

A Five-Year Breast Cancer-Specific Survival Disadvantage of African American Women

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Abstract

Racial/ethnic disparities in female breast cancer survival continue to persist in United States. However, disparities comparing African Americans (AA), Asians and Caucasians remain to be assessed. We aimed to assess multi-racial/ethnic disparities in breast cancer survival, and to examine the factors that may explain the variability. A total of 6,951 women diagnosed with breast cancer between 1992 and 1998 were identified from Surveillance, Epidemiology, and End Results tumor registries. The effect of race/ethnicity and the prognostic factors on survival was assessed using Cox proportional hazard model. AA demonstrated a survival disadvantage. Compared to Asians, Caucasians had 74% increased risk of dying (HR= 1.74, 95% CI = 1.31 – 2.33), while AA were almost three times as likely as Asians to die, (HR=2.78, 95% CI 2.02 – 3.86). After adjustment for the relevant covariates the survival disadvantage of AA persisted. Relative to Asians, Caucasians were 45% more likely to die (HR=1.45, 95% CI 1.10 – 1.93), while AA were more than two times as likely to die (HR=2.57, 95% CI 1.86 - 3.55). There were substantial racial/ethnic disparities in breast cancer survival among United States women. AA demonstrated survival disadvantage compared with either Caucasians or Asians, which persisted even after controlling factors known to influence breast cancer survival (*Afr. J. Reprod. Health* 2010; 14[3]: 195-200).

Résumé

Désavantage de la survie spécifique du cancer du sein à cinq ans chez les femmes afro-américaines. Les disparités raciales/ethniques dans la survie du cancer du sein chez la femme persistent encore aux Etats-Unis. Néanmoins, l'on n'a pas encore évalué les disparités de manière comparative chez les Afro-Américains (AA), les Asiatiques et les Caucasiens. Nous avons comme objectif d'avancer les disparités dans la survie du cancer du sein et d'examiner les facteurs qui puissent expliquer la variabilité. Au total, on a diagnostiqué le cancer du sein chez 6951 femmes entre 1992 et 1998 qui ont été identifiées à travers la surveillance, l'épidémiologie et des listes des résultats définitifs de la tumeur. L'effet de la race / l'ethnie et les facteurs pronostiqués sur la survie ont été évalués à l'aide du modèle du danger proportionnel de Cox. L'AA a démontré un désavantage de la survie. Par rapport aux Asiatiques, les Caucasiens couraient un risque accru à 74% de mourir (HR=1,74, 95% CI = 1,31-2,33), alors que les AA avaient presque trois fois plus la possibilité de mourir que les Asiatiques (HR=2,78, 95%CI 2,92-3,86). Après les ajustements pour arriver aux co-variables, le désavantage de la survie de l'AA a persisté. Par rapport aux Asiatiques, les Caucasiens avaient 45% plus la possibilité de mourir (HR=1,45, 95% CL 110-1,93), tandis que les AA avaient plus de deux fois la possibilité de mourir (HR=2,57, 95%CL 1,86-3,55). Il y avait beaucoup de disparités raciales/ethniques à l'égard de la survie du cancer du sein chez les femmes américaines. Les AA ont démontré un désavantage de la survie par rapport soit aux Caucasiens soit aux Asiatiques qui ont persisté même après avoir contrôlé les facteurs qui influent sur la survie du cancer du sein (*Afr. J. Reprod. Health* 2010; 14[3]: 195-200).

Key words: African American Women; breast cancer survival; racial/ethnic disparities; United States.

Introduction

Breast cancer is the most diagnosed non-dermatologic neoplasm among United States women, and incidence as well as survival varies by race/ethnicity¹⁻⁸. The incidence of breast cancer is higher among white women compared to black, Hispanic,

or Asian women⁵⁻¹¹. However, black women are more likely to be diagnosed with breast cancer at an early age and are also more likely to die from the disease relative to other ethnic and racial groups.

This racial/ethnic variances may be in part associated with hereditary, since an aggressive type of breast cancer called basal-like tumor seems most

likely to affect young African-American women^{12,13}. Secondly, the lower survival rates among black women may be related to limited access and lower quality health care¹⁴, as well as clinicians' preference not to treat American women with the proven aggressive therapy.

