorical clinical characteristics and outcomes. Pearson's Chi square and Fisher's exact tests were used to assess associations between categorical variables and treatment. Univariate analysis and a multivariable generalized estimating equation (GEE) model were used to evaluate the risk factors for complications. A backward selection algorithm was used to fit the most parsimonious multivariable model. The final multivariate GEE model controlled for body mass index (BMI), diabetes, and immediate contralateral mastopexy for symmetry (bilateral surgery). Simple imputation was applied to handle missing data in model selection. Subgroup analysis was performed to compare outcomes relative to the timing of surgery after completion of NAC. A p value lower than 0.05 was considered statistically significant. The analyses were performed using SAS 9.2 (SAS Institute Inc., Cary, NC, USA).

RESULTS

The study included 429 patients, 284 of whom underwent immediate contralateral mastopexy/breast-reduction surgery for symmetry of 713 breasts. The median patient age was 55 years (range, 24–78 years), and the median BMI was 32 kg/m^2 (range, 17.6–64 kg/m^2). A total of 122 patients (199 breasts, 28.4%) received NAC, and 307 patients (514 breasts; 71.6%) did not (Table 1). The NAC and non-NAC groups were similar, except that the patients in the NAC group were younger ($p < 0.001$), had more

TABLE 1 Characteristics of patients undergoing oncoplastic breast-conserving surgery: comparison of patients who underwent neoadjuvant systemic chemotherapy with those who did not

	Total *n* (%)	Neoadjuvant chemotherapy *n* (%)	No neoadjuvant chemotherapy *n* (%)	*p* Value
No. of patients	429	122 (28.4)	307 (71.6)	
Median age: years (range)	55 (24–78)	52 (24–73)	57 (31–78)	< 0.001
Median BMI: kg/m^2 (range)	32 (17.6–64)	31.5 (20.2–58)	32 (17.6–64)	0.6
Median follow-up period: months (range)	51.6 (27.8–112.7)	49.8 (28.1–112.7)	53.2 (27.8–110.5)	0.16
Comorbidities				
Hypertension	182 (42.4)	45 (36.9)	137 (44.6)	0.14
Diabetes mellitus	62 (14.5)	19 (15.6)	43 (14)	0.68
Coronary artery disease	33 (7.7)	9 (7.4)	24 (7.8)	0.88
Pulmonary disease	31 (7.2)	11 (9)	20 (6.5)	0.37
Active cigarette smoker	10 (2.3)	3 (2.5)	7 (2.3)	1
No of comorbidities				
None	211 (49.2)	67 (54.9)	144 (46.9)	0.13
1	148 (34.5)	34 (27.9)	115 (37.5)	0.06
≥ 2	70 (16.3)	21 (17.2)	48 (15.6)	0.69
Bra cup size				0.65
A	0 (0)	0 (0)	0 (0)	
B	19 (4.4)	4 (3.3)	15 (4.9)	
C	72 (16.8)	24 (19.7)	48 (15.6)	
D	12 (2.8)	34 (27.9)	78 (25.4)	
DD	92 (21.4)	28 (23.0)	64 (20.8)	
DDD or larger	36 (8.4)	8 (6.6)	28 (9.1)	
Unknown	98 (22.8)	24 (19.7)	74 (24.1)	
Breast cancer stage				< 0.001
0	76 (17.7)	0 (0)	76 (24.4)	
1	127 (29.6)	4 (3.3)	123 (40.1)	
2	198 (46.1)	97 (79.5)	101 (32.9)	
3	28 (6.5)	21 (17.2)	7 (2.3)	
Clinical tumor (T) category				< 0.001
0	75 (17.5)	0 (0)	75 (24.4)	
1	141 (32.9)	13 (10.7)	128 (41.7)	
2	184 (42.9)	87 (71.3)	97 (31.6)	
3	26 (6.1)	19 (15.6)	7 (2.3)	
4	3 (0.7)	3 (2.5)	0 (0)	
Clinical nodal (N) category				< 0.001
0	329 (76.7)	54 (44.2)	275 (89.6)	
1	74 (17.2)	45 (36.9)	29 (9.4)	
2	7 (1.6)	6 (4.9)	1 (0.3)	
3	19 (4.4)	17 (13.9)	2 (0.7)	
Mean preoperative WBC count	6.87 ± 2.46	6.4 ± 3.4	7 ± 1.9	0.01
Mean preoperative ANC	4.09 ± 1.87	4 ± 2.5	4.1 ± 1.5	1
Postoperative chemotherapy	96 (22.4)	12 (9.8)	84 (27.4)	<0.001
Postoperative radiation therapy	409 (96.3)	120 (98.4)	289 (94.1)	0.01

