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Tradeoffs Associated with Contralateral Prophylactic Mastectomy in Women Choosing Breast Reconstruction: Results of a Prospective Multicenter Cohort

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Abstract

OBJECTIVE—Assess postoperative morbidity and patient reported outcomes following unilateral and bilateral breast reconstruction in patients with unilateral breast cancer.

BACKGROUND—Relatively little is known about the morbidity associated with and changes in quality of life experienced by patients who undergo contralateral prophylactic mastectomy (CPM) and breast reconstruction. This information would be valuable for decision making in patients with unilateral breast cancer.

METHODS—Women undergoing mastectomy and breast reconstruction for unilateral breast cancer were recruited for this prospective observational study. Postoperative complications following implant and autologous breast reconstruction in patients undergoing unilateral or bilateral mastectomy were recorded. Preoperative and one year patient reported outcomes were measured. Univariate tests and logistic regression analyses were performed, studying the effects of reconstructive method, laterality, and risk factors on surgical complication rates, patient satisfaction and anxiety.

RESULTS—We identified 1144 women who underwent either unilateral (47.2%) or bilateral (52.8%) mastectomies with reconstruction. Bilateral autologous (OR 1.73, 95% CI 1.07–2.81) and implant reconstructions (OR 1.73, 95% CI 1.22–2.47) were associated with a higher risk of complications compared to unilateral reconstructions. Baseline anxiety was greater in women who chose bilateral compared to unilateral implant reconstructions (p=0.001). There was no difference in anxiety levels between groups postoperatively. Postoperatively, women who chose CPM with

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implant reconstructions were more satisfied with their breasts than women with unilateral reconstructions (p=0.034).

CONCLUSIONS—Though higher postoperative complications were observed following CPM and reconstruction, these procedures were associated with decreased anxiety levels and improved satisfaction with breasts for women who underwent implant reconstructions.

Keywords

Contralateral Prophylactic Mastectomy; Breast Reconstruction; Complications; Patient Reported Outcomes; Satisfaction; Anxiety; MROC; BREAST-Q

INTRODUCTION

The benefit of a contralateral prophylactic mastectomy (CPM), in patients without a genetic predisposition or oncologic risk factors remains unclear. Yet trends demonstrate that the number of women with stage I-III breast cancer opting for CPM in the Surveillance, Epidemiology, and End Results (SEER) registry more than doubled (4.2% to 11%) over a six-year period.[1] Moreover, the proportion of breast conserving procedures performed for treatment of early stage breast cancer has declined, with a compensatory rise in the number of CPMs.[2] The role of breast reconstruction in the choice to undergo CPM is also unclear, but it appears to influence patient decision-making. For example, women who choose a bilateral mastectomy undergo reconstruction at rates nearly double those in patients with unilateral mastectomy.[2]

The choice to undergo a CPM involves a number of tradeoffs to be weighed by the patient. On one hand is the possibility of greater morbidity following bilateral mastectomy with reconstruction. On the other is the potential for improvements in health-related quality-of-life (HR-QOL) aspects such as breast cancer related anxiety and body image (including satisfaction with breast appearance and symmetry).[3] Effectively balancing these tradeoffs is a significant challenge for patients who are often actively wrestling with a recent diagnosis of breast cancer. Prospectively obtained objective data on the expected morbidity and HR-QOL that results after reconstruction in patients who opt for CPM instead of a unilateral mastectomy would be essential to help facilitate well informed patient decisions.

The aim of this study is to prospectively measure surgical complications and patient reported outcomes (PROs) in a multicenter cohort undergoing either unilateral or bilateral breast reconstruction for unilateral breast cancer. The first hypothesis is that women who choose CPM have greater surgical complication rates than women with unilateral mastectomies. The second hypothesis is that bilateral reconstructions result in greater HR-QOL relative to similar unilateral reconstructions.

METHODS

Study Population

Patients were recruited as part of the Mastectomy Reconstruction Outcomes Consortium (MROC) Study, a five-year prospective, multicenter cohort study of mastectomy

reconstruction patients funded by the National Cancer Institute. Women 18 years or older undergoing first-time, immediate post-mastectomy breast reconstruction for unilateral carcinoma in situ or cancer treatment were eligible for participation. Women who underwent bilateral mastectomy had the contralateral breast removed prophylactically (CPM) with no genetic, pathologic or radiographic abnormalities present at the time of surgery. Both unilateral and bilateral implant or abdominally based autologous reconstructions were included. Choices of reconstructive options were based on patient and surgeon preferences. Patients were excluded from the study if they answered less than 50% of the preoperative baseline panel of questionnaires; these questionnaires were a combination of PRO instruments and questions on demographic information. Patients were also excluded if they had metastatic breast cancer (Stage IV disease), had a prior mastectomy or underwent bilateral reconstruction with two different methods (Figure 1, Supplemental Digital Content 1, study flow diagram). Over 60 plastic surgeons from 11 centers in the USA (Michigan, New York, Illinois, Ohio, Massachusetts, Washington, D.C., Georgia and Texas) and Canada (British Columbia and Manitoba) contributed patients to the study, which began in February 2012. Appropriate Institutional Review Board (IRB) approval was obtained from all participating sites.

