Racial, Ethnic, and Socioeconomic Disparities in Curative Treatment Receipt and Survival in Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) disproportionately affects racial, ethnic, and low socioeconomic status (SES) populations. However, the interaction between race, ethnicity, and neighborhood SES in HCC prognosis is not well explored. This study evaluates the interaction between race and ethnicity and neighborhood SES on curative treatment utilization and overall survival among patients with HCC in the United States. We conducted a retrospective cohort study of 13,874 patients aged ≥65 years diagnosed with HCC from 2001 through 2015 using the Surveillance, Epidemiology, and End Results Medicare-linked database. We performed multivariable logistic regression to examine the association between race, ethnicity, and curative treatment receipt across SES. We also evaluated the association between curative treatment receipt and overall survival using a Cox proportional hazards model. Among 13,874 patients, only 2,617 (18.9%) patients received curative treatment. Overall, Black patients had lower odds of receiving curative treatment than White patients (odds ratio [OR], 0.76; 95% confidence interval [CI], 0.64-0.91). When stratified by neighborhood SES, Black patients living in high-poverty neighborhoods had lower odds of curative treatment receipt (OR, 0.64; 95% CI, 0.49-0.84) and worse survival (hazard ratio, 1.13; 95% CI, 1.02-1.25). Conversely, Hispanic and Asian patients had similar curative treatment receipt compared to White patients across all socioeconomic levels. *Conclusion:* Disparities in curative treatment receipt and overall survival are pronounced between Black and White patients. Black–White disparities appear to be moderated by neighborhood SES and are particularly evident among those living in high-poverty neighborhoods. (*Hepatology Communications* 2022;6:1186-1197).

Hepatocellular carcinoma (HCC) results in over 700,000 deaths globally every year and is one of the fastest rising causes of cancer-related mortality in the United States.[1] The 5-year survival for HCC remains below 20%. Prognosis markedly differs by tumor stage at diagnosis.[2] Patients with early stage HCC are eligible for curative surgical therapy, such as resection or liver transplantation, and can achieve 5-year survival rates exceeding 60%.[3] Conversely, median survival is typically 1-2 years for those with a more advanced tumor burden.[4]

HCC disproportionately affects racial and ethnic minorities and low socioeconomic status (SES) populations, with significantly higher HCC incidence and mortality rates in Black and Hispanic patients than non-Hispanic White patients.[4-6] However, fewer studies examine racial and ethnic and socioeconomic disparities in HCC prognosis, including overall survival. A prior systematic review found curative treatment is often underused in clinical practice, with only 22% of all patients with HCC and 59% of patients with early stage HCC undergoing curative treatment.[7] However,

Abbreviations: CI, confidence interval; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HR, hazard ratio; ICD, International Classification of Diseases; MAFLD, metabolic-associated fatty liver disease; NCI, National Cancer Institute; OR, odds ratio; SEER, Surveillance, Epidemiology and End Results; SES, socioeconomic status.

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The data underlying this article cannot be shared publicly because the National Cancer Institute does not permit others to use the data except for collaborators at our institution involved with this research as described in our research proposal. However, the data can be obtained through https://healthcaredelivery.cancer.gov/seermedicare/obtain/ by paying the cost mentioned.

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only five studies in this systematic review described racial, ethnic, or socioeconomic disparities in treatment receipt.[7] Similarly, a recent systematic review found Black patients with HCC had lower odds of early tumor detection and worse overall survival than non-Hispanic White patients, although the study did not directly address the interaction between race–ethnicity and SES. Although race, ethnicity, and SES are interrelated, they may impact health outcomes distinctly and have additive contributions to observed health disparities. Studies in other cancer types, including lung, ovarian, breast, prostate, and colorectal cancer, have shown that lower neighborhood SES is independently associated with worse survival.[8-12] However, there are few if any data examining the interaction between race, ethnicity, and neighborhood SES in patients with HCC.[13]

Therefore, we performed a retrospective cohort study to characterize the interaction of racial, ethnic, and neighborhood socioeconomic disparities in curative treatment use and overall survival in the United States among a large population-based sample of patients with HCC.

Materials and Methods

DATA SOURCES

We performed a retrospective cohort study using the National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results (SEER) Medicare data between the years 2001 and 2015. SEER is an epidemiological surveillance program that collects data on incident cancer cases from population-based cancer registries covering 34.6% of the United States.[14] The linked SEER-Medicare database combines these two population-based databases providing information on diagnosis, survival, demographics, and health services utilization of patients with cancer from Medicare eligibility until death.[15] This study protocol was reviewed and deemed not human subjects research by the Institutional Review Board at Texas A&M University.

STUDY POPULATION

We included all Medicare beneficiaries aged 65 years and older who were diagnosed with HCC (International Classification of Diseases [ICD] for Oncology, Third Edition, histology code 8170 and site code C22.0 for liver) between 2001 and 2015.[16] Only patients with diagnostically confirmed HCC (positive histology, cytology, laboratory test, positive radiology tests) were included. We excluded patients who (1) were not continuously enrolled in Medicare Part A and B 1 year before and after HCC diagnosis; (2) were enrolled in health maintenance organizations (HMOs)[15,17]; (3) had missing characteristics that could not be imputed[17]; (4) died within 30 days after HCC diagnosis; or (5) were diagnosed with other cancers 1 year before HCC diagnosis (Supporting Fig. S1).

