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Survival Disparities in Male Patients With Breast Cancer

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Abstract. *Background/Aim: We evaluated factors associated with mortality among men with breast cancer. Materials and Methods: We used the National Cancer Database to identify men with breast cancer and evaluated factors associated with mortality, using a Cox regression model. Results: Black patients experienced an increased risk of death from any cause compared to white patients [hazard ratio (HR)=1.19, 95%CI=1.05-1.37]. Patients with government insurance had a greater risk of death compared to privately insured patients (HR=1.57, 95%CI=1.41-1.75). When compared to patients with an income of >$46,000, those with an income <$30,000 presented an increased risk of death (HR=1.35, 95%CI=1.14-1.60). Finally, patients treated at a comprehensive community cancer program (HR=1.129, 95%CI=1.021-1.248), community cancer program (HR=1.164, 95%CI=1.010-1.343), or integrated network cancer program (HR=1.216; 95%CI=1.056-1.401) experienced elevated risk of death compared to those treated at academic/research-programs. Conclusion: Race, insurance, income, education, and facility type are associated with the risk of mortality in male patients with breast cancer.*

Male breast cancer is a rare disease, representing 1% of all cancers in male patients and is also accountable for less than 0.2% of cancer deaths reported in men (1). Risk factors for male breast cancer include diseases that increase estrogen level, such as Klinefelter syndrome, obesity, testicular damage, cirrhosis, and exogenous source (2). In addition, African American ancestry has also been associated with increased risk of male breast cancer, and up to 40% of male breast cancer is hereditary compared to only 5% to 10% in female breast cancer (3). Finally, previous studies have shown that male breast cancer has a higher mortality when compared to stage- and subtype-matched female breast cancer (4).

Due to the low incidence of this disease, there is limited available information on the impact socioeconomic characteristics can have on overall survival. Furthermore, to our knowledge, no reports on disparities among patients with male breast cancer have been reported. The purpose of this study was to analyze if there are disparities in overall survival based on patient, facility, and disease characteristics.

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Patients and Methods

The National Cancer Database (NCDB) is sponsored by the American College of Surgeons and the American Cancer Society. The NCDB collects information from approximately 70% of the newly diagnosed oncologic patients in the United States (5). Information found in the NCDB is entered by Certified Tumor Registrars, where it is then revised for accuracy (5). This retrospective cohort analysis was exempt from institutional review board evaluation due to the unidentified population-based nature of the NCDB.

We included male patients, 18 years of age or older, diagnosed with breast cancer between January 1st, 2004 and December 31st, 2010. We excluded female patients, those with stage IV disease, Paget disease, or inflammatory cancer, and those diagnosed between 2011 and 2015. Patients presenting with stage IV disease were excluded because they were beyond the reach of curative treatment. Patients diagnosed between 2011 and 2015 were also excluded from the analysis because they do not have 5 years of follow-up, potentially affecting survival analysis. Inclusion and exclusion criteria are illustrated in Figure 1.

Our primary outcome was patient overall survival. The NCDB defines survival as the number of months from the date of diagnosis to the date of death, until patients are lost to follow-up, or until the last date of the study (December 31, 2015). It is important to note that the NCDB does not collect specific cancer survival information.

Our primary independent variables included the following demographic covariates: age (categorized by age groups), race,

