



Tumor Biology and Racial Disparities in Reconstruction After Mastectomy: A SEER Database Analysis

Journal of Health Disparities Research and Practice

Volume 11 | Issue 3

Article 9

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2018

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Recommended Citation

Ullrich, Sarah J.; Smith, Michael C.; Chung, Paul J.; Kim, Sara Y.; and Sugiyama, Gainosuke (2018) "Tumor Biology and Racial Disparities in Reconstruction After Mastectomy: A SEER Database Analysis," *Journal of Health Disparities Research and Practice*: Vol. 11: Iss. 3, Article 9.

Available at: <https://digitalscholarship.unlv.edu/jhdrp/vol11/iss3/9>

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Tumor Biology and Racial Disparities in Reconstruction After Mastectomy: A SEER Database Analysis

Abstract

Introduction:

Significant disparities in immediate breast reconstruction after mastectomy have persisted, and may even be increasing, despite large-scale efforts to minimize them, such as the Women's Health and Cancer Rights Act of 1998. Immediate breast reconstruction has been shown to lead to higher rates of surgical satisfaction, minimize delay in post-operative cancer treatment, and improve the quality of life and overall well-being of mastectomy patients. However only 25-40% of eligible women in the United States receive reconstruction. The rate of reconstruction is even lower in African American and Hispanic women compared to White women. To better understand this disparity, this study uses national population-based data to examine how demographic factors, socioeconomic factors, and disease characteristics interact and affect the rate of immediate breast reconstruction (IBR) after mastectomy.

Methods:

Women with AJCC7 Stage 0-III breast cancer who underwent mastectomy from 2010 to 2012 were identified in the Surveillance, Epidemiology and End Results Program (SEER) database. Race, Hispanic ethnicity, age, marital status, insurance status, tumor grade, AJCC7 stage and hormone receptor/Her2Neu profile were compared between women undergoing mastectomy with IBR and mastectomy alone using univariate and multivariate analysis.

Results:

We identified 51,115 women who underwent mastectomy for Stage 0-III breast cancer from 2010-2012, of whom 15,389 (30.1%) received IBR. On multivariate analysis, age (p

Conclusion:

The decision to undergo reconstruction after mastectomy is influenced by many factors. Our results show that even after adjusting for tumor characteristics, socioeconomic factors are independently associated with receiving IBR after mastectomy. Further research is needed to elucidate the factors that influence the decision to undergo IBR in order to eliminate these persistent disparities.

Keywords

breast; reconstruction; race

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Journal of Health Disparities Research and Practice
Volume 11, Issue 3, Fall 2018, pp. 128-136
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ABSTRACT

Introduction: Significant disparities in immediate breast reconstruction after mastectomy have persisted, and may even be increasing, despite large-scale efforts to minimize them, such as the Women's Health and Cancer Rights Act of 1998. Immediate breast reconstruction has been shown to lead to higher rates of surgical satisfaction, minimize delay in post-operative cancer treatment, and improve the quality of life and overall well-being of mastectomy patients. However only 25-40% of eligible women in the United States receive reconstruction. The rate of reconstruction is even lower in African American and Hispanic women compared to White women. To better understand this disparity, this study uses national population-based data to examine how demographic factors, socioeconomic factors, and disease characteristics interact and affect the rate of immediate breast reconstruction (IBR) after mastectomy.

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INTRODUCTION

Breast cancer is the most common cancer in women in the United States, with 224,147 cases diagnosed in women in 2012, and is the second leading cause of cancer deaths in women, with increasing incidence (Centers for Disease Control and Prevention, 2018, June 12). Black women have a worse prognosis than White women, often presenting at a later stage and with a shortened survival rate. Numerous investigators have explored this difference, which has been attributed to differences in screening, socioeconomic status, insurance status, treatment regimen and timing, comorbidities, and tumor biology (Byers et al., 2008; Carey et al., 2006; Chagpar, Crutcher, Cornwell, & McMasters, 2011; Clarke et al., 2012; Cross, Harris, & Recht, 2002; Curtis, Quale, Haggstrom, & Smith-Bindman, 2008; Dent et al., 2007; Gorey et al., 2009; Gorin, Heck, Cheng, & Smith, 2006; Grann et al., 2006; Haas et al., 2008; Hershman et al., 2005; McBride et al., 2007; McCarthy et al., 1998; Ooi, Martinez, & Li, 2011; Smith-Bindman et al., 2006; Tammemagi, Nerenz, Neslund-Dudas, Feldkamp, & Nathanson, 2005; Ward et al., 2004).

