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ORIGINAL ARTICLE

The Impact of Race on Survival After Hepatocellular Carcinoma in a Diverse American Population

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Abstract

Background and Aims Hepatocellular carcinoma (HCC) incidence is increasing at differential rates depending on race. We aimed to identify associations between race and survival after HCC diagnosis in a diverse American population.

Methods Using the cancer registry from Sylvester Comprehensive Cancer Center, University of Miami and Jackson Memorial Hospitals, we performed retrospective analysis of 999 patients diagnosed with HCC between 9/24/2004 and 12/19/2014. We identified clinical characteristics by reviewing available electronic medical records. The association between race and survival was analyzed using Cox proportional hazards regression.

Results Median survival in days was 425 in Blacks, 904.5 in non-Hispanic Whites, 652 in Hispanics, 570 in Asians, and 928 in others, $p < 0.01$. Blacks and Asians presented at more advanced stages with larger tumors. Although Whites had increased severity of liver disease at diagnosis compared to other races, they had 36% reduced rate of death compared to Blacks, [hazard ratio (HR) 0.64, 95% confidence interval (CI) 0.51–0.8, $p < 0.01$]. After adjusting for significant covariates, Whites had 22% (HR 0.78, 95% CI 0.61–0.99, p 0.04) reduced risk of death, compared to Blacks. Transplant significantly reduced rate of death; however, only 13.3% of Blacks had liver transplant, compared to 40.1% of Whites, $p < 0.01$.

Conclusions In this diverse sample of patients, survival among Blacks is the shortest after HCC diagnosis. Survival differences reflect a more advanced tumor stage at presentation rather than severity of underlying liver disease precluding treatment. Improving survival in minority populations, in whom HCC incidence is rapidly increasing, requires identification and modification of factors contributing to late-stage presentation.

Keywords Hepatocellular carcinoma · Disparities · Race

Introduction

Hepatocellular carcinoma (HCC), the fifth leading cause of cancer [1] and the second cause of cancer mortality worldwide [2], represents the fastest growing cause of cancer-related death among men in the USA [1]. In 2012, nearly 25,000 new cases of HCC were diagnosed in the USA [3]. It develops primarily in patients with cirrhosis, hepatitis C virus (HCV) and advanced fibrosis [4], or hepatitis B virus (HBV). Though increased HCC incidence is due partly to the aging cohort of HCV patients [5, 6], the increasing prevalence of nonalcoholic fatty liver disease (NAFLD),

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driven by the obesity [7] and diabetes epidemics [8, 9], contributes greatly to HCC development [10]. Heavy drinking (≥ 3 drinks/day) may independently increase HCC risk [11]. Further, alcohol acts synergistically with viral hepatitis to increase HCC risk [12].The greatest proportional increase in incidence was observed in persons between ages 45 and 60 [1, 13]. Since HCC has significant mortality, increased incidence at younger ages translates into greater productivity losses and years of potential life lost [14]. Regardless of stage, 5-year survival ranges from 12% [13] to 28% [15].

Incidence and mortality are increasing faster in Blacks than Whites [1, 3, 16]. In 2012, incidence rates in Hispanics exceeded those in Asians, who historically had the highest rates of HCC [3]. Blacks present with advanced HCC more often and receive appropriate surgical therapy less frequently [17–19]. Despite lower rates of transplantation, ablation, and hepatic resection for HCC, Blacks have higher in-hospital mortality than Whites [20]. Blacks are less likely to be referred [21], receive liver transplant for HCC [22], and have worse survival after transplant than Whites [17, 23]. Retrospective analyses of the Surveillance, Epidemiology, and End Results (SEER) [17, 18, 24] and United Network for Organ Sharing (UNOS) [17, 23] databases demonstrate that Blacks with HCC have decreased survival compared to Whites.

Although national databases offer large study populations, they have inherent limitations. SEER extracts information from regional cancer registries representing approximately 28% of the US population, 26% of African Americans, and 38% of Hispanics [25]. Many states are excluded from SEER, including Florida. Incidence rates of HCC are the highest in the South [3, 26], where unique demographic differences may impact HCC epidemiology. Database studies provide insufficient clinical information to explain why Blacks fare worst. It is unknown if treatment setting modifies the association between race and survival, especially where most patients are minorities. Other factors, including decompensated liver disease and socioeconomic status, influence treatment options and survival after HCC diagnosis [27, 28]. This study aimed to evaluate how race impacts survival in a diverse American population and to identify clinical factors contributing to survival differences by race.

Methods

Study Cohort

We performed retrospective analysis of patients with a radiologic, surgical, or biopsy-proven diagnosis of HCC, diagnosed consecutively between 9/24/2004 and 12/19/2014 at Sylvester Comprehensive Cancer Center (SCCC), University of Miami or Jackson Memorial Hospital (JMH) in Miami, Florida. Both institutions are academic tertiary care hospitals located within a joint medical campus and staffed by the same group of physicians; JMH is the major healthcare provider for indigent and uninsured patients in Miami-Dade County and also houses the transplant program. Since 2011, most patients diagnosed with HCC at SCCC or JMH are referred for discussion at the joint weekly multidisciplinary tumor board. We excluded all patients with a prior history of HCC. The University of Miami Miller School of Medicine Institutional Review Board approved the study.

Variables and Data Source

The cancer registry contains demographics, diagnosis date, treatment details, tumor size, and date of death or last follow-up. Race and ethnicity were ascertained by documentation in the medical record and defined by the North American Association of Central Cancer Registries (NAACCR) criteria [29]. Although the registry contains International Classification of Diseases, Ninth Edition (ICD-9) codes, using ICD-9 codes to define comorbidities is susceptible to error from underreporting. Therefore, we reviewed the electronic medical record to obtain clinical information regarding the etiology of liver disease, Barcelona Clinic Liver Cancer (BCLC) stage at diagnosis and treatment details.

Outcomes

The primary outcome variable was survival after HCC diagnosis, defined as the number of days between diagnosis date and date of death or last follow-up, if the patient was alive. Secondary outcome variables were time to transplant, chemotherapy, and radiation therapy, also measured in days.

Statistical Analysis

Categorical variables were expressed using proportions and continuous variables using medians and interquartile range (IQR). We identified associations between baseline characteristics, race, and vital status using Wilcoxon rank-sum and Kruskal–Wallis tests for continuous and Pearson's Chi-square for categorical variables. We used stratified analysis and logistic regression modeling with multiple degree-of-freedom likelihood ratio tests to assess for effect modification between race/ethnicity and all variables. Our analysis for missing data determined that all values were missing completely at random. Overall, there was a low rate of missing data, < 5%, with the exception of alpha-fetoprotein (AFP) at diagnosis, which was unavailable in 24.5% of the sample. We included age at diagnosis

and gender in the multivariate model as potential confounders based on clinical reasoning a priori. Also, we included potential confounders in the multivariate model, if $p < 0.10$ in bivariate analysis. Transplant was included in multivariate survival analyses as a time-dependent variable.

We addressed missing data in the models by categorizing continuous clinical variables into quartiles and then adding a category for unknown data. We compared these results to results obtained from multivariate models utilizing multiple imputation. We eliminated confounders via hierarchical backwards elimination strategy using a change in estimate approach (< 10%). We determined crude and adjusted hazard ratios (HR) for mortality after HCC diagnosis using Cox proportional hazards modeling and Kaplan–Meier survival curves were generated. For multivariate analyses, two-sided p values ≤ 0.05 were considered statistically significant. Analyses were performed using Stata versions 12.1 and 14.1 (College Station, TX).