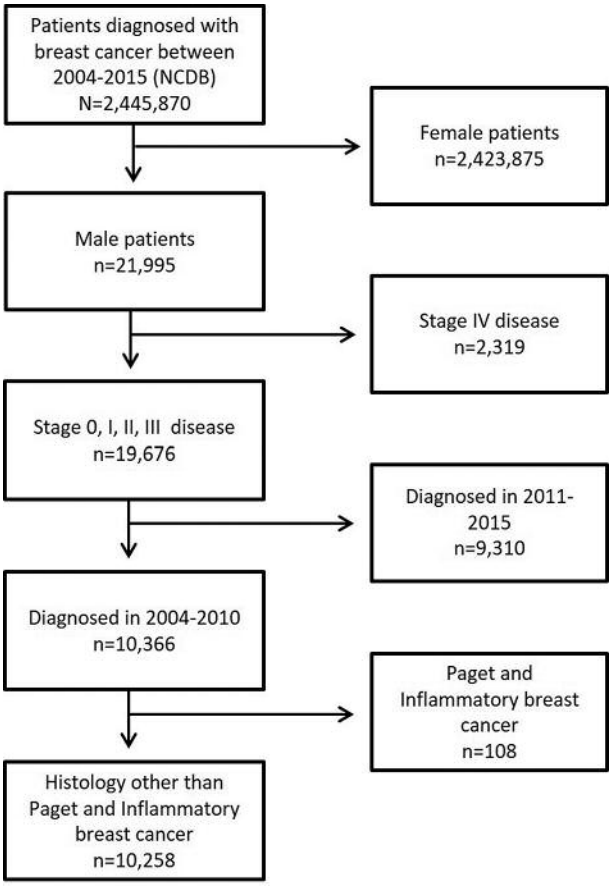

Figure 1. *Patient inclusion and exclusion criteria.*

insurance status, income, education, and population density. It is important to note that the NCDB does not include patient-specific income or education level information. Based on census information from 2000, income is calculated using the average household income within the patient's zip code, and education level is calculated using the percentage of people without a high school diploma in the zip code of residence. We also included facility type and location in our analysis. Facility type defines the type of hospital at which a patient received care (*e.g.*, academic/research center, comprehensive community cancer program). Facility location was used to describe our patient population, but was not included in the multivariate analysis due to its low clinical relevance. Disease-specific characteristics, including stage of disease, Charlson Deyo Score (comorbidity index), histology, estrogen receptor (ER) status, and tumor size, were also included as independent variables. We intended to include hormonal status triple negative assessment, but this was not possible because the human epidermal growth factor receptor 2 status was not included in the NCDB until after 2010, making this information unavailable for the population in question. These covariates were selected because they characterize the patient, facility, and disease-specific variables that could have an impact on patient mortality.

Using a multivariable Cox regression model, we analyzed the impact of patient, facility, and disease-specific characteristics on the odds of mortality after adjusting for the mentioned covariates. Patients with 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

We identified 2,445,870 patients with a diagnosis of breast cancer. After meeting the inclusion criteria, 10,258 patients were included. Mean (SD) age was 64.47 (13.13) years; 8,585 (83.7%) were white, 1,255 (12.2%) black, 188 (1.8%) Asian, and 12 (0.1%) Native American. Demographic, facility, and disease-specific characteristics are further described on Table I.

In the adjusted Cox Regression model (Table II), our results showed that as age increased, the hazard ratio (HR) for overall death increased. When compared with patients aged 40 to 60, 60- to 80-year-old patients (HR=1.53, 95%CI=1.34-1.73) and those older than 80 years (HR=4.28, 95%CI=3.70-4.94) had an increased risk of dying. Black patients (HR=1.19, 95%CI=1.05-1.37) were found to have significantly greater risk of overall death than white patients. However, no significant differences were found when comparing Asian and Native American patients to white patients. No significant differences were found when independently calculating the risk of death based on education. Patients with government insurance (HR=1.57, 95%CI=1.41-1.75) were found to have greater risk of overall death when compared to those with private insurance. Interestingly, no significant difference was found in uninsured patients. Patients with an estimated income of $35,000 to $45,999 (HR=1.13, 95%CI=1.01-1.27), $30,000 to $34,999 (HR=1.32, CI=1.15-1.52), and less than $30,000 (HR=1.35, CI=1.14-1.60) independently had significantly increased risk of overall mortality when compared to patients with estimated income of $46,000 or more. Patients receiving treatment at a comprehensive community cancer program (HR=1.13, 95%CI=1.02-1.25), community cancer program (HR=1.16, 95%CI=1.01-1.34), or integrated network cancer program (HR=1.22, 95%CI=1.06-1.40) had a greater risk of death than patients receiving treatment at academic/research programs.

