

# Characteristics of Breast Cancer Patients Who Refuse Surgery

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**Abstract.** *Aim: This study describes the demographic, socioeconomic, and tumor-specific characteristics of patients who refuse breast cancer surgery. Materials and Methods: This is a retrospective study of breast cancer patients from 2004-2015 captured by the National Cancer Data Base. Demographic, socioeconomic, and tumor-specific predictors were compared between patients who refused breast cancer surgery versus those who agreed to surgery, using bivariate and multivariate models. Results: A total of 2,445,870 patients met the inclusion criteria. On multivariate analysis, black and Asian patients had higher odds of refusing surgical treatment compared to whites (OR=2.16, CI=2.05-2.28,  $p<0.001$ ), (OR=1.58, CI=1.41-1.76,  $p<0.001$ ), respectively. Moreover, patients with government insurance (OR=1.97, CI=1.86-2.09,  $p<0.001$ ) and uninsured patients (OR=3.91, CI=3.50-4.36,  $p<0.001$ ) were found to have higher odds of surgical treatment refusal when compared to patients with private insurance. Conclusion: Specific demographic and disease-specific characteristics are related to refusing potentially life-saving breast cancer surgery.*

In 2019, 1,762,450 new breast cancer cases and 606,880 cancer deaths are projected to occur in the United States (1). Furthermore, breast cancer is the most common cancer in women and second most common cause of cancer death (1). Refusing surgery is a brave decision that has a deleterious effect on breast cancer mortality and is more commonly related to advanced disease, which has a poor prognosis (2). Previous studies focused on patients with pancreatic cancer who refused

surgery demonstrated that there were disparities in the refusal of cancer-directed surgery and that several variables, such as insurance, sex, and race, were independently associated to this outcome (3, 4). However, studies on breast cancer have not elucidated groups likely to refuse surgical treatment. Therefore, this study's objective was to describe the demographic, socioeconomic, and tumor-specific characteristics related to surgery refusal in the United States (US) breast cancer population using the National Cancer Database (NCDB).

## Materials and Methods

This study was a retrospective cohort analysis of the NCDB, which is a program of the Commission on Cancer of the American College of Surgeons and the American Cancer Society. NCDB captures approximately 70% of newly diagnosed US cancer patients (5). This study was exempt from Institutional Board Review due to the de-identified data.

Women and men diagnosed with breast cancer (disease stages I, II, and III) between January 1st, 2004 and December 31st, 2015 were included in the study. Patients who were diagnosed at autopsy or who were only reported to have breast cancer on death certificate, but not on clinical record were excluded. Patients with stage IV disease were also excluded because this group typically is not offered surgical treatment per guidelines (6). The inclusion and exclusion criteria are outlined in Figure 1.

The NCDB variable "Reason for no Surgery" was used to identify the cohort of patients who refused surgery even when it was recommended by the treating physician. Patients were filtered and separated into two groups for comparison: patients who refused surgery vs. patients who received surgery.

The following patient-specific variables abstracted: age, gender, race, insurance status, income, education, population density and facility type. Disease-specific characteristics abstracted include: disease behavior, disease stage, histology, tumor size, laterality, and triple-negative disease assessment. These covariates were selected because they characterize the patient- and disease-specific variables that could influence the decision to refuse surgical treatment for breast cancer.

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Patient- and disease-specific characteristics were compared between patients who had surgery *versus* patients who refused surgery. The  $\chi^2$  test was used to compare explanatory variables and the rate of surgery treatment refusal. A multivariate regression model was created to adjust for potential confounders, patient-specific characteristics and disease-specific characteristics affected the odds of refusing surgical treatment. Patients with any missing data were excluded from regression models. Significance was set at a  $p < 0.05$ . Statistical analysis was performed using SPSS 25.0 statistical software (SPSS Inc., Chicago, IL, USA).

**Results**

Our NCDB search identified 2,445,870 patients diagnosed with breast cancer during the study period, 2,259,024 of whom met inclusion criteria. The  $\chi^2$  test revealed that demographic characteristics had an association with surgical treatment refusal (Table I). Patients who were 80 years of age or older were associated with surgery refusal ( $p < 0.001$ ) when compared to patients who were younger. Furthermore, black race had a significant association with treatment refusal ( $p < 0.001$ ), while white patients were less prone to refuse treatment. Government insurance and patients with no insurance were associated to surgery refusal ( $p < 0.001$ ) when compared to patients with private insurance.