Results

Characteristics of the Overall Sample

During this period, 999 patients were diagnosed with HCC; however, we excluded 88 patients with inadequate information in the electronic medical record. Additionally, ten patients were excluded after chart review leaving a final sample of 901 patients (Supplementary Figure 1). In this sample, 55.9% of patients with HCC received the initial care at JMH and 44.1% at SCCC. For a detailed comparison of baseline characteristics by hospital, see Supplementary Table 1. Median age at diagnosis was 60.3 years and 77% were men. The cohort was diverse: 46% were non-Hispanic White, 15% Black, 34.4% Hispanic, 2.4% Asian, 2.2% were other or unknown race, and 21.6% were Caribbean-born. Only 7.6% were uninsured, others had private insurance, 42.4%, Medicare, 30.9%, or Medicaid, 18.3%. Median body mass index (BMI) was 26.9 kg/m^2 and 25.3% were obese. Hepatitis C was reported in 63.6%, HBV in 12.4%, ALD in 26.3%, and NAFLD in 12.1%. In many patients, CLD was caused by multiple etiologies (Fig. 1). Diabetes was reported in 31.5%. Cirrhosis was noted in 86.9% of the patients, and median Model for End-Stage Liver Disease (MELD) score at diagnosis was 8; MELD-Na was 10.1. At diagnosis, 42.4% had current or previous ascites, 50.3% had had varices detected, 20.3% had had prior gastrointestinal bleeding, and 29% had had an episode of hepatic encephalopathy. See Table 1 for additional details.

Median size of the largest tumor was 38 mm, and median AFP at diagnosis was 56 ng/mL. At diagnosis, 47.8% of patients were within Milan criteria, while 47.6% were beyond Milan [30]. For 4.6%, Barcelona Clinic Liver Cancer (BCLC) stage could not be determined by available documentation. Metastases and tumor thrombus were present at diagnosis in 9.3% and 9.4%, respectively. Liver transplant was performed in 284 patients, resection in 110 patients, transarterial radioembolization (TARE) in 51 patients, transarterial chemoembolization (TACE) in 268 patients, and ablative therapies, including radiofrequency ablation, microwave ablation, and Nanoknife™ in 236 patients. Chemotherapy was administered to 236 patients, 83% of whom had received Sorafenib.

Characteristics of the Sample, Stratified by Race and Ethnicity

More Blacks and Hispanics, 65.9 and 56.8%, respectively, had received their initial care at JMH. The majority of Blacks and Whites were born in North America, while Hispanics and Asians were predominantly foreign-born. Blacks, Hispanics, and Asians were significantly more likely than Whites to be uninsured or have Medicaid, $p < 0.01$ (Table 1). Obesity was most prevalent in Hispanics, who had the highest median BMI. Diabetes was present in 42.9% of Asians, 37.6% of Hispanics, 36.8% of others, 19.2% of Blacks, and 29.9% of Whites, $p < 0.01$.

Hepatitis B was more common in Blacks, 35%, and Asians, 60%, compared to 6.1% of Whites, 8% of Hispanics, and 20% of others, $p < 0.01$. Blacks, Hispanics, and others had the lowest rates of HBV treatment prior to HCC diagnosis, 39, 31.8, and 25%, respectively, compared to 68.2% of Whites and 75% of Asians, p 0.02. Hepatitis C was more common in Whites, 68%, and Hispanics, 61.7%, compared to 58.7% of Blacks, 57.9% of others, and 40% of Asians, p 0.04. Additionally, Blacks were least likely to receive HCV treatment before HCC diagnosis, p 0.04. Hispanics, 15.3%, and others, 25%, had the highest rates of NAFLD, compared to 3.2% of Blacks, 5% of Asians, and 12.1% of Whites, $p < 0.01$. There were no significant racial differences in the prevalence of ALD, primary sclerosing cholangitis (PSC), primary biliary cholangiopathy (PBC), or autoimmune hepatitis (AIH). Human immunodeficiency virus (HIV) was more prevalent in Blacks, 10.9%. As such, there were higher rates of HIV–HBV and HIV–HCV coinfection in Blacks.

Only 54.6% of Asians and 77% of Blacks had documented cirrhosis, compared to 85% of others, 87.9% of Whites, and 92.3% of Hispanics, $p < 0.01$. There was no significant difference in MELD score, but MELD-Na score was highest in Whites, 10.7, followed by 10.1 in Hispanics, 9 in Blacks, 8.6 in Asians, and 5.7 in others, $p < 0.01$. Varices and GI bleeding were most common in Hispanics, followed by Whites,