Disease-specific characteristics were also found to independently affect the overall mortality in male patients with breast cancer. As stage of disease increased, mortality risk progressively increased when compared to stage 0 disease: stage I (HR=1.64, 95%CI=1.31-2.05), stage II (HR=2.28, 95%CI=1.85-2.82), stage III (HR=3.57, 95%CI=2.87-4.45). Furthermore, patients with positive lymph node assessment (HR=1.37, 95%CI=1.23-1.51) had an increased risk of death when compared to patients with negative lymph node assessment.

Table I. *Characteristics of patients with male breast cancer.*

	No.	%
Total	10258	100
Age		
18-40 years	298	2.9
40-60 years	3356	32.7
60-80 years	5165	50.4
≥80 years	1439	14
Race		
White	8585	83.7
Black	1255	12.2
Asian	188	1.8
Native American	12	0.1
Missing	218	2.1
Insurance		
Private	4715	46
Government	5099	49.7
Not insured	231	2.3
Missing	213	2.1
Income		
≥$46,000	4605	44.9
$35,000-$45,999	2592	25.3
$30,000-$34,999	1525	14.9
<$30,000	1160	11.3
Missing	376	3.7
Education		
<14%	4182	40.8
14%-19.9%	2292	22.3
20%-28.9%	2080	20.3
≥29%	1326	12.9
Missing	378	3.7
Population density		
Metropolitan	8632	84.1
Urban	1134	11.1
Rural	143	1.4
Missing	349	3.4
Facility type		
Academic/Research Program	2844	27.7
Comprehensive Community Cancer Program	4796	46.8
Community Cancer Program	1170	11.4
Integrated Network Cancer Program	1150	11.2
Missing	298	2.9
Facility location		
New England	693	6.8
Middle Atlantic	1702	16.6
South Atlantic	2406	23.5
East North Central	1880	18.3
East South Central	550	5.4
West North Central	725	7.1
West South Central	683	6.7
Mountain	439	4.3
Pacific	882	8.6
Missing	298	2.9
Stage		
Stage 0	1473	14.4
Stage I	3473	33.9
Stage II	3700	36.1
Stage III	1612	15.7
Charlson Deyo score		
0	8334	81.2
1	1492	14.5
≥2	338	3.3
Missing	94	0.9
Histology		
Ductal	8702	84.8
Lobular	399	3.9
Others	1157	11.3
ER status		
Positive	8494	82.8
Negative	763	7.4
Unknown	1001	9.8
Lymph nodes		
Negative	5094	49.7
Positive	5164	50.3

No.: Number of patients.

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Discussion

Male breast cancer, though not common, can be deadly. In 2019, more deaths are expected to occur due to male breast cancer than testicular cancer (500 vs. 410) in the United States (6). Men usually present at a higher stage of disease than women, possibly due to low awareness and no prevention programs (7). Previous studies have focused on identifying reasons for the disparity between increased survival outcomes of women with breast cancer when compared to men (8-10). Results suggested that disparity is associated with lack of screening and the only few randomized trials performed to define appropriate treatment for male breast cancer (8-10). However, to our knowledge, no studies have analyzed the gap among male patients, comparing survival outcomes by socioeconomic, facility, and disease-specific characteristic. The importance of our study lies in the fact that it is the first to analyze the presence of disparities in the survival of male breast cancer. Our results fill this gap in the literature and create awareness to enhance public health strategies to reduce disparities.

Prevention programs, early detection, and treatment improvement have increased the survival outcomes for most types of cancer. However, these resources have not been made available equally, and poorer outcomes have been reported in vulnerable populations, like minorities or those with less access to the health care system (11, 12). The incidence of female breast cancer has been greater in white patients than black; however, mortality is higher for black patients than white (13). Furthermore, the decrease in female breast cancer mortality since 1999 was higher in white patients than black (13). This shows that prevention

Table II. *Multivariate Cox regression analysis*.

