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At diagnosis of hepatocellular carcinoma, African Americans with hepatitis C have better liver function than other patients

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Introduction

Liver cancer is the fifth most common site of cancer in men worldwide and the second leading cause of site-specific cancer-related death.(1) Hepatocellular carcinoma (HCC) is by far the most common histological cell type, accounting for 90% of all liver cancer in the United States (US).(2) As of 2008, the worldwide incidence and mortality of liver cancer were essentially equal, highlighting the urgent need for better strategies for prevention and treatment. The prognosis for most patients with HCC is grim—5-year survival ranges between 6% and 28% in the West. (3–6) Early detection allows the use of life-saving interventions that have the potential to be curative. When these interventions are applied to early-stage HCC, 5-year survival rates are reported to exceed 50%, underscoring the importance of early detection and equal access to potentially curative treatments. (7)

Published data show that there are race-related and ethnicity-related differences in HCC incidence, surveillance, diagnosis, and treatment in the United States. Black and African American (AA) patients have an elevated incidence of HCC and have high HCC-related mortality. According to the NIH Surveillance, Epidemiology, and End Results (SEER) database, during the 2005–2007 time interval, the HCC incidence in AAs was 7.6 per 100,000—over 1.5-fold higher than the national average.(4) Additionally, Black patients have lower rates of HCC screening than patients of other races.(8, 9) Black and AA patients present with more advanced HCC and are offered curative surgical therapy less often than members of other races.(10–13) Black patients have significantly higher in-hospital HCC-related mortality than Whites, as well as decreased overall survival.(10–14)

In the United States, chronic infection with the hepatitis C virus (HCV) is a leading risk factor for HCC and has elevated prevalence in AAs. This study sought to identify clinical

characteristics of patients with a history of hepatitis C (HCV) infection and HCC that might put Non-Hispanic AAs at a survival disadvantage.

Methods

We examined medical records of patients with a history of hepatitis C infection and a radiographic or biopsy-proven diagnosis of HCC between 2007 and 2015 at the Mount Sinai Hospital in New York City, with IRB approval. Most data were from the time of HCC diagnosis. We examined age, race, ethnicity, clinical laboratory values and tumor characteristics (number and size of lesions, Milan criteria status, and total tumor volume). Data on HCC treatments (transarterial chemoembolization (TACE)/radiofrequency ablation (RFA)/Yttrium 90 radioembolization (Y90), resection, and/or liver transplantation) were also collected. Non-Hispanic AAs were compared to a pooled group of all other patients using t-tests and Levene's test.

Results

We analyzed data of 154 patients, 34% of whom were female with an average age at HCC diagnosis of 61 years. Our population was diverse and included 42 (27%) non-Hispanic AAs, 54 (35%) non-Hispanic Caucasians, 46 (30%) Hispanics, and 12 (8%) people of other races/ethnicities. At the time of HCC diagnosis there were no differences between AAs and non-AAs in age (61.7 years and 62.1 years, respectively) or sex (31% vs 35% female), but AAs had a significantly lower BMI (26.1 kg/M^2 vs 28.7 kg/M^2). See Table 1.

At the time of HCC diagnosis, AAs had better liver function and less liver injury than other patients as indicated by higher albumin measurements (p=0.009), higher platelet counts (p=0.010), lower international normalized ratio (p=0.015), lower total bilirubin measurements (p=0.001), lower FIB-4 scores (p=0.037), and lower MELD scores (p=0.026). See Table 2. Differences in tumor size (3.2 cm vs. 2.7 cm), tumor number (1.80 vs 1.47), total tumor volume (46.4cm^3 vs. 29.3cm^3), and presentation within Milan Criteria (76% vs 88%) all tended to be worse in the AA group but the differences did not reach statistical significance.(15) Of the 90 patients who underwent LT, 18 (20%) were African American. We found no evidence in our population that AAs had less access to local-regional therapy or liver transplantation. There was no significant difference between insurance status defined as public (i.e. Medicaid or Medicare) or commercial (29% vs. 30%).

