Racial and Ethnic Disparities in the Refusal of Surgical Treatment in Women 40 years and older with Breast Cancer in the United States between 2010 and 2017

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Abstract

Purpose

Although surgical resection is the main modality of treatment for breast cancer, some patients elect to refuse the recommended surgery. We assessed racial and ethnic differences in women 40 years and older who received or refused to receive surgical treatment for breast cancer in the United States and whether racial disparities in mortality were affected by their differences in the prevalence of refusal for surgical treatment

Methods

We studied 277,127 women with breast cancer using the Surveillance, Epidemiology, and End Results (SEER) data and performed multivariable logistic regressions to investigate the association between surgery status of breast cancer and race/ethnicity. Additionally, we performed Cox logistic regression analyses to determine the predictors of mortality outcomes.

Results

Of 277,127 patients with breast cancer, 1,468 (0.53%) refused to receive the recommended surgical treatment in our cohort. Non-Hispanic Black women were 112% more likely to refuse recommended surgical treatment for breast cancer compared to their non-Hispanic White counterparts [adjusted odds ratio: 2.12, 95% confidence interval (CI)=1.82-2.47]. Women who underwent breast conserving surgery [hazards ratio (HR): 0.15, 95% CI: 0.13-0.16] and mastectomy (HR:0.21, 95% CI: 0.18-0.23) had lower hazard ratios of mortality as compared to women who refused the recommended treatment after adjusting for covariates.

Conclusion

Race/ethnicity was associated with refusal for recommended surgery, especially among non-Hispanic Black women. Also, surgery refusal was associated with a higher risk of all-cause and breast cancer-related mortality. These disparities stress the need to tailor interventions aimed at raising awareness of the importance of following physician recommendations among minorities.

Introduction

Breast cancer is the most prevalent cancer and the second leading cause of cancer-related deaths after lung cancer among U.S. women [1–4]. In 2021, it is estimated that approximately 281,550 new cases of invasive breast cancer will be diagnosed, and 43,600 women will die from breast cancer in the U.S. Approximately 3.8 million U.S. women currently live with a history of breast cancer [2, 3]. Additionally, nearly 1 in 8 (13%) women in the U.S. will be diagnosed with invasive breast cancer, and 1 in 39 (2.6%) will die of it [1, 2, 4, 5]. Breast cancer incidence rates are highest among non-Hispanic (NH) Whites (130.8 per 100,000 women) and NH Blacks (126.7 per 100,000 women). NH Black women have the highest

recorded breast cancer death rate (28.4 deaths per 100,000) and are more likely at any age to die from breast cancer as compared to other ethnic groups [2, 6] .

It is well documented that the main modality of treatment for breast cancer is surgical resection either in the form of lumpectomy (breast-conserving surgery – BCS) or modified mastectomy (removal of the entire breast) based on pathological characteristics, which is often followed by adjuvant treatment such as radiation therapy and/or chemotherapy [2, 7, 8]. However, corroboration from controlled clinical trials showed that there has been increasing concern that cancer patients in the U.S. do not receive the full benefit of effective and appropriate cancer treatment [9, 10].

Although surgical treatment has been proven effective, research showed that some patients develop various setbacks. Post-surgery patients may develop declining psychosocial functioning with respect to their quality of life, cancer-related distress, sexual dysfunction, body image dysmorphism, anxiety, and depression, hence affecting surgery refusal rates [7, 11–13]. Previous studies have also found age, race, marital status, and income level to be associated with surgery refusal, with NH Black patients being less likely to receive breast cancer surgical treatment [7, 14–19]. However, these studies focused on data prior to 2014. Information and data on patients diagnosed in more recent years is needed. Also, the extent to which these disparities result from differences in cancer molecular subtype characteristics among a large and ethnically diverse cohort of older women remains unexplored.

The acknowledgement of treatment refusal has led to various quality improvement measures to better direct strategies to improve surgical utilization, patient satisfaction, and cancer care outcome [20–22]. Understanding which patients are potentially likely not to abide by the recommended treatment and when the treatment is most likely to be curative, would be of great clinical benefit. This information should also help address, identify, and reduce cancer care outcome disparities.

Therefore, this study aimed to determine if there were racial and ethnic disparities in the prevalence of refusals for definitive surgeries (i.e., mastectomy or lumpectomy) in women with early-stage breast cancer who were eligible and recommended for surgeries, whether the refusal of receiving the recommended surgeries was associated with an increased risk of mortality, and whether racial disparities in mortality were affected by their differences in the prevalence of refusal for surgical treatment.

Methods

Data source, study design and patient selection

This analysis utilized the Surveillance, Epidemiology, and End Results (SEER) database. SEER is a cancer registry program supported by the National Cancer Institute (NCI) that aims to provide reliable incidence and survival data [23]. We selected the SEER research plus data, 18 registries, Nov 2020 database, which covers nearly 28% of the U.S. population [24]. A detailed description of the database and data collection can be found elsewhere [23]. The study subjects were de-identified and there was no patient contact; thus, the study is exempt from an Institutional Review Board's review.

We conducted a retrospective cohort study using secondary data of women aged 40 years and older with a primary diagnosis of breast cancer between 2010 and 2017 in the SEER areas of the U.S. We focused on women 40 years and older to capture women at risk of being diagnosed with breast cancer based on the American Cancer Society breast cancer screening recommendation [25]. We investigated the racial and ethnic disparities between women who received surgery to treat their breast cancer and those who refused the surgical recommendation. Additionally, we assessed the differences in breast cancer survival outcomes by surgery type (recommended but refused surgery versus BCS versus Mastectomy).

We used the SEER Stat software 8.3.8 to identify all women over 40 years old with breast cancer as the first primary diagnosis from 2010 to 2017 ($n = 404,240$). We included eligible patients for whom surgery was recommended and performed or for whom surgery was not performed due to patients' refusal. We excluded patients with grade IV tumor, distant tumor stage, or unknown race, income, marital status, area of residence, tumor sites, breast cancer subtypes, and ineligible for surgery (Fig. 1). The new sample size was 277,127 and then 267,999 following logistic and cox regression analyses when observations with missing values were dropped.

Study Variables

Main exposure

Race/ethnicity was classified into non-Hispanic White, non-Hispanic Black, Hispanic, and other. For the secondary analysis, surgery type was categorized into breast conserving surgery (BCS), mastectomy, and no surgery (i.e., patient refused) was assessed as a predictor of death. Only those ineligible cases for surgery were excluded (Fig. 1).

Outcomes

Surgery treatment was the main outcome of interest and dichotomized as "surgery performed" and "surgery recommended but not performed, patient refused". We also looked at death from any causes, death from breast cancer, and 5-year survival as secondary outcomes. *All-cause mortality* was a dichotomous variable (yes/no). Patients who died of any causes at end of the study were categorized as "yes", and those who did not were categorized as "no". *Breast cancer related death* was a dichotomous variable. Patients who died of breast cancer at the end of the study were categorized as "yes", and those who died of other causes were "censored".

Survival months

For overall mortality, survival time was calculated from the date of diagnosis to the date of death, or the date of last follow-up (December 31, 2017) as indicated in the SEER registry. For the breast cancer-related mortality, survival time was calculated from the date of diagnosis to the date of breast cancer related death, or the date of last follow-up as indicated in the SEER registry.

Tumor characteristics and adjuvant treatment

The following tumor characteristics and treatment variables were obtained from SEER and assessed based on findings from previous studies [7, 8, 11, 14]: year of diagnosis (2010, 2011, 2012, 2013, 2014, 2015, 2016, and 2017); tumor subtype (luminal A, luminal B, HER2 enriched, and triple negative); tumor grade (Grade I, grade II, and grade III); tumor site (nipple, centra portion of the breast, upper-inner quadrant of the breast, lower-inner quadrant of the breast, upper-outer quadrant of the breast, lower-outer quadrant of the breast, and axillary tail of the breast); tumor stage (localized only, regional with direct extension, regional with lymph nodes only, and regional with both direct extension and lymph nodes); and adjuvant treatment: radiotherapy (yes/no) and chemotherapy (yes/no).