Data Collection

Patients enrolled in the MROC Study completed a series of questionnaires at five specific time-points while enrolled in the study: preoperatively; and one week; three months; one year; and two years post reconstruction. Site staff also performed medical chart reviews and collected clinical data preoperatively, and at one-week, one-year, and two-years post reconstruction. Patients were recruited in person preoperatively and completed the questionnaires either electronically or on paper. These questionnaires consisted of a series of validated PRO instruments that solicited information on health-related quality of life outcomes, treatment satisfaction and socio-demographics. The medical record for each patient was also accessed to obtain demographic and clinical data related to treatment, reconstruction method, and postoperative complications retrospectively. For this study we analyzed PRO data collected preoperatively and at 1 year as well as complications at one year postoperatively.

Questionnaires

The BREAST-Q, is a validated, procedure specific PRO instrument for women undergoing different types of breast surgery.[4] This questionnaire is composed of independent scales, in a variety of domains that assess both satisfaction and health-related quality of life outcomes. Response options are four-point scales ranging from one (very dissatisfied) to four (very satisfied). Item responses for each scale are summed and transformed utilizing the Q-Score program[5] into a range from 0 to 100 for each scale. Higher scores are indicative of greater patient satisfaction.

The Generalized Anxiety Disorder 7 (GAD 7) Scale is a self-reported questionnaire for screening and measuring the severity of generalized anxiety disorder.[6] The questionnaire consists of seven items that are summed to form a total score. A higher score correlates to more anxiety over the past two weeks. The Patient Reported Outcome Measurement

Information System (PROMIS-29) is a self-administered survey for patient reported symptoms. The PROMIS-29 is a short profile form of a longer instrument developed for use in a wide range of conditions.[7] The anxiety instrument measures patient reported anxiety with the questionnaire consisting of four items. A higher score correlates to more anxiety over the past seven days.

Dependent Variables

The dependent variables of the analysis were complications and PRO scores (BREAST-Q, GAD 7, and PROMIS Anxiety). Major complications were defined as complications that required an operative intervention or readmission while minor complications could be managed conservatively on an outpatient basis. Major complications included hematoma, infection requiring intravenous antibiotics, total flap loss, partial flap loss, implant or tissue expander removal, implant malposition, implant leakage or rupture, and capsular contracture (Baker grade III and IV). Minor complications included wound dehiscence, infection requiring oral antibiotics only, mastectomy skin flap necrosis, fat necrosis, scarring, and seroma.

Independent Variables

Demographic variables included age, race, ethnicity (Hispanic/Non-Hispanic), body mass index (BMI), marital status, highest level of education, and household income. The racial group “other” included Asians, Pacific Islanders, Hawaiians, and American Indians. Highest level of education obtained was defined as college degree or not. Household income was categorized into low income (<$50,000 per year), mid income ($50,000 to $99,999 per year), and high income (>$100,000 per year). Clinical variables included comorbidities (Charlson Score), extent of disease, histology, chemotherapy, and radiation therapy. The extent of disease was defined as the following: local disease - disease confined to the breast; or regional disease- axillary or internal mammary lymph nodes positive for cancer. Chemotherapy and radiation therapy were defined as receipt before or after reconstruction.

Statistical Analysis

Sociodemographic and clinical characteristics were compared between those who underwent unilateral versus bilateral reconstruction using chi-square or Fisher’s exact test. All analyses presenting differences in complications between unilateral and bilateral groups were separated by reconstruction type – autologous or implant. Rates of specific types of minor and major complications are given as the observed proportion for those with unilateral versus bilateral reconstructions. To compare the proportion of women who had any complication to those with none by laterality, chi-square tests were performed. A stepwise model building technique with logistic regression was used to build a multivariable model for the odds of any complication. Sociodemographic and clinical characteristics were potential independent variables in the model with the criteria to entry of 0.30 and the criteria to stay of 0.35.

PRO analysis preoperatively and at one year was measured by the BREAST-Q (five scales: satisfaction of breasts, psychological well-being, physical well-being chest, physical well-being abdomen, sexual well-being), PROMIS 29 (anxiety section), and GAD 7. Changes in

PRO scores from baseline to 1 year were analyzed for individual patients. Some of the PRO measures were missing for a proportion of individuals at baseline and at the one year follow-up. To account for this missingness, multiple imputations with chained equations were used to create 10 complete imputed data sets. PROs at one year were approximately normally distributed. Separate linear regression models were run for women who had implants and autologous reconstruction, respectively. Initially, changes in PRO scores were modelled univariably to find the difference in those who had bilateral versus unilateral reconstruction. Then, multivariable models were run controlling for age, BMI, race (white, black, or other), and prior receipt of chemotherapy. Analyses were performed for each imputed data set and the results were combined using Rubin's rules.[8] Analyses were performed in R using packages MI and Zelig.[9,10]

RESULTS

Between February 2012 and July 2014, 3517 patients were recruited from 11 centers in Canada and the USA. Of these, 1144 patients (32.53 %) met the inclusion criteria and had complete data available on post-reconstruction complications and PROs at one year. Details of the study cohort selection are presented in a flow diagram (Figure 1). Among eligible patients, 540 underwent unilateral reconstruction: 343 with implants and 197 with autologous tissue. In comparison 604 patients had CPM with bilateral reconstruction: 482 with implants and 122 with autologous tissue. Table 1 outlines the demographic and oncologic characteristics of the study cohort. Patients who underwent CPM were more likely to be white, younger, college graduates, and earn a higher income compared with those who chose unilateral mastectomy ($P< .05$).