Discussion

In the United States, Black and AA patients with liver disease are developing HCC at rates greater than Whites, are offered definitive therapy less often and have worse overall survival. These healthcare disparities could be the result of biological/genetic factors (worse tumor biology, less vigorous tumor immune-surveillance, *IL28B* polymorphisms) and/or socioeconomic factors that create barriers to optimal healthcare. While barriers to healthcare are likely to be significant contributors, our findings suggest that biological/genetic factors may play an unexpectedly important role. They reveal a distinctive profile of HCC in HCV-positive AAs. This group of patients had relatively well-preserved liver function at the time

of HCC diagnosis, and a trend toward more advanced/aggressive HCC at the time of diagnosis as indicated by higher tumor number and tumor volume, and greater likelihood of presenting with HCC outside the Milan criteria.

This distinctive profile was also reported in single center study conducted in south Florida by Jones and colleagues, who analyzed a large, diverse group of patients with cirrhosis and found that despite having better liver function, Blacks with HCC had worse tumor characteristics and the shortest survival of any group examined.(16) Based on the consistency of their results and our findings, we propose that healthcare providers should be alerted to the fact that AA may have a higher HCC risk than expected based on standard indicators of liver function (albumin, bilirubin, and platelet measurements). It is possible that HCC screening strategies need to be adjusted to provide maximal benefit to AAs.

We suggest five areas of future research to increase understanding of the HCC clinical profile we and Jones et al. uncovered: (a) increasing the number of patients studied both at our institution and others to further establish a pattern in addition to further delineating differences among other races, (b) molecular analysis to determine whether HCCs in AA concentrate in a particular (and aggressive) subclass, similar to breast cancer, which has an elevated prevalence of triple negative tumors in young AA women and an aggressive clinical course, (c) co-factor studies to determine whether HCV-positive AA with HCC have been exposed to specific oncogenic agents (aflatoxin, smoking, environmental pollution, HBV infection) that might drive HCC development, (d) additional medical record review to determine whether the profile we describe is specific to HCC in which HCV infection is the underlying etiology of liver disease, or is typical of HCC in AAs, regardless of liver disease etiology, and (e) healthcare utilization analysis to determine whether AAs fare more poorly because they are less likely to be engaged in HCC screening, are more likely to develop HCC without meeting HCC screening criteria (which rely heavily on a diagnosis of cirrhosis) and/or are less likely to be offered optimal HCC treatment.

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Table 1:

Baseline Characteristics

		By Ethnicity		
	Total (154)	**AA (42)**	**Non-AA (112)**	
Age (y)	61.8	62.1	61.7	p=0.72
Female sex	33.80%	31% (13)	35% (39)	p=0.7
BMI (kg/m2)	28	28.7	26	p=0.008
Commercial Insurance	29.90%	28.6% (12)	30.4% (34)	p=0.47

Table 2:

Lab Values, Clinical Scores, and Tumor Characteristics at Diagnosis of HCC by Ethnicity

	AA M (SD)	Non-AA M (SD)	95% CI	p-value
Albumin (g/dL)	3.6 (0.59)	3.3 (.65)	0.3 (0.08-0.53)	0.009
Platelet Count (1 × 10^3)	128.6 (64.67)	99.4 (61.67)	29.2 (6.86-51.54)	0.011
INR	1.12 (0.19)	1.26 (0.35)	0.14 (0.03-0.125)	0.015
Total Bilirubin (mg/dL)	1.02 (0.86)	1.9 (2.47)	0.89 (0.35-1.42)	0.001
FIB-4	6.5 (5.11)	9.2 (7.58)	2.7 (0.17-5.18)	0.037
MELD	9.9 (4.05)	11.9 (6.49)	1.98 (0.24-3.71)	0.026
Tumor Size (cm)	3.2 (2.05)	2.7 (1.51)	0.54 (0.16-1.20)	0.126
Number of Tumors	1.8 (2.12)	1.47 (0.82)	0.37 (0.34-1.00)	0.33
Tumor Volume (cm^3)	46.6 (100.6)	29.3 (110.9)	17.1 (22.6-56.7)	0.396
Within Milan Criteria	73.8% (31)	87.5% (98)	0.46 (0.185-1.129)	0.085