There are three molecular markers currently used to classify breast cancer; Estrogen Receptors, Progesterone Receptors and Her2Neu receptors. Triple Negative Breast Cancer (TNBC) does not express any of these receptors, and has the most aggressive tumor biology. TNBC is associated with diagnosis at a younger age, high-tumor grade, larger mean tumor size at presentation, and higher rates of mortality compared to other tumor subtypes. The highest rate of TNBC occurs in young Black women (Clarke et al., 2012; Dent et al., 2007).

Though breast-conserving therapy is more prevalent, mastectomy is a commonly performed procedure, accounting for 38% of resections for early-stage breast cancer (Mahmood et al., 2013). After mastectomy, immediate breast reconstruction (IBR) has been shown to improve surgical satisfaction, minimize pain, improve physical and sexual function while not delaying time to adjuvant treatment or increasing the risk of disease recurrence (Eltahir et al., 2013; Yang, Newman, Lin, et al., 2013). However, only thirty-seven percent of women in one large database study were noted to undergo IBR (Eltahir et al., 2013). This is the case despite efforts such as the Women's Health and Cancer Rights Act of 1998, which mandates insurance coverage for reconstruction in women who undergo mastectomy.

Further compounding the issue, Black women undergo IBR at a rate significantly lower than their White counterparts after mastectomy (Tseng et al., 2004; Yang, Newman, Reinke, et al., 2013). The objective of this study was to use a national population-based data to examine how demographic factors, socioeconomic factors, and disease characteristics interact and affect the rate of IBR after mastectomy.

METHODS

Participants

This study was granted exempt status approved by the Institutional Review Board. Women with American Joint Committee on Cancer (AJCC) 7 Stage 0 – III breast cancer who underwent surgical treatment for pathologically confirmed breast cancer were selected from all 18 registries of the Surveillance, Epidemiology, and End Results (SEER) database. Subjects were categorized as having undergone mastectomy alone or mastectomy with immediate breast reconstruction (IBR). The following patients were excluded: male patients, patients with stage IV disease, patients whose case was reported via death certificate or autopsy, and patients whose type of surgery was

unknown. Stage IV patients were excluded as surgical resection is not typically a first-line treatment for patients presenting at this disease stage.

Design

Both tumor specific and socioeconomic factors were analyzed. Patients were divided into four mutually exclusive subtypes based on their Her2-Neu and Hormone Receptor (HR) status. Patients who are Estrogen and/or Progesterone receptor positive were considered to be HR positive. Patients were also stratified based on their AJCC and pathologic grade (1-4). Women were split into age groups (<40, 40-49, 50-59, 60-69, 70-79 and ≥ 80) and further categorized by race (Caucasian, African-American and Other - American Indian/Alaska Native, Asian/Pacific Islander), Hispanic ethnicity, marital status (married, single, separated/divorced, and widowed), and insurance status (private insurance, uninsured, and Medicaid).

Statistical Analysis

A chi squared test for association was used to determine which variables were associated with IBR. A multivariate logistic regression analysis using all statistically significant variables was then performed to evaluate which variables were independently associated with IBR. Tumor subtype, AJCC7 stage, pathologic grade, race, Hispanic ethnicity, marital status and insurance type were included in the multivariate regression. Both tests were two-tailed and a p-value < 0.05 was considered statistically significant. The C-statistic was used to determine the model's discriminative ability. The Hosmer-Lemeshow statistic was used to determine goodness of fit. All analyses were conducted using SPSS version 24 ("IBM SPSS Statistics for Macintosh," 2016).

RESULTS

From 2010 – 2012, there were 51,115 patients who underwent mastectomy for breast cancer. The rate of IBR was 30.10% (n = 15,386).