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Potential conflict of Interest: Dr. Singal consults for Genentech, AstraZeneca, Bayer, Eisai, Exelixis, Bristol-Myers Squibb, Roche, Exact Sciences, Wako, Glycotest, and GRAIL. Dr. Rich consults for AstraZeneca. The other authors have nothing to report.

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STUDY VARIABLES

Outcomes

The primary outcome of interest was the receipt of curative treatment. Curative treatment was defined as liver transplantation, surgical resection, or local ablation and was identified from Medicare data using the ICD, Ninth and Tenth Revision, Clinical Modification (ICD-9 and ICD-10-Procedure Coding System), and Current Procedure Terminology codes within 12 months after HCC diagnosis.[18] Our secondary outcome was overall survival, defined as the time from HCC diagnosis (in months) to the date of death from any cause.

Neighborhood-Level SES

Census tract poverty level (CPL) was abstracted from the SEER Patient Entitlement and Diagnosis Summary File (PEDSF) and used as a proxy for neighborhood-level SES, defined as the proportion of the population living in poverty in the patient's residential census tract at the time of HCC diagnosis. We used 2000 US Census tract data for diagnosis years 2000-2005 and 2010 US Census tract data for diagnosis years 2006-2015 and categorized CPL for each patient as follows: high-poverty neighborhoods (20% to 100% poverty), moderate-poverty neighborhoods (10% to less than 20% poverty), and low-poverty neighborhoods (0% to less than 10% poverty), as described in the literature.[12,19,20]

Race, Ethnicity, and Other Sociodemographic Characteristics

SEER PEDSF was used to abstract information on race and ethnicity, age, sex, geographic region (Northeast, West, Midwest, and South), year of diagnosis, and census tract-level educational attainment. Race and ethnicity variable was categorized as non-Hispanic White (White), non-Hispanic Black (Black), Hispanic, Asian/Pacific Islander (Asian), and "other/unknown." Educational attainment was defined as the proportion of the population 25 years or older with at least 12 years of education.

Clinical Characteristics

Liver disease etiology was identified using Medicare data and was hierarchically categorized as hepatitis C virus (HCV), hepatitis B virus (HBV), alcohol-related liver disease, other liver diseases (hemochromatosis, disorders of copper metabolism, porphyria), metabolic-associated fatty liver disease (MAFLD), and no identifiable liver diseases. The severity of liver dysfunction was assessed by the presence of ascites (ICD-9: 789.51, 789.59 and ICD-10 code R18.0, R18.8) or hepatic encephalopathy (ICD-9: 572.2 and ICD-10 code K72.90, K72.91) at least 12 months before HCC diagnosis by using Medicare claims. We used diagnosis and procedure codes in the year preceding HCC diagnosis to calculate the National Cancer Institute (NCI) comorbidity index as a measure of noncancer comorbidity.[21,22] Receipt of abdominal ultrasound within 1 year before HCC diagnosis was captured as a proxy for screening from outpatient and physician/supplier claims data. Patients with early stage HCC were defined as patients with unifocal lesion ≤5 cm with no evidence of vascular invasion or distant metastases. We conducted a sensitivity analysis using SEER stage, classified as localized, regional, or distant.

STATISTICAL ANALYSIS

Chi-squared tests were used to compare characteristics of the study population by receipt of curative treatment. Multivariable logistic regression with time-fixed effects was performed to examine the impact of race and ethnicity on receipt of curative treatment across socioeconomic strata. We calculated robust standard errors to account for clustering at the census tract level. Survival time was measured in months from HCC diagnosis to death from any cause. People who were alive on December 31, 2017, were censored on that date. We estimated overall survival by race and ethnicity across the socioeconomic strata using Kaplan-Meier analysis. Log-rank tests were used to compare survival distributions by race, ethnicity, and SES. We then performed univariable and multivariable Cox proportional hazards analyses for each SES subgroup to examine the association between race, ethnicity, and survival across socioeconomic strata. We reported the associations from our multivariable models as adjusted odds ratios (ORs) and adjusted hazard ratios (HRs) with 95% confidence intervals (CIs). All P values were two-sided with a statistical significance $P < 0.05$. We conducted a subgroup analysis among patients with early stage HCC. All statistical analyses were performed using Stata version 16.1 (StataCorp, College Station, TX).

Results

A total of 46,998 patients were diagnosed with HCC between 2001 and 2015 (Supporting Fig. S1). We excluded 25,084 patients (12.1% Black, 5.8% Hispanic) due to lack of continuous enrollment in Medicare Part A and B or enrollment in HMOs; 4,653 patients with missing sociodemographic information; 2,901 patients who died within 30 days after HCC diagnosis (11.3% Black, 4.6% Hispanic); and 486 patients with other cancers 1 year before HCC diagnosis. There were 13,874 patients with HCC who remained eligible for inclusion in the final sample set (Supporting Fig. S1).