Tumor-specific characteristics were also found to influence treatment refusal (Table II). Invasive behavior and tumor stages II and III showed a positive association with treatment refusal ( $p < 0.001$ ). On histology examination, ductal carcinoma and mixed carcinomas ( $p < 0.001$ ) had a negative association with surgical refusal ( $p < 0.001$ ), while lobular carcinomas showed a significant association with surgical treatment refusal ( $p < 0.001$ ). Laterality of the tumor showed no significant difference. Patients who refused breast cancer surgery had a lower rate of triple-negative breast cancer ( $p < 0.001$ ) when compared to patients who accepted treatment.

When adjusted for confounders (Table III), our results showed that patients aged 60 to 80 years (OR=1.2; CI=1.12-1.28) and more than 80 years (OR=8.14; CI=7.60-8.72) had higher odds of refusing surgical treatment than patients aged 40 to 60 years. Women (OR=1.48; CI=1.48-1.85) were found to have higher odds of refusing breast cancer surgery than men with breast cancer. Black (OR= 2.30; CI=2.17-2.43) and Asian (OR=1.62; CI=1.44-1.82) patients were also found to have higher odds of refusing surgical treatment, compared to white patients. No significant difference was found in Native American patients when compared to white patients. Moreover, patients with government insurance (OR=1.97; CI=1.85-2.09) and uninsured patients (OR=3.91; CI=3.46-4.42) were found to have higher odds of surgical treatment refusal when compared to patients with private insurance. Also, we found that patients that live in a zip code in which <7% of the population did not graduate high school (OR=1.11; CI=0.85-0.98) have higher odds of breast cancer

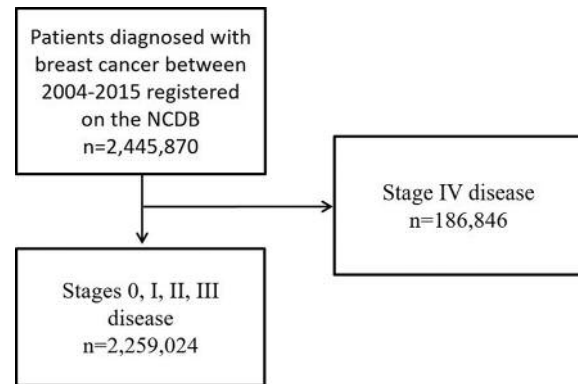


Figure 1. Inclusion and exclusion criteria. NCDB, National Cancer Database.

surgery refusal than patients that live in a zip code in which >21% of the population did not graduate high school. Patients with breast cancer stages II (OR=1.88; CI=1.45-2.44) and III (OR=2.99; CI=2.30-3.89) were more likely to refuse surgical treatment when compared to stage 0 patients. When compared to triple-negative breast cancer, patients with non-triple-negative disease had higher odds of refusing breast cancer surgery (OR=1.81; CI=1.64-2.00).

**Discussion**

Our study results show that there is a number of patient and disease characteristics associated with refusing surgical treatment. These characteristics include higher age at diagnosis, female gender, black and Asian race, government or no insurance, living in zip codes in which a higher percentage of the population did not graduate high school, disease stages II and III, adenocarcinomas, and non-triple-negative breast cancer. It has been shown that refusing surgery for breast cancer, at any stage, can significantly decrease survival and therefore, it is important to understand what factors may impact a patient’s choice of refusing surgery (2).

Our findings that medical treatment is more often refused by patients with higher age have been also found in other cancer studies (7, 8). Previous studies have demonstrated that higher age independently increases the odds of refusing cancer surgery (2, 9, 10). This could be caused by different factors, such as shorter life expectancy, higher likelihood of surgical adverse events, or higher rate of comorbidities. It has also been demonstrated that elderly patients are less likely to get surgery for cancer than younger patients (11).

An interesting finding of this study is that women have independently higher odds of refusing breast cancer surgery than men. Although not easy to explain, it could be due to

Table I. Chi-square analysis of demographic characteristics.