Sociodemographic characteristics

Age at diagnosis was categorized into 40–49, 50–59,60–69,70–79, and 80+. Marital status was classified as married, unmarried/domestic partner, divorced, widowed, separated, and never married. Median household income inflation adjusted to 2019 was grouped into <\$35k; \$35,000–44,999, \$ 45,000–54,999, \$ 55,000–64,999, \$65,000–74,999, and ≥\$75k at the census tract level. Area of residence was organized into counties in metropolitan areas greater than 1 million, counties in metropolitan areas of 250k to 1 million, counties in metropolitan areas less than 250k, nonmetropolitan counties adjacent to a metropolitan area, and nonmetropolitan counties non-adjacent to a metropolitan area.

Statistical Analysis

We performed descriptive statistics to review the characteristics of the cohort stratified by race/ethnicity and by surgery status. We used Pearson’s Chi-square test to determine if the differences were statistically significant. We performed crude and multivariable logistic regression to assess the association between the surgical treatment of breast cancer and its predictors, mainly race/ethnicity. We performed crude and adjusted Cox proportional hazards regressions to determine the association between surgery types and race/ethnicity and the mortality outcomes (death and survival). SAS version 9.4 and STATA 16.1 were used to perform the analyses.

Results

Sociodemographic Characteristics

A description of the sample baseline characteristics stratified by race/ethnicity is provided in Table 1. The proportion of patients with triple negative breast cancer was 20.38% among non-Hispanic Black patients while the proportion was 9.15% and 10.88% among non-Hispanic and Hispanic patients respectively. The proportion of patients with Grade 3 tumors was 43.78% among non-Hispanic Black patients, 26.78% among non-Hispanic White, and 33.56% among Hispanic patients. The descriptive analysis also showed differences in marital status within racial groups. Non-Hispanic Black had the lowest percentage of being married or with a domestic partner (37.80%) while it was 61.99% and 58.39% among non-Hispanic Whites and Hispanics respectively.

Table 1
Socio-demographic and cancer characteristics of women 40 and above in the U.S. by Race/Ethnicity
(2010–2017)

Variable	Number of patients (n = 277,127)	Non-Hispanic White (n = 191,777)	Non-Hispanic Black (n = 28,250)	Hispanic (All races) (n = 30,813)	Other (n = 26,287)	Pearson Chi square
Surgery						86.4692***
Patients with surgery recommended but not performed, patients refused	1,486	938 (0.49)	257 (0.91)	140 (0.45)	151 (0.57)	
Patients who received surgery	275,641	190,839 (99.51)	27,993 (99.09)	30,673 (99.55)	26,136 (99.43)	
Subtypes						4.6exp(3)***
Luminal A	209,996	149,932 (78.18)	17,973 (63.62)	22,437 (72.82)	19,654 (74.77)	
Luminal B	27,478	17,776 (9.27)	3,064 (10.85)	3,585 (11.63)	3,053 (11.61)	
HER2 enriched	10,838	6,530 (3.40)	1,456 (5.15)	1,438 (4.67)	1,414 (5.38)	
Triple negative	28,815	17,539 (9.15)	5,757 (20.38)	3,353 (10.88)	2,166 (8.24)	
Age at diagnosis						5.7exp(3)***
40–49	48,079	28,312 (14.76)	5,566 (19.70)	7,963 (25.84)	6,238 (23.73)	
50–59	72,810	47,643 (24.84)	8,443 (29.89)	9,225 (29.94)	7,499 (28.53)	
60–69	81,609	58,454 (30.48)	8,031 (28.43)	7,819 (25.38)	7,305 (27.79)	
70–79	51,583	39,045 (20.36)	4,509 (15.96)	4,225 (13.71)	3,804 (14.47)	
80+	23,046	18,323 (9.55)	1,701 (6.02)	1,581 (5.13)	1,441 (5.48)	
Tumor grade						4.2exp(3)***
Grade I; well differentiated	69,674	52,293 (27.27)	4,722 (16.72)	6,675 (21.66)	5,984 (22.76)	

Variable	Number of patients (n = 277,127)	Non-Hispanic White (n = 191,777)	Non-Hispanic Black (n = 28,250)	Hispanic (All races) (n = 30,813)	Other (n = 26,287)	Pearson Chi square
Grade II; moderately differentiated	125,240	88,117 (45.95)	11,160 (39.50)	13,796 (44.77)	12,167 (46.29)	
Grade III; poorly differentiated	82,213	51,367 (26.78)	12,368 (43.78)	10,342 (33.56)	8,136 (30.95)	
Tumor site						367.0890***
Nipple	1,008	647 (0.34)	101 (0.36)	142 (0.46)	118 (0.45)	
Central portion of the breast	14,156	9,912 (5.17)	1,234 (4.37)	1,516 (4.92)	1,494 (5.68)	
Upper-inner quadrant of the breast	40,050	27,181 (14.17)	4,102 (14.52)	4,486 (14.56)	4,281 (16.29)	
Lower-inner quadrant of the breast	17,578	12,006 (6.26)	2,098 (7.43)	1,875 (6.09)	1,599 (6.08)	
Upper-outer quadrant of the breast	108,230	75,762 (39.51)	11,157 (39.49)	11,808 (38.32)	9,503 (36.15)	
Lower-outer quadrant of the breast	23,767	16,572 (8.64)	2,442 (8.64)	2,580 (8.37)	2,173 (8.27)	
Axillary tail of the breast	1,305	885 (0.46)	197 (0.70)	135 (0.44)	88 (0.33)	
Overlapping lesion of the breast	71,033	48,812 (25.45)	6,919 (24.49)	8,271 (26.84)	7,031 (26.75)	
Tumor stage						1.3exp(3)***
Localized only	197,500	139,928 (72.96)	18,501 (65.49)	20,277 (65.81)	18,794 (71.50)	
Regional, direct extension only	3,423	2,437 (1.27)	368 (1.30)	332 (1.08)	286 (1.09)	
Regional, lymph nodes only	68,290	44,318 (23.11)	8,323 (29.46)	9,169 (29.76)	6,480 (24.65)	
Regional, both direct extension and lymph nodes	7,914	5,094 (2.66)	1,058 (3.75)	1,035 (3.36)	727 (2.77)	
Marital status						1.1exp(4)***
Married/Domestic Partner	165,394	118800 (61.99)	10,678 (37.80)	17,991 (58.39)	17,845 (67.89)	

Variable	Number of patients (n = 277,127)	Non-Hispanic White (n = 191,777)	Non-Hispanic Black (n = 28,250)	Hispanic (All races) (n = 30,813)	Other (n = 26,287)	Pearson Chi square
Divorced	32,038	22,181 (11.57)	4,457 (15.78)	3,456 (11.22)	1,944 (7.40)	
Widowed	37,364	27,269 (14.22)	4,096 (14.50)	3,142 (10.20)	2,857 (10.87)	
Separated	3,073	1,407 (0.73)	681 (2.41)	724 (2.35)	261 (0.99)	
Never married	39,258	22,040 (11.49)	8,338 (29.52)	5,500 (17.85)	3,380 (12.86)	
Year of diagnosis						348.4360***
2010	30,717	22,092 (11.52)	2,999 (10.62)	2,953 (9.58)	2,673 (10.17)	
2011	31,810	22,487 (11.73)	3,110 (11.01)	3,375 (10.95)	2,838 (10.80)	
2012	33,035	23,131 (12.06)	3,415 (12.09)	3,521 (11.43)	2,968 (11.29)	
2013	34,302	23,840 (12.43)	3,480 (12.32)	3,753 (12.18)	3,229 (12.28)	
2014	34,957	24,208 (12.62)	3,629 (12.85)	3,838 (12.46)	3,282 (12.49)	
2015	36,769	25,244 (13.16)	3,716 (13.15)	4,210 (13.66)	3,599 (13.69)	
2016	37,470	25,276 (13.18)	3,899 (13.80)	4,559 (14.80)	3,736 (14.21)	
2017	38,067	25,499 (13.30)	4,002 (14.17)	4,604 (14.94)	3,962 (15.07)	
Median income						1.8exp(4)***
< \$35,000	3,797	2,946 (1.54)	645 (2.28)	135 (0.44)	71 (0.27)	
\$35,000 - \$44,999	19,617	13,749 (7.17)	4,795 (16.97)	840 (2.73)	233 (0.89)	
\$45,000 - \$54,999	40,359	29,846 (15.56)	5,508 (19.50)	3,940 (12.79)	1,065 (4.05)	
\$55,000 - \$64,999	66,982	43,241 (22.55)	7,620 (26.97)	10,239 (33.23)	5,882 (22.38)	

