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Racial Disparities in the Outcomes of Patients With Stage IV Pancreatic Adenocarcinoma are Mediated by Chemotherapy Utilization

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To the Editor

Khawja et al.¹ recently reported, based on a systematic review, that blacks diagnosed with pancreatic adenocarcinoma have worse outcomes than their white counterparts. They concluded that differences in disease biology and treatment variations alone do not fully explain the disparity. We commend the authors for their thorough review of the literature; however, we disagree with their conclusion.

A recent study of patients with pancreatic adenocarcinoma treated in the Department of Defense (DoD) health care system found no difference in survival based on race.² Importantly, in this cohort, there was no difference in the rates of chemotherapy utilization between black and white patients, contrary to that reported in other studies.^{3–4} Additionally, black patients tended to be younger than whites at the time of diagnosis, but there was no difference in baseline tumor stage or site of distant disease. These findings suggest that the differences in outcomes of black patients with pancreatic adenocarcinoma reported elsewhere are likely secondary to disparities in chemotherapy utilization, a variable not commonly controlled, as treatment data is not available in many databases including the Surveillance, Epidemiology, and End Results (SEER) database. To investigate this further, we performed an analysis of patients treated at our institution for pancreatic adenocarcinoma to determine if disparities in outcomes among whites and blacks exist after controlling for chemotherapy utilization.

MATERIALS AND METHODS

We performed a retrospective chart review of 384 patients whom were diagnosed or treated for biopsy proven Stage IV pancreatic adenocarcinoma from January 2009 through August 2012 at Washington University School of Medicine. Data on age at diagnosis, year of diagnosis, sex, race comorbidities, chemotherapy utilization and survival were collected from the Barnes-Jewish hospital Oncology Data Service. Seven patients were excluded from

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all analyses as chemotherapy utilization could not be determined and 4 because they were a race other than white or black. This resulted in an analysis cohort of 373 patients.

STATISTICAL ANALYSIS

All data was analyzed using IBM SPSS Statistics version 21. We used standard descriptive statistics to describe the sample. Median overall survival was determined by Kaplan-Meier estimates. Multivariate survival analysis was performed by Cox proportional hazards modeling; initially only variables commonly available in population studies were entered (age at diagnosis, year of diagnosis, race, sex); then chemotherapy utilization was added to the model. To determine if the model improved we used the likelihood ratio test.

RESULTS

The median age at diagnosis was 64 years (range 33–86); 54% were male. Seventy-eight percent were white, 22% were black. Seventy-two percent received chemotherapy while 28% did not. The estimated median overall survival of the entire study population was 6.2 months (95% CI 5.3–7.0 months).

A multivariate logistic Cox proportional hazards model of age at diagnosis, year of diagnosis, sex, and race was significantly better than the baseline at explaining chemotherapy utilization ($\chi^2(4) = 26.983$; $p < 0.001$). When age at diagnosis, year of diagnosis, and sex were controlled, black race was associated with a 33% (95% CI 24–73%) increase in mortality rate ($p = 0.033$). After adding chemotherapy utilization, the model improved ($\chi^2(5) = 192.391$; $p < 0.001$). Based on the results of the likelihood ratio test adding chemotherapy utilization significantly improved the model ($p < 0.001$). When age at diagnosis, year of diagnosis, sex, and chemotherapy utilization were controlled, race was not associated with survival. Results of the multivariate models are summarized in Table 1.

DISCUSSION

Similar to the study in the DoD health care system, we found that race was not associated with survival in patients with Stage IV pancreatic adenocarcinoma. These results conflict with many of the other published reports; however those studies did not control for chemotherapy utilization.^{5–7} This suggests that the differences in outcomes of black patients with pancreatic adenocarcinoma are secondary to disparities in chemotherapy utilization.

Many studies have found that black patients with pancreatic adenocarcinoma were less likely to receive chemotherapy than their white counterparts. In a secondary analysis of our dataset, we also observed this; however, when insurance provider at diagnosis and/or SES (as determined by median household income of the home census tract) were controlled for, race was no longer associated with chemotherapy utilization (data not shown). This suggests that the disparity in treatment is not associated with a preference in black patients to forego chemotherapy; rather, it may be associated with barriers to access in healthcare.

While many of the other studies examining the association of race and outcomes of patients with pancreatic adenocarcinoma included all stages, the current study only included patients

with Stage IV disease at diagnosis. A survival benefit for adjuvant chemotherapy in resectable pancreatic adenocarcinoma was only recently reported in 2014;⁸ the initial report from 2007 did not find a difference.⁹ This suggests that variations in the use of adjuvant chemotherapy based on physician or institution discretion likely occurred in the interim. Thus, the current study included only stage IV pancreatic adenocarcinoma in an attempt to eliminate this potential confounding variable.

In conclusion, barriers to access are associated with a lower rate of chemotherapy utilization in patients with Stage IV pancreatic adenocarcinoma; not receiving chemotherapy is associated with poorer outcomes. Our study suggests that the poorer outcomes associated with black race in population studies actually reflects race as a surrogate for chemotherapy utilization.

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Table 1

Multivariate Analysis of Overall Survival for Pancreatic Adenocarcinoma

	Model 1			Model 2		
	aHR	95% CI	p value	aHR	95 % CI	p value
Age (per year)	1.02	1.01–1.03	<0.001	1.01	1.00–1.02	NS
Year of Diagnosis (per year)	0.91	0.84–0.97	0.004	0.93	0.87–1.00	0.050
Sex						
Female	1*			1*		
Male	1.31	1.05–1.63	0.017	1.22	0.97–1.52	NS
Race						
White	1*			1*		
Black	1.33	1.02–1.73	0.033	1.15	0.88–1.50	NS
Chemotherapy Utilization						
Yes				1*		
No				4.47	3.43–5.83	<0.001

aHR indicates adjusted hazard ratio; CI, Confidence Interval; NS, not significant ($p > 0.050$)

* Reference level