The risk factors in breast cancer incidence include race/ethnicity, dietary pattern, body mass index, high cholesterol diet, and age at menarche, gravida, parity, family history of breast cancer, family support system, and genetic predisposition^{12,13}. Also, factors associated with survival have been shown to include race/ethnicity, socio-economic status, comorbidities tumor stage, treatment options, marital status, age and race¹⁵⁻²².

Although breast cancer survival has improved over the last 30 years, disparities in survival between blacks and whites have not declined and remain sizeable²³. The 5-year survival rates in 1995-2000 for black and white breast cancer patients were 75% and 89%, respectively²⁴. In addition differences in comorbidities which had been shown in other tumors and in men, may explain disparities in breast cancer survival²⁵. The extent to which racial/ethnic differences in comorbidities explain disparities in breast cancer survival has not been well studied. Despite the identification of racial/ethnic disparities in tumor prognostic factors such as advanced cancer stage, lack of access to medical care, inferior treatment, and lower socio-economic status (SES), it is not fully understood which factors explain these disparities²⁶.

This current study aimed to examine the impact of race/ethnicity as a single predictor of breast cancer survival among the United State's women as well as to determine the prognostic factors which may explain racial disparities in survival. Therefore given the knowledge from other tumors with respect to racial/ethnic variation in survival, we postulated that the racial variation in breast cancer survival may be explained in part by the differences in treatment received, tumor stage, age at diagnosis and marital status.

Materials and Methods

After an approval from the appropriate Institutional Review Board (IRB), we conducted a retrospective cohort study to assess health disparities in the survival of women in the United State diagnosed with early and late stage breast cancer and treated for the disease.

Data sources

The merged Surveillance Epidemiology and End Result (SEER)-Medicare database for women aged 22 and older diagnosed with breast cancer from 1992 through 1998 in eleven SEER areas were

used. The SEER areas comprise the metropolitan areas of San Francisco/Oakland, Detroit, Atlanta, and Seattle; Los Angeles county, the San Jose Monterey area; and the states of Connecticut, Iowa, New Mexico, Utah, and Hawaii¹. This area represents an estimated 14% of the United States population.

Study population

The detail on study population has been described elsewhere². The study population comprised 6,951 female patients, aged 22 years or older, diagnosed with early and late stage breast cancer in the eleven SEER areas between 1992 and 1998.

Variables ascertainment

Breast Cancer, Treatment and Clinico-pathologic features

Breast cancer diagnosis was ascertained through the registries from multiple reporting sources³. The registries provide information on age at diagnosis, tumor stage, tumor size, tumor volume, grade, race, and treatment received (surgery, radiation), marital status and geography (region/location), cause, vital and time of death. Tumor stage was defined at diagnosis and classified into five distinct groups (0-IV), with 0 being tumor insitu and stage IV, the late or most advanced stage. Surgery received following the diagnosis of breast cancer was classified into two categories, namely breast conservative surgery (BCS) and mastectomy; and were compared to women without either BCS or mastectomy. Radiation was categorized into dichotomous variable, with those who received radiation therapy compared with women without, following diagnosis. Patients diagnosed with breast cancer at early and late stages were treated with breast conservative surgery. Radiotherapy was received by some patients who had BCS and those who did not.

Survival and Mortality

Breast cancer-specific death was ascertained and defined by breast cancer being the underlying cause of death or if patients with breast cancer died from unknown cause. All patients who died from other causes or were lost due to follow up were censored. Thus the event, a five-year cause-specific only considered breast cancer specific mortality – only count of those who died of breast cancer as having the event of interest, other causes are censored (event = 0). The five year survival, termed fix-year survival was obtained by dividing the number of persons known to survive for five years by the number of persons at risk for five years. Survival time was defined as the survival from the date of diagnosis to the date of death or the date of last follow-up. Vital status was defined as alive, or dead at the end of follow-up.