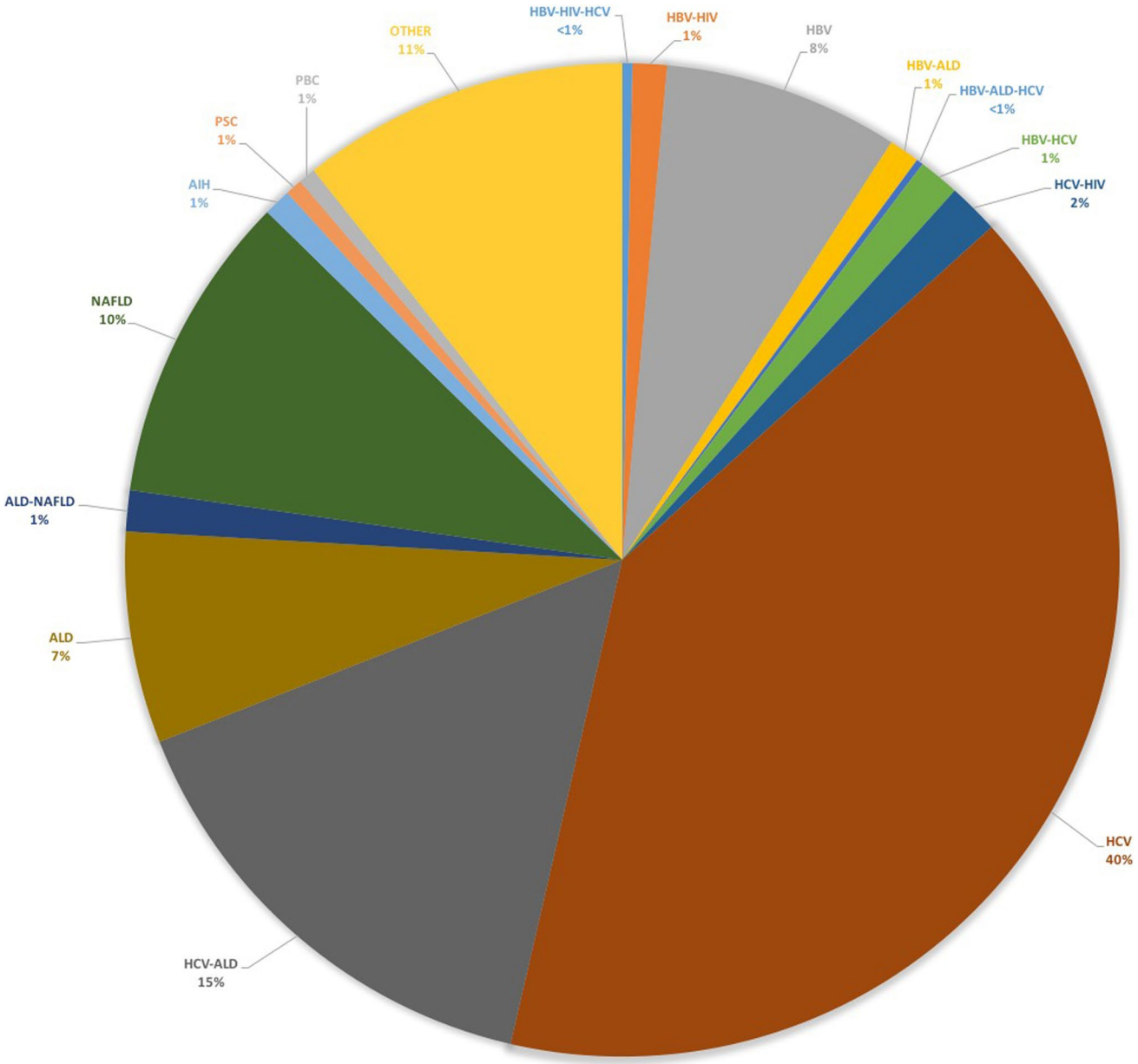

Fig. 1 Etiology of chronic liver disease in the overall sample. *AIH* autoimmune hepatitis, *ALD* alcoholic liver disease, *HBV* hepatitis B virus, *HCV* hepatitis C virus, *HIV* human immunodeficiency virus, *NAFLD* nonalcoholic fatty liver disease, *PBC* primary biliary cholangiopathy, *PSC* primary sclerosing cholangitis

others, Blacks, and Asians, $p < 0.01$. Hepatic encephalopathy was more common in Whites and Hispanics. There were no significant racial differences in ascites, portopulmonary hypertension, hepatopulmonary syndrome, or hepatorenal syndrome (HRS).

Cancer Characteristics of the Sample, Stratified by Race and Ethnicity

Blacks were the youngest at diagnosis, median 58.1 years, compared to 59.6 in Hispanics, 60.3 in others, 61.7 in Whites, and 61.8 in Asians, $p < 0.01$. Median size of the largest tumor was 50 mm in Blacks, 35 mm in Whites, 40 mm in Hispanics, 45 mm in Asians, and 39 mm in others, $p < 0.01$. Blacks were most likely to present with advanced disease; 65.9% of Blacks were beyond Milan criteria at

Table 1 Baseline clinical characteristics of the overall sample and the sample stratified by race

	Overall ($n = 901$)	Stratified by race					
		Black ($n = 135$)	White ($n = 414$)	Hispanic ($n = 310$)	Asian ($n = 22$)	Other ($n = 20$)	p value
Male, *n* (%)	695 (77.1)	101 (74.8)	330 (79.7)	236 (76.1)	16 (72.7)	12 (60)	0.22
Age at diagnosis, years, median (IQR)	60.3 (54.8–66.5)	58.1 (52.1–61.9)	61.7 (56.1–67.7)	59.6 (53.7–67)	61.8 (54.4–72.7)	60.3 (57–66.5)	< 0.01
Payer, *n* (%)							< 0.01
Medicaid	162 (18.3)	42 (31.1)	38 (9.4)	78 (25.7)	3 (14.3)	1 (5.6)	
Private	375 (42.4)	48 (35.6)	196 (48.3)	109 (35.9)	9 (42.9)	13 (72.2)	
Medicare	273 (30.9)	26 (19.3)	156 (38.4)	84 (27.6)	6 (28.6)	1 (5.6)	
Uninsured	67 (7.6)	18 (13.3)	13 (3.2)	30 (9.9)	3 (14.3)	3 (16.7)	
Military/VA/IPHS	7 (0.8)	1 (0.7)	3 (0.7)	3 (1)	0	0	
Hospital, *n* (%)							< 0.01
JMH	504 (55.9)	89 (65.9)	226 (54.6)	176 (56.8)	9 (40.9)	4 (20)	
SCCC	397 (44.1)	46 (34.1)	188 (45.4)	134 (43.2)	13 (59.1)	16 (80)	
Birth continent, *n* (%)							< 0.01
North America	405 (45)	75 (55.6)	297 (71.7)	25 (8.1)	1 (4.6)	7 (35)	
Central America	35 (3.9)	1 (0.7)	2 0.5)	31 (10)	1 (4.6)	0	
Caribbean	195 (21.6)	34 (25.2)	4 (1)	155 (50)	1 (4.6)	1 (5)	
South America	50 (5.6)	3 (2.2)	1 (0.2)	46 (14.8)	0	0	
Asia	25 (2.8)	0	8 (1.9)	1 (0.3)	15 (68.2)	1 (5)	
Africa	3 (0.3)	2 (1.5)	1 (0.2)	0	0	0	
Europe	22 (2.4)	1 (0.7)	19 (4.6)	1 (0.3)	0	1 (5)	
Unknown	166 (18.4)	19 (14.1)	82 (19.8)	51 (16.5)	4 (18.2)	10 (50)	
Current alcohol, *n* (%)	242 (26.9)	42 (31.1)	103 (24.9)	91 (29.4)	2 (9.1)	4 (20)	0.02
Current tobacco, *n* (%)	159 (17.7)	28 (20.7)	76 (18.4)	47 (15.2)	2 (9.1)	6 (30)	< 0.01
Family history of cancer, *n* (%)	240 (26.6)	34 (25.2)	117 (28.3)	80 (25.8)	5 (22.7)	4 (20)	0.05
Obese, *n* (%)	217 (25.3)	30 (23.6)	86 (21.7)	96 (32.5)	0	5 (26.3)	< 0.01
Body mass index (kg/m^2), median (IQR)	26.9 (23.8–30.3)	25.7 (22.9–30)	26.8 (23.6–29.9)	27.6 (24.5–31.2)	23.5 (21.2–26)	25.9 (22.4–31.5)	< 0.01
Diabetes, *n* (%)	278 (31.5)	25 (19.2)	122 (29.9)	115 (37.6)	9 (42.9)	7 (36.8)	< 0.01
Metavir fibrosis stage, *n* (%)							< 0.01
F0	10 (1.1)	3 (2.2)	5 (1.2)	1 (0.3)	1 (4.6)	0	
F1	8 (0.9)	1 (0.7)	4 (1)	2 (0.7)	0	1 (5)	
F2	13 (1.4)	2 (1.5)	6 (1.5)	3 (1)	2 (9.1)	0	
F3	6 (0.7)	0	2 (0.5)	2 (0.7)	2 (9.1)	0	
F4/cirrhosis	783 (86.9)	104 (77)	364 (87.9)	286 (92.3)	12 (54.6)	17 (85)	
No information available	81 (9)	25 (18.5)	33 (8)	16 (5.2)	5 (22.7)	2 (10)	
PV thrombosis, *n* (%)	180 (21.1)	34 (26.2)	68 (17.5)	72 (24.2)	4 (21.1)	2 (10.5)	0.09
Hepatitis B, *n* (%)	107 (12.4)	43 (35)	24 (6.1)	24 (8)	12 (60)	4 (20)	< 0.01
Treated prior to HCC	48 (47.5)	16 (39)	15 (68.2)	7 (31.8)	9 (75)	1 (25)	0.02
Hepatitis C, *n* (%)	554 (63.6)	74 (58.7)	274 (68)	187 (61.7)	8 (40)	11 (57.9)	0.04
Treated prior to HCC	193 (36.4)	15 (20.8)	108 (40.8)	64 (36.6)	2 (25)	4 (40)	0.04
SVR prior to HCC	25 (13.2)	1 (6.7)	18 (17)	6 (9.5)	0	0	0.47
Alcoholic liver disease, *n* (%)	229 (26.3)	37 (29.8)	100 (24.9)	87 (28.6)	2 (9.1)	3 (15)	0.15
NAFLD, *n* (%)	105 (12.1)	4 (3.2)	49 (12.1)	46 (15.3)	1 (5)	5 (25)	< 0.01
PSC, *n* (%)	6 (0.7)	2 (1.6)	2 (0.5)	1 (0.3)	0	1 (5)	0.09
PBC, *n* (%)	6 (0.7)	0	2 (0.5)	3 (1)	1 (5.3)	0	0.11
AIH, *n* (%)	11 (1.3)	1 (0.8)	5 (1.2)	4 (1.3)	1 (4.8)	0	0.63
HIV, *n* (%)	30 (3.4)	14 (10.9)	9 (2.2)	7 (2.3)	0	0	< 0.01

