

BONE METASTATIC PROSTATE CANCER AMONG AFRICAN AMERICANS: THE SURVIVAL EQUIVALENCE PARADOX

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ABSTRACT

Prostate cancer (PC) is one of the leading causes of cancer-related deaths among men. It is well-documented that African American (AA) men in general have poorer survival outcomes than European American (EA) men. In this study, a retrospective review of prostate cancer patient charts from the past 12 years was conducted using an academic medical center's cancer registry and electronic health records. Sixty-nine AA and twenty-one EA PC patients with bone metastases were included in this study. Our analyses indicated that when treatments were equal, the survival outcomes for AA and EA were not significantly different, which conflicts with the current notion in the literature, but supports findings in a few recent studies. This study should add to the growing body of literature indicating that when equal access to treatments is provided, less racial disparities will be observed among AA and EA men.

Keywords: prostate cancer, bone metastasis, African American, European American, survival outcomes

INRODUCTION

Prostate Cancer (PC) has many disease characteristics that are different among African Americans (AA) compared to European Americans (EA) [1-6]. These differences are listed in Table 1. These differences contribute to poorer overall survival outcomes among AA compared to EA. Health outcomes are not determined just by tumor characteristics; they are also determined by 'Social Determinants of Health' [SDH]. This is true in PC also. PC outcomes are poorer among AA compared to EA due to many disadvantaged factors among the SDH in AA population. These are listed in Table 2[7-12].

Overall survival rates are poorer among AA compared to EA [13-15]. However, most the studies have focused on either overall survival outcomes or survival among patients without metastatic disease. PC has a tendency to preferentially metastasize to bones, but few studies have looked into the survival outcomes of PC patients with bone metastasis, specifically among AA.

The purposes of the current study are as follows:

- To determine the survival outcomes among AA men with bone metastasis from PC from the time of diagnosis of metastatic disease at an academic medical center.
- To compare these survival outcomes among AA with that of EA for our population diagnosed with bone metastasis from PC.

Based on previous reports in the literature, we hypothesized that the overall survival rates of AA men with bone metastasis from PC would be statistically different.

Table 1. Differences in the disease profile between African Americans and European Americans in prostate cancer

DIFFERENCES IN THE DISEASE PROFILE BETWEEN AFRICAN AMERICANS AND EUROPEAN AMERICANS IN PROSTATE CANCER[1-6]
1. Younger age at presentation for AA
2. Higher incidence rate for AA
3. Lower overall survival rates for AA
4. Higher Prostate Specific Antigen Levels among AA
5. Worse prognostic profile at presentation for AA
6. Differences in tumor genetics between AA and EA

Table 2. Social determinants of health that influence poorer outcomes in prostate cancer among African Americans

SOCIAL DETERMINANTS OF HEALTH THAT INFLUDENCE POORER OUTCOMES IN PROSTATE CANCER AMONG AFRICAN AMERICANS[7-12]
1. Lack of access to health insurance among AA versus EA
2. Reluctance to participate in prostate cancer screening
3. Lack of trust in health systems and health system professionals
4. Lack of sufficient knowledge about prostate cancer risk and outcomes
5. Risk perception inconsistent with epidemiological facts

MATERIAL AND METHODS

Institutional Review Board (IRB) approval was obtained first for this study. A retrospective review of PC patient charts diagnosed in the past 12 years was conducted using an academic medical center's cancer registry and Electronic Health Records (EPIC). Twenty-one EA and sixty-nine AA patients with bone metastases were identified. Only patients who had been diagnosed with bone metastasis at presentation were included in this study. PC patients who

had been diagnosed with local or regional disease and who subsequently developed bone metastasis were not included in this analysis.

Statistical Methods: Descriptive statistics were compiled, stratified by race. Mann-Whitney U tests and Fisher's exact tests were used for statistical comparisons of univariate associations. Kaplan-Meier (KM) analysis was performed to examine survival outcomes between races. A log-rank test was performed to test the difference in KM curves. We then undertook a Bayesian analysis, allowing us to incorporate the wealth of prior information that suggests AA have worse survival than EA. We did this in two separate models: (1) using a non-informative Normal (0, 10000) prior on the AA indicator coefficient in a parametric Weibull survival model, and (2) the same as (1) but changing the prior to a highly informative Cauchy (log(2), 0.5) prior. This second model, particularly the log(2) location parameter, allows us to use the previously published information that AA men have twice the hazard of death compared to EA. All Bayesian posterior checks were performed to assure proper model convergence. All statistical analysis was performed with Stata v15.1 (StataCorp, College Station, TX).