BMI body mass index, *WBC* white blood cell, *ANC* absolute neutrophil count

TABLE 2 Postoperative complications: comparison of patients who underwent neoadjuvant systemic chemotherapy with those who did not

	Total *n* (%)	Neoadjuvant chemotherapy *n* (%)	No neoadjuvant chemotherapy *n* (%)	OR (95% CI)	*p* Value
No. of patients	429	122 (28.4)	307 (71.6)	–	
No. of breasts	713	199 (27.9)	514 (72.1)	–	
Overall complications (per patient)	111 (25.9)	28 (23)	83 (27.04)	1.24 (0.76–2.03)	0.4
Delayed wound healing	62 (14.4)	16 (13.1)	46 (15)	1.17 (0.63–2.15)	0.65
Dehiscence	18 (4.2)	4 (3.3)	14 (4.6)	1.41 (0.45–4.37)	0.61
Hematoma/seroma	10 (2.3)	3 (2.5)	7 (2.3)	0.93 (0.24–3.64)	1
Fat necrosis	24 (5.6)	5 (4.1)	19 (6.2)	1.54 (0.56–4.23)	0.49
Wound infection	29 (6.8)	5 (4.1)	24 (7.8)	1.98 (0.74–5.33)	0.204
Skin necrosis	6 (1.4)	1 (0.8)	5 (1.6)	2 (0.23–17.3)	0.68
T-junction necrosis	15 (3.5)	3 (2.5)	12 (3.9)	1.61 (0.45–5.82)	0.57
Multiple complications	35 (8.2)	2 (1.6)	11 (3.6)	1.65 (0.7–3.88)	0.33
Major complication (per patient)	39 (9.1)	14 (11.5)	25 (8.1)	1.46 (0.73–2.92)	0.35
Complication causing delayed adjuvant radiation (for those who received it)	13 (3.2)	2 (1.7)	11 (3.8)	0.43 (0.09–1.96)	0.36
Complication causing delayed adjuvant chemotherapy (for those who received it first)	5 (5.2)	0 (0)	5 (6.0)	–	1
Reexcision for involved margins (per patient)	30 (7.0)	12 (6)	22 (4.3)	0.48 (0.18–1.29)	0.15
Additional surgery for complication (per patient)	21 (4.9)	7 (5.7)	14 (4.6)	1.27 (0.5–3.24)	0.62

OR odds ratio, *CI* confidence interval

advanced stage cancer ($p < 0.001$), and were more likely to receive postoperative radiation therapy ($p = 0.01$). The patients in the NAC group had a lower preoperative white blood cell count (WBC) at the time of surgery ($p = 0.01$), but the ANC was similar between the two groups. The demographic data for the patients who underwent uni- or bilateral surgery were similar, except that the incidence of hypertension was higher in the bilateral surgery group ($p = 0.04$). The mean postoperative follow-up period was 59.2 ± 22.4) months.

The total complication rate for the first stage of reconstruction was 25.9% per patient (15.6% per breast), with major complications occurring for 9.1% of the patients (9.3% of the breasts). Additional surgery for treatment of complications was required for 4.9% of the patients (Table 2; Fig. 1). Complications occurred in the index breast in 10.9%, the contralateral breast in 2.4%, and both breasts in 2.2% of the cases. Any complication resulted in a delay of any adjuvant therapy (defined as longer than 8 weeks) for 18 patients (4.2%). Delayed radiation therapy occurred for 13 patients who received adjuvant radiation therapy (3.2%) and for 5 patients who received adjuvant chemotherapy first (5.2%).

Higher BMI and diabetes mellitus were correlated with a higher risk of overall complications, whereas bilateral surgery was not associated with a higher risk of complications than unilateral surgery (Table 3). We observed the same findings after adjustment for BMI, diabetes mellitus, and bilateral surgery in the multivariate analysis (Table 3). Higher BMI ($p < 0.001$), breast size greater than a D cup ($p = 0.034$), higher WBC ($p = 0.003$), and higher ANC ($p = 0.002$) were correlated with a higher risk of major complications in the univariate analysis. Youden's index suggested a BMI cutoff of 29.6 kg/m^2 for increased risk of complications, but complications increased gradually with an increase in BMI.