Table 1. Study characteristics by race/ethnicity of United States women diagnosed and treated for early and late stages breast cancer

Variables	White	Black	Asian	Others	Total
Age at Diagnosis (year)					
22-54	2,077 (82.16)	250 (9.89)	143 (5.66)	58 (2.29)	2,528 (36.7)
55-65	1,310 (84.30)	123 (7.92)	97 (6.24)	24 (1.54)	1,554 (22.36)
66-76	1,596 (89.51)	91 (5.10)	79 (4.43)	17 (0.95)	1,783 (25.62)
77+	998 (91.90)	42 (3.87)	40 (3.68)	6 (0.55)	1,086 (15.62)
Marital Status					
Single	582 (77.60)	113 (15.07)	40 (5.33)	15 (2.0)	750 (10.79)
Married	3,504(87.01)	213(5.29)	239(5.93)	71(1.76)	4,027 (57.93)
Separated	26 (72.22)	10(27.78)	0 (0.00)	0(0.00)	36(0.52)
Divorced	541(83.75)	74 (11.46)	22(3.47)	9 (1.39)	646 (9.29)
Widowed	1,328 (89.01)	96(6.43)	58(3.89)	10(0.6)	1,492 (21.46)
Tumor stage at diagnosis					
0	333 (81.02)	37 (9.0)	35 (8.52)	6 (1.46)	411 (5.91)
I	3,050 (88.28)	173 (5.01)	179(5.18)	53 (1.53)	3,455 (49.71)
II	2,162 (84.22)	238 (9.27)	129 (5.03)	38(1.48)	2,567 (36.93)
III	326 (84.24)	42 (10.85)	12 (3.10)	7 (1.81)	387 (5.57)
IV	110 (83.7)	16 (12.21)	4 (3.05)	1(0.76)	131 (1.88)
Surgery Received					
No surgery	58(82.86)	10(14.29)	1(1.43)	1(1.43)	70 (1.01)
Breast conservative surgery (BCS)	3,005(86.47)	250(7.19)	163(4.69)	57(1.64)	3,475(49.99)
Mastectomy	2,918 (85.67)	246(7.22)	195(5.73)	47(1.38)	3,406(49.00)

Race/Ethnicity

Race was defined as white (Anglo American), black (African Americans) and Asian (women of the East / South/West/North) Asia and others (American Indian, Alaska Natives, Hispanics not classified as whites are blacks).

Statistical Analyses

Frequency and percentage were used to summarize the study variables by race and ethnicity. The Kaplan-Meier survival curve was used to estimate the survival function as well as survival estimate by race/ethnicity. To determine the equality of survival by race, the log rank test was used. We tested proportionality of hazard assumption, and used Cox proportional hazard model to assess the effect of clinico-pathologic features on survival. Further, to examine the confounding effect of the clinico-pathologic features on the differences on survival by race /ethnicity, a multivariable Cox regression model was built. The significance level was 0.05, and all tests were two-tailed. All analyses were performed using STATA statistical package, version 10.0 (StataCorp, College Station, Texas).

Results

This result represents the survival experience of wo-

men diagnosed with breast cancer and treated for the disease. Table 1 presents the number and percentages of the age of the study population at the diagnosis of breast cancer stratified by race/ethnicity. Though not shown on table, white women made up the largest proportion of the sample, 5,981 (86.05%), blacks, 506(7.28%), Asians, 359 (5.16%) and others, 105(1.51%). The tumor stages at diagnosis were stratified by race/ethnicity. Compared with the proportion of blacks in the sample (5.16%), blacks were relatively more likely to be diagnosed with stage III (10.85%versus 5.16%) and IV (12.85% versus 5.16%) tumors. The study population with stage I and II breast cancer at diagnosis constituted 86.64% of all stages of breast tumor.

Table 2 presents the effects of clinico-pathologic features on marital status on breast cancer survival. This is the unadjusted hazard ratio of the effect of marital status, radiation, surgery, age, and tumor stage on cancer survival. In this model, compared with age group, 22-54 years, the was no significant difference by race/ethnicity among women, age 55-65 years, but white women in age group 66-76 had 92% increased risk of dying relative to white women in 22-54 age group. Compared to single black women, there was a 36% reduction in the risk of dying among married black women, HR=0.64, 95% Confidence Interval (CI), 0.42 – 0.97. Relative to white women with stage 0 tumor, white women stages I, II,

Table 2. The effects of prognostic factors on survival of United States Women diagnosed with early and late stage breast cancer