Variable	Number of patients (n = 277,127)	Non-Hispanic White (n = 191,777)	Non-Hispanic Black (n = 28,250)	Hispanic (All races) (n = 30,813)	Other (n = 26,287)	Pearson Chi square
\$65,000 - \$74,999	58,796	42,341 (22.08)	4,776 (16.91)	7,209 (23.40)	4,470 (17.00)	
> \$75,000	87,576	59,654 (31.11)	4,906 (17.37)	8,450 (27.42)	14,566 (55.41)	
Urban-Rural						6.7exp(3)***
Counties in metropolitan areas greater than 1 million	172,590	112,780 (58.81)	19,349 (68.49)	21,765 (70.64)	18,696 (71.12)	
Counties in metropolitan areas of 250k to 1 million	58,086	40,567 (21.15)	4,942 (17.49)	6,737 (21.86)	5,840 (22.22)	
Counties in metropolitan areas less than 250k	19,049	14,817 (7.73)	1,950 (6.90)	1,440 (4.67)	842 (3.20)	
Nonmetropolitan counties adjacent to a metropolitan area	15,984	13,759 (7.17)	1,505 (5.33)	499 (1.62)	221 (0.84)	
Nonmetropolitan counties non-adjacent to a metropolitan area	11,418	9,854 (5.14)	504 (1.78)	372 (1.21)	688 (2.62)	
Radiation therapy						983.2506***
No	106,188	71,589 (37.33)	10,494 (37.15)	12,957 (42.05)	11,148 (42.41)	
Yes	161,811	114,632 (59.77)	16,559 (58.62)	16,347 (53.05)	14,273 (54.30)	
Missing	9,128	5,556 (2.90)	1,197 (4.24)	1,509 (4.90)	866 (3.29)	
Chemotherapy						3.0exp(3)***
No	171,081	124,213 (64.77)	14,039 (49.70)	17,061 (55.37)	15,768 (59.98)	
Yes	106,046	67,564 (35.23)	14,211 (50.30)	13,752 (44.63)	10,519 (40.02)	
Values are n (% of column total). For the p-value: ns indicates not significant, *p < 0.05, ** < 0.01, *** < 0.001						
Abbreviation: HER2 = Human epidermal growth factor receptor 2						

A description of the sample baseline characteristics stratified by surgery treatment status is provided in Table 2. Overall, 0.53% of women with breast cancer refused the recommended breast cancer treatment. The surgery refusal rate was higher in non-Hispanic Black women (0.91%) than in non-Hispanic Whites (0.49%), Hispanics (0.45%), and others (0.57%). Chi-square test comparing women who underwent surgery as recommended versus those who did not reveal statistically significant differences ($p < 0.0001$) by patient and tumor characteristics. Although non-Hispanic Black patients represented 10.19% of all women with breast cancer, they accounted for 17.29% of breast cancer women who refused to get the treatment as recommended as compared to 10.19% of those who did in our cohort. On the other hand, non-Hispanic White patients accounted for 63.12% of the patients who refused to undergo surgery as prescribed. The proportion of women who refused the recommended surgery were higher for ≥ 80 years and for those who had a localized, luminal A, grade II moderately differentiated tumor located in the upper-outer quadrant of the breast.

Table 2
Socio-demographic and cancer characteristics of women 40 and above in the US by Surgery status
(2010–2017)

Variable	Number of patients (n = 277,127)	Patients who received surgery (n = 275,641)	Patients with surgery recommended but not performed (n = 1,486)	Pearson Chi square
Race and ethnicity				86.4692***
Non-Hispanic White	191,777	190,839 (99.51)	938 (0.49)	
Non-Hispanic Black	28,250	27,993 (99.09)	257 (0.91)	
Hispanic (All races)	30,813	30,673 (99.55)	140 (0.45)	
Other	26,287	26,136 (99.43)	151 (0.57)	
Subtypes				10.2803*
Luminal A	209,996	208,897 (99.48)	1,099 (0.52)	
Luminal B	27,478	27,296 (99.34)	182 (0.66)	
HER2 enriched	10,838	10,775 (99.42)	63 (0.58)	
Triple negative	28,815	28,673 (99.51)	142 (0.49)	
Age at diagnosis				2.3exp(3)***
40–49	48,079	47,940 (99.71)	139 (0.29)	
50–59	72,810	72,571 (99.67)	239 (0.33)	
60–69	81,609	81,362 (99.70)	247 (0.30)	
70–79	51,583	51,355 (99.56)	228 (0.44)	
80+	23,046	22,413 (97.25)	633 (2.75)	
Tumor grade				26.4617***
Grade I; well differentiated	69,674	69,362 (99.55)	312 (0.45)	
Grade II; moderately differentiated	125,240	124,473 (99.39)	767 (0.61)	
Grade III; poorly differentiated	82,213	81,806 (99.50)	407 (0.50)	
Tumor site				49.6519***
Nipple	1,008	1,000 (99.21)	8 (0.79)	

Variable	Number of patients (n = 277,127)	Patients who received surgery (n = 275,641)	Patients with surgery recommended but not performed (n = 1,486)	Pearson Chi square
Central portion of the breast	14,156	14,030 (99.11)	126 (0.89)	
Upper-inner quadrant of the breast	40,050	39,842 (99.48)	208 (0.52)	
Lower-inner quadrant of the breast	17,578	17,496 (99.53)	82 (0.47)	
Upper-outer quadrant of the breast	108,230	107,710 (99.52)	520 (0.48)	
Lower-outer quadrant of the breast	23,767	23,656 (99.53)	111 (0.47)	
Axillary tail of the breast	1,305	1,298 (99.46)	7 (0.54)	
Overlapping lesion of the breast	71,033	70,609 (99.40)	424 (0.60)	
Tumor stage				615.9641***
Localized only	197,500	196,538 (99.51)	962 (0.49)	
Regional, direct extension only	3,423	3,311 (96.73)	112 (3.27)	
Regional, lymph nodes only	68,290	67,990 (99.56)	300 (0.44)	
Regional, both direct extension and lymph nodes	7,914	7,802 (98.58)	112 (1.42)	
Marital status				759.8123***
Married	164,397	163,925 (99.71)	472 (0.29)	
Unmarried/Domestic partner	997	996 (99.90)	1 (0.10)	
Divorced	32,038	31,855 (99.43)	183 (0.57)	
Widowed	37,364	36,837 (98.59)	527 (1.41)	
Separated	3,073	3,044 (99.06)	29 (0.94)	
Never married	39,258	38,984 (99.30)	274 (0.70)	
Year of diagnosis				72.0314***

Variable	Number of patients (n = 277,127)	Patients who received surgery (n = 275,641)	Patients with surgery recommended but not performed (n = 1,486)	Pearson Chi square
2010	30,717	30,611 (99.65)	106 (0.35)	
2011	31,810	31,678 (99.59)	132 (0.41)	
2012	33,035	32,871 (99.50)	164 (0.50)	
2013	34,302	34,142 (99.53)	160 (0.47)	
2014	34,957	34,783 (99.50)	174 (0.50)	
2015	36,769	36,532 (99.36)	237 (0.64)	
2016	37,470	37,219 (99.33)	251 (0.67)	
2017	38,067	37,805 (99.31)	262 (0.69)	
Median income				15.7957**
< \$35,000	3,797	3,780 (99.55)	17 (0.45)	
\$35,000 - \$44,999	19,617	19,525 (99.53)	92 (0.47)	
\$45,000 - \$54,999	40,359	40,130 (99.43)	229 (0.57)	
\$55,000 - \$64,999	66,982	66,674 (99.54)	308 (0.46)	
\$65,000 - \$74,999	58,796	58,476 (99.46)	320 (0.54)	
> \$75,000	87,576	87,056 (99.41)	520 (0.59)	
Urban-Rural				6.8024 ^{ns}
Counties in metropolitan areas greater than 1 million	172,590	171,648 (99.45)	942 (0.55)	
Counties in metropolitan areas of 250k to 1 million	58,086	57,756 (99.43)	330 (0.57)	
Counties in metropolitan areas less than 250k	19,049	18,963 (99.55)	86 (0.45)	
Nonmetropolitan counties adjacent to a metropolitan area	15,984	15,913 (99.56)	71 (0.44)	
Nonmetropolitan counties non-adjacent to a metropolitan area	11,418	11,361 (99.50)	57 (0.50)	

Variable	Number of patients (n = 277,127)	Patients who received surgery (n = 275,641)	Patients with surgery recommended but not performed (n = 1,486)	Pearson Chi square
Radiation therapy				2.2exp(3)***
No	106,188	104,747 (98.64)	1,441 (1.36)	
Yes	161,811	161,787 (99.99)	24 (0.01)	
Missing	9,128	9,107 (99.77)	21 (0.23)	
Chemotherapy				579.0282***
No	171,081	169,714 (99.20)	1,367 (0.80)	
Yes	106,046	105,927 (99.89)	119 (0.11)	
Values are n (% of column total). For the p-value: ns indicates not significant, *p < 0.05, ** < 0.01, *** < 0.001				
Abbreviation: HER2 = Human epidermal growth factor receptor 2				

Trend of surgery refusal over time

Results from Fig. 2 showed an increasing trend in refusing the recommended surgery by year of diagnosis in women with breast cancer. Compared to 2010 (0.35%), the proportion of those who refused surgery increased by about 97% in 2017 (0.69%).