Postoperative complications between the NAC and no-NAC groups were evaluated independently per breast. The findings showed that NAC did not increase overall complications ($p = 0.62$) or major complications ($p = 0.35$), and did not delay adjuvant radiation therapy ($p = 0.37$; Table 4). After adjustment for confounders (BMI, diabetes, and immediate contralateral mastopexy for symmetry) in a multivariate GEE model, NAC was not found to be associated with an increased risk of complications (adjusted OR 0.85; 95% CI 0.53–1.37; $p = 0.50$), major complications (adjusted OR 1.46; 95% CI 0.69–3.06; $p = 0.32$), or multiple complications (OR 1.65; 95% CI 0.7–3.88; $p = 0.33$).

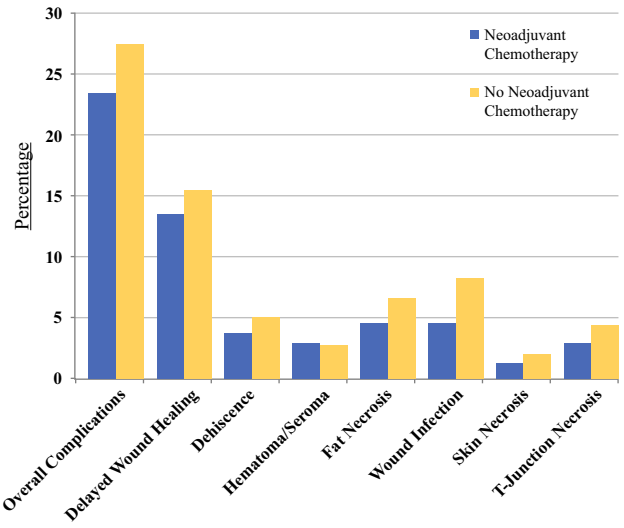

FIG. 1 Complications (per patient) for patients who underwent oncoplastic breast-conserving surgery according to neoadjuvant systemic chemotherapy administration ($p \geq 0.05$ for all variables)

In the multivariate analysis, higher BMI ($p = 0.001$) and higher preoperative WBC ($p = 0.001$) were correlated with a higher risk of complications for patients who received NAC (Table 4). Higher BMI (OR 1.1; 95% CI 1.02–1.19; $p = 0.01$) and higher preoperative WBC (OR 1.19; 95% CI 1.06–1.34; $p = 0.003$) also were correlated with a higher risk of major complications in the multivariate analysis of the patients who received NAC.

Of the patients who received NAC at MD Anderson Cancer Center whose regimens therefore were known, 80 received an anthracycline-based combination as the last component of their chemotherapy, and 28 received single-agent paclitaxel as the last component of their chemotherapy regimen. The groups were similar except that the patients treated last with single-agent paclitaxel were older (average, 55.3 vs. 49.2 years; $p = 0.003$) and more likely to have hypertension ($p = 0.02$) and coronary artery disease ($p = 0.007$). In the univariate analysis, the different regimens did not influence overall complications

TABLE 3 Univariate and multivariate analyses of overall complications for all patients

	Univariate analysis		Multivariate analysis	
Variable	OR (95% CI)	*p* Value	OR (95% CIl)	*p* Value
Neoadjuvant chemotherapy	0.89 (0.55–1.43)	0.62	–	
BMI (continuous)	1.05 (1.03–1.08)	< 0.001	1.05 (1.02–1.07)	0.002
Diabetes mellitus	2.37 (1.45–3.87)	0.001	1.91 (1.14–3.20)	0.001
Hypertension	1.61 (1.06–2.44)	0.025	–	
Immediate contralateral mastopexy for symmetry (per breast)	0.56 (0.35–0.88)	0.013	0.57 (0.36–0.91)	0.002
Preoperative WBC count	1.09 (1.01–1.17)	0.024	–	
ANC	1.09 (0.98–1.22)	0.11	–	
Bra cup size ≥ D	1.29 (0.80–2.09)	0.29	–	

OR odds ratio, *CI* confidence interval, *BMI* body mass index, *WBC* white blood cell, *ANC* absolute neutrophil count