Table 1 (continued)

	Overall ($n = 901$)	Stratified by race					
		Black ($n = 135$)	White ($n = 414$)	Hispanic ($n = 310$)	Asian ($n = 22$)	Other ($n = 20$)	p value
Ascites, *n* (%)	378 (42.4)	49 (36.8)	181 (44.4)	135 (43.7)	4 (18.2)	9 (45)	0.1
Varices, *n* (%)	383 (50.3)	38 (38.4)	183 (51.8)	150 (55)	4 (21.1)	7 (46.7)	< 0.01
Prior GI bleeding, *n* (%)	179 (20.3)	17 (13.2)	81 (19.9)	77 (25.5)	1 (4.6)	3 (15.8)	0.01
Encephalopathy, *n* (%)	258 (29)	20 (15.3)	137 (33.3)	93 (30.4)	3 (13.6)	5 (25)	< 0.01
Hepatorenal syndrome, *n* (%)	21 (2.4)	3 (2.3)	12 (2.9)	6 (2)	0	0	0.77
MELD, median (IQR)	8 (5–12.6)	7.2 (3.8–13.3)	8.4 (5.2–13.3)	8.1 (5.4–12.3)	9.2 (4.3–11.1)	5.7 (0.8–9.74)	0.17
MELD-Na, median (IQR)	10.1 (5.7–15.3)	9 (4.6–15.1)	10.7 (6.6–16.3)	10.1 (5.9–14.9)	8.6 (5.5–12.9)	5.7 (0.4–10.3)	0.01
INR, median (IQR)	1.2 (1.1–1.4)	1.2 (1.1–1.4)	1.2 (1.1–1.4)	1.2 (1.1–1.4)	1.1 (1–1.1)	1.1 (1.1–1.2)	0.07
Sodium (mmol/L), median (IQR)	138 (135–140)	138 (136–141)	138 (135–140)	138 (135–140)	140 (137–142)	139.5 (138–142)	0.01
Creatinine (mg/dL), median (IQR)	0.9 (0.7–1.1)	0.9 (0.7–1.1)	0.9 (0.7–1.1)	0.8 (0.7–1)	0.9 (0.8–1.1)	0.8 (0.7–0.9)	0.20
Total bilirubin (mg/dL), median (IQR)	1.3 (0.8–2.4)	0.9 (0.6–2)	1.4 (0.8–2.6)	1.3 (0.8–2.5)	0.8 (0.6–1.3)	0.8 (0.5–2)	< 0.01
Albumin (g/dL), median (IQR)	3.4 (2.8–3.9)	3.6 (3.1–4)	3.2 (2.8–3.9)	3.3 (2.8–3.9)	3.8 (2.8–4.3)	3.4 (3–4)	0.02
Alkaline phosphatase (U/L), median (IQR)	143 (103–208)	166.5 (115–233)	132 (97–186)	146 (106–215)	128.5 (102–225.5)	143.5 (113–207)	< 0.01
ALT (U/L), median (IQR)	57 (38–90)	63 (42–87)	56 (37–90)	57 (39–91.5)	42 (31–71)	55 (41–84)	0.52
AST (U/L), median (IQR)	83 (51–134)	103 (63–168)	73 (47–128)	86.5 (56–129.5)	64.5 (38–139)	78 (50–97)	< 0.01
Hematocrit (%), median (IQR)	38 (33.5–42.2)	39.1 (35.2–42.4)	37.6 (32.8–41.7)	38 (33.9–41.8)	39.3 (32.2–42.9)	44 (37.9–45.5)	0.01
Hemoglobin 10^3/μL, median (IQR)	12.9 (11.2–14.1)	12.9 (11.3–13.8)	12.7 (11.2–14.2)	12.9 (11.3–14.1)	12.7 (11–14)	14.6 (12.6–15.3)	0.26
Platelets 10^3/μL, median (IQR)	118 (77–191.5)	166 (116–264)	104 (70–168)	108 (71–188)	165 (110–224)	157 (111–238)	< 0.01
WBC 10^3/μL, median (IQR)	5.7 (4.1–7.6)	6.2 (4.7–8.9)	5.2 (4–7.4)	5.6 (4.1–7.4)	6.2 (4.7–6.5)	7.1 (4.7–9.9)	< 0.01

AIH autoimmune hepatitis, *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *HIV* human immunodeficiency virus, *INR* international normalized ratio, *IPHS* Indian Public Health System, *IQR* interquartile range, *JMH* Jackson Memorial Hospital, *MELD* Model for End-Stage Liver Disease; Formula: 10 * ((0.957 * ln(creatinine)) + (0.378 * ln(bilirubin)) + (1.12 * ln(INR))) + 6.43, MELD − Na = MELD corrected for sodium Formula: MEL D − sodium − ((0.025) * (MELD) * (140 − sodium)) + 140, *NAFLD* nonalcoholic fatty liver disease, *PBC* primary biliary cholangiopathy, *PSC* primary sclerosing cholangitis, *PV* portal vein, *SCCC* Sylvester Comprehensive Cancer Center, *VA* Veteran's Administration

diagnosis, compared to 54.6% of Asians, 49.7% of Hispanics, 45% of others, and 39.9% of Whites, $p < 0.01$. Blacks also had higher rates of metastatic disease and tumor thrombus at diagnosis, $p < 0.01$ and 0.02, respectively. Median AFP at diagnosis was 266 ng/mL in Blacks, compared to 14.3 in others, 38.2 in Whites, 47.8 in Hispanics, and 68.5 in Asians, $p < 0.01$.

Hispanics and Blacks received chemotherapy significantly more often than Whites, Asians, and others. Also, time to chemotherapy was shorter in Blacks, compared to Hispanics, p 0.01. Transplant was performed in 40.1% of Whites, 30.3% of Hispanics, 18.2% of Asians, 13.3% of Blacks, and 10% of others, $p < 0.01$. There was a trend toward significant racial differences in receipt of resection, p 0.07, and TACE, p 0.06. There were no significant racial differences in receipt of external beam radiation, bland embolization, TARE, ablative therapies, or in time to surgery, transplant, or radiation. More Blacks, 73.3%, had evidence of cancer at follow-up, compared to 42% of Whites, 58.4% of Hispanics, 60% of others, and 59.1% of Asians, $p < 0.01$ (Table 2).

Survival After HCC Diagnosis

For the 604 deceased patients, median survival was 350.5 days, IQR 133.5–848.5, compared to 2004 days (IQR 1276–2870), in those alive at last follow-up. In 30 patients, recurrent disease was documented and 53.6% of the sample were never cancer-free. Cause of death was largely unknown. In bivariate analysis, the following variables were significantly associated with vital status: gender, age at diagnosis, payer, hospital, alcohol, tobacco, family history of cancer, portal vein thrombosis (PVT), treatment for HBV or HCV prior to HCC diagnosis, ALD, hepatorenal syndrome, tumor size, BCLC stage, metastasis at diagnosis, tumor thrombus at diagnosis, AFP at diagnosis, receipt of chemotherapy, external beam radiation, TARE, ablation, transplant, and

cancer status at follow-up. Additionally, sodium, alkaline phosphatase, aspartate aminotransferase (AST), platelet count, and white blood cell (WBC) count were significantly associated with vital status (Supplementary Table 2).

