

Original article

Lack of association between breast reconstructive surgery and the development of chronic pain after mastectomy: A propensity matched retrospective cohort analysis



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ABSTRACT

Objectives: To compare if mastectomy with reconstructive surgery had greater incidence of chronic pain compared to mastectomy surgery alone.

Materials and methods: The study was a retrospective cohort. Patients who underwent mastectomies with and without reconstruction responded to the modified short form Brief Pain Inventory and the short form McGill pain questionnaire to identify and characterize pain at least 6 months after the surgical procedure. Propensity matching analysis was used to control for covariates differences in the study groups.

Results: 310 subjects were included and 132 patients (43%) reported the presence of chronic pain. After propensity score matching to adjust for covariate imbalances, the incidence of chronic pain in the mastectomy group who had additional surgery for breast reconstruction was not different compared to the group who had mastectomy surgery alone, 26 out of 68 (38%) and 27 out of 68 (39%), respectively $P = 1.0$. Among patients who had chronic pain, breast reconstruction did not increase the intensity of worst pain in the last 24 h, median (IQR) of 2 (1–5) compared to 4 (1–5) in the no reconstruction group, $P = 0.41$. Type of reconstruction (breast implants vs. flap tissue) did not result in greater incidence and/or intensity of chronic pain.

Conclusions: Breast reconstruction after mastectomy does not result in a greater incidence of chronic pain compared to mastectomy alone. Female patients undergoing breast cancer surgery should not incorporate chronic pain in their decision to undergo reconstructive surgery after mastectomy.

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Introduction

Chronic postsurgical pain has recently been called an epidemic potentially affecting millions of patients undergoing surgical procedures each year [1,2]. Common surgical procedures associated with the development of chronic postsurgical pain included amputation surgery, inguinal hernia repair, thoracic surgery and mastectomies [3–8]. The FDA recently organized a panel named ACTION (Analgesic Clinical Trial Innovations, Opportunities and Network) to hasten the development of preventive strategies to reduce the incidence of chronic postsurgical pain [9]. However, few

strategies seems to be effective to preventive or treat chronic postsurgical pain [10–13].

The incidence of chronic postsurgical pain has been estimated to affect around fifty percent of patients undergoing breast cancer surgery [14]. Well established factors associated with the development of chronic pain after mastectomy include younger patients' age and the performance of axillary lymph node dissection during the surgical procedure [15]. The involvement of a plastic reconstructive surgery after mastectomy has also been considered as a potential contributor to the development of chronic postsurgical pain but the association between reconstructive surgery and the development of chronic pain after breast cancer surgery has yet to be confirmed or refuted [16].

The main objective of the current investigation was to examine an association between breast reconstructive surgery and the development of chronic pain after mastectomy. We hypothesized

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that patients undergoing breast reconstructive surgery after mastectomy would have greater incidence of propensity adjusted chronic pain than the ones having mastectomies without reconstructive surgery. We also sought to determine if the type of reconstruction (breast implants vs. tissue flaps) would affect the development of chronic postsurgical pain.

Material and methods

The study was a retrospective cohort study. Study approval was granted by the Institutional Review Board. Informed consent was obtained from all participant subjects. Subjects with breast cancer who had surgery from January 2008 through August 2013 were sequentially evaluated after at least 6 months of their last surgical procedure. Patients with prior history of chronic pain in the breast or axillary area before surgery and with history of other chronic pain conditions requiring opioid usage were excluded.

Subjects responded to the modified short form Brief Pain Inventory and the short form McGill pain questionnaire to identify and characterize subjects' pain [17,18]. The following data were also extracted from patient's electronic medical records: patient characteristics (age, height and weight), preoperative medications, history of preoperative psychiatric disease (depression and/or anxiety), history of preoperative chronic pain in a different body region (osteoarthritis, back pain, migraines), surgical procedure, surgical duration, surgeon performing the procedure, surgical procedure on axilla, tumor staging, presence and type of breast reconstruction, postoperative opioid consumption, presence, type and number of cycles of chemotherapy, use of radiation treatment. The inpatient and outpatient medical records of all eligible subjects were evaluated by two authors (JB and LN).