TABLE 4 Univariate and multivariate analyses of overall complications for patients undergoing oncoplastic breast-conserving surgery who received neoadjuvant systemic chemotherapy

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p* Value	OR (95% CI)	*p* Value
Surgery >4 weeks after preoperative chemotherapy versus ≤4 weeks	0.89 (0.36–2.21)	0.81	–	
Taxol chemotherapy	1.05 (0.40–2.76)	0.92	–	
BMI (continuous)	1.07 (1.03–1.11)	< 0.001	1.08 (1.02–1.13)	0.006
Diabetes mellitus	2.70 (1.05–6.97)	0.04	–	
Hypertension	1.93 (0.84–4.41)	0.12	–	
Immediate contralateral mastopexy for symmetry (per breast)	0.34 (0.15–0.80)	0.013	0.17 (0.07–0.46)	0.002
Preoperative WBC count	1.13 (1.04–1.24)	0.005	1.16 (1.06–1.28)	0.001
Preoperative ANC	1.16 (1.02–1.33)	0.024	–	

OR odds ratio, *CI* confidence interval, *BMI* body mass index, *WBC* white blood cell, *ANC* absolute neutrophil count

($p = 0.89$) or major complications ($p = 0.91$), and in subgroup multivariate analysis, the observations remained unchanged. Lower preoperative ANC was not correlated with an increase in the complication rate. The interval between NAC and surgery did not differ significantly between the patients who received a single-agent paclitaxel last and those who received an anthracycline-based regimen (mean, 32.6 vs. 35.1 days; $p = 0.11$).

Among the patients who underwent NAC, 88 (145 breasts) underwent surgery more than 4 weeks after completion of NAC, and 32 (52 breasts) received surgery within 4 weeks. Both the uni- and multivariate analyses demonstrated that the interval between completion of NAC and surgery did not increase overall complications or major complications (Table 4). It should be noted that due to the retrospective study design, this analysis was underpowered to detect a difference and may have been subject to a type 2 error.

DISCUSSION

In this large study of patients treated with complex OBCS involving the mastopexy/breast-reduction technique, the administration of preoperative chemotherapy was not associated with a higher rate of postoperative overall ($p = 0.33$), major ($p = 0.35$), or multiple ($p = 0.33$) complications. The results of this study are in accord with those of others demonstrating similar complication rates for patients undergoing oncologic breast surgery after NAC.[11,12,24–31,40] This is the first study specifically to examine the effect of NAC on outcomes of OBCS.

Despite evidence that overall and recurrence-free survival rates are similar when the oncologic surgery is performed any time up to 8 weeks after completion of NAC, in clinical practice, this interval is significantly shorter due to concerns for adverse oncologic outcomes. Chemotherapy affects rapidly dividing cells, which can impair wound healing and may increase susceptibility to infection in patients undergoing surgery. A short interval between completion of NAC and surgery therefore raises concerns that cell counts may not have recovered, potentially increasing the risk of wound infection and delayed wound healing, with the consequent potential for delayed adjuvant radiotherapy, particularly for patients undergoing more complex OBCS procedures with immediate symmetrizing surgeries.

The recommendation for earlier surgery in the setting of NAC often comes from medical oncologists, particularly when patients receive single-agent paclitaxel as the last component of their chemotherapy regimen because cell count recovery from paclitaxel (usually administered weekly) is faster than with anthracycline-based regimens (which usually are administered every 3 weeks). This is the first study to examine the effect of NAC timing on the rate of complications in breast surgery. No increase in complications was found for patients with an interval shorter than 4 weeks between completion of NAC and surgery compared with an interval of 4 weeks or longer. Our study was underpowered to detect an absolute cutoff, but at least a 4-week interval between NAC and oncologic surgery seems to be a practical and safe compromise. Interestingly, no difference in complication rates based on the last chemotherapy component was found.