Prognostic factors	Asian	White	Black
	HR, 95% CI	HR, 95% CI	HR, 95% CI
Age (yrs)			
22-54	1.0 reference	1.0 reference	1.0 reference
55-65	1.71(0.78-3.74)	1.18(0.98-1.42)	0.87(0.56-1.35)
66-76	2.11(0.93-4.79)	1.92(1.63-2.26)	0.66(0.39-1.10)
77+	2.54(0.94-6.86)	3.93(3.29-4.68)	1.78(0.98-3.25)
Marital status			
Single	1.0	1.0	1.0
Married	1.04(0.37-2.88)	0.91(0.74-1.11)	0.64(0.42-0.97)
Separated	----	1.19(0.48-2.93)	0.51(0.15-1.66)
Divorced	1.90(0.52-6.94)	1.28(0.99-1.66)	0.60(0.33-1.08)
Widowed	0.92(0.27-3.08)	1.17(0.94-1.45)	1.39(0.81-2.39)
Tumor Stage			
0	1.0	1.0 reference	1.0 reference
I	0.83(0.23-2.93)	2.14(1.35-3.39)	1.32(0.51-3.41)
II	2.54(0.79-8.70)	3.98(2.51-6.30)	2.23(0.93-5.84)
III	2.43(0.37-16.0)	7.78(4.81-12.60)	8.35(3.13-22.28)
IV	13.10(2.39-71.62)	25.83(15.38-43.37)	12.32(4.24-35.79)
Surgery*			
No	1.0	1.0 reference	1.0 reference
BCS	---	0.72(0.49-1.07)	0.15(0.07-0.35)
Mastectomy	---	0.91(0.49-1.07)	0.19(0.08-0.41)
Radiation			
No	1.0	1.0 reference	1.0 reference
Yes	0.84(0.41-1.73)	0.74(0.64-0.86)	1.0(0.68-1.46)

Note: --- means that the HR was not computed due to small sample size in this subgroup. Black is interchangeable with African American in this study.

Table 3. The effect of race/ethnicity with and without adjustment on breast cancer survival among United States women diagnosed with early and late stage tumor and treated for the disease.

Race/ethnicity	Univariable Model Hazard Ratio (95% CI)	p	Multivariable Model Adjusted Hazard Ratio* (95% CI)	p
Asian	1.0	referent	1.0	referent
White	1.74(1.31-2.33)	0.001	1.45(1.10-1.93)	0.012
Black	2.78 (2.02-3.86)	0.001	2.57(1.86-3.55)	0.001

Notes and Abbreviations: * Adjusted for marital status, tumor stage at diagnosis, age at diagnosis, and other prognostic factors. The significance level is 0.05. CI=Confidence Interval.

III, and IV had 2, 3, 7, and 25 times increased risk of dying respectively, $p < 0.05$. Relative to black women who receive no surgery for the treatment of their disease those who received breast cancer conservative therapy had 85% decreased risk of dying (HR = 0.15, 95% CI 0.07 – 0.35), while those who received mastectomy had 81% decrease risk of dying (HR = 0.19, 95% CI 0.08 – 0.41). Compared with white women who received no radiation those who received radiation were 26% less likely to die from breast cancer, HR=0.74, 95% CI 0.64 – 0.86).

Table 3 presents the crude and adjusted hazard ratios of dying for Blacks and Whites, with Asian women as the reference group. In the unadjusted model, relative to Asian women, black women were almost 3 times (HR = 2.78, 95% CI, 2.02-3.86) as likely to die from breast cancer, while white women were 74% more likely to die from breast cancer (HR= 1.74, 95% CI 1.31 – 2.33). After adjustment for the relevant covariates namely marital status, tumor stage, age at diagnosis, and treatment (surgery, radiation) received, the significant racial/ethnic sur-

vival differences in breast cancer persisted. Compared with Asian women, black women were 2 times as likely to die from breast cancer while white women were 45% more likely to die (Table 3).

Discussion

This study was conducted to examine the effect of race/ethnicity on a five year breast cancer-specific survival of United States women in a population-based or community setting, and to determine whether or not survival disparities is explained by racial/ethnic variability in tumor prognostic factors and demographics. There are few relevant findings from this study. First, African American women demonstrated survival disadvantage from breast cancer relative to white and Asian women. Secondly, treatment received, tumor stage, age at diagnosis, and marital status had significant impacts on breast cancer survival in this cohort. Finally, racial/ethnic significant difference in breast cancer survival persisted after adjustment for tumor prognostic factors.

We demonstrated a statistically significant increased risk of dying from breast among black women compared to Asian women. Likewise we have shown that after adjustment for tumor prognostic factors, white women had survival disadvantage compared to Asian women. In fact, there was 45% increased risk of dying in this 5 year cause-specific mortality assessment. Overall, black women have the lowest breast cancer survival rate, indicating highest mortality in a five year cause-specific survival. Our finding supports previous studies in this direction^{6-11,14}.