The primary outcome was the presence of chronic pain in the breast and/or axillae after the surgical procedure in patients who had mastectomy with and without breast reconstruction. Assuming a 50% incidence of chronic pain, it would be required 66 subjects per group in order to achieve 80% power to detect a 25% reduction in the incidence of chronic pain in the mastectomy only group compared to the mastectomy and reconstruction group using a two tailed alpha set at 0.05.

The Shapiro–Wilk and Kolmogorov–Smirnov tests were used to test the hypothesis of normal distribution. Univariate associations of normally distributed interval data are reported as mean (SD) and were evaluated between subjects with and without breast reconstruction after mastectomy. Non-normally distributed interval and ordinal data are reported as median (range or Interquartile range (IRQ)) and compared between groups using the Mann–Whitney *U* test [19,20]. Categorical data are presented as counts (percentages) and univariate associations were performed by constructing cross tabulations and compared between groups using Fisher's exact test.

To control for covariate bias, we performed a propensity score matched analysis to examine the study groups. The propensity score was the conditional probability for subjects after mastectomy that had breast reconstruction and did not have breast reconstruction, as a binary dependent variable, under a set of pre-determined covariates, added into a multiple logistic regression. Individualized propensity score derived from the logistic regression were determined. Using the estimated propensity scores a one-to-one matched analysis (nearest neighbor with caliber matching) followed by a random selection of a subject who had breast reconstruction with one who did not have breast reconstruction among the closest estimated propensity score matches. The pair of subjects was eligible for matching if the caliber width of pair was within 0.6 SD (standard deviation) of all selected pairs. Cochran and Rubin had suggested that a caliber width of 0.6 SD will remove approximate 90% of the bias in observed confounders [21]. Subjects

who did not have an acceptable range of match were excluded. A $P < 0.05$ was required to reject the null hypothesis. Data were analyzed using Stata version 11 (College Station, Texas, USA).

Results

Three hundred and ten subjects were included in the study. The median time (IQR) time from last surgery to subject's evaluation was 17 (8–27) months. One hundred and thirty two patients (43%) reported the presence of chronic pain in the breast and/or axillary region. Baseline unadjusted surgical and patient characteristics were significantly different in regards to age, body mass index, type of surgery and radiation therapy between the group of patients who had reconstructive surgery and the ones who did not have reconstructive surgery (Table 1).

The unadjusted incidence of chronic postsurgical pain was not different between the mastectomy/no reconstruction group, 31 out of 78 (39%) compared to the mastectomy/reconstruction group, 101 out of 232 (43%), $P = 0.6$. Among subjects reporting chronic postsurgical pain, the rating of worst pain in the last 24 h was not different in the reconstruction group, median (IQR) of 2 (1–5) compared to the no reconstruction group, 4 (1–5), $P = 0.38$. The incidence of chronic pain was not different in patients who had reconstruction with breast implants 77 out of 177 (43%) compared

Table 1
Unadjusted baseline characteristics of patients who had a mastectomy with and without plastic reconstruction.

	No breast reconstruction (n = 78)	Breast reconstruction (N = 234)	P value
Age (years)	57.8 ± 12.2	48.7 ± 9.3	<0.001
BMI (kg/m ²)	29.6 ± 8.3	25.6 ± 5.6	<0.001
History of preoperative depression and/or anxiety			0.23
Yes	15	61	
No	63	171	
History of preoperative pain in other body location			1.0
Yes	12	36	
No	66	196	
Type of surgery			0.001
Unilateral Mastectomy	56	115	
Bilateral mastectomy	22	117	
Axillary lymph node dissection			0.02
Yes	30	57	
No	48	175	
Tumor stage			0.18
0	20	41	
I	26	88	
II	18	68	
III	11	33	
IV	3	2	
Tumor size (cm)	1.3 (0.6–3)	1.65 (0.8–2.6)	0.22
Grade			0.09
0	0	1	
I	17	25	
II	36	120	
III	25	86	
Radiation			0.001
Yes	39	65	
No	39	167	
Chemotherapy			0.70
Yes	38	119	
No	40	113	

Continuous data are presented as mean (SD) or median (IQR). Categorical data are presented as counts (n).

to the one who had reconstruction with flaps 20 out of 44 (42.5%), $P = 1.0$. Among the patients who developed chronic pain in the reconstruction group, patients who had reconstruction with flaps had similar worst pain ratings, median (IQR) of 2 (1–5) as patients who had reconstruction with tissue implants, 2 (1–4.5), $P = 0.87$.