Univariate Analysis

Univariate analysis (Table 1) revealed statistically significant difference in IBR rates associated with tumor subtype (χ^2 (3) = 75.15, p <0.0001), age (χ^2 (5) = 6116.67 p <0.0001) AJCC7 stage (χ^2 (3) = 649.40, p <0.0001) pathologic grade (χ^2 (3) = 36.21, p <0.0001), race (χ^2 (2) = 186.81 p <0.0001), Hispanic ethnicity (χ^2 (1) = 68.70, p <0.0001), marital status (χ^2 (3) = 1913.11, p <0.0001) and insurance type (χ^2 (2) = 953.35, p <0.0001).

Table 1: Univariate analyses of factors associated with IBR

	Sample Size	% of sample	Reconstruction rate (%)	χ^2	<i>p</i> value
Subtype				75.15	<0.0001
Her2 + / HR +	5988	11.70	32.2		
Her2 + / HR -	2947	5.8	28.6		
Her2 - / HR +	35584	69.6	30.7		
TNBC	6596	12.9	25.9		
Age				6116.67	<0.0001
< 40	3696	7.2	49.8		
40-49	10425	20.4	48		
50-59	12812	25.1	37.5		
60-69	12009	23.5	24.8		
70-79	7722	15.1	9		
≥ 80	4451	8.7	1.6		
Stage				649.40	<0.0001
is	1046	2	42.3		
I	19846	38.8	34.9		
II	19975	39.1	29.1		
III	10248	20	21.6		
Grade				36.21	<0.0001
1	9276	18.1	32.1		
2	22411	43.8	30.4		
3	19139	37.4	28.7		
4	289	0.6	30.4		
Marital Status				1913.11	<0.0001
Married	30156	59	35.7		
Single	7804	15.3	28.5		
Separated	/				
Divorced	6221	12.2	12.2		
Widowed	6934	13.6	13.6		
Race				186.81	<0.0001
White	40607	79.4	31.5		
Black	5339	10.4	25.9		
Other	5169	10.1	23.6		
Hispanic				68.70	<0.0001
No	45297	88.6	30.7		
Yes	5818	11.4	25.4		
Insurance Status				953.35	<0.0001
Uninsured	1046	2	19.6		
Medicaid	7268	14.2	15.4		
Insured	42801	83.7	32.9		

Multivariate Analysis

A logistic regression model was created using the factors found to be associated with patients receiving IBR. In the multivariate logistic regression analysis, age ($p < 0.0001$), marital status ($p < 0.0001$), race ($p < 0.0001$), Hispanic ethnicity ($p < 0.0001$), grade ($p = 0.0045$), insurance status ($p < 0.0001$), AJCC7 stage ($p < 0.0001$), and ER/PR/Her2 receptor status ($p < 0.0001$) were all independently associated with IBR. Patients more likely to undergo mastectomy with IBR were younger (age < 40: OR = 2.11; age 40 – 49: OR = 1.66) and presented at a less advanced stage

(stage is: OR = 1.87; stage I: OR = 1.37). Factors independently associated with not undergoing IBR were Black race (OR = 0.75), Hispanic ethnicity (OR = 0.62), being uninsured (OR = 0.39) or insured by Medicaid (OR = 0.36), tumor grade 3 (OR = 0.93), presenting at an advanced stage (stage III: OR 0.64), and having triple negative disease (OR = 0.79).

The C-statistic for this model was 0.768, demonstrating good discriminative ability. The Hosmer-Lemeshow statistic ($p = 0.928$) suggesting that the model does not over-fit the data.