RESULTS

The characteristics of patients with bone metastases are presented in Table 3. Tumors of the patients were classified with TNM staging systems. No significant differences were shown as to the stage of disease between AA and EA. No significant differences existed found in average age and treatments among AA and EA. Kaplan-Meier survival curves are shown in Figure 1. The five-year survival rates for AA and EA men are 0.30 (0.17 – 0.44) and 0.26 (0.10 – 0.46) [p-value 0.855] (Figure 1). There were no differences in survival rates for AA and EA. Pooling across race, the 5-year survival probability was 0.29 (0.19 – 0.41).

Figure 2 shows the histograms for posterior hazard ratios for our two Bayesian models. Model 1 had posterior mean and median of 0.97 and 0.92, respectively, and 95% equal-tailed credible interval of (0.57 – 1.68). Model 2, using a highly informative prior of hazard ratio equal to two, our data still overwhelmed the prior. Posterior mean and median for this model were 1.15 and 1.10, respectively, with 95% equal-tailed credible interval of (0.64 – 1.92). These results suggest our conclusions are robust to choice of prior and that there lacks a difference in the hazard of death between AA and EA.

Table 3 Characteristics of PC patients with bone metastases

	EAs (N=21)	AAs (N=69)	*p*-value
Age at Diagnosis (mean, median, SD, IQR)	66.0, 61, 10.9, 60 – 70	63.3, 62, 10.9, 57 – 71	0.517
T Class			0.111
1	7 (33%)	18 (26%)	
2	6 (28%)	12 (18%)	
3	2 (10%)	5 (8%)	
4	5 (24%)	9 (13%)	
X	1 (5%)	24 (35%)	
N Class			0.816
0	8 (38%)	33 (49%)	
1	7 (33%)	18 (27%)	
X	6 (29%)	16 (24%)	
Chemotherapy	5 (24%)	8 (12%)	0.173
Radiation therapy	1 (5%)	14 (20%)	0.177
Hormone therapy	16 (76%)	54 (78%)	0.999
Immunotherapy	4 (19%)	8 (12%)	0.464
Other	4 (19%)	7 (10%)	0.275

(*P*-value is significant at 0.05 level)