Performing contralateral mastopexy for symmetry at the time of OBCS to the index breast did not increase the risk of overall complications compared with performing delayed or no surgery to the contralateral breast, and no differences in the rate of delayed adjuvant radiation therapy were observed. The decision to delay surgery to the contralateral breast likely was due to greater medical comorbidity. Consistent with previous breast surgery literature, BMI was found to be an independent predictor of complications in this study.[25,27,30,41–44] The number of active cigarette smokers was too small for statistical conclusions to be reached regarding independent or multivariable risk in this population. A gradual increase in complication rate was demonstrated with an increase in BMI, and the inflection point was at an approximate BMI of 30 kg/m^2, consistent with other literature.[45,46] Although higher preoperative WBC also correlated with an increased risk of complications for the patients who received NAC, this likely was a confounder due agents often used in the setting of chemotherapy (e.g., pegfilgrastim) to stimulate WBC production artificially.

Evidence exists to support better surgical outcomes for patients treated in high-volume hospitals or by high-volume or specialized surgeons,[47,48] suggesting that these complex patients are optimally managed in high-volume breast cancer centers that have careful patient selection within a multidisciplinary framework. Delayed adjuvant therapy is an unintended consequence of surgical procedures, and although immediate contralateral mastopexy for symmetry was not associated with an increased risk of complications or delayed adjuvant radiation therapy in this patient population, patient selection should strongly take comorbidities, including the presence of obesity, into account. Clinicians should always bear in mind that OBCS is an oncologic procedure with cure as the goal of care, so all efforts should be concentrated on avoiding delays in adjuvant treatments to preserve the associated survival benefit.

The current study had several limitations including the retrospective design and the inherently heterogeneous surgical group of patients given the multiple ablative and reconstructive surgeons. This study also did not evaluate

whether OBCS in the setting of NAC could have an impact on long-term disease control, and this is an area for future investigation. Despite these limitations, this is the first study specifically to evaluate complications after NAC among patients undergoing OBCS. The study focused on the most complex OBCS procedures involving the mastopexy/breast-reduction technique, including patients undergoing synchronous symmetrizing mastopexy/breast reduction. The findings are therefore likely to be generalizable to less complex local parenchymal tissue rearrangement procedures. The findings of this study provide much needed real evidence for the low rates of complications from these procedures in the setting of NAC and highlight the importance of multidisciplinary care and careful patient selection.

CONCLUSIONS

In a high-volume center and with careful patient selection, OBCS can be safely performed for patients receiving NAC without an increased the risk of complications or delayed adjuvant radiation therapy. An interval of at least 4 weeks between completion of NAC and surgery can be regarded as safe irrespective of the chemotherapy regimen used.

ACKNOWLEDGMENT Mariana C.-MacGregor is supported by CPRIT (RP160674) and by a Susan G. Komen Breast Cancer Foundation grant (SAC150061). This study was supported by a cancer center support grant from the National Cancer Institute to the University of Texas MD Anderson Cancer Center (CA016672).

DISCLOSURE There are no conflicts of interest.

