



At Diagnosis of Hepatocellular Carcinoma, African Americans With Hepatitis C Have Better Liver Function Than Other Patients

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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 cancers in the United States.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 rate ranges between 6% and 28% North America and Western Europe.³⁻⁶ Early detection allows the use of lifesaving 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. African American patients have an elevated incidence of HCC and high HCC-related mortality. According to the National Institutes of Health Surveillance, Epidemiology, and End Results database, during the 2005 to 2007 time interval, the HCC incidence rate in African American individuals was 7.6 per 100,000, which is more than 1.5-fold higher than the national average.⁴ In addition, African Americans have lower rates of HCC screening than patients of other races.^{8,9} African American patients present with more advanced HCC and are offered curative surgical therapy less often than members of other races.¹⁰⁻¹³ African American patients have significantly higher

Abbreviations: BMI, body mass index; FIB-4, Fibrosis-4; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; LT, liver transplantation; MELD, Model for End-Stage Liver Disease; SD, standard deviation.

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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 African American individuals. This study sought to identify clinical characteristics of patients with a history of HCV infection and HCC that might place non-Hispanic black patients at a survival disadvantage.

METHODS

We examined medical records of patients with a history of HCV infection and a radiographic- or biopsy-proven diagnosis of HCC between 2007 and 2015 at the Mount Sinai Hospital in New York City, with institutional review board 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/radiofrequency ablation/yttrium 90 radioembolization, resection, and/or liver transplantation [LT]) were also collected. Non-Hispanic black patients were compared with a pooled group of all other patients using *t* tests and Levene 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 blacks, 54 (35%) non-Hispanic whites, 46 (30%) Hispanics, and 12 (8%) people of other races/ethnicities. At the time of HCC diagnosis, there were no differences between African American and non-African American patients in age (61.7 and 62.1 years, respectively) or sex (31% versus 35% female), but African American patients had a significantly lower body mass index (BMI; 26.1 versus 28.7 kg/m²; Table 1).

At the time of HCC diagnosis, African American patients 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 Fibrosis-4 (FIB-4) scores (*P* = 0.037), and lower Model for End-Stage Liver Disease (MELD) scores (*P* = 0.026; Table 2). Differences in tumor size (3.2 versus 2.7 cm), tumor number (1.80 versus 1.47), total tumor volume (46.4 versus 29.3 cm³), and presentation within Milan criteria (76% versus 88%) all tended

TABLE 1. BASELINE CHARACTERISTICS

	Total (154)	By Ethnicity		<i>P</i>
		African American (42)	Not African American (112)	
Age, years	61.8	62.1	61.7	0.72
Female sex, % (n)	33.80%	31% (13)	35% (39)	0.7
BMI, kg/m ²	28	28.7	26	0.008
Commercial insurance, % (n)	29.90%	28.6% (12)	30.4% (34)	0.47

TABLE 2. LABORATORY VALUES, CLINICAL SCORES, AND TUMOR CHARACTERISTICS AT DIAGNOSIS OF HCC BY ETHNICITY

	African American, Mean (SD)	Not African American, Mean (SD)	95% Confidence Interval	<i>P</i>
Albumin (g/dL)	3.6 (0.59)	3.3 (0.65)	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
International normalized ratio	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

to be worse in the African American patient 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 African American patients had less access to local–regional therapy or LT. There was no significant difference between insurance status defined as public (i.e., Medicaid or Medicare) or commercial (29% versus 30%).

DISCUSSION

In the United States, African American patients with liver disease are experiencing HCC at rates greater than white patients, are offered definitive therapy less often, and have worse overall survival. These health care 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 health care. Although barriers to health care 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 African American patients. 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 a single-center study conducted in south Florida by Jones et al.,¹⁶ who analyzed a large, diverse group of patients with cirrhosis and found that despite having better liver function, African American patients 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 health care providers should be alerted to the fact that African American individuals 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 African American patients.

We suggest five areas of future research to increase understanding of the HCC clinical profile that we and Jones et al.¹⁶ uncovered: (1) 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; (2) molecular analysis to determine whether HCCs in African American patients concentrate in a particular (and aggressive) subclass, similar to breast cancer, which has an elevated prevalence of triple-negative tumors in young African American women and an aggressive clinical course; (3) cofactor studies to determine whether HCV-positive African American patients with HCC have been exposed to specific oncogenic agents (aflatoxin, smoking, environmental pollution, HBV infection) that may drive HCC development; (4) additional medical record review to determine whether the profile we describe is specific to HCC in which HCV infection is the underlying cause of liver disease, or is typical of HCC in African American patients, regardless of liver disease cause; and (5) health care utilization analysis to determine whether African American patients fare more poorly because they are less likely to be engaged in HCC screening, are more likely to experience development of 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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