Primary outcome on surgery refusal

The surgery refusal rate was higher in non-Hispanic Black women (0.91%) than in non-Hispanic Whites (0.49%), Hispanics (0.45%), and others (0.57%). The multivariable logistic regression analysis showed that non-Hispanic Black women had 112% higher odds (AOR: 2.12, 95% CI = 1.82–2.47) of refusing the recommended surgery performed compared to non-Hispanic Whites after adjusting for sociodemographic and tumor characteristics as shown in Table 3. Additionally, women aged ≥ 80 years compared to those aged 40–49 years old and those with luminal B, HER2, triple negative compared to those with luminal A were less likely to undergo the recommended surgery as recommended (Table 3). There was an increasing trend in the proportion of women receiving the recommended surgery by year of diagnosis from 2013 to 2017. Women residing in metropolitan counties of 250 thousand to 1 million residents had the highest odds (AOR = 1.17, 95% CI = 1.02–1.34) of receiving the recommended surgery compared to women residing in counties in metropolitan areas with populations greater than 1 million.

Table 3

Crude and multivariable logistic regression analyses of factors associated with refusing to undergo surgery as recommend among US. Women 40 or above between 2010–2017

Variable	Crude Odds Ratio of refusing the recommended surgery (95% Confidence Interval)	Adjusted Odds Ratio of refusing the recommended surgery (95% Confidence Interval)
Race and ethnicity		
Non-Hispanic White	1.00 (reference)	1.00 (reference)
Non-Hispanic Black	1.87 (1.63–2.15)***	2.12 (1.82–2.47)***
Hispanic (All races)	0.93 (0.78–1.11) ^{ns}	0.97 (0.81–1.17) ^{ns}
Other	1.18 (0.99–1.397) ^{ns}	1.18 (0.99–1.42) ^{ns}
Subtypes		
Luminal A	1.00 (reference)	1.00 (reference)
Luminal B	1.27 (1.08–1.48)**	1.93 (1.62–2.28)***
HER2 enriched	1.11 (0.86–1.43) ^{ns}	1.64 (1.25–2.16)***
Triple negative	0.94 (0.79–1.12) ^{ns}	1.36 (1.12–1.66)**
Age at diagnosis		
40–49	1.00 (reference)	1.00 (reference)
50–59	1.14 (0.92–1.4) ^{ns}	1.15 (0.93–1.43) ^{ns}
60–69	1.05 (0.85–1.29) ^{ns}	1.04 (0.84–1.29) ^{ns}
70–79	1.53 (1.24–1.89)***	0.97 (0.77–1.21) ^{ns}
80+	9.74 (8.10–11.71)***	3.06 (2.48–3.78)***
Tumor grade		
Grade I; well differentiated	1.00 (reference)	1.00 (reference)
Grade II; moderately differentiated	1.37 (1.20–1.56)***	1.31 (1.14–1.49)***
Grade III; poorly differentiated	1.11 (0.954–1.282) ^{ns}	1.11 (0.94–1.32) ^{ns}
Tumor site		
Nipple	1.00 (reference)	1.00 (reference)

Variable	Crude Odds Ratio of refusing the recommended surgery (95% Confidence Interval)	Adjusted Odds Ratio of refusing the recommended surgery (95% Confidence Interval)
Central portion of the breast	1.12 (0.55–2.30) ^{ns}	1.73 (0.83–3.60) ^{ns}
Upper-inner quadrant of the breast	0.65 (0.32–1.33) ^{ns}	1.85 (0.89–3.84) ^{ns}
Lower-inner quadrant of the breast	0.59 (0.28–1.21) ^{ns}	1.54 (0.73–3.25) ^{ns}
Upper-outer quadrant of the breast	0.60 (0.30–1.22) ^{ns}	1.78 (0.87–3.66) ^{ns}
Lower-outer quadrant of the breast	0.59 (0.9–1.21) ^{ns}	1.57 (0.75–3.28) ^{ns}
Axillary tail of the breast	0.67 (0.24–1.86) ^{ns}	1.75 (0.62–4.99) ^{ns}
Overlapping lesion of the breast	0.75 (0.37–1.52) ^{ns}	1.92 (0.93–3.96) ^{ns}
Tumor stage		
Localized only	1.00 (reference)	1.00 (reference)
Regional, direct extension only	6.91 (5.67–8.43) ***	4.2 (3.39–5.21) ***
Regional, lymph nodes only	0.90 (0.79–1.03) ^{ns}	1.57 (1.37–1.81) ***
Regional, both direct extension and lymph nodes	2.93 (2.41–3.57) ***	4.02 (3.23–4.98) ***
Marital status		
Married	1.00 (reference)	1.00 (reference)
Unmarried/Domestic partner	0.35 (0.05–2.48) ^{ns}	0.4 (0.05–2.84) ^{ns}
Divorced	2.00 (1.68–2.37) ***	1.69 (1.42–2.02) ***
Widowed	4.97 (4.39–5.63) ***	1.66 (1.43–1.93) ***
Separated	3.31 (2.27–4.82) ***	2.79 (1.88–4.15) ***
Never married	2.44 (2.10–2.83) ***	1.88 (1.61–2.19) ***
Year of diagnosis		
2010	1.00 (reference)	1.00 (reference)
2011	1.20 (.93-1.56) ^{ns}	1.26 (0.97–1.64) ^{ns}
2012	1.44 (1.13–1.84) **	1.51 (1.18–1.93) **

Variable	Crude Odds Ratio of refusing the recommended surgery (95% Confidence Interval)	Adjusted Odds Ratio of refusing the recommended surgery (95% Confidence Interval)
2013	1.35 (1.058–1.731) *	1.45 (1.13–1.87) **
2014	1.45 (1.134–1.84) **	1.61 (1.25–2.06) ***
2015	1.87 (1.489–2.357) ***	2.09 (1.66–2.65) ***
2016	1.95 (1.55–2.44) ***	2.26 (1.79–2.85) ***
2017	2.00 (1.60–2.51) ***	2.25 (1.79–2.84) ***
Median income		
< \$35,000	1.00 (reference)	1.00 (reference)
\$35,000 - \$44,999	1.05 (0.62–1.76) ^{ns}	1.08 (0.632–1.85) ^{ns}
\$45,000 - \$54,999	1.27 (0.774–2.079) ^{ns}	1.52 (0.89–2.57) ^{ns}
\$55,000 - \$64,999	1.03 (0.63–1.676) ^{ns}	1.20 (0.71–2.06) ^{ns}
\$65,000 - \$74,999	1.22 (0.746–1.984) ^{ns}	1.48 (0.86–2.54) ^{ns}
> \$75,000	1.33 (0.82–2.16) ^{ns}	1.85 (1.08–3.16) *
Urban-Rural		
Counties in metropolitan areas greater than 1 million	1.00 (reference)	1.00 (reference)
Counties in metropolitan areas of 250k to 1 million	1.04 (0.918–1.181) ^{ns}	1.17 (1.02–1.337) *
Counties in metropolitan areas less than 250k	0.83 (0.662–1.031) ^{ns}	0.91 (.712-1.159) ^{ns}
Nonmetropolitan counties adjacent to a metropolitan area	0.81 0(.638-1.035) ^{ns}	0.96 (.728-1.265) ^{ns}
Nonmetropolitan counties non-adjacent to a metropolitan area	0.91 (0.70–1.20) ^{ns}	1.02 (0.75–1.40) ^{ns}
Radiation therapy		
No	1.00 (reference)	1.00 (reference)
Yes	0.01 (0.01–0.02) ***	0.02 (0.01–0.02) ***
Chemotherapy		