Complications after reconstruction were categorized as minor or major [Tables 2 (Supplemental Digital Content 2), 3 and 4]. Compared with unilateral implant procedures, bilateral implant reconstructions were associated with higher complication rates (25.7% vs 18.4%, p=0.013, Figure 2) and a higher major complication rate (17.2% vs 11.3%, p=0.027). Bilateral autologous procedures were also associated with higher complication rates relative to unilateral autologous reconstructions (55.7% vs 42.6%, p=0.023, Figure 2). A trend toward a higher rate of major complications after bilateral autologous reconstruction was also observed (39.3% vs 30.5%, p=0.10). Controlling for demographic and clinical covariates, bilateral autologous (OR 1.81, 95% CI 1.10–3.00, p=0.020) and bilateral implant reconstructions (OR 1.76, 95% CI 1.21–2.54, p=0.003) were independently associated with a greater odds of complications compared to similar unilateral reconstructions (Table 5).

PROs for the cohort are recorded in Table 6. Baseline BREAST-Q scores for patients undergoing unilateral or bilateral mastectomy with reconstruction were similar. However, baseline anxiety was greater in women who chose bilateral compared to unilateral implant reconstructions as measured by both the GAD (5.95 vs 4.77, p=0.001) and PROMIS (60.19 vs 58.48, p=0.005). Baseline anxiety was not significantly different in patients who chose unilateral or bilateral mastectomy with autologous reconstruction. At one-year postoperatively, multivariable analysis demonstrated that women who chose CPM with implant reconstructions were more satisfied with their breasts than those who chose similar unilateral reconstructions (p=0.0009). There was no difference in satisfaction with breasts at

one year between unilateral and bilateral autologous reconstructions. Anxiety scores at one year (GAD and PROMIS) did not differ significantly between unilateral and bilateral mastectomies with reconstruction.

DISCUSSION

The oncologic benefit of CPM in women with early stage unilateral breast cancer is uncertain with multiple studies reporting no survival advantage.[11–14] The five year risk of developing a second primary tumor in the contralateral breast is relatively low, estimated at 0.5–1% per year in the average breast cancer survivor.[15] This risk is greater in select groups such as patients with genetic predispositions to developing breast cancer, strong personal or family histories of cancer, and prior chest wall radiation; however, the observed rise in the rate of CPM use has been driven primarily by patients who are not at high risk for contralateral breast cancer.[16] Interestingly, the sociodemographic profile of the young, white, educated patients who choose CPM is consistent across studies. Associations between these factors and the decision to undergo CPM are unclear, but highlight the influence of sociocultural aspects on surgical decision-making.

Though the HR-QOL benefits of post-mastectomy breast reconstruction compared to mastectomy alone are well documented,[17] reconstruction is not without potential for significant morbidity. The complications associated with breast reconstruction take on an even greater significance in the context of an elective procedure such as prophylactic mastectomy. The potential for increased morbidity with bilateral, as opposed to unilateral breast reconstruction, has not been evaluated prospectively in this patient population. One recent single institution retrospective study showed that patients undergoing CPM were 2.7 times more likely to have a major complication requiring readmission or additional intervention.[18] Overall complication rates of 28.6% were observed in patients undergoing unilateral mastectomy and 41.6% in those who had CPM. Of note 33% of the included patients were not reconstructed and these patients had significantly lower complication rates, potentially lowering the reported complication rates; complications were also not presented by type of reconstruction. An evaluation of 30 day complications using the NSQIP database also revealed greater odds for overall complications in patients undergoing bilateral mastectomy with implant or autologous breast reconstruction.[19] Patients undergoing bilateral mastectomy and reconstruction with either technique had significantly longer hospital stays and were more likely to require transfusions. With limited follow up time and a focus on complications that occur in the in-patient setting, the overall complication rates reported for unilateral versus bilateral implants (8.8% vs 10.1%) and autologous reconstruction (14.7% vs 21.2%) were relatively lower than has been published by others.[18, 20] Our implant complication rates (18.4%, unilateral and 25.7%, bilateral) and autologous complication rates (42.6%, unilateral and 55.7%, bilateral) are on the higher end of what is reported in the literature. This is likely explained by the prospective nature of this study with rigorous documentation of all complications encountered over the course of a year. Many such complications tend to be overlooked or entirely missed in retrospective studies. In the current cohort, after adjusting for confounders, rates of complications were significantly greater in women undergoing CPM with either autologous or implant based reconstruction (Table 3 and 4). Although greater complication rates and side-effects can be

anticipated following any bilateral compared to unilateral procedure, women may continue to choose CPM for a variety of reasons. One consideration is that although complications may be significantly higher from a statistical standpoint, the rate may be acceptable to patients and/or physicians. An alternate interpretation is that women remain willing to accept complications for other perceived benefits of CPM.