Table 2: Multivariate logistic regression of factors predicting IBR

	OR	95% CI	<i>p</i> value
Subtype			
Her2 + / HR +	Ref		
Her2 + / HR -	0.94	.85 - 1.05	0.291
Her2 - / HR +	1.05	.99 - 1.13	0.115
TNBC	0.83	.77 - .91	<0.0001
Age			
< 40	2.11	1.95 - 2.29	<0.0001
40-49	1.66	1.57 - 1.75	<0.0001
50-59	Ref		
60-69	0.50	.47 - .52	<0.0001
70-79	0.14	.13 - .16	<0.0001
≥ 80	0.03	.02 - .03	<0.0001
Stage			
is	1.87	1.62 - 2.16	<0.0001
I	1.37	1.30 - 1.44	<0.0001
II	Ref		
III	0.64	.60 - .68	<0.0001
Grade			
1	Ref		
2	0.96	.91 - 1.02	0.203
3	0.89	.83 - .95	0.001
4	0.88	.66 - 1.18	0.397
Marital Status			
Married	Ref		
Single	0.82	.77 - .87	<0.0001
Separated	/		
Divorced	0.94	.88 - 1.00	0.056
Widowed	0.67	.60 - .74	<0.0001
Race			
White	Ref		
Black	0.75	.70 - .81	<0.0001
Other	0.49	.45 - .52	<0.0001
Hispanic			
No	Ref		
Yes	0.62	.58 - .66	<0.0001
Insurance Status			
Uninsured	0.39	.34 - .46	<0.0001
Medicaid	0.37	.34 - .39	<0.0001
Insured	Ref		

DISCUSSION

Our analysis of immediate breast reconstruction after mastectomy demonstrates that there are significant disparities among women who undergo this procedure. This disparity was multifactorial, with race, ethnicity, insurance status, age, stage, grade, and tumor subtype all shown to be independently associated with rate of reconstruction on multivariate logistic regression. Though previous studies have these demographic variables to be significant, tumor subtype has not been extensively studied as a predictor of the likelihood of immediate reconstruction (Tseng et al., 2004; Yang, Newman, Reinke, et al., 2013).

In our study, Black women were significantly less likely to undergo immediate breast reconstruction than their White counterparts. Previous studies have associated inferior breast cancer care with socioeconomic status and lack of insurance (Gorey et al., 2009; Haas et al., 2008). However, even controlling for marital and insurance status in our multivariate logistic regression, Black women were less likely to undergo reconstruction. Additionally, we know of no other study which has investigated the hormone receptor status as an independent predictor of reconstruction. Perhaps armed with knowledge of aggressive tumor biology, physicians and patients are less apt to pursue immediate reconstruction.

A diagnosis of breast cancer, particularly one requiring mastectomy, is an anxiety-provoking situation in which a woman faces both medical concerns of longevity as well as psychosocial concerns related to mastectomy. The benefits of immediate breast reconstruction are well-demonstrated. Eltahir et al. (2013) demonstrated that women who underwent IBR showed a significant improvement in satisfaction with their physical appearance. This cohort also had improved psychological and sexual outcomes, along with improved physical performance and had less pain and physical limitations than their counterparts who did not undergo reconstruction (Eltahir et al., 2013).

The Women's Health and Cancer Rights Act of 1998 aimed to improve rates of reconstruction by requiring that health insurance companies pay for reconstruction after mastectomy. However, actual rates of reconstruction remain low. Our study demonstrates the complex, multifactorial nature of this issue. In a multivariate logistic regression analysis, we have demonstrated that even while controlling for age, race, socioeconomic status, and tumor stage women with triple-negative breast cancer are 17% less likely to get IBR than women with Her2 positive, hormone receptor positive breast cancer.

Our study has several limitations. It is a retrospective database study, and thus is limited to the variables contained in that database. This may lead to biased estimates if other variables, which are not recorded in the SEER database, influence the likelihood a woman undergoes IBR. The molecular variation of breast cancer is far more complex than the four subtypes described by SEER, so we could potentially be over- or understating the effect of molecular markers on rates of reconstruction. Additionally, with such a large sample size, clinically insignificant differences can be seen as statistically significant.

This study also has a number of strengths. It is representative of nationwide cases of breast cancer, and thus highly generalizable to the United States population. The SEER database represents roughly 28% of cancer cases in the United States. Second, the large sample size of the study increased our statistical power and decreased the probability of committing a type 2 error. Third, we were able to control our statistical models for a number of confounders in a way that includes tumor biology subtypes. This is important as the knowledge of the molecular biology of

breast cancer continues to grow.

In conclusion, we have demonstrated that several factors, including receptor status, influence the rate of immediate reconstruction post-mastectomy. Further research should aim to identify the particular reasons for this disparity. Rates of reconstruction following mastectomy could potentially be used as an indicator of the quality of care of an institution. This may serve to improve rates of reconstruction and eliminate the disparities that persist.

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