We have also demonstrated that advancing age decreases breast cancer survival. Indeed, this observation was very outstanding among white women in our study. Age is a strong predictor of breast cancer survival, and the role of race/ethnicity in predicting survival may be confounded by age. In general, advancing age is associated with decreased breast cancer survival, and had been shown in other studies^{4,5}.

Tumor stage at diagnosis is a strong predictor of breast cancer survival. In our sample, especially among black and white women, there is a monotonic increase in breast cancer mortality with advancing stage of tumor at diagnosis. This finding supports a previous study²⁵. Marital status is a potent predictor of breast cancer survival, especially in black and white women. Compared to women who were single, our analysis indicated a significant decrease in breast cancer survival among married black women, and a statistically significant increase in breast cancer survival among white women who were single as well. Next, our data indicated that radiation has a protective effect in decreasing breast cancer mortality, and this beneficial effect was significant among white women. Surgery received com-

pared to no surgery significantly impacted on survival. Compared with no surgery and mastectomy, breast conservative surgery increases survival in breast cancer. Our findings are consistent with other findings in literature¹⁴⁻¹⁸.

The results in this analysis raise a number of issues related to race/ethnicity and disease etiology in general, race and cancer etiology in particular as well as race and cancer survival. There is no doubt that race plays a role in cancer survivability in general and breast cancer survival in particular. Previous studies have shown that black women relative to whites have poorer survival following breast cancer survival^{14, 18-22}. Our result therefore is consistent with most findings in this vein. An interesting and important finding in this analysis is the fact that Asian women compared with white and black women have the best breast cancer survival rate, while AA women have the worst survival, after adjustment for marital status, age and tumor stage at diagnosis.

Whether there is a biologic element in racial categorization remains to be fully evaluated, but race reflects both psycho-social and physical-environmental attributes. Using race in understanding survivability in breast cancer is indicative of factors outside treatment and tumor behavior that may affect breast cancer outcomes. The interpretation of race as a factor in breast cancer survival may be compromised by misclassification. Therefore the avoidance of misclassification bias in race category requires fine categories in epidemiologic investigation; such as inter-racial, bi-racial etc. Often bi-racial (white and black; Asian and black, Hispanic and black) and sometimes inter-racial are classified as blacks in spite of the shared population genes.

What are the possible causes or sources of variation in breast cancer survival? Studies have shown racial disparities in access to the health care delivery system, health resources utilization and quality care. Access to the health care system may illustrate why tumors are diagnosed at late stage among black women compared to Asians or white women (Table 1). One could argue that black women have a biologically aggressive breast tumor, which might explain decreased survival even after early stage diagnosis. It may also be possible that black women respond differently to chemotherapy and radiation therapy. It will also be important to examine data on surgical intervention of tumor and the variance in clinical practice with respect to black and white women. With respect to Asian women, early tumor detection, compliance to treatment regimen and dietary intake may play a role in the breast cancer survival advantage of this sub-population (Asian women). Finally, if diet, compliance to the treatment regimen and early detection are not associated with racial difference in breast cancer survival, then could this be biologic variance in breast tumor presentation? Whatever the cause of the racial va-

riation in breast cancer survival, this data support the consideration of race as a significant variable in breast cancer prognosis and survival.

Whereas the approach used in this study to illustrate the disadvantage of AA women in breast cancer survival presents some methodological strengths, there are some limitations as well. First, we used a retrospective design, which is prone to selection and misclassification and information biases. However, it is highly unlikely that the significant survival disadvantage of black women demonstrated in our data is driven solely by these internal validity issues. Secondly, we adjusted for some potential confounding factors in breast cancer survival, but there are factors known to drive breast cancer survival mainly comorbidities, SES, etc which were not available for adjustment in this study. These factors may very well influence in part our result. Finally, like in all epidemiologic studies, this study may be influenced by unmeasured and residual confounding factors.

Conclusion

In summary, there were substantial racial/ethnic disparities in breast cancer survival among United States women. African American women demonstrated survival disadvantage compared with either white or Asian women, which persisted even after controlling for factors known to predict breast cancer survival. Therefore, prospective studies are needed to determine whether or not the survival disadvantage of AA women in this cohort may be explained by racial/ethnic variance in dietary patterns, treatment compliance as well as other prognostic factors.

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