A number of studies have evaluated factors influencing the decision to proceed with CPM. Broadly these can be broken down into clinical or decisional characteristics.[21] Clinical characteristics include, but are not limited to features such as family history of breast cancer, ipsilateral recurrence of breast cancer, history of prior breast biopsy, preoperative Magnetic Resonance Imaging (MRI) testing and availability of reconstruction. Decisional characteristics comprise aspects such as anxiety, fear, or worry of cancer recurrence, desire to avoid future surveillance, desire for reconstructive symmetry, and desire to improve on breast aesthetics. Multiple investigators have cited anxiety as an important factor in the decision making process for women to choose CPM,[21, 22, 23] but few have directly measured preoperative anxiety levels using validated PRO instruments.[24, 25] A prospective questionnaire based study on the surgical decision-making process for CPM showed that patients with less knowledge about breast cancer and greater worry were more interested in CPM.[25] Greater cancer worry ultimately was a significant predictor for patients who went on to have CPM. An evaluation of 45 patients undergoing CPM, using the Hospital Anxiety and Depression Scale, demonstrated no difference in baseline or two-year postoperative anxiety and depression scores when compared to women from the general population.[24] By contrast, in evaluating only patients with unilateral breast cancer, the current study showed significantly greater preoperative anxiety in women who chose a bilateral compared to a unilateral implant reconstruction. With an evaluation of changes in anxiety levels in individual patients from base line to one year postoperatively, no significant difference was found. Appreciating the greater baseline anxiety levels of women undergoing CPM with implant reconstruction, it is fair to consider that these patients have a distinct set of concerns that differentiates them from those choosing autologous tissue.[26] For example, patients who undergo prosthetic reconstruction tend to be younger, lack the abdominal adiposity necessary for autologous reconstruction (Table 8, Supplemental Digital Content 4) and have aesthetic concerns about the donor site scars associated with autologous reconstruction. These younger women are also potentially at a stage in life when careers, relationships and family life are just beginning so a diagnosis of breast cancer tends to have a profound effect. The differences notwithstanding, this data provides objective evidence of the potential benefit of CPM on relieving anxiety in a select group of patients.

Beyond the effect of CPM on anxiety and vice versa, it is important to understand how CPM impacts other aspects of quality of life. Hwang and colleagues approached this question by administering the BREAST-Q to 2,760 patients who had undergone unilateral or bilateral mastectomy with reconstruction. Without evaluating specific reconstruction types, they found that patients undergoing CPM reported higher breast satisfaction scores with lower physical and psychosocial well-being scores.[27] In our assessment of reconstruction types, women who chose a unilateral compared to bilateral prosthetic based breast reconstruction were significantly less satisfied with their breasts as measured by the BREAST-Q; this difference did not exist for autologous reconstructions. Such a difference likely reflects the

asymmetry noted by women when comparing their native breast to an implant and may underlie the choice made by many for CPM as an alternative to a contralateral symmetry procedure (e.g. mastopexy or reduction).[3,26,28] Previous studies demonstrate strong independent associations between the choice for CPM and implant, not autologous, breast reconstruction.[30,31] It is likely that the simplicity of prosthetic breast reconstruction, combined with its absent donor site morbidity and ease of removal in cases of complications has served to facilitate recent U.S. trends towards CPM.[2]

Not surprisingly no difference in satisfaction with breasts was measurable for women who chose unilateral versus bilateral autologous transfer. This makes sense intuitively since in unilateral autologous transfer, the tissue used for reconstruction is very similar in appearance and consistency to breast tissue. It is also interesting to note that women who underwent autologous transfers experienced increased satisfaction with their breasts compared to baseline. This is in contradistinction to women who had either unilateral or bilateral implant reconstructions where postoperative scores were lower than baseline. Taken together, perhaps these findings should be used to advocate for greater numbers of unilateral autologous reconstructions when feasible, since this solution minimizes surgical complications, maximizes chest well-being, and has satisfaction with breasts comparable with bilateral reconstructions. Moreover, health related quality of life data demonstrates greater long-term satisfaction with autologous transfer compared with prosthetic reconstructions.[32] An important negative finding was the absence of a difference in sexual well-being between women who chose unilateral mastectomy and those who chose CPM with either method of breast reconstruction.

Strengths of the current study include its prospective design and patient accrual from multiple institutions with a host of reconstructive surgeons which lends to the generalizability of our findings. This is the first study using preoperative BREAST-Q scores as a covariate to adjust for measured differences in postoperative levels of satisfaction and HR-QOL. Because the BREAST-Q is the only condition specific PRO instrument for breast reconstruction, it may more effectively highlight subtle differences between groups than generic instruments used in previous analyses. A fundamental limitation of this study has to do with the fact that data was not collected on first degree relatives with genetic mutations predisposing them to breast cancer, tumor staging and hormone receptor status, variables known to increase the risk for breast cancer recurrence. In comparing patients who chose CPM versus unilateral mastectomy there may be unmeasured confounders which could not be adjusted for between groups in the final multivariate analyses. This study is also limited by the fact that most of the institutions included are major academic medical centers, making it difficult to comment on subtle variations that might be encountered in community based practices and hospitals. Furthermore, a selection bias is possible with a potential for retention of patients with greater satisfaction and fewer complications. Based on our comparison of included patients and those with missing PRO data (Table 7, Supplemental Digital Content 3, demographic and clinical characteristics of patients with complete or missing PRO data), we have no evidence of missing data in a preferential fashion that would support a selection bias.

CONCLUSIONS

This prospective study demonstrates subjective benefits to CPM including gains in HR-QOL and psychosocial aspects of disease management. Such findings can be used to substantiate CPM especially in the era of patient centeredness advocated by the Institute of Medicine.[33] Despite its higher complications rates, the choice for CPM should remain with patients to decide upon in shared decision-making process with their doctors. Lastly, physicians need to be aware of the current findings in order to present a balanced picture not only to patients considering CPM, but to those considering unilateral mastectomy as well.