Using Cox modeling, older age at diagnosis, male gender, current alcohol or tobacco use, PVT, ALD, and ascites were negatively associated with survival. White race, private insurance, and Medicare were protective. Interestingly, obesity, hepatic encephalopathy, and HRS were associated with increased survival. Liver transplant was performed in 71.4% of patients with HRS, which likely explains this finding. Increasing tumor size, advanced BLCLC stage, metastasis or tumor thrombus, and increasing AFP at diagnosis were negatively associated with survival. While chemotherapy, external beam radiation, and TARE were negatively associated with survival, treatment with ablative therapies, resection, or liver transplant were associated with increased survival. Interestingly, neither fibrosis stage nor TACE influenced survival. These findings are likely a function of stage at presentation as persons with advanced (BCLC-C) and terminal (BCLC-D) tumor stage on presentation were unlikely to receive TACE, TARE, resection, transplant, or ablative therapies. Baseline sodium, bilirubin, alkaline phosphatase, AST, platelet count, and white blood cell count were all associated with survival. Univariate hazard ratios (HR), confidence intervals (CI), and *p*-values are in Table 3.

Impact of Race and Ethnicity on Survival

Stratified by race, median survival in days was 425 in Blacks, 570 in Asians, 652 in Hispanics, 904.5 in Whites, and 928 in others, statistically significant when comparing Blacks to Whites, $p < 0.01$, Blacks to Hispanics, p 0.03, and Hispanics to Whites, $p < 0.01$. One-year survival was 54.8, 70.5, 61.6, 59.1, and 70% for Blacks, Whites, Hispanics, Asians, and others, respectively, $p < 0.01$. Five-year survival was 14.8, 27.5, 21.6, 27.3, and 25% for Blacks, Whites, Hispanics, Asians, and others, respectively, p 0.04. Whites had 36% reduced rate of death, HR 0.64, 95% confidence interval (CI) 0.51–0.8, $p < 0.01$ and Hispanics had 20% reduced rate of death, HR 0.8, 95% CI 0.63–1.02, p 0.07, compared to Blacks. After adjusting for age at diagnosis, gender, insurance, hospital, birth continent, alcohol, tobacco, family history of cancer, PVT, encephalopathy, initial BCLC stage, AFP at diagnosis, chemotherapy, resection, transplant, and cancer status at last follow-up, Whites had a 22% reduced rate of death compared to Blacks, HR 0.78, 95% CI 0.61–0.99, p 0.04 (Table 3; Figs. 2, 3).

Race, Transplant, and Survival

Receipt of transplant was strongly associated with survival. Unadjusted, transplant was associated with a 79% reduction in death, HR 0.21, 95% CI 0.17–0.26, $p < 0.01$. When adjusted for race/ethnicity, age at diagnosis, gender, insurance, hospital, birth continent, alcohol, tobacco, family history of cancer, PVT, encephalopathy, initial BCLC stage, AFP at diagnosis, chemotherapy, resection, and cancer status at last follow-up, transplant was associated with an 80% reduction in death, HR 0.2, 95% CI 0.15–0.26, $p < 0.01$. Whites were fourfold more likely to have received transplant, 95% CI 2.44–6.48, $p < 0.01$ and Hispanics twofold more likely, 95% CI 1.4–3.85, $p < 0.01$, compared to Blacks. Numerically, a higher percentage of Blacks had HCC incidentally diagnosed on explant compared to Whites and Hispanics. Thus, in these cases, liver transplant was not an intentional treatment for HCC.

Discussion

Worldwide, HCC is the second most frequent cause of cancer-related deaths [2]. Its incidence has increased more rapidly in Blacks than Whites [1, 16, 31], and Blacks are less likely to receive curative treatments [32], including liver transplantation [22, 33]. Our understanding regarding racial and socioeconomic disparities in HCC survival is mostly derived from analyses of the SEER database. Artinyan et al. [17] analyzed HCC cases using SEER and found that black race predicts poorer survival. Additionally, they found that Blacks with HCC had the worst graft and overall survival after liver transplant using UNOS data [17]. A recent analysis of SEER demonstrated Blacks have the lowest 5-year survival rate, 21.3%, compared to 23.8% in Hispanics, 25% in non-Hispanic whites, and 26.1% in Asians [19]. SEER is the most widely used cancer registry database and includes specific geographic regions. Results are often generalized to the entire USA. There is significant inter-region geographic variability in HCC incidence [34], thus it may be ill-advised to extrapolate SEER results to non-SEER regions.

South Florida presents a unique population for study; over 50% of residents are foreign-born and 20% live in poverty. Immigrant status and lower neighborhood-level socioeconomic status increase HCC risk, especially among minorities [35]. Patients born in the Caribbean had a 39% higher rate of death after HCC diagnosis, when compared to those born in North America, $p < 0.01$. Although minorities are grouped for analysis by race and ethnicity, there is significant intra-racial diversity. In our sample, Hispanics were born in twenty-three and Blacks in seventeen different countries; Haitian Blacks lived only 173 days compared to US-born Blacks, 521 days, and other Blacks, 523 days, p 0.02. In Hispanics, there were no significant survival differences based on birthplace. Race, ethnicity, and country of origin have important implications as we seek to understand how etiology of liver disease, HCC risk factors, and survival differ by race as there may be significant intra-racial genetic variation.

Table 2 Cancer characteristics of the overall sample and the sample stratified by race