Variable	Crude Odds Ratio	Adjusted Odds Ratio
	of refusing the recommended surgery	of refusing the recommended surgery
	(95% Confidence Interval)	(95% Confidence Interval)
No	1.00 (reference)	1.00 (reference)
Yes	0.14 (0.12–0.17) ***	0.17 (0.13–0.20) ***
For the p-value: ns indicates not significant, *p < 0.05, ** < 0.01, *** < 0.001		
Abbreviation: HER2 = Human epidermal growth factor receptor 2		

Secondary outcome on mortality

All-cause mortality

Table 4 presents the Cox proportional hazards regression analysis of the association between surgery type and overall mortality adjusted for covariates. To account for the violation of the proportional hazard assumption, the final model treated race, subtypes, tumor grade, and age as time-varying variables by adjusting for the interaction between these variables and the natural log of survival time. Women who underwent BCS (HR = 0.34, 95% CI = 0.31–0.37) or mastectomy (HR = 0.37, 95% CI = 0.34–0.40) had significantly lower hazards of death from any cause than women who refused the recommended surgery adjusted for covariates. Using non-Hispanic Whites as the reference group, non-Hispanic Black women had the highest crude hazard of all-cause mortality (HR = 1.40, 95% CI = 1.36–1.45). After adjusting for surgery type and other covariates, the hazard of all-cause mortality decreased but was still significantly higher among NH Black women (HR = 1.18, 95% CI = 1.01–1.37).

Table 4

Crude and multivariable Cox regression analyses of factors associated with all-cause mortality and breast cancer-related mortality among US. Women 40 or above between 2010–2017

Variable	Overall Mortality		Breast Cancer Mortality	
	Crude Proportional Hazard Ratio (95% Confidence Interval)	Adjusted Proportional Hazard Ratio (95% Confidence Interval)	Crude Proportional Hazard Ratio (95% Confidence Interval)	Adjusted Proportional Hazard Ratio (95% Confidence Interval)
Surgery type				
No surgery	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Breast conservatory surgery (BCS)	0.12 (0.11–0.13)***	0.34 (0.31–0.37)***	0.07 (0.06–0.08)***	0.14 (0.13–0.16)***
Mastectomy	0.19 (0.18–0.21)***	0.37 (0.34–0.40)***	0.18 (0.16–0.20)***	0.21 (0.19–0.23)***
Race and ethnicity				
Non-Hispanic White	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Non-Hispanic Black	1.40 (1.36–1.45)***	1.18 (1.01–1.37)*	1.88 (1.80–1.98)***	1.13 (0.90–1.42) ^{ns}
Hispanic (All races)	0.91 (0.87–0.95)***	0.80 (0.66–0.96)*	1.22 (1.16–1.30)***	0.82 (0.62–1.08) ^{ns}
Other	0.63 (0.60–0.66)***	0.59 (0.47–0.75)***	0.78 (0.73–0.84)***	0.47 (0.32–0.68)***
Subtypes				
Luminal A	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Luminal B	1.00 (0.95–1.04) ^{ns}	1.25 (1.03–1.52)*	1.40 (1.31–1.49)***	1.56 (1.14–2.15)**
HER2 enriched	1.37 (1.29–1.45)***	2.71 (2.15–3.42)***	2.42 (2.25–2.61)***	5.31 (3.82–7.40)***
Triple negative	2.21 (2.15–2.28)***	5.81 (5.12–6.60)***	4.20 (4.03–4.37)***	12.93 (10.62–15.73)***
Age at diagnosis				

Variable	Overall Mortality		Breast Cancer Mortality	
	Crude Proportional Hazard Ratio (95% Confidence Interval)	Adjusted Proportional Hazard Ratio (95% Confidence Interval)	Crude Proportional Hazard Ratio (95% Confidence Interval)	Adjusted Proportional Hazard Ratio (95% Confidence Interval)
40–49	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
50–59	1.16 (1.11–1.22) ^{***}	1.01 (0.81–1.26) ^{ns}	0.99 (0.94–1.05) ^{ns}	0.92 (0.69–1.22) ^{ns}
60–69	1.44 (1.38–1.51) ^{***}	1.57 (1.27–1.93) ^{***}	0.83 (0.79–0.88) ^{***}	1.65 (1.23–2.20) ^{**}
70–79	2.70 (2.58–2.83) ^{***}	2.73 (2.22–3.35) ^{***}	1.06 (1.00–1.13) [*]	4.44 (3.30–5.95) ^{***}
80+	7.96 (7.62–8.32) ^{***}	5.45 (4.45–6.67) ^{***}	2.38 (2.24–2.54) ^{***}	9.97 (7.41–13.41) ^{***}
Tumor grade				
Grade I; well differentiated	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Grade II; moderately differentiated	1.32 (1.28–1.37) ^{***}	1.20 (1.16–1.24) ^{***}	2.82 (2.61–3.05) ^{***}	2.09 (1.93–2.27) ^{***}
Grade III; poorly differentiated	2.29 (2.21–2.37) ^{***}	1.86 (1.79–1.94) ^{***}	8.71 (8.09–9.39) ^{***}	4.42 (4.07–4.80) ^{***}
Tumor site				
Nipple	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Central portion of the breast	0.86 (0.73–1.00) ^{ns}	1.11 (0.94–1.30) ^{ns}	0.97 (0.75–1.25) ^{ns}	1.19 (0.92–1.55) ^{ns}
Upper-inner quadrant of the breast	0.56 (0.48–0.66) ^{***}	1.14 (0.97–1.34) ^{ns}	0.60 (0.46–0.77) ^{***}	1.28 (0.99–1.65) ^{ns}
Lower-inner quadrant of the breast	0.64 (0.55–0.75) ^{***}	1.17 (1.00–1.38) ^{ns}	0.70 (0.54–0.90) ^{**}	1.37 (1.05–1.77) [*]
Upper-outer quadrant of the breast	0.60 (0.51–0.70) ^{***}	1.11 (0.95–1.30) ^{ns}	0.66 (0.51–0.84) ^{**}	1.16 (0.90–1.49) ^{ns}

Variable	Overall Mortality		Breast Cancer Mortality	
	Crude Proportional Hazard Ratio (95% Confidence Interval)	Adjusted Proportional Hazard Ratio (95% Confidence Interval)	Crude Proportional Hazard Ratio (95% Confidence Interval)	Adjusted Proportional Hazard Ratio (95% Confidence Interval)
Lower-outer quadrant of the breast	0.62 (0.53–0.73) ^{***}	1.13 (0.96–1.33) ^{ns}	0.71 (0.55–0.91) ^{**}	1.24 (0.95–1.60) ^{ns}
Axillary tail of the breast	0.70 (0.56–0.87) ^{**}	1.19 (0.95–1.48) ^{ns}	0.79 (0.56–1.11) ^{ns}	1.16 (0.82–1.64) ^{ns}
Overlapping lesion of the breast	0.64 (0.55–0.75) ^{***}	1.15 (0.98–1.35) ^{ns}	0.69 (0.54–0.88) ^{**}	1.21 (0.94–1.56) ^{ns}
Tumor stage				
Localized only	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regional, direct extension only	4.00 (3.75–4.28) ^{***}	4.76 (3.67–6.17) ^{***}	5.92 (5.34–6.56) ^{***}	3.35 (3.01–3.73) ^{***}
Regional, lymph nodes only	1.75 (1.70–1.79) ^{***}	2.41 (2.14–2.71) ^{***}	3.86 (3.71–4.02) ^{***}	3.20 (3.06–3.34) ^{***}
Regional, both direct extension and lymph nodes	4.80 (4.60–5.00) ^{***}	6.90 (5.80–8.21) ^{***}	11.88 (11.23–12.56) ^{***}	7.11 (6.67–7.58) ^{***}
Marital status				
Married/Domestic Partner	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Divorced	1.50 (1.45–1.56) ^{***}	1.34 (1.29–1.39) ^{***}	1.39 (1.32–1.48) ^{***}	1.24 (1.17–1.31) ^{***}
Widowed	3.35 (3.26–3.45) ^{***}	1.45 (1.41–1.50) ^{***}	1.97 (1.88–2.07) ^{***}	1.29 (1.22–1.36) ^{***}
Separated	1.48 (1.32–1.66) ^{***}	1.53 (1.36–1.72) ^{***}	1.62 (1.39–1.90) ^{***}	1.35 (1.16–1.58) ^{***}
Never married	1.52 (1.47–1.58) ^{***}	1.45 (1.39–1.50) ^{***}	1.59 (1.51–1.67) ^{***}	1.35 (1.28–1.42) ^{***}
Median income				
< \$35,000	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)