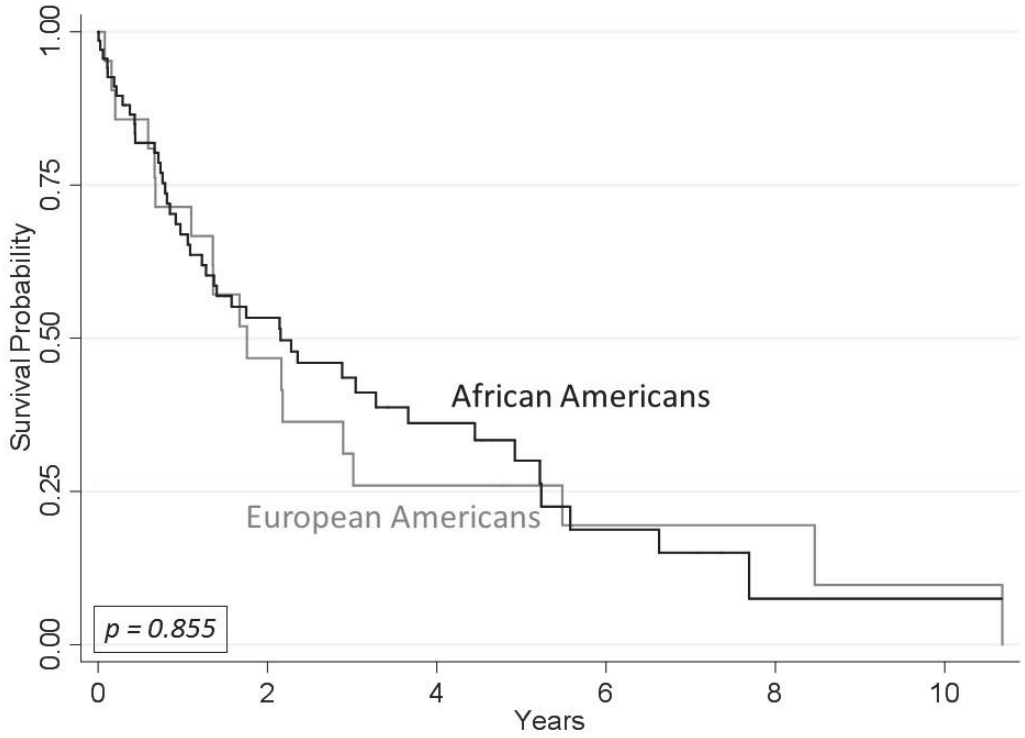

Figure 1. Kaplan-Meier Survival Curves for AA and EA

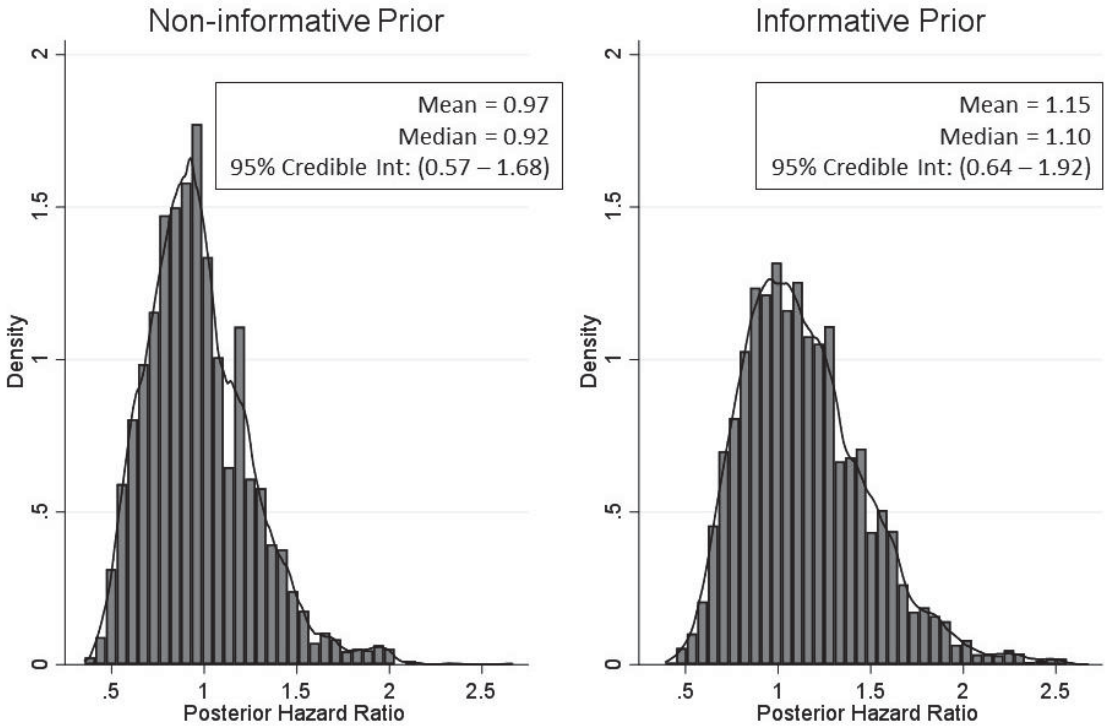

Figure 2. Hazard of Death for African Americans and European Americans (Bayesian analysis (posterior hazard ratios: The left panel used a non-informative Normal(0,10000) prior and thus did not incorporate the prior info of AA PC patients having higher hazard of death. Contrastingly, the right panel, incorporated this info, by assigning an informative Cauchy(log(2), 0.5) prior. In either case, the hazard of death is similar for AA and EA.