	Overall ($n = 901$)	Stratified by race					
		Black ($n = 135$)	White ($n = 414$)	Hispanic ($n = 310$)	Asian ($n = 22$)	Other ($n = 20$)	p value
Median size of the largest tumor size, mm (IQR)	38 (25–60)	50 (30–80)	35 (24–55)	40 (25–60)	45 (20–60)	39 (26–58)	< 0.01
BCLC stage, *n* (%)							< 0.01
Very early	58 (6.4)	7 (5.2)	30 (7.3)	19 (6.1)	0	2 (10)	
Early	373 (41.4)	34 (25.2)	195 (47.1)	126 (40.7)	9 (40.9)	9 (45)	
Intermediate	283 (31.4)	45 (33.3)	124 (30)	97 (31.3)	8 (36.4)	9 (45)	
Advanced	102 (11.3)	30 (22.2)	34 (8.2)	36 (11.6)	2 (9.1)	0	
Terminal	44 (4.9)	14 (10.4)	7 (1.7)	21 (6.8)	2 (9.1)	0	
Unstaged	41 (4.6)	5 (3.7)	24 (5.8)	11 (3.6)	1 (4.6)	0	
Within milan criteria, *n* (%)							< 0.01
Yes	431 (47.8)	41 (30.4)	225 (54.4)	145 (46.8)	9 (40.9)	11 (55)	
No	429 (47.6)	89 (65.9)	165 (39.9)	154 (49.7)	12 (54.6)	9 (45)	
Unknown	41 (4.6)	5 (3.7)	24 (5.8)	11 (3.6)	1 (4.6)	0	
Mets at diagnosis, *n* (%)	80 (9.3)	28 (22.2)	14 (3.6)	35 (11.6)	2 (10)	1 (5)	< 0.01
Tumor thrombus at diagnosis, *n* (%)	85 (9.4)	22 (16.3)	32 (7.7)	29 (9.4)	2 (9.1)	0	0.03
AFP at diagnosis (ng/mL)	56	266	38.2	47.8	68.5	14.3	< 0.01
Median (IQR)	(8.3–951.8)	(16.9–5744)	(6–350)	(9.1–797.5)	(3.1–1454)	(7.8–137.9)	
Treatments received							
Chemotherapy, *n* (%)	236 (27.8)	41 (32.3)	80 (20.8)	106 (35.7)	5 (23.8)	4 (20)	< 0.01
Sorafenib, *n* (%)[a]	185 (83)	36 (90)	65 (85.5)	78 (79.6)	3 (60)	3 (75)	0.33
External beam radiation, *n* (%)	26 (3)	4 (3.1)	10 (2.6)	10 (3.3)	2 (9.5)	0	0.4
Bland embolization, *n* (%)	16 (1.9)	2 (1.6)	10 (2.6)	3 (1)	1 (4.8)	0	0.45
TARE, *n* (%)	51 (6)	9 (7)	19 (4.9)	21 (7)	1 (4.8)	1 (5)	0.79
TACE, *n* (%)	268 (31.5)	29 (22.8)	123 (32)	97 (32.4)	9 (42.9)	10 (50)	0.06
Ablation, *n* (%)	236 (27.7)	27 (21.1)	121 (31.4)	76 (25.5)	6 (28.6)	6 (30)	0.18
Resection, *n* (%)	110 (12.7)	14 (11)	61 (15.5)	27 (8.9)	4 (19.1)	4 (20)	0.07
Transplant, *n* (%)	284 (31.5)	18 (13.3)	166 (40.1)	94 (30.3)	4 (18.2)	2 (10)	< 0.01
Diagnosed at explant, *n* (%)[b]	32 (11.3)	3 (16.7)	19 (11.5)	10 (10.6)	0	0	0.86
Time to transplant, days[c]	142	197	124	158	311	308.5	0.39
Median (IQR)	(55–269)	(31–350)	(59–264)	(33–245)	(126–820)	(195–422)	
Survival days	722	425	904.5	652	570	928	< 0.01
Median (IQR)	(214–1766)	(90–1277)	(319–1937)	(174–1555)	(144–1864)	(263–1843)	
Alive at 1 year, *n* (%)	584 (64.8)	74 (54.8)	292 (70.5)	191 (61.6)	13 (59.1)	14 (70)	< 0.01
Alive at 3 years, *n* (%)	352 (39.1)	41 (30.4)	184 (44.4)	107 (34.5)	10 (45.6)	10 (50)	< 0.01
Alive at 5 years, *n* (%)	212 (23.5)	20 (14.8)	114 (27.5)	67 (21.6)	6 (27.3)	5 (25)	0.04
Evidence of cancer at follow-up, *n* (%)	479 (53.6)	99 (73.3)	174 (42)	181 (58.4)	13 (59.1)	12 (60)	< 0.01
Vital status at study end, *n* (%)							0.06
Dead	604 (67)	101 (74.8)	264 (63.8)	214 (69)	15 (68.2)	10 (50)	
Alive	297 (33)	34 (25.2)	150 (36.2)	96 (31)	7 (31.8)	10 (50)	

AFP alpha-fetoprotein, *BCLC* Barcelona Clinic Liver Cancer, *IQR* interquartile range, *TACE* transarterial chemoembolization, *TARE* transarterial radioembolization

[a]Percentage based on those who received chemotherapy

[b]Percentage based on those who were transplanted

[c]Time to transplant calculated for those where HCC was diagnosed prior to transplant

Table 3 Univariate hazard ratios and adjusted hazard ratio, stratified by race/ethnicity

Unadjusted univariate Cox model				Adjusted multivariate Cox model[a]			
Variable	Hazard ratio	95% confidence interval	*p* value		Hazard ratio	95% confidence interval	*p* value
Race/ethnicity							
Black	1			Black	1		
White	0.64	0.51–0.8	< 0.01	White	0.78	0.61–0.99	0.04
Hispanic	0.80	0.63–1.02	0.07	Hispanic	0.88	0.69–1.13	0.32
Asian	0.74	0.43–1.28	0.28	Asian	0.89	0.5–1.54	0.68
Other/unknown	0.53	0.27–1.01	0.05	Other/unknown	0.75	0.38–1.46	0.39
Payer							
Medicaid	1						
Private	0.47	0.37–0.58	< 0.01				
Medicare	0.77	0.62–0.96	0.02				
Uninsured	0.85	0.6–1.2	0.35				
VA/IPHS	1.2	0.53–2.72	0.67				
Birth continent							
N. America	1						
C. America	1.27	0.85–1.1	0.24				
Caribbean	1.39	1.13–1.7	< 0.01				
S. America	1.07	0.74–1.55	0.71				
Asia	0.80	0.46–1.39	0.42				
Africa	0.35	0.05–2.46	0.29				
Europe	0.59	0.32–1.08	0.09				
Missing	1.28	1.03–1.60	0.03				
Alcohol use							
None	1						
Current	1.48	1.21–1.8	< 0.01				
Past	1.22	0.97–1.52	0.09				
Unknown	0.88	0.67–1.15	0.36				
Tobacco							
Never	1						
Current	1.45	1.16–1.8	< 0.01				
Former	1.17	0.97–1.41	0.11				
Unknown	0.75	0.56–1.02	0.07				
Family history							
No	1						
Yes	1.13	0.94–1.37	0.18				
Unknown	0.85	0.69–1.05	0.12				
Hospital							
JMH	1						
SCCC	1.44	1.23–1.7	< 0.01				
Male gender	1.31	1.07–1.59	< 0.01				
Age at diagnosis	1.01	1–1.02	< 0.01				
Obesity	0.82	0.68–1	0.05				
BMI	0.99	0.98–1	0.42				
Diabetes	1.05	0.89–1.25	0.55				
PVT	2.48	2.05–2.99	< 0.01				
ALD	1.29	1.08–1.55	< 0.01				
Ascites	1.19	1–1.39	0.04				

Table 3 (continued)

Unadjusted univariate Cox model				Adjusted multivariate Cox model[a]		
Variable	Hazard ratio	95% confidence interval	*p* value	Hazard ratio	95% confidence interval	*p* value
Varices	0.92	0.77–1.1	0.35			
Encephalopathy	0.82	0.69–0.99	0.04			
HRS	0.37	0.16–0.82	0.01			
Disease type						
HCV	1					
HBV	1.39	1.02–1.91	0.04			
NAFLD	1.01	0.75–1.34	0.97			
ALD	1.61	1.14–2.11	< 0.01			
AIH	0.44	0.14–1.39	0.16			
PSC	0.56	0.14–2.25	0.41			
PBC	0.9	0.29–2.8	0.85			
ALD–HCV	1.28	1.01–1.62	0.04			
ALD–NAFLD	0.85	0.4–1.8	0.66			
HIV–HBV	1.47	0.69–3.12	0.32			
HBV–HCV	0.9	0.42–1.9	0.78			
HIV–HCV	1.54	0.86–2.75	0.14			
HBV–HCV–HIV	1.29	0.32–5.21	0.72			
ALD–HBV	2.65	1.25–5.64	0.01			
ALD–HBV–HCV	2.78	0.69–11.21	0.15			
Crypotgenic	1.35	1.03–1.78	0.03			
Metavir fibrosis stage						
F0	1					
F1	0.66	0.19–2.33	0.52			
F2	0.95	0.33–2.75	0.93			
F3	1.15	0.35–3.75	0.82			
F4/Cirrhosis	0.97	0.43–2.16	0.94			
Unknown	1.09	0.47–2.53	0.84			
Tumor size	1	1–1	< 0.01			
Mets at diagnosis	4.29	3.34–5.5	< 0.01			
Tumor thrombus	3.52	2.76–4.49	< 0.01			
AFP at diagnosis	1	1–1	< 0.01			
AFP in quartiles[b]						
1st	1					
2nd	1.07	0.81–1.41	0.62			
3rd	1.31	1–1.71	0.05			
4th	2.82	2.18–3.66	< 0.01			
Unavailable	1.23	0.95–1.59	0.12			
BCLC						
Very early	1					
Early	1.35	0.88–2.08	0.17			
Intermediate	2.99	1.95–4.61	< 0.01			
Advanced	8.01	5.05–12.68	< 0.01			
Terminal	23.36	13.93–39.14	< 0.01			
Unstaged	4.01	2.37–6.8	< 0.01			
Milan criteria						
Within Milan	1					
Beyond Milan	3.08	2.59–3.65	< 0.01			