Variable	Overall Mortality		Breast Cancer Mortality	
	Crude Proportional Hazard Ratio (95% Confidence Interval)	Adjusted Proportional Hazard Ratio (95% Confidence Interval)	Crude Proportional Hazard Ratio (95% Confidence Interval)	Adjusted Proportional Hazard Ratio (95% Confidence Interval)
\$35,000 - \$44,999	0.87 (0.80–0.96)**	0.89 (0.81–0.98)*	0.83 (0.72–0.95)**	0.92 (0.80–1.06) ^{ns}
\$45,000 - \$54,999	0.79 (0.72–0.86)***	0.87 (0.79–0.95)**	0.74 (0.65–0.84)***	0.94 (0.82–1.09) ^{ns}
\$55,000 - \$64,999	0.67 (0.61–0.73)***	0.79 (0.72–0.87)***	0.68 (0.60–0.77)***	0.92 (0.80–1.06) ^{ns}
\$65,000 - \$74,999	0.61 (0.56–0.66)***	0.76 (0.69–0.83)***	0.57 (0.50–0.65)***	0.83 (0.71–0.96)*
> \$75,000	0.53 (0.48–0.57)***	0.70 (0.63–0.77)***	0.50 (0.44–0.57)***	0.77 (0.66–0.89)***
Urban-Rural				
Counties in metropolitan areas greater than 1 million				
Counties in metropolitan areas of 250k to 1 million	1.07 (1.03–1.10)***	1.04 (1.01–1.07)*	0.97 (0.93–1.02) ^{ns}	0.97 (0.92–1.02) ^{ns}
Counties in metropolitan areas less than 250k	1.26 (1.21–1.32)***	1.08 (1.03–1.14)**	1.16 (1.08–1.24)***	1.03 (0.96–1.12) ^{ns}
Nonmetropolitan counties adjacent to a metropolitan area	1.28 (1.22–1.34)***	1.05 (0.99–1.10) ^{ns}	1.15 (1.06–1.23)***	1.00 (0.92–1.09) ^{ns}
Nonmetropolitan counties non-adjacent to a metropolitan area	1.37 (1.30–1.45)***	1.07 (1.00–1.14)*	1.30 (1.20–1.41)***	1.12 (1.02–1.23)*
Radiation therapy				
No	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Yes	0.53 (0.52–0.55)***	0.69 (0.67–0.71)***	0.66 (0.63–0.68)***	0.81 (0.77–0.84)***
Chemotherapy				

Variable	Overall Mortality		Breast Cancer Mortality	
	Crude Proportional Hazard Ratio (95% Confidence Interval)	Adjusted Proportional Hazard Ratio (95% Confidence Interval)	Crude Proportional Hazard Ratio (95% Confidence Interval)	Adjusted Proportional Hazard Ratio (95% Confidence Interval)
No	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Yes	0.95 (0.92–0.97)***	0.93 (0.90–0.96)***	2.44 (2.36–2.54)***	1.16 (1.11–1.22)***
For the p-value: ns indicates not significant, *p < 0.05, ** < 0.01, *** < 0.001				
Abbreviation: HER2 = Human epidermal growth factor receptor 2				

Breast cancer-specific mortality: Women who underwent BCS had a significantly lower hazard of breast cancer-specific mortality as compared to women who refused the recommended treatment [HR:0.15 (95% CI = 0.13–0.16)], after adjusting for covariates. Women who underwent mastectomy were also significantly less likely to die of breast cancer than women who refused the recommended surgery (HR: 0.21, 95% CI = 0.18–0.23). Similar to that of all-cause mortality, non-Hispanic Black women had the highest crude hazard of breast cancer mortality (HR = 1.88, 95% CI = 1.80–1.98). After adjusting for surgery type and other covariates, the hazard of breast cancer-specific mortality remained significantly higher among non-Hispanic Blacks (HR = 1.13, 95% CI = 1.01–1.37). Women with HER2 enriched and triple negative tumors were significantly more likely to die of breast cancer as compared to luminal A with hazard ratios of 3.06 (95% CI = 2.11–4.44) and 7.30 (95% CI = 5.88–9.06) respectively. A significantly higher hazards of breast cancer-specific mortality were observed in those with grade III cancer, regional tumors with both direct and lymph node involvement, tumors located in the lower-inner quadrant of the breast, and 80 years or more.

Discussion

Racial disparities in access to healthcare, including breast cancer treatment, have been widely reported in the U.S. [26–28]. In this nation-wide large cohort of women aged 40 years and above with a primary diagnosis of breast cancer in the United States from 2010 to 2017, we sought to assess racial and ethnic disparities in undergoing the recommended surgery. The findings from our study suggest that race/ethnicity, increasing age, tumor subtypes, income, area of residence (rural vs. urban), and year of diagnosis are significant predictors of whether the recommended surgery for breast cancer was performed for women aged 40 years and older.

Non-Hispanic Blacks were more likely to refuse getting surgery as recommended for breast cancer compared to Non-Hispanic Whites. This is consistent with similar studies that have assessed the predictors of breast cancer recommended surgery refusal [7, 14–19]. This finding can be attributed to low socioeconomic status (SES) and distrust of health care among racial minorities [7, 27, 29]. Evidence suggests that income and employment are major determinants of a person's refusal to undergo recommended surgery [7, 30]. This is partly explained in that people with low income may not have health insurance or the financial resources to cover the cost of treatment or any additional out-of-pocket expenses required for a recommended surgery for breast cancer [7, 30]. However, contrary to what has been previously documented in other studies, higher median household income (> 75,000) at the census tract level was significantly associated with an increased odds of refusing the recommended surgery in our study. The reason for this finding is unclear. Additionally, this study is limited since we did not have access to insurance coverage and employment status data for different racial and ethnic groups. This study also revealed that non-Hispanic Black women were diagnosed at more advanced stages of breast cancer for which surgery may not be curative. This is similar to a study that found that NH Black women were 3 times (OR, 3.00 [95% CI, 2.41 to 3.75]) more likely to not undergo mammography screening and 2.5 times (OR, 2.49 [CI, 1.59 to 3.92]) more likely to present with a more advanced stage of breast cancer at diagnosis as compared to White women [31]. For persons who present with more advanced stages of breast cancer for which surgery may not be curative, a decision to undergo a recommended surgery may not seem favorable especially when it weighed against the economic burden following the procedure.

Increasing age was also significantly associated with an increased odds of refusing recommended surgery being performed, which was disproportionate for women aged 80 years and older compared to those aged 40–49 years consistent with other studies on the topic [7, 14–19]. Advanced age is associated with an increased risk for comorbidities and decreased survival after cancer treatment [32, 33]. As such, these patients may not have had the recommended surgery performed because they may be sicker or have a decreased life expectancy from other comorbidities or from advanced age. Additionally, breast cancer screening after the age of 74 years is controversial and not recommended especially for average-risk older women with less than 10 years life expectancy [33–35]. Hence, women with breast cancer after 70 years could present with an advanced stage of breast cancer or may refuse surgery as this treatment may not impact life expectancy. We were unable to assess the relationship between advanced age, comorbidities, and likelihood of undergoing recommended surgery because the publicly available SEER data does not include clinical information on comorbid conditions.