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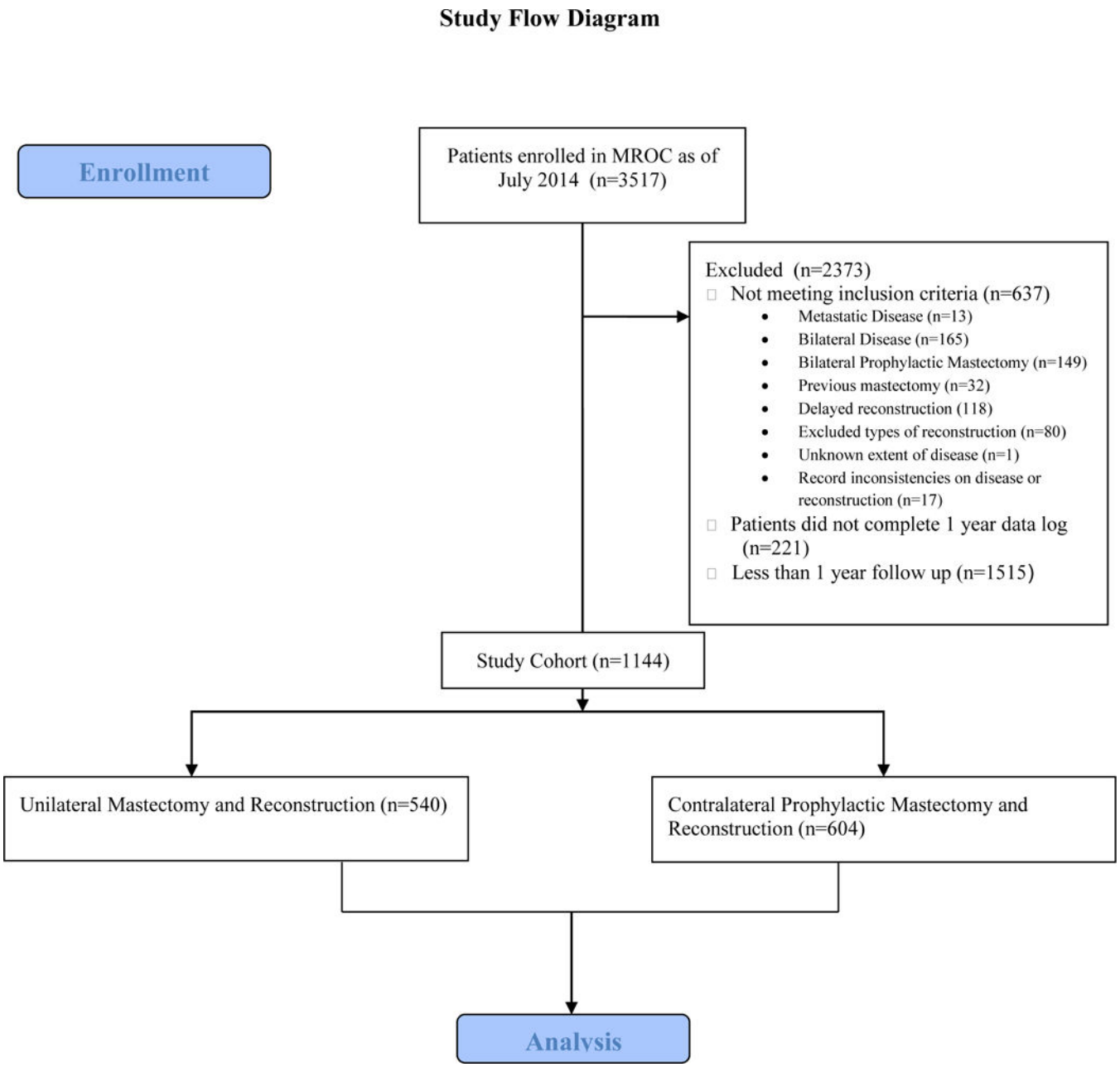

Figure 1.
Study flow diagram. (Supplemental Digital Content 1)