Table 3 (continued)

Unadjusted univariate Cox model				Adjusted multivariate Cox model[a]		
Variable	Hazard ratio	95% confidence interval	*p* value	Hazard ratio	95% confidence interval	*p* value
Unstaged	2	2.1–4.3	< 0.01			
Transplant	0.21	0.17–0.26	< 0.01			
Diagnosed at explant[c]	0.36	0.2–0.66	< 0.01			
Chemotherapy	1.71	1.43–2.04	< 0.01			
External beam radiation	1.75	1.16–2.64	< 0.01			
TARE	1.48	1.09–2.02	0.01			
TACE	0.89	0.74–1.06	0.2			
Ablation	0.68	0.56–0.83	< 0.01			
Resection	0.68	0.52–0.88	< 0.01			
MELD	1	0.99–1.02	0.56			
MELD-Na	1.01	1–1.02	0.08			
Sodium	0.97	0.95–0.99	< 0.01			
Bilirubin	1.03	1–1.05	0.02			
Albumin	0.94	0.84–1.04	0.24			
Alkaline phosphatase	1.00	1.00–1.00	< 0.01			
AST	1.00	1.00–1.00	< 0.01			
Platelet count	1.00	1.00–1.00	< 0.01			
White blood cell	1.04	1.02–1.06	< 0.01			
Cancer status at follow-up						
No evidence of cancer	1					
Evidence of cancer	4.68	3.86–5.66	< 0.01			
Unknown	2.23	1.5–3.29	< 0.01			

AFP alpha-fetoprotein, *AIH* autoimmune hepatitis, *ALD* alcoholic liver disease, *AST* aspartate aminotransferase, *BCLC* Barcelona Clinic Liver Cancer, *BMI* body mass index, measured in kg/m^2, *C. America* Central America, *HBV* hepatitis B virus, *HCV* hepatitis C virus, *HIV* human immunodeficiency virus, *HRS* hepatorenal syndrome, *IPHS* Indian Public Health System, *JMH* Jackson Memorial Hospital, *MELD* Model for End-Stage Liver Disease, *Mets* metastasis, *Na* sodium, *NAFLD* nonalcoholic fatty liver disease, *N. America* North America, *PBC* primary biliary cholangiopathy, *PSC* primary sclerosing cholangitis, *PVT* portal vein thrombosis, *S. America* South America, *SCCC* Sylvester Comprehensive Cancer Center, *TACE* transarterial chemoembolization, *TARE* transarterial radioembolization, *VA* Veteran's Administration

[a]Adjusted for age at diagnosis, gender, insurance, hospital, birth continent, alcohol use, tobacco use, family history of cancer, portal vein thrombosis, encephalopathy, BCLC stage at diagnosis, AFP at diagnosis, receipt of chemotherapy, resection, cancer status at last follow-up, transplant, and type of underlying chronic liver disease

[b]AFP at diagnosis was stratified into quartiles; first quartile: AFP ≤ 8.285, second quartile: 8.285 < AFP ≤ 56, third quartile: 56 < AFP ≤ 951.8, fourth quartile AFP > 951.8, fifth category: AFP at diagnosis not available ($n = 221$)

[c]Comparing those diagnosed at explant to the overall sample. When comparing in only transplant recipients, there were no significant survival differences; HR 1.12, 95% CI 0.6–2.1

In this retrospective study of 901 patients diagnosed with HCC consecutively over 10 years, Blacks had the shortest median survival, 425 days. At diagnosis, Blacks were younger, had higher AFP and more advanced BCLC stage. Surgical treatment differed by race and Blacks had surgery, including liver transplant, less often. After controlling for confounders, Whites had a 22% decrease in the rate of death after a diagnosis for HCC, compared to Blacks.

Analyses of national databases are fraught with challenges, including missing or inaccurate data. A single-center study affords several advantages. In this study, the same healthcare providers practice at SCCC and JMH, both tertiary care centers on a combined medical campus, ensuring reasonable uniformity of healthcare. Patients with HCC receive healthcare both at SCCC and at JMH during their treatment course, and cancer information is entered by abstractors into the joint registry. Since 2011, there has been a joint weekly multidisciplinary conference to develop and discuss treatment plans for patients with HCC, further standardizing the approach to care.

Cancer registries typically collect minimal data regarding the severity of underlying liver disease. The inclusion of clinical data in this study greatly strengthens our ability to interpret differences in survival. To accurately assess how clinical status and comorbidities differ by race and impact survival, we reviewed all available medical records. Whites

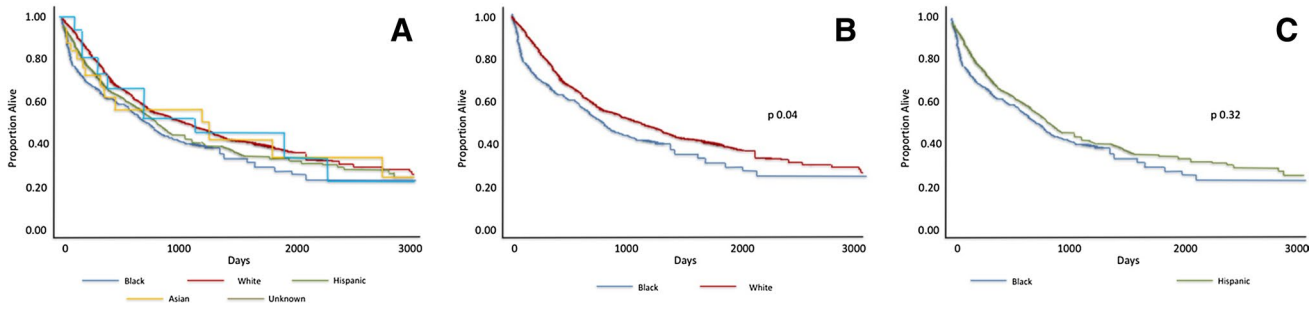

Fig. 2 Kaplan–Meier curves, adjusted for age at diagnosis, gender, insurance, hospital, birth continent, alcohol, tobacco, family history of cancer, portal vein thrombosis, encephalopathy, initial Barcelona Clinic Liver Cancer stage, alpha-fetoprotein at diagnosis, chemotherapy, resection, transplant, and cancer status at last follow-up, **a** stratified by race, **b** comparing Whites to Blacks, and **c** comparing Hispanics to Blacks