This study also explored the extent to which disparities in receipt of breast cancer surgery were due to molecular subtype characteristics in an ethnically diverse cohort of older women in the United States. Our study revealed that women with breast cancer subtypes luminal B and HER2 enriched and triple negative as compared to luminal A subtype were more likely to refuse recommended breast cancer surgery. This was particularly true for HER2 enriched tumors and triple negative tumors, which have been more closely associated with aggressive tumor features such as increased tumor size, positive lymph nodes and lymphovascular invasion [36]. Although different negative prognostic factors exist for different breast cancer subtypes, studies have found that cases with HER2 and triple negative tumors, predominantly

diagnosed among racial minorities such as African American and American Indian/ Native Alaska women, have the worst 5-year survival and overall survival among the other subtypes [36, 37]. As such, cases with more aggressive subtypes such as HER2 enriched may likely present at more advanced stages of breast cancer at diagnosis for which surgery may not be curative and this may impact the decision to pursue recommended surgery for breast cancer.

Similar to other studies, women who received a recommended surgery for breast cancer treatment had a better survival probability as compared to those who refused recommended treatment [4, 8]. Significant predictors of death following a breast cancer diagnosis included age 80 years or more, HER2 enriched and triple negative tumors and tumor features suggestive of advanced disease such as tumor grade III and lymph node involvement. As previously discussed, HER2 enriched and triple negative tumors, which were mostly present among African American women, were associated with aggressive disease [36–39]. This suggests that breast tumor subtypes' impact on breast cancer disease progression may be a significant contributor of whether recommended surgery is refused or performed and could ultimately affect survival benefit from breast cancer surgery particularly among NH Black women.

The study strengths include the use of the SEER database, a large nationally representative cancer registry which allows for generalizability of results to the general population in the US. Additionally, to our knowledge, this is one of the few studies to examine the refusal of surgery for breast cancer specifically by examining and adjusting for tumor stage, grade, and molecular subtype.

One of the limitations of this study is that the information on chemotherapy and radiation therapy were incomplete, thus their interpretations should be done with caution. Another limitation of the study is that it is possible that an eligible patient with recommended surgery purposely chose to have a surgery outside SEER areas or abroad. This has a potential of introducing differential bias in the analysis. Additionally, the SEER database lacks the detailed clinical and circumstantial information for each patient. There is therefore the potential for residual confounding as we were limited in our ability to control for other potential confounders such as comorbidities. Furthermore, the lack of detailed clinical information limits our ability to fully understand the reasons why a recommended surgery for breast cancer treatment was not performed. There is also the potential for selection bias since individuals who were excluded from the analysis could be significantly different in examined characteristics from those included in the analysis.

Conclusion

In conclusion, this study highlights the racial and ethnic disparity in the receipt of a recommended surgery for breast cancer treatment in the United States. Although NH Black women are disproportionately affected by breast cancer, they are more likely to refuse a recommended surgery for breast cancer treatment even when it is the main modality of treatment. Refusal of surgery for breast cancer treatment can negatively impact survival in this vulnerable group. Physicians should be cognizant

of the predictors of surgery refusal. Also, targeted and culturally relevant interventions should be implemented for this at-risk population.

Statements and Declarations

Declarations

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Ethics Approval: The study subjects were de-identified and there was no patient contact; thus, the study is exempt from an Institutional Review Board's review.

Data Availability: *The datasets generated during and/or analyzed during the current study are not publicly available due to SEER's Data use agreement and terms. The data access requests should be directly made to SEER <https://service.cancer.gov/seer-data-access>*

References

- [1] Guo F, Kuo Y-f, Berenson AB (2019) Breast Cancer Incidence by Stage Before and After Change in Screening Guidelines. *American journal of preventive medicine* **56**(1): 100-108.
<https://doi.org/10.1016/j.amepre.2018.08.018>
- [2] American Cancer Society (2021). *Cancer Facts & Figures 2021*.
<https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2021/cancer-facts-and-figures-2021.pdf>. Accessed 15 December 2021
- [3] DeSantis CE, Ma J, Gaudet MM, Newman LA, Miller KD, Goding Sauer A, Jemal A, Siegel RL (2019) Breast cancer statistics, 2019. *CA: A Cancer Journal for Clinicians* **69**(6): 438-451.
<https://doi.org/https://doi.org/10.3322/caac.21583>
- [4] Harper S, Lynch J, Meersman SC, Breen N, Davis WW, Reichman MC (2009) Trends in Area-Socioeconomic and Race-Ethnic Disparities in Breast Cancer Incidence, Stage at Diagnosis, Screening,

Mortality, and Survival among Women Ages 50 Years and Over (1987-2005). *Cancer Epidemiology Biomarkers & Prevention* **18**(1): 121-131. <https://doi.org/10.1158/1055-9965.Epi-08-0679>

[5] Waks AG, Winer EP (2019) Breast Cancer Treatment: A Review. *JAMA* **321**(3): 288-300. <https://doi.org/10.1001/jama.2018.19323>

[6] Wheeler SB, Carpenter WR, Peppercorn J, Schenck AP, Weinberger M, Biddle AK (2012) Predictors of timing of adjuvant chemotherapy in older women with hormone receptor-negative, stages II-III breast cancer. *Breast Cancer Res Treat* **131**(1): 207-16. <https://doi.org/10.1007/s10549-011-1717-6>

[7] Gaitanidis A, Alevizakos M, Tsalikidis C, Tsaroucha A, Simopoulos C, Pitiakoudis M (2018) Refusal of Cancer-Directed Surgery by Breast Cancer Patients: Risk Factors and Survival Outcomes. *Clin Breast Cancer* **18**(4): e469-e476. <https://doi.org/10.1016/j.clbc.2017.07.010>

[8] Joseph K, Vrouwe S, Kamruzzaman A, Balbaid A, Fenton D, Berendt R, Yu E, Tai P (2012) Outcome analysis of breast cancer patients who declined evidence-based treatment. *World journal of surgical oncology* **10**(1): 118-118. <https://doi.org/10.1186/1477-7819-10-118>

[9] Edwards BK, Brown ML, Wingo PA, Howe HL, Ward E, Ries LA, Schrag D, Jamison PM, Jemal A, Wu XC, Friedman C, Harlan L, Warren J, Anderson RN, Pickle LW (2005) Annual report to the nation on the status of cancer, 1975-2002, featuring population-based trends in cancer treatment. *J Natl Cancer Inst* **97**(19): 1407-27. <https://doi.org/10.1093/jnci/dji289>

[10] Hewitt ME, Simone JV, *Ensuring quality cancer care*. 1999, Washington, D.C: National Academy Press.

[11] Nissen MJ, Swenson KK, Ritz LJ, Farrell JB, Sladek ML, Lally RM (2001) Quality of life after breast carcinoma surgery: A comparison of three surgical procedures. *Cancer* **91**(7): 1238-1246. [https://doi.org/10.1002/1097-0142\(20010401\)91:7<1238::AID-CNCR1124>3.0.CO;2-X](https://doi.org/10.1002/1097-0142(20010401)91:7<1238::AID-CNCR1124>3.0.CO;2-X)

[12] Metcalfe KA, Semple J, Quan M-L, Vadaparampil ST, Holloway C, Brown M, Bower B, Sun P, Narod SA (2011) Changes in Psychosocial Functioning 1 Year After Mastectomy Alone, Delayed Breast Reconstruction, or Immediate Breast Reconstruction. *Annals of surgical oncology* **19**(1): 233-241. <https://doi.org/10.1245/s10434-011-1828-7>

[13] Verkooijen HM, Fioretta GM, Rapiti E, Bonnefoi H, Vlastos G, Kurtz J, Schaefer P, Sappino AP, Schubert H, Bouchardy C (2005) Patients' refusal of surgery strongly impairs breast cancer survival. *Ann Surg* **242**(2): 276-80. <https://doi.org/10.1097/01.sla.0000171305.31703.84>

[14] Lund MJ, Brawley OP, Ward KC, Young JL, Gabram SS, Eley JW (2008) Parity and disparity in first course treatment of invasive breast cancer. *Breast Cancer Res Treat* **109**(3): 545-57. <https://doi.org/10.1007/s10549-007-9675-8>