REFERENCES

1. Agarwal S, Pappas L, Neumayer L, Kokeny K, Agarwal J. Effect of breast conservation therapy vs mastectomy on disease-specific survival for early-stage breast cancer. *JAMA Surg.* 2014;149: 267.
2. Jacobson JA, Danforth DN, Cowan KH, et al. Ten-year results of a comparison of conservation with mastectomy in the treatment of stage I and II breast cancer. *N Engl J Med.* 1995;332:907.
3. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med.* 2002;347:1233.
4. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med.* 2002;347:1227.
5. Kronowitz SJ, Kuerer HM, Buchholz TA, Valero V, Hunt KK. A management algorithm and practical oncoplastic surgical techniques for repairing partial mastectomy defects. *Plast Reconstr Surg.* 2008;122:1631.
6. Bajaj AK, Kon PS, Oberg KC, Miles DA. Aesthetic outcomes in patients undergoing breast conservation therapy for the treatment of localized breast cancer. *Plast Reconstr Surg.* 2004;114:1442.
7. Clough KB, Cuminet J, Fitoussi A, Nos C, Mosseri V. Cosmetic sequelae after conservative treatment for breast cancer: classification and results of surgical correction. *Ann Plast Surg.* 1998;41:471.
8. Losken A, Ghaz B. An update on oncoplastic surgery. *Plast Reconstr Surg.* 2012;129:382.
9. Carter SA, Lyons GR, Kuerer HM, et al. Operative and oncologic outcomes in 9861 patients with operable breast cancer: single-institution analysis of breast conservation with oncoplastic reconstruction. *Ann Surg Oncol.* 2016;23:3190.
10. Losken A, Dugal CS, Styblo TM, Carlson GW. A meta-analysis comparing breast conservation therapy alone to the oncoplastic technique. *Ann Plast Surg.* 2014;72:145.
11. Clough KB, Lewis JS, Couturaud B, Fitoussi A, Nos C, Falcou MC. Oncoplastic techniques allow extensive resections for breast-conserving therapy of breast carcinomas. *Ann Surg.* 2003;237:26.
12. Clough KB, van la Parra R, Thygesen HH, et al. Long-term results after oncoplastic surgery for breast cancer: a 10-year follow-up. *Ann Surg.* 2017;268:165.
13. Mazouni C, Naveau A, Kane A, et al. The role of oncoplastic breast surgery in the management of breast cancer treated with primary chemotherapy. *Breast.* 2013;22:1189.
14. Da Costa Vieira RA, Carrara GFA, Neto CS, Morini MA, Bretani MM, Folgueira MAAK. The role of oncoplastic breast-conserving treatment for locally advanced breast tumors: a matching case-control study. *Ann Med Surg.* 2016;10:61.
15. Fitoussi AD, Berry MG, Fama F, et al. Oncoplastic breast surgery for cancer: analysis of 540 consecutive cases. *Plast Reconstr Surg.* 2010;125:454.
16. De La Cruz L, Blankenship SA, Chatterjee A, et al. Outcomes after oncoplastic breast-conserving surgery in breast cancer patients: a systematic literature review. *Ann Surg Oncol.* 2016;23:3247.
17. Veiga DF, Veiga-Filho J, Ribeiro LM, et al. Quality-of-life and self-esteem outcomes after oncoplastic breast-conserving surgery. *Plast Reconstr Surg.* 2010;125:811.
18. Chen AM, Meric-Bernstam F, Hunt KK, et al. Breast conservation after neoadjuvant chemotherapy: the M.D. Anderson Cancer Center Experience. *J Clin Oncol.* 2004;22:2303.
19. Mittendorf EA, Buchholz TA, Tucker SL, et al. Impact of chemotherapy sequencing on local-regional failure risk in breast cancer patients undergoing breast-conserving therapy. *Ann Surg.* 2013;257:173.
20. Rastogi P, Anderson SJ, Bear HD, et al. Preoperative chemotherapy: updates of National Surgical Adjuvant Breast and Bowel Project Protocols B-18 and B-27. *J Clin Oncol.* 2008;26:778.
21. Van Nes JGH, Putter H, Julien JP, et al. Preoperative chemotherapy is safe in early breast cancer, even after 10 years of follow-up; clinical and translational results from the EORTC trial 10902. *Breast Cancer Res Treat.* 2009;115:101.
22. Caudle AS, Kuerer HM. Breast conservation therapy after neoadjuvant chemotherapy: optimization of a multimodality approach. *J Surg Oncol.* 2014;110:32.
23. Decker MR, Greenblatt DY, Havlena J, Wilke LG, Greenberg CC, Neuman HB. Impact of neoadjuvant chemotherapy on wound complications after breast surgery. *Surgery.* 2012;152:382.
24. Broadwater JR, Edwards MJ, Kuglen C, Hortobagyi GN, Ames FC, Balch CM. Mastectomy following preoperative chemotherapy. *Ann Surg.* 1991;213:126.