DISCUSSION

Our study data were obtained from the cancer registry of the only academic center in Mississippi. The American Cancer Society has reported the following about PC: between 2010 and 2014, it was the leading type of cancer among men, and between 2011 and 2015 it was the second leading cause of male cancer deaths in Mississippi (MS) [16]. African Americans make up almost two fifths of the total population in the state[17]. For decades the PC survival rates for AA have been consistently lower than EA. The 5-year survival rates were 69% for EA and 61% for AA in 1970s; 84% for EA and 71% for AA in 1980s; and >99% for EA and 97% for AA in 2010s)[18].

It is well known that T-stage, Gleason Sum and PSA levels are important prognostic factors that determine outcomes in prostate cancer. Why some PC have tendency to metastasize to the bone and some do not is a subject of significant research and is beyond the scope of this paper. In this study, we evaluated survival outcomes of PC patients with bone metastases. Nationally, even though the overall PC 5-year survival rate is approaching 100%, the survival rate for PC at advanced stage is only 30%. The death rates for AA patients (40.8%) is two times higher than EA (18.2%)[19]. Some studies in the literature have reported similar findings. Williams *et al* [15] reviewed 25-year data of over 7000 patients with PC and discovered that even after adjusting clinicodemographic and other risk factors, AA experienced a higher risk of mortality than EA. Akinyemiju et al [20] analyzed data from Surveillance Epidemiology and Ends Results (SEER) and concluded that AA PC patients were more likely to have metastasis to the bone and demonstrated higher risk of mortality when compared with EA.

Based on current statistics and study findings on PC, it was reasonable to hypothesize that AA in our study would have lower survival outcomes than EA. However, our study indicated that the survival outcomes of AA with bone metastases from PC did not differ from those of their EA counterparts. From Table 3, it was evident that the treatments received by AA and EA in our study did not differ. According to Chhatre *et al* [21], who retrospectively reviewed SEER-Medicare data of over 10,000 men with advanced-stage PC, survival outcomes for AA and EA were not significantly different after controlling for the treatment. Most recently, Halabi [22] analyzed pooled data from nine large randomized clinical trials involving 8,820 men with advanced PC and discovered that AA in the trials actually had at least the same, if not better, chance of survival as EA when they were all provided with equal access to treatment. After adjusting for age, site of metastasis, PSA levels and a few other factors that influenced survival, the risk of death was actually 19% lower for AA. Our current investigation supports the findings of those studies and adds to the growing body of evidence that racial disparities can be reduced when equal treatments are provided.

Our finding may be explained by one or more of the following mechanisms: first, lack of the 'Will Rogers' phenomenon in metastatic prostate cancer. It is well known that Will Rogers phenomenon exists in PC [23-25]. In this phenomenon, sub-stages exist within broader TNM stages; these sub-stages are hypothesized to be of higher (worse) stages among AA. This is evidenced by higher PSA (prostate specific antigen) levels among AA even after adjustments for stage and grade [26-28]. It is likely that such differences do not exist in metastatic PC. Second, there is a lack of effective curative treatment in metastatic PC in the past, thus leading to a lack of differences in outcomes. In non-metastatic PC, effective treatments exist. Due to limited access to medical care (see Table 2), AA are likely to have poorer outcomes in non-metastatic PC. However, since no effective curative treatments exist in metastatic PC, no differences in survival are expected. Third, our study is underpowered to detect differences.

The study has a few limitations: first, we only evaluated PC patients with bone metastases and did not compare them to those patients without metastases. Second, even though our study included 12 years' data, the number of patients who met our inclusion criteria was limited. It is recommended that future research include comparative analyses of PC patients with and without bone metastasis, enlarge the sample size, and further assess the significance of race in PC.

Conclusion

In this study, we compared the survival outcomes of AA and EA PC patients with bone metastases. Our data suggested that the survival outcomes of AA PC patients with bone metastases were not significantly different from their EA counterparts when equal treatments were given. This finding contradicts the current notion of AA enduring poorer survival outcomes than EA and adds a different perspective to the current body of literature. Future research is recommended to further evaluate the role of race in PC.

Disclosure

The authors of this article have no affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter discussed in this manuscript.

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