- [15] Aizer AA, Chen MH, Parekh A, Choueiri TK, Hoffman KE, Kim SP, Martin NE, Hu JC, Trinh QD, Nguyen PL (2014) Refusal of curative radiation therapy and surgery among patients with cancer. *Int J Radiat Oncol Biol Phys* **89**(4): 756-64. <https://doi.org/10.1016/j.ijrobp.2014.03.024>
- [16] Rapp J, Tuminello S, Alpert N, Flores RM, Taioli E (2019) Disparities in surgery for early-stage cancer: the impact of refusal. *Cancer Causes Control* **30**(12): 1389-1397. <https://doi.org/10.1007/s10552-019-01240-9>
- [17] Hamidi M, Moody JS, Kozak KR (2010) Refusal of radiation therapy and its associated impact on survival. *American journal of clinical oncology* **33**(6): 629-632. <https://doi.org/10.1097/COC.0b013e3181d270ce>
- [18] Hu X, Ye H, Yan W, Sun Y (2022) Factors Associated With Patient's Refusal of Recommended Cancer Surgery: Based on Surveillance, Epidemiology, and End Results. *Frontiers in public health* **9**: 785602-785602. <https://doi.org/10.3389/fpubh.2021.785602>
- [19] Wang S, Chen S, Huang Y, Hu D, Zeng W, Zhou L, Zhou W, Chen D, Feng H, Wei W, Zhang C, Liu Z, Wang M, Guo L (2021) Refusal of cancer-directed surgery in male breast cancer. *Medicine* **100**(13): e25116-e25116. <https://doi.org/10.1097/MD.00000000000025116>
- [20] Tohme S, Kaltenmeier C, Bou-Samra P, Varley PR, Tsung A (2018) Race and Health Disparities in Patient Refusal of Surgery for Early-Stage Pancreatic Cancer: An NCDB Cohort Study. *Ann Surg Oncol* **25**(12): 3427-3435. <https://doi.org/10.1245/s10434-018-6680-6>
- [21] Mehta RS, Lenzner D, Argiris A (2012) Race and health disparities in patient refusal of surgery for early-stage non-small cell lung cancer: a SEER cohort study. *Ann Surg Oncol* **19**(3): 722-7. <https://doi.org/10.1245/s10434-011-2087-3>
- [22] Landrum MB, Keating NL, Lamont EB, Bozeman SR, McNeil BJ (2012) Reasons for underuse of recommended therapies for colorectal and lung cancer in the Veterans Health Administration. *Cancer* **118**(13): 3345-55. <https://doi.org/10.1002/cncr.26628>
- [23] Duggan MA, Anderson WF, Altekruse S, Penberthy L, Sherman ME (2016) The Surveillance, Epidemiology, and End Results (SEER) Program and Pathology: Toward Strengthening the Critical Relationship. *The American journal of surgical pathology* **40**(12): e94-e102. <https://doi.org/10.1097/PAS.0000000000000749>
- [24] Surveillance, Epidemiology, and End Results Program (2021) Number of persons by race and Hispanic ethnicity for SEER participants based on 2020 Census data. <https://seer.cancer.gov/registries/data.html>. Accessed on 04 December 2021
- [25] Oeffinger KC, Fontham ETH, Etzioni R, Herzig A, Michaelson JS, Shih Y-CT, Walter LC, Church TR, Flowers CR, LaMonte SJ, Wolf AMD, DeSantis C, Lortet-Tieulent J, Andrews K, Manassaram-Baptiste D,

- Saslow D, Smith RA, Brawley OW, Wender R (2015) Breast Cancer Screening for Women at Average Risk: 2015 Guideline Update From the American Cancer Society. *JAMA* **314**(15): 1599-1614.
<https://doi.org/10.1001/jama.2015.12783>
- [26] Davis BA, Aminawung JA, Abu-Khalaf MM, Evans SB, Su K, Mehta R, Wang S-Y, Gross CP (2017) Racial and Ethnic Disparities in Oncotype DX Test Receipt in a Statewide Population-Based Study. *Journal of the National Comprehensive Cancer Network* **15**(3): 346-354.
<https://doi.org/10.6004/jnccn.2017.0034>
- [27] Dreyer MS, Nattinger AB, McGinley EL, Pezzin LE (2017) Socioeconomic status and breast cancer treatment. *Breast cancer research and treatment* **167**(1): 1-8. <https://doi.org/10.1007/s10549-017-4490-3>
- [28] McCarthy EP, Burns RB, Coughlin SS, Freund KM, Rice J, Marwill SL, Ash A, Shwartz M, Moskowitz MA (1998) Mammography use helps To explain Differences in breast cancer stage at diagnosis between Older Black and white women. *Annals of internal medicine* **128**(9): 729-736.
<https://doi.org/10.7326/0003-4819-128-9-199805010-00005>
- [29] Jacobs EA, Rolle I, Ferrans CE, Whitaker EE, Warnecke RB (2006) Understanding African Americans' views of the trustworthiness of physicians. *Journal of General Internal Medicine* **21**(6): 642.
<https://doi.org/10.1111/j.1525-1497.2006.00485.x>
- [30] Singh GK, Daus GP, Allender M, Ramey CT, Martin EK, Perry C, Reyes AADL, Vedamuthu IP (2017) Social Determinants of Health in the United States: Addressing Major Health Inequality Trends for the Nation, 1935-2016. *International journal of MCH and AIDS* **6**(2): 139-164.
<https://doi.org/10.21106/ijma.236>
- [31] McCarthy EP, Burns RB, Coughlin SS, Freund KM, Rice J, Marwill SL, Ash A, Shwartz M, Moskowitz MA (1998) Mammography use helps to explain differences in breast cancer stage at diagnosis between older black and white women. *Ann Intern Med* **128**(9): 729-36. <https://doi.org/10.7326/0003-4819-128-9-199805010-00005>
- [32] Harper S, Lynch J, Meersman SC, Breen N, Davis WW, Reichman MC (2009) Trends in Area-Socioeconomic and Race-Ethnic Disparities in Breast Cancer Incidence, Stage at Diagnosis, Screening, Mortality, and Survival among Women Ages 50 Years and Over (1987-2005). *Cancer epidemiology, biomarkers & prevention* **18**(1): 121-131. <https://doi.org/10.1158/1055-9965.EPI-08-0679>
- [33] Hawley ST, Fagerlin A, Janz NK, Katz SJ (2008) Racial/Ethnic Disparities in Knowledge about Risks and Benefits of Breast Cancer Treatment: Does It Matter Where You Go? *Health services research* **43**(4): 1366-1387. <https://doi.org/10.1111/j.1475-6773.2008.00843.x>
- [34] Wedding U, Röhrig B, Klippstein A, Pientka L, Höffken K (2007) Age, severe comorbidity and functional impairment independently contribute to poor survival in cancer patients. *Journal of cancer research and clinical oncology* **133**(12): 945-950. <https://doi.org/10.1007/s00432-007-0233-x>

- [35] Demb J, Abraham L, Miglioretti DL, Sprague BL, O'Meara ES, Advani S, Henderson LM, Onega T, Buist DSM, Schousboe JT, Walter LC, Kerlikowske K, Braithwaite D (2020) Screening Mammography Outcomes: Risk of Breast Cancer and Mortality by Comorbidity Score and Age. *JNCI : Journal of the National Cancer Institute* **112**(6): 599-606. <https://doi.org/10.1093/jnci/djz172>
- [36] Xue C, Wang X, Peng R, Shi Y, Qin T, Liu D, Teng X, Wang S, Zhang L, Yuan Z (2012) Distribution, clinicopathologic features and survival of breast cancer subtypes in Southern China. *Cancer science* **103**(9): 1679-1687. <https://doi.org/10.1111/j.1349-7006.2012.02339.x>
- [37] Perou CM, Børresen-Dale A-L (2011) Systems biology and genomics of breast cancer. *Cold Spring Harbor perspectives in biology* **3**(2): a003293-a003293. <https://doi.org/10.1101/cshperspect.a003293>
- [38] Dietze EC, Sistrunk C, Miranda-Carboni G, O'Regan R, Seewaldt VL (2015) Triple-negative breast cancer in African-American women: disparities versus biology. *Nature reviews. Cancer* **15**(4): 248-254. <https://doi.org/10.1038/nrc3896>
- [39] Prakash O, Hossain F, Danos D, Lassak A, Scribner R, Miele L (2020) Racial Disparities in Triple Negative Breast Cancer: A Review of the Role of Biologic and Non-biologic Factors. *Front Public Health* **8**: 576964. <https://doi.org/10.3389/fpubh.2020.576964>

Figures

Figure 1

Sample Selection

Figure 2

Surgery refusal prevalence over time