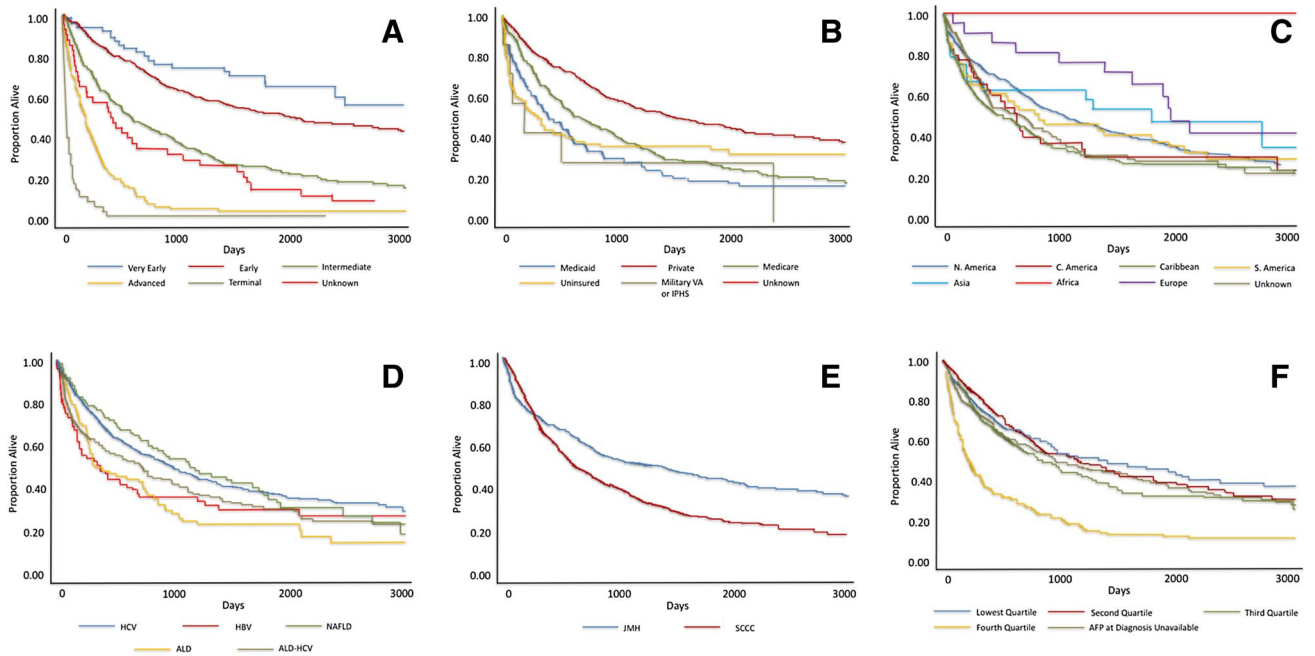

Fig. 3 Unadjusted Kaplan–Meier curves, **a** stratified by Barcelona Clinic Liver Cancer stage at diagnosis, **b** stratified by insurance, **c** stratified by birth continent, and **d** stratified by etiology of chronic liver disease. **e** Kaplan–Meier curve, adjusted for transplant and stratified by hospital. **f** Unadjusted Kaplan–Meier curve, stratified by alpha-fetoprotein at diagnosis. *AFP* alpha-fetoprotein, *ALD* alcoholic liver disease, *C. America* Central America, *HBV* hepatitis B, *HCV* hepatitis C, *IPHS* Indian Public Health System, *JMH* Jackson Memorial Hospital, *NAFLD* nonalcoholic fatty liver disease, *N. America* North America, *S. America* South America, *SCCC* Sylvester Comprehensive Cancer Center, *VA* Veterans Administration

had more advanced underlying liver disease as measured by MELD-Na and the greater prevalence of encephalopathy and ascites. Therefore, differences in HCC treatments offered by race are most likely attributable to patient-level differences in tumor stage and socioeconomic factors, rather than severity of underlying liver disease. In this sample, Blacks were less likely to have received treatment for HBV and HCV prior to HCC diagnosis and many were not diagnosed with hepatitis until HCC diagnosis. Even in the subset of patients diagnosed with HCC after the advent of direct-acting antiviral (DAA) medications, which have no significant racial differences in efficacy, only 10% of Blacks with HCV were treated prior to diagnosis compared to 46.5% of Whites, 50% of Hispanics, and 80% of others, $p < 0.01$.

Inadequate treatment of underlying liver disease and suboptimal surveillance for HCC in high-risk populations may partially explain racial differences in survival. In this study, approximately 19% of Blacks were born in Haiti, a highly HBV-endemic country [36], and were candidates for HBV screening based on the Centers for Disease Control (CDC) guidelines and screening for HCC as recommended by American Association for the Study of Liver Diseases

(AASLD) [37] and European Association for Study of the Liver (EASL) [38] guidelines. In 68% of Haitian Blacks, there was documented HBV infection; however, only 11.8% received HBV treatment prior to HCC diagnosis. Unfortunately, our experience has been that the diagnoses of HBV and HCC are often made concurrently.

In our sample, Blacks were presented with larger tumors at more advanced stages; 65.9% were beyond Milan compared to only 39.9% of Whites, 49.7% of Hispanics, and 54.6% of Asians, $p < 0.01$. African-American race and insurance status are associated with inconsistent HCC surveillance. In some settings, fewer than 2% of patients receive biannual surveillance [39]. Screening increases the proportion of cancers found at early stages, when curative treatment is possible. Presenting with a large tumor burden, as many of our Black patients did, affects eligibility for treatment options such as TACE and liver transplant. It is unclear why Blacks weren't transplanted commensurately with their proportion of the population. Given the retrospective design, this question cannot be answered by the current study. We found that Blacks were more often uninsured or insured by Medicaid. Underinsurance and lack of insurance are barriers to many interventions, including liver transplantation.

Situated in an urban setting with a diverse physician workforce, this study offers a large sample for the comparison of diverse patients. The number of Asian patients with HCC treated in our center was low, which did limit our ability to compare survival differences between Asian patients and patients of other races. Most patients, 55%, in our sample are immigrants to the USA, which influences the etiology of liver disease leading to HCC and may create additional barriers to accessing healthcare for screening. Also, patient engagement with the healthcare system is affected by race and culture. Our chart review yielded multiple cases where patients under age 30 died from ruptured or multifocal HCC. These patients were all minorities, some were immigrants, and several had a strong family history of liver cancer. Despite these risk factors, they did not seek medical attention until the only options were palliative. For HCC treatment, access to appropriate care is critical and depends on healthcare insurance. The existence of disparities is irrefutable; now, we must explore why these disparities exist and intervene. To improve racial disparities in survival after a diagnosis of HCC, additional research should specifically focus on reducing risk for chronic liver disease and improving surveillance for HCC in minority populations.

Author's contribution PDJ contributed to project conception, study design, data collection, statistical analysis, manuscript drafting, and critical revision. PDJ has approved the final draft submitted. CD contributed to data collection, data analysis, manuscript drafting, and critical revision. CD has approved the final draft submitted. DW contributed to data collection, data analysis, manuscript drafting, and critical revision. DW has approved the final draft submitted. JGD contributed to data collection, manuscript drafting, and critical revision. JGD has approved the final draft submitted. PM contributed to study design, data collection, data analysis, manuscript drafting, and critical revision. PM has approved the final draft submitted. EK contributed to project conception, study design, data collection, statistical analysis, manuscript drafting, and critical revision. EK has approved the final draft submitted.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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