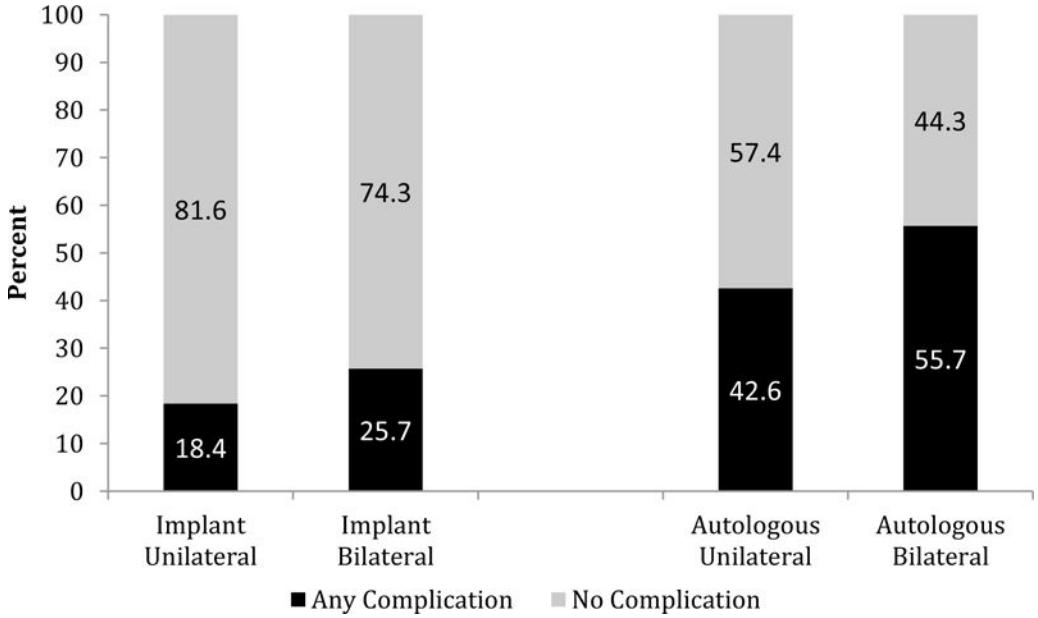

Figure 2.

Rates of any postoperative complication (*) following implant and autologous breast reconstruction by laterality

*Some patients had more than one complication- for this evaluation complications in individual patients were only counted once.

Table 1

Patient Socio-Demographic and Clinical Characteristics (N=1144)

Variable	Unilateral n= 540		Bilateral n= 604		p-value
	n	%	n	%	
Age					<0.0001
≤30	7	1.3	22	3.6	
30–39	36	6.7	122	20.2	
40–49	177	32.8	261	43.2	
50–59	184	34.1	147	24.3	
≥60	136	25.2	52	8.6	
BMI					0.08
≤30	400	74.1	473	78.3	
>30	140	25.9	130	21.5	
Missing	0	0	1	0.2	
Race					0.043
White	460	85.2	539	89.2	
Black	43	8.0	28	4.6	
Other	32	5.9	29	4.8	
Missing	5	0.9	8	1.3	
Ethnicity					0.88
Hispanic	31	5.7	36	6.0	
Non-Hispanic	498	92.2	556	92.1	
Missing	11	2.0	12	2.0	
Education Level					0.009
College degree	381	70.6	467	77.3	
No college degree	157	29.1	135	22.4	
Missing	2	0.4	2	0.3	
Employed					0.004
Yes	356	65.9	446	73.8	

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Variable	Unilateral n= 540		Bilateral n= 604		p-value
	n	%	n	%	
No	177	32.8	152	25.2	
Missing	7	1.3	6	1.0	
Income					0.016
<50,000	101	18.7	94	15.6	
50,000–99,999	190	35.2	181	30.0	
≥100,000	234	43.3	313	51.8	
Missing	15	2.8	16	2.6	
Marital Status					0.054
Single	164	30.4	153	25.3	
Married	373	69.1	449	74.3	
Missing	3	0.6	2	0.3	
Extent of Disease					0.97
Local	392	72.6	439	72.7	
Regional	148	27.4	165	27.3	
Histology*					
DCIS	408	75.6	403	66.7	0.001
LCIS	74	13.7	85	14.1	0.86
Invasive	383	70.9	430	71.2	0.92
Comorbidities					0.42
0	14	1.82.6	11	1.8	
1	468	86.7	538	89.1	
2–3	58	10.7	55	9.1	
Chemotherapy					
Before	57	10.5	99	16.4	0.005
After	202	37.4	218	36.1	0.65
Radiation					
Before	37	6.8	45	7.4	0.78
After	117	21.7	128	21.2	0.85

Using Chi-Square test of independence or Fisher's exact test without unknown group

*Some patients had more than one histopathologic abnormality at the time of the initial diagnosis.

Table 2

Rates of Minor Complications for Unilateral and Bilateral Autologous and Implant Breast Reconstruction. (Supplemental Digital Content 2)

	Autologous n=319		Implant n=825	
	Unilateral	Bilateral	Unilateral	Bilateral
Minor Complication	**n=197 (%)**	**n=122 (%)**	**n=343 (%)**	**n=482 (%)**
Any Minor Complication*	53 (26.9)	36 (29.5)	32 (9.3)	62 (12.9)
Wound dehiscence	10 (5.1)	7 (5.7)	1 (0.3)	11 (2.3)
Wound infection requiring oral antibiotics	11 (5.6)	7 (5.7)	13 (3.8)	28 (5.8)
Mastectomy skin flap necrosis	22 (11.2)	6 (4.9)	15 (4.4)	29 (6.0)
Hypertrophic or keloid scarring	0 (0)	2 (1.6)	1 (0.3)	1 (0.2)
Wound dehiscence at donor site	19 (9.6)	9 (7.4)	–	–
Wound infection requiring oral antibiotics at donor site	9 (4.6)	9 (7.4)	–	–
Hypertrophic or keloid scarring at donor site	2 (1.0)	1 (0.8)	–	–
Abdominal wall bulge, laxity or hernia requiring surgical repair	0	1 (0.8)	–	–
Donor site necrosis	0	1 (0.8)	–	–
Other Minor Complications	4 (2.0)	5 (4.1)	3 (0.9)	3 (0.6)

*Some patients had more than one complication- for this evaluation complications in individual patients were only counted once.