Variable	Treated		Refused treatment		p-Value
	N	%	N	%	
Age					<0.001
18-40 years	101805	4.5	164	1.6	
40-60 years	972155	42.9	2072	20.7	
60-80 years	992631	43.8	3062	30.5	
>80 years	200420	8.8	4732	47.2	
Total	2267011	100.00	10030	100.00	
Gender					0.904
Male	19862	0.9	89	0.9	
Female	2247149	99.1	9941	99.1	
Total	2267011	100.0	10030	100.0	
Race					<0.001
White	1904096	85.50	7448	75.80	
Black	243873	10.90	2012	20.50	
Asian	73648	3.30	346	3.50	
Native American	5677	0.30	24	0.20	
Total	2227294	100.00	9830	100.00	
Insurance status					<0.001
Private	1225996	55.00	2218	22.50	
Government	961410	43.10	7282	73.90	
Not insured	40988	1.80	355	3.60	
Total	2228394	100.00	9855	100.00	
Average income in zip code					<0.001
Less than \$38,000	323536	14.4	1905	19.1	
\$38,000 \$47,999	859538	38.2	3232	32.5	
\$48,000 \$62,999	597992	26.6	2581	25.9	
\$63,000 +	468077	20.8	2240	22.5	
Total	2249143	100.0	9958	100.0	
% with no HSD in zip code					<0.001
21% or more	317605	14.1	1567	15.7	
13-20.9%	659225	29.3	2534	25.4	
7-12.9%	747453	33.2	3312	33.3	
Less than 7%	525788	23.4	2546	25.6	
Total	2250071	100.0	9959	100.0	
Population density					<0.001
Metropolitan	1910033	86.80	8621	88.30	
Urban	257411	11.70	1028	10.50	
Rural	32508	1.50	118	1.20	
Total	2199952	100.00	9767	100.00	
Facility type					<0.001
Academic/Research*	657054	30.30	3098	31.40	
Comprehensive community*	1047765	48.40	4409	44.70	
Community*	217882	10.10	1178	11.90	
Integrated network*	242505	11.20	1181	12.00	
Total	2165206	100.00	9866	100.00	
Charlson-Deyo score					<0.001
No Comorbidity	1926315	85.40	8162	83.00	
Score 1	279551	12.40	1236	12.60	
Score 2 or more	48667	2.20	441	4.50	
Total	2254533	100.00	9839	100.00	

HSD, High school diploma. \*Cancer Program.

the deformity and greater psychological impact that mastectomy can have on women when compared to men. A previous study on patients with resectable pancreatic cancer

Table II. Chi-square analysis for disease-specific characteristics.

Variable	Treated		Refused treatment		p-Value
	N	%	N	%	
Behavior					<0.001
<i>In situ</i>	456720	21.00%	1579	15.70%	
Invasive	1718396	79.00%	8447	84.30%	
Total	2175116	100.00%	10026	100.00%	
Stage					<0.001
Stage 0	471464	21.70%	1613	16.10%	
Stage I	945658	43.50%	2770	27.60%	
Stage II	568330	26.10%	3673	36.60%	
Stage III	189664	8.70%	1970	19.60%	
Total	2175116	100.00%	10026	100.00%	
Histology					<0.001
Papillary	8064	0.40%	76	0.80%	
Squamous	766	0.00%	3	0.00%	
Ductal	1477737	67.90%	6224	62.10%	
Adenocarcinoma	5775	0.30%	144	1.40%	
Lobular	206186	9.50%	1189	11.90%	
Mixed	273980	12.60%	879	8.80%	
Inflammatory	4776	0.20%	75	0.70%	
Paget	6520	0.30%	39	0.40%	
Phyllodes	2521	0.10%	5	0.00%	
Others	188791	8.70%	1392	13.90%	
Total	2175116	100.00%	10026	100.00%	
Tumor size					<0.001
<2 cm	26382	1.20%	96	1.00%	
2-4.9 cm	141316	6.50%	213	2.10%	
≥5 cm	2007418	92.30%	9717	96.90%	
Total	2175116	100.00%	10026	100.00%	
Laterality					0.595
Right	1070460	49.30%	4897	49.00%	
Left	1102797	50.70%	5099	51.00%	
Total	2173257	100.00%	9996	100.00%	
Triple-negative					<0.001
Triple-negative	108460	5.00%	419	4.20%	
Non-triple-negative	804542	37.00%	4579	45.70%	
Unknown	1262114	58.00%	5028	50.10%	
Total	2175116	100.00%	10026	100.00%	

showed that women had higher odds of refusing surgery (OR=1.52; 95% CI=1.33-1.73) when compared to men (3). Additionally, previous research has identified that body disfigurement caused by the surgery can affect the psychological state of female breast cancer patients (12, 13).

In our study, when compared to white patients, black and Asian patients were shown to have an independently higher risk of refusing surgery when diagnosed with breast cancer. There may be cultural or access to care components secondary to socioeconomic disparities (14). Furthermore, studies have reported independently increased odds of refusing cancer-directed surgery in black and Asian patients in pancreatic, breast, and hepatocellular carcinomas (2, 3, 10).

Table III. Odds of refusing breast cancer surgery.