After propensity score matching to adjust for covariate imbalances (Table 2), the incidence of chronic pain in the mastectomy group who had additional surgery for breast reconstruction was not different compared to the group who had mastectomy surgery alone, 26 out of 68 (38%) and 27 out of 68 (39%), respectively $P = 1.0$ (Fig. 1). Among patients who had chronic pain, breast reconstruction did not increase the intensity of worst pain in the last 24 h, median (IQR) of 2 (1–5) compared to 4 (1–5) in the no reconstruction group, $P = 0.41$ (Fig. 2).

Discussion

The most important finding of the current investigation was the lack of association between breast surgery reconstruction and the development of chronic pain after mastectomy for breast cancer. In addition, plastic reconstruction did not lead to greater pain

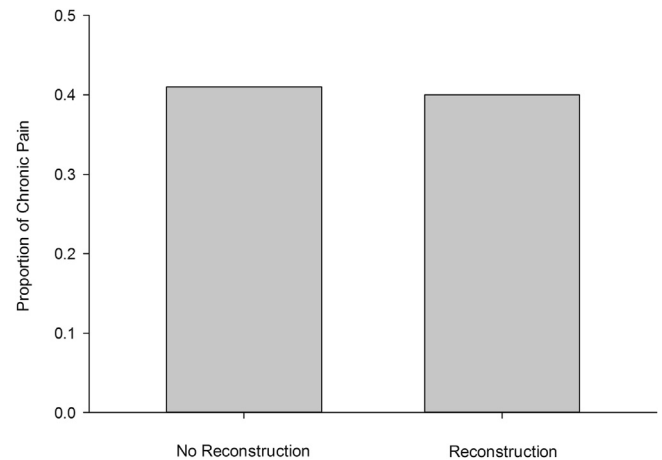


Fig. 1. Bar Charts demonstrating a similar the incidence of chronic post-mastectomy pain in propensity matched patients undergoing mastectomy with breast reconstruction compared to patients undergoing mastectomy without breast reconstruction, $P = 1.0$. Data was analyzed using Fisher's exact test.

Table 2

Propensity matched variables for subjects undergoing total mastectomy with and without breast reconstructive surgery.

	Reconstruction (N = 68)	No reconstruction (n = 68)	Bias reduction (%)	P
Age (years)			35.4	0.43
≥50	53	48		
<50	15	20		
BMI(kg/m ²)			15	0.71
≥25	46	43		
<25	22	25		
History of preoperative depression and/or anxiety			100	1.0
Yes	15	14		
No	53	54		
History of preoperative pain in other body location			100	1.0
Yes	12	11		
No	56	57		
Type of surgery			100	1.0
Unilateral mastectomy	49	49		
Bilateral mastectomy	19	19		
Axillary lymph node dissection			86	0.86
Yes	25	27		
No	43	41		
Tumor stage			25	0.54
0	11	17		
I	25	22		
II	17	16		
III	14	10		
IV	1	3		
Tumor size (cm)	1.7 (0.75–3.65)	1.3 (0.6–2.75)	20.8	0.28
Grade				0.45
0	1	0		
I	11	17		
II	26	31		
III	20	20		
Radiation			100	1.0
Yes	35	35		
No	33	33		
Chemotherapy			–	0.49
Yes	38	33		
No	30	35		

Continuous data are presented as mean (SD) or median (IQR). Categorical data are presented as counts (n).

intensity scores in patients who developed chronic pain. After controlling for covariates in a propensity matched analysis, the incidence of chronic pain was identical in the group who had breast reconstruction and the group who did not have breast reconstruction. Contrary to what we hypothesized, our results deny a relationship between breast reconstruction and the development of chronic post-mastectomy pain in breast cancer patients.