Table 3

Rates of Major Complications for Unilateral and Bilateral Autologous Breast Reconstructions

Major Complication	**Autologous**	
	Unilateral	**Bilateral**
	N=197 (%)	**N=122 (%)**
Any Major Complication	60 (30.5)	48 (39.3)
Post-operative bleeding or hematoma requiring needle aspiration or re-operation	12 (6.1)	10 (8.2)
Wound infection requiring IV antibiotics	7 (3.6)	2 (1.6)
Wound infection requiring surgical drainage	2 (1.0)	3 (2.5)
Acute partial flap necrosis within 30 days	9 (4.6)	5 (4.1)
Flap loss	0 (0)	3 (2.5)
Chronic flap necrosis	18 (9.1)	14 (11.5)
Seroma	4 (2.0)	1 (0.8)
Post-operative bleeding or hematoma requiring needle aspiration or re-operation at donor site	4 (2.0)	2 (1.6)
Wound infection at donor site requiring IV antibiotics	0	3 (2.5)
Wound infection at the donor site requiring surgical or percutaneous drainage of abscess	0	5 (4.1)
Donor site necrosis	5 (2.5)	10 (8.2)
Chronic fat necrosis of the donor site	3 (1.5)	2 (1.6)
Donor site seroma	9 (4.6)	8 (6.6)
Abdominal wall bulge, laxity or hernia requiring surgery	3 (1.5)	7 (5.7)
Deep vein thrombosis	1 (0.5)	0
Pulmonary embolus	0	2 (1.6)
Other Major Complications	8 (4.1)	9 (7.4)

Table 4

Rates of Major Complications for Unilateral and Bilateral Implant-Based Breast Reconstructions

Major Complication	**Implant**	
	Unilateral	**Bilateral**
	N=343 (%)	**N=482 (%)**
Any Major Complication	40 (11.7)	83 (17.2)
Post-operative bleeding or hematoma requiring needle aspiration or re-operation	9 (2.6)	19 (3.9)
Wound infection requiring IV antibiotics	11 (3.2)	25 (5.2)
Wound infection requiring surgical drainage	3 (0.9)	6 (1.2)
Capsular contracture (Baker Class III or IV)	1 (0.3)	8 (1.7)
Implant malposition	1 (0.3)	3 (0.6)
Seroma	12 (3.5)	18 (3.5)
Implant leakage	3 (0.9)	2 (0.4)
Abdominal wall bulge, laxity or hernia requiring surgery	0	1 (0.2)
Tissue expander removal	20 (5.8)	47 (9.8)
Implant removal	7 (2.0)	24 (5.0)
Deep vein thrombosis	3 (0.9)	0
Pulmonary embolus	0	2 (0.4)
Other Major Complications **	2 (0.6)	2 (0.4)

** Other major complications include: negative exploration & washout for suspected hematoma, (n=1); nipple flap necrosis (n=2); pneumothorax (n=1).

Table 5

Multivariable model of any complication for implant and autologous reconstruction

Implant (n=823)		
Variable	**Odds Ratio (95% CI)**	**p-value**
Laterality		0.003
Unilateral	-Reference-	
Bilateral	1.76 (1.21–2.54)	
Age	1.02 (0.99–1.06)	0.21
BMI	1.05 (1.02–1.08)	0.002
Disease Extent		0.07
Local	-Reference-	
Regional	0.67 (0.44–1.03)	
Radiation		0.0001
None	-Reference-	
Ever	2.25 (1.49–3.39)	
Autologous (n=309)		
Variable	**Odds Ratio (95% CI)**	**p-value**
Laterality		0.020
Unilateral	-Reference-	
Bilateral	1.81 (1.10–3.00)	
BMI	1.06 (1.01–1.11)	0.015
Age	1.02 (0.99–1.05)	0.26
Income		0.025
<50,000	-Reference-	
50,000–99,999	1.96 (1.07–3.59)	
≥100,000	1.00 (0.54–1.86)	
Charlson Comorbidity Index		0.28
0	-Reference-	
1	2.13 (0.60–7.51)	
2–3	3.11 (0.75–12.95)	
Disease Extent		0.015
Local	-Reference-	
Regional	2.02 (1.15–3.57)	

Table 6

Comparison of Patient Reported Outcome Scores at Baseline and One Year Post Reconstruction (N=1144)

Outcome	Subset	N Missing	Mean Score at Baseline		Mean Change (Score at 1 year-Score at BL)		Bilateral vs. Unilateral	Multivariable p-value*
			Bilateral	Unilateral	Bilateral	Unilateral		
Breast-Q Satisfaction with Breast	Implant	274	63.69	65.83	−4.48	−10.14	5.67	0.0009
	Autologous	76	57.37	59.68	8.53	6.97	1.56	0.35
Breast-Q Physical Well-Being Abdomen	Implant		91.55	90.28				
	Autologous	83	86.74	87.62	−6.76	−5.57	−1.19	0.99
Breast-Q Psycho-Social Well being	Implant	278	71.73	72.45	−8.68	−7.38	−1.30	0.70
	Autologous	75	66.46	70.05	−0.89	2.83	−3.72	0.37
Breast-Q Physical Well Being Chest/Upper Body	Implant	270	79.41	80.02	−13.19	−10.91	−2.28	0.10
	Autologous	75	74.07	77.11	−6.31	−5.07	−1.23	0.76
Breast-Q Sexual Well Being	Implant	315	59.70	58.63	−9.05	−6.46	−2.59	0.92
	Autologous	91	51.54	55.46	0.87	1.31	−0.45	0.49
GAD7	Implant	280	5.95	4.77	−0.50	0.01	−0.51	0.85
	Autologous	77	5.52	5.31	0.55	−0.40	0.95	0.17
PROMIS- Anxiety Score	Implant	295	60.19	58.48	−5.86	−6.52	0.66	0.45
	Autologous	82	58.66	58.15	−4.88	−6.35	1.47	0.21