		95%CI		
	HR	Lower	Upper	*p*-Value
Age				
40-60 years				0
60-80 years	1.525	1.347	1.728	<0.001
>80 years	4.276	3.703	4.938	<0.001
Race				
White				0.022
Black	1.194	1.048	1.36	0.008
Asian	0.764	0.51	1.143	0.19
Native American	1.547	0.577	4.149	0.386
Insurance				
Private				<0.001
Government	1.573	1.414	1.75	<0.001
Not insured	1.253	0.905	1.735	0.175
Income				
≥$46,000				0
$35,000-$45,999	1.134	1.012	1.27	0.031
$30,000-$34,999	1.32	1.148	1.517	<0.001
<$30,000	1.352	1.139	1.603	0.001
Education				
<14%				0.173
14%-19.9%	1.106	0.986	1.24	0.086
20%-28.9%	0.995	0.87	1.136	0.936
≥29%	0.96	0.81	1.139	0.642
Facility type				
Academic/Research Program				0.022
Comprehensive Community Cancer Program	1.129	1.021	1.248	0.018
Community Cancer Program	1.164	1.01	1.343	0.036
Integrated Network Cancer Program	1.216	1.056	1.401	0.007
Stage				
Stage 0				0
Stage I	1.638	1.31	2.049	<0.001
Stage II	2.284	1.847	2.823	<0.001
Stage III	3.573	2.87	4.447	<0.001
Charlson Deyo score				
0				0
1	1.602	1.449	1.771	<0.001
≥2	2.78	2.37	3.26	<0.001
Histology				
Ductal				0
Lobular	0.744	0.587	0.942	0.014
ER status				
Positive				0
Negative	1.107	0.938	1.307	0.229
Lymph nodes				
Negative				
Positive	1.366	1.233	1.513	<0.001
Tumor size				
<2 cm				0.692
2-4.9 cm	1.075	0.501	2.308	0.853
≥5 cm	1.205	0.601	2.416	0.599

HR: Hazard ratio; ER: estrogen receptor.

programs and equal care can potentially decrease the mortality of male breast cancer.

We found that having a lower income increases the likelihood of dying in patients with male breast cancer. In a 2004 meta-analysis, Subramanian and colleagues (12) observed that poverty was a contributing factor for poor overall health and premature mortality from diseases considered curable, and in 2006, Cormier and colleagues

(14) noted that low income was a risk factor for poorer outcomes in cancer.

Our results show that black men with breast cancer have a lower overall survival than white men. We did not find studies that analyzed male breast cancer overall survival by race to compare our results with, however, it has been shown that black women with breast cancer are negatively affected by racial disparities, ranging from decreased survival to receipt of elective procedures like breast reconstruction (15-17).

This study also demonstrated that insurance status can independently affect overall survival. Insurance disparities are expected, since patients with private insurance have better access to physicians and screening procedures. It is interesting to see that patients with government insurance, despite having access to health care, still had lower survival. Efforts to give patients the best care possible, despite their insurance, must be made to reduce this gap. It has been reported that disparities tend to disappear in populations in which everyone has equal access to health care services (16).

In terms of income (estimated by average income in zip code of residence), we also found that as the level of income decreases, overall mortality secondary to male breast cancer increases. Male breast cancer is not the only malignancy that has been found to have a higher mortality in patients with lower income. It has been previously reported by Singh and colleagues (18) that patients with lower income are more likely to have overall higher cancer mortality than patients with higher income (18).

In our multivariate model, type of facility where a patient received care had a significant impact on survival. It was demonstrated that receiving care at an academic facility decreased mortality when compared to comprehensive community, community cancer, and integrated network cancer programs. Our results are in concordance with Bhatt and colleagues (19), whose study showed that patients treated for acute myeloid leukemia at academic centers had a lower mortality than patients treated at nonacademic centers (19).

Our study is not without limitations. Our analysis was conducted using the NCDB because it includes data from approximately 70% of the cancer population in the USA; however, its overall fidelity could be affected by individual centers' incomplete reports. Furthermore, the NCDB does not have 5-year follow-up for patients diagnosed from 2011 to 2015 because the study ended December 31, 2015. Additionally, income and education are based on the zip code where the patients reside rather than specific characteristics of the patients, leading to assumptions of income or education level that might not be accurate for every patient.

Race, insurance, income, education, and facility type seem to affect mortality in patients with male breast cancer. Future efforts are warranted to reduce deaths that can be prevented with equal care.

Conflicts of Interest

All Authors report no conflicts of interest regarding this study.

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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