Variables	OR	95% CI		p-Value	Variables	OR	95% CI		p-Value
		Lower	Upper				Lower	Upper	
Age					Charlson-Deyo score				
40-60 years				0	No comorbidity				0
60-80 years	1.2	1.124	1.282	<0.001	Score=1	0.732	0.688	0.78	<0.001
>80 years	8.139	7.596	8.721	<0.001	Score=2 or more	1.233	1.116	1.363	<0.001
Gender					Behavior				
Male				0	<i>In situ</i>				0
Female	1.482	1.189	1.847	<0.001	Invasive	0.73	0.562	0.949	0.019
Race					Stage				
White				0	Stage 0				<0.001
Black	2.296	2.167	2.432	<0.001	Stage I	0.867	0.668	1.124	0.281
Asian	1.622	1.444	1.823	<0.001	Stage II	1.877	1.446	2.435	<0.001
Native American	1.313	0.843	2.043	0.228	Stage III	2.994	2.302	3.894	<0.001
Insurance status					Histology				
Private				0	Papillary				0
Government	1.966	1.848	2.092	<0.001	Squamous	0.293	0.071	1.203	0.088
Not insured	3.911	3.463	4.416	<0.001	Intraductal	0.702	0.549	0.897	0.005
Average income in zip code					Adenocarcinoma	3.174	2.338	4.309	<0.001
Less than \$38,000				0	Lobular	0.811	0.631	1.043	0.103
\$38,000 \$47,999	0.821	0.755	0.893	<0.001	Mixed	0.542	0.421	0.699	<0.001
\$48,000 \$62,999	0.852	0.79	0.918	<0.001	Inflammatory	1.658	1.17	2.35	0.004
\$63,000 +	0.913	0.851	0.98	0.012	Angiomyosarcoma	0.847	0.564	1.273	0.425
% with no HSD in zip code					Paget	0.43	0.173	1.073	0.071
21% or more				0	Others	1.317	1.025	1.692	0.031
13-20.9%	1.222	1.119	1.335	<0.001	Tumor size				
7-12.9%	1.205	1.117	1.301	<0.001	<2 cm				0
Less than 7%	1.105	1.03	1.186	0.005	2-4.9 cm	0.471	0.362	0.614	<0.001
Population density					≥5 cm	1.028	0.821	1.286	0.812
Metropolitan				0	Laterality				
Urban	0.881	0.82	0.947	0.001	Right				0
Rural	0.776	0.641	0.939	0.009	Left	0.993	0.953	1.036	0.754
Facility type					Triple-negative				
Academic/Research Program				0	Triple-negative				0
Comprehensive Community*	0.838	0.797	0.88	<0.001	Non-triple-negative	1.737	1.561	1.932	<0.001
Community*	0.942	0.876	1.014	0.11	Unknown	1.185	1.064	1.319	0.002
Integrated network*	0.939	0.875	1.009	0.086					

Multivariate analysis for odds of refuse treatment. HSD, High school diploma. \*Cancer Program.

Another important study finding is that patients with no insurance or those with government insurance had independently increased odds of refusing breast cancer surgery. This result is supported by Gaitanidis and colleagues (2) who performed a study using the Surveillance Epidemiology and End Results (SEER) database in which the lack of insurance was found to increase the odds of surgery refusal (OR=2.11; 95% CI=1.59-2.8;  $p<0.001$ ) (2). Tohme and colleagues (3), using the NCDB, found that patients with resectable pancreatic cancer were more likely to refuse surgery when they had government insurance (OR=2.75; 95% CI=1.54-4.92) when compared to patients with private insurance (3). Further health economic analysis is required to understand the real or perceived economic

impact of breast cancer surgery on patients with government or without insurance options.

Higher stage of disease was found to be an important risk factor for refusing breast cancer surgery. Multiple reasons may be driving this situation. Patients who have lower survival chances might consider that surgery will decrease their quality of life and decide not to have it. Also, higher stage of disease could imply a bigger surgical resection, which would increase cosmetic deformity, and patients might consider this unacceptable. Patients with hepatocellular carcinoma have also been shown to increase surgery refusal at higher stages (10). However, prostate cancer patients with higher stage of disease have been reported to embrace surgical treatment more often (9).

Our study is not without limitations. Our analysis was conducted using the NCDDB because it encompasses approximately 70% of all the cancer population in the US; however, due to the nature of large national databases, the fidelity of the information can be affected by incorrect or incomplete reports. Furthermore, the number of patients who refused surgery was considerably smaller than the number of patients who refused treatment. However, the large number of patients included in our study allows us to perform an analysis that is comparable to the United States cancer population and draw conclusions.

In conclusion, this study describes demographic and disease-specific characteristics related to breast cancer surgery refusal, which could be of immediate use to clinicians counseling selected populations. Further studies are needed to elucidate the underlying reasons for surgery refusal in the identified demographic and disease-specific populations.

### Authors' Contributions

All Authors contributed to the study design, commented on previous versions of the manuscript, read and approved the final manuscript. Material preparation, data collection and analysis were performed by DJR, ACS and AJF. The first draft of the manuscript was written by DJR and DB.

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