Our findings have important clinical implications since previous studies have supported the role of breast surgery reconstruction in the development of chronic pain after mastectomy [16,22,23]. Since chronic pain can drastically affect overall quality of life of patients, breast surgeons and patients may avoid breast reconstruction [24–26]. In contrast, breast reconstruction surgery after mastectomy for breast cancer offers women the chance of modifying important emotional and esthetic consequences of this devastating disease and should not be avoided in order to prevent the development of chronic pain [27].

It was also interesting to note that despite the more extensive surgical procedure patients who undergone breast reconstruction with tissue flaps had the same incidence of chronic pain as patients who had breast reconstruction with breast implants. In addition, there was also no difference in pain intensity in patients who developed chronic pain after reconstruction with breast implants vs. tissue flaps. The likelihood of developing chronic pain should not interfere with patients' decision on the type of breast reconstruction.

Despite the fact that breast reconstruction did not increase the incidence of chronic pain after mastectomy, it was disappointing to report that currently 43% of patients undergoing mastectomy still develops chronic pain. Our current study is, to the best of our knowledge, the largest investigation performed on chronic pain after mastectomy in the United States. The current incidence rate of chronic pain is similar to ones reported by older studies performed in different countries in Europe [28,29].

No pharmacological strategy is currently established to prevent the development of chronic pain after mastectomy. However, few small studies suggest that the perioperative period is an important therapeutic window in order to reduce the development of post-operative pain [30–33]. Since postoperative pain can be a marker for the development of chronic pain, it is possible that by reducing acute pain may also reduce the rate of transition to chronic pain [34,35]. Nevertheless, larger studies evaluating preventive

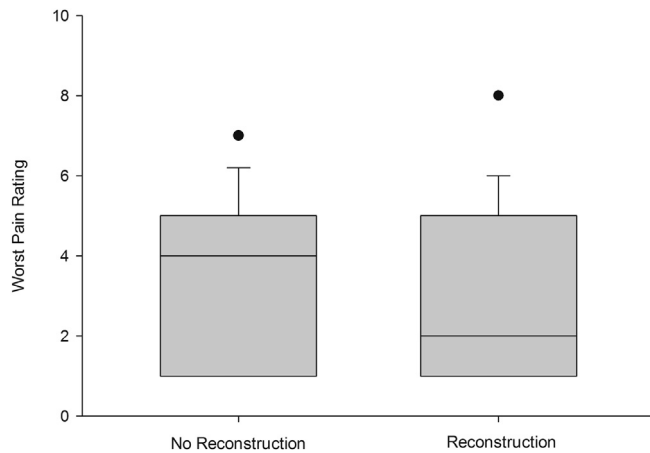


Fig. 2. Box Plots demonstrating worst pain scores in propensity matched patients who did not have breast reconstruction compared to patients who had breast reconstruction, $P = 0.41$. Data was analyzed using the Mann–Whitney U test.

analgesic strategies to reduce chronic persistent surgical pain are needed.

Our study should only be interpreted within the context of its limitations. We did not randomize our subjects to breast reconstruction vs. no breast reconstruction; therefore, we cannot completely exclude the possibility of unknown confounding factors that could have affected our results. However, we utilized propensity matched analysis in order to minimize the possibility of bias. We did not perform sensory testing of the subjects and it is possible that despite similar incidences of pain, the mechanisms that resulted in chronic pain in patients undergoing mastectomy with reconstruction may be different from the mechanisms that resulted in chronic pain in patients who had only mastectomy without reconstruction. Another limitation is that our propensity matched sample was underpowered to detect a difference in worst pain scores in the no reconstruction group compared to the reconstruction group.

Conclusions

In summary, breast reconstruction after mastectomy for breast cancer does not result in a greater incidence and/or severity of chronic pain compared to mastectomy alone. In addition, the type of reconstruction (breast implants vs. flap tissue) also did not alter the incidence and/or severity of chronic pain. Female patients undergoing breast cancer surgery should not incorporate chronic pain in their decision to undergo reconstructive surgery after mastectomy.

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Conflict of interest statement

The authors have no conflict of interest to declare.

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