25. Forouhi P, Dixon JM, Leonard RCF, Chetty U. Prospective randomized study of surgical morbidity following primary systemic therapy for breast cancer. *Br J Surg.* 1995;82:79.
26. Godfrey PM, Godfrey NV, Romita MC. Immediate autogenous breast reconstruction in clinically advanced disease. *Plast Reconstr Surg.* 1995;95:1039.
27. Selber JC, Kurichi JE, Vega SJ, Sonnad SS, Serletti JM. Risk factors and complications in free TRAM flap breast reconstruction. *Ann Plast Surg.* 2006;56:492.
28. Azzawi K, Ismail A, Earl H, Forouhi P, Malata CM. Influence of neoadjuvant chemotherapy on outcomes of immediate breast reconstruction. *Plast Reconstr Surg.* 2010;126:1.
29. Van der Hage JH, van de Velde CCJH, Mieog SJSD. Preoperative chemotherapy for women with operable breast cancer. *Cochrane Database Syst Rev.* 2:2012.
30. McCarthy CM, Mehrara BJ, Riedel E, et al. Predicting complications following expander/implant breast reconstruction: an outcomes analysis based on preoperative clinical risk. *Plast Reconstr Surg.* 2008;121:1886.
31. Abt NB, Flores JM, Baltodano PA, et al. Neoadjuvant chemotherapy and short-term morbidity in patients undergoing mastectomy with and without breast reconstruction. *JAMA Surg.* 2014;149:1068.
32. Sanford RA, Lei X, Barcenas CH, et al. Impact of time from completion of neoadjuvant chemotherapy to surgery on survival outcomes in breast cancer patients. *Ann Surg Oncol.* 2016;23:1515–21.
33. Sultan MR, Smith ML, Estabrook A, Schnabel F, Singh D. Immediate breast reconstruction in patients with locally advanced disease. *Ann Plast Surg.* 1997;38:345.
34. Deutsch MF, Smith M, Wang B, Ainsle N, Schusterman MA. Immediate breast reconstruction with the TRAM flap after neoadjuvant therapy. *Ann Plast Surg.* 1999;42:240.
35. Huang J, Barbera L, Brouwers M, Browman G, Mackillop WJ. Does delay in starting treatment affect the outcomes of radiotherapy? A systematic review. *J Clin Oncol.* 2003;21:555–63.
36. Tsoutsou PG, Koukourakis MI, Azria D, Belkacemi Y. Optimal timing for adjuvant radiation therapy in breast cancer: a comprehensive review and perspectives. *Crit Rev Oncol Hematol.* 2009;71:102–16.
37. Hebert-Croteau N, Freeman CR, Latreille J, Rivard M, Brisson J. A population-based study of the impact of delaying radiotherapy after conservative surgery for breast cancer. *Breast Cancer Res Treat.* 2004;88:187–96.
38. Shurell E, Olcese C, Patil S, McCormick B, Van Zee KJ, Pilewskie ML. Delay in radiotherapy is associated with an increased risk of disease recurrence in women with ductal carcinoma *in situ. Cancer.* 2018;124:46–54.
39. Chavez-MacGregor M, Clarke CA, Lichtensztajn DY, Giordano SH. Delayed initiation of adjuvant chemotherapy among patients with breast cancer. *JAMA Oncol.* 2016;2:322–9.
40. Song J, Zhang X, Liu Q, Peng J, Liang X, Shen Y, Liu H, Li H. Impact of neoadjuvant chemotherapy on immediate breast reconstruction: a meta-analysis. *PLOS One.* 2014;9:e98225.
41. Mehrara BJ, Santoro TD, Arcilla E, Watson JP, Shaw WW, Da Lio AL. Complications after microvascular breast reconstruction: experience with 1195 flaps. *Plast Reconstr Surg.* 2006;118:1100.
42. Schaverien M, Munnoch DA. Effect of neoadjuvant chemotherapy on outcomes of immediate free autologous breast reconstruction. *EJSO.* 2013;39:430.
43. Schaverien M, McCulley SJ. Effect of obesity on outcomes of free autologous breast reconstruction: a meta-analysis. *Microsurgery.* 2014;34:484.
44. Tong WMY, Baumann DP, Villa MT, et al. Obese women experience fewer complications after oncoplastic breast repair following partial mastectomy than after immediate total breast reconstruction. *Plast Reconstr Surg.* 2016;137:777.
45. Munhoz AM, Aldrighi CM, Montag E, et al. Outcome analysis of immediate and delayed conservative breast surgery reconstruction with mastopexy and reduction mammaplasty techniques. *Ann Plast Surg.* 2011;67:220–5.
46. de Blacam C, Ogunleye AA, Momoh AO, Colakoglu S, Tobias AM, Sharma R, et al. High body mass index and smoking predict morbidity in breast cancer surgery: a multivariate analysis of 26,988 patients from the national surgical quality improvement program database. *Ann Surg.* 2012;255:551–5.
47. Guller U, Safford S, Pietrobon R, Heberer M, Oertli D, Jain NB. High hospital volume is associated with better outcomes for breast cancer surgery: analysis of 233,247 patients. *World J Surg.* 2005;29:994–9.
48. Hebert-Croteau N, Brisson J, Lemaire J, Latreille J, Pineault R. Investigating the correlation between hospital of primary treatment and the survival of women with breast cancer. *Cancer.* 2005;104:1343–8.