*P-value from multivariable model controlling for age, BMI, race (white, black or other) and prior chemotherapy

Negative Effect indicates the score decreased over time

Table 7

Demographic and Clinical Characteristics in patients with complete PRO data (n=711) or any missing PRO data (n=433). (Supplemental Digital Content 3)

Variable	PRO Complete		PRO Missing	
	N	%	N	%
Age				
≤30	20	2.8	9	2.1
30–39	92	12.9	66	15.2
40–49	277	39.0	161	37.2
50–59	212	29.8	119	27.5
≥60	110	15.5	78	18.0
BMI				
≤30	566	79.6	307	70.9
>30	145	20.4	125	28.9
Missing	0	0	1	0.2
Race				
White	643	90.4	356	82.2
Black	26	3.7	45	10.4
Other	33	4.6	28	6.5
Missing	9	1.3	4	0.9
Ethnicity				
Hispanic	34	4.8	33	7.6
Non-Hispanic	661	93.0	393	90.8
Missing	16	2.3	7	1.6
Education Level				
College degree	550	77.4	298	68.8
No college degree	160	22.5	132	30.5
Missing	1	0.1	3	0.7
Employed				
Yes	514	72.3	288	66.5
No	191	26.9	138	31.9
Missing	6	0.8	7	1.6
Income				
<50,000	108	15.2	87	20.1
50,000–99,999	235	33.1	136	31.4
≥100,000	354	49.8	193	44.6
Missing	14	2.0	17	3.9
Marital Status				
Single	177	24.9	140	32.3
Married	532	74.8	290	67.0

Variable	PRO Complete		PRO Missing	
	N	%	N	%
Missing	2	0.3	3	0.7
Extent of Disease				
Local	527	74.1	304	70.2
Regional	184	25.9	129	29.8
Histology (both sides)				
DCIS	509	71.6	302	69.8
IDC	485	68.2	328	75.8
LCIS	104	14.6	55	12.7
Comorbidities				
0	3	0.4	2	0.5
1	5	0.7	4	0.9
2 or more	703	98.9	427	98.6
Chemotherapy				
Before	88	12.4	68	15.7
After	257	36.2	163	37.6
Radiation				
Before	40	5.6	42	9.7
After	139	19.6	106	24.5
Complications				
Minor	104	14.6	79	18.2
Major	138	19.4	93	21.5

Table 8

Patient Socio-Demographic and Clinical characteristics by Procedure Type- Implant vs. Autologous. (N=1144) (Supplemental Digital Content 4)

Variable	Implant n=825		Autologous n=319		p-Value
	n	%	n	%	
Age					<.0001
<30	29	3.5	0	0.0	
30–39	129	15.6	29	9.1	
40–49	320	38.8	118	37.0	
50–59	216	26.2	115	36.1	
>=60	131	15.9	57	17.9	
BMI					<.0001
<=30	677	82.1	196	61.4	
>30	147	17.8	123	38.6	
Missing	1	0.1	0	0.0	
Race					0.047
White	731	88.6	268	84.0	
Black	49	5.9	22	6.9	
Other	36	4.4	25	7.8	
Missing	9	1.1	4	1.3	
Ethnicity					0.032
Hispanic	56	6.8	11	3.5	
Non-Hispanic	753	91.3	301	94.4	
Missing	16	1.9	7	2.2	
Education Level					<.0001
College degree	643	77.9	205	64.3	
No college degree	179	21.7	113	35.4	
Missing	3	0.4	1	0.3	
Employed					0.567
Yes	574	69.6	228	71.5	

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Variable	Implant n=825		Autologous n=319		p-Value
	n	%	n	%	
No	241	29.2	88	27.6	
Missing	10	1.2	3	0.9	
Income					<.0001
<50,000	116	14.1	79	24.8	
50,000–99,999	251	30.4	120	37.6	
>=100,000	436	52.9	111	34.8	
Missing	22	2.7	9	2.8	
Marital status					0.744
Single	226	27.4	91	28.5	
Married	594	72.0	228	71.5	
Missing	5	0.6	0	0.0	
Extent of Disease					0.050
Local	586	71.0	245	76.8	
Regional	239	29.0	74	23.2	
Histology*					
DCIS	583	70.7	228	71.5	0.788
LCIS	132	16.0	27	8.5	0.001
Invasive	605	73.3	208	65.2	0.007
Comorbidities					0.009
0	12	1.5	13	4.1	
1	740	89.7	266	83.4	
2–3	73	8.8	40	12.5	
Chemotherapy					
Before	113	13.7	43	13.5	0.924
After	307	37.2	113	35.4	0.574
Radiation					
Before	36	4.4	46	14.4	<.0001
After	182	22.1	63	19.8	0.393

* Some patients had more than one histopathologic abnormality at the time of the initial diagnosis.