Baseline patient characteristics are detailed in Table 1. The median age was 75 years, and over two thirds (68.0%) of patients were men. The cohort was racially diverse (69.1% Whites, 8.4% Blacks, 12.1% Asians, and 4.1% Hispanics) and had socioeconomic diversity, with 46.8% of patients residing in low-poverty neighborhoods, 29.9% in moderate-poverty neighborhoods, and 23.3% in high-poverty neighborhoods. Most (61.0%) patients did not receive ultrasound-based screening within 1 year before HCC diagnosis, although screening was higher (52.6%) among those with early stage HCC. Blacks had lower receipt of ultrasound in the year before HCC diagnosis than Whites and Hispanics (33.8% vs. 36.7% and 46.9%, respectively). Although more than half (52.5%) of the patients had localized SEER stage, only one fifth (17.7%) were detected with a unifocal HCC ≤5 cm without vascular invasion or distant metastases.

RECEIPT OF CURATIVE TREATMENT

A minority of patients received curative treatment, including 2,617 (18.9%) of the entire cohort of patients. Of the 2,617 who received curative treatment, 68.0% were White, 7.2% were Black, 13.3% were Asian, and 3.3% were Hispanic (Supporting Table S1). Of the 2,457 patients with early stage HCC, 911 (37.1%) received curative treatment; among those who received curative treatment, 62.9% were White, 7.8% were Black, 15.1% were Asian, and 4.2% were Hispanic.

In multivariable analyses (Table 2), men, older patients, and those with higher comorbidity had lower

TABLE 1. CHARACTERISTICS OF PATIENTS DIAGNOSED WITH HCC (2001-2015)

	Overall (n = 13,874)		Early stage HCC* (n = 2,457)	
	n (%)		n (%)	
Curative treatment				
Not received	11,257	81.10%	1,546	62.90%
Received	2,617	18.90%	911	37.10%
Age at diagnosis				
65-69 years	3,438	24.80%	757	30.80%
70-74 years	3,665	26.40%	677	27.60%
75-79 years	3,244	23.40%	523	21.30%
80 years and over	3,527	25.40%	500	20.40%
Sex				
Female	4,442	32.00%	944	38.40%
Male	9,432	68.00%	1,513	61.60%
Race and ethnicity				
White	9,594	69.20%	1,593	64.80%
Black	1,161	8.40%	189	7.70%
Asian	1,675	12.10%	356	14.50%
Hispanic	573	4.10%	116	4.70%
Other/unknown	871	6.30%	203	8.30%
Neighborhood-level SES				
Low-poverty neighborhoods	6,489	46.80%	1,092	44.40%
Moderate-poverty neighborhoods	4,145	29.90%	765	31.10%
High-poverty neighborhoods	3,240	23.40%	600	24.40%
Census tract education level (mean, SD)	17.7	13.6	17.2	13.5
Geographic region				
Northeast	2,469	17.80%	319	13.00%
West	7,377	53.20%	1,497	60.90%
Midwest	1,334	9.60%	222	9.00%
South	2,694	19.40%	419	17.10%
Abdominal ultrasound				
No	8,463	61.00%	1,165	46.40%
Yes	5,411	39.00%	1,292	52.60%
Unifocal lesion				
No	6,603	47.60%		
Yes	2,457	17.70%	N/A	N/A
Nondeterminable	4,814	34.70%		
SEER stage				
Localized	7,290	52.50%		
Regional	3,592	25.90%	N/A	N/A
Distant	1,764	12.70%		
Unknown	1,228	8.90%		
NCI comorbidity index				
0	3,186	23.00%	457	18.60%
1	2,974	21.40%	453	18.40%

TABLE 1. *Continued*

	Overall (n = 13,874)		Early stage HCC* (n = 2,457)	
	n (%)		n (%)	
2	2,372	17.10%	681	27.70%
3	2,312	16.70%	684	27.80%
4	831	6.00%	210	8.50%
≥5	2,199	15.80%	576	23.40%
Liver disease etiology				
No identifiable liver disease	2,885	20.80%	281	11.40%
HCV	3,589	25.90%	979	39.80%
HBV	587	4.20%	176	7.20%
Alcohol-related liver disease	1,379	9.90%	302	12.30%
Other liver disease†	244	1.80%	51	2.10%
MAFLD	5,190	37.40%	668	27.20%
Liver dysfunction				
Presence of hepatic encephalopathy	815	5.90%	265	10.80%
Presence of ascites	1,481	10.70%	457	18.60%
Year of diagnosis				
2001	627	4.50%	62	2.50%
2002	735	5.30%	75	3.10%
2003	694	5.00%	85	3.50%
2004	807	5.80%	124	5.00%
2005	802	5.80%	99	4.00%
2006	783	5.60%	132	5.40%
2007	881	6.40%	139	5.70%
2008	918	6.60%	161	6.60%
2009	953	6.90%	166	6.80%
2010	998	7.20%	209	8.50%
2011	1,068	7.70%	195	7.90%
2012	1,111	8.00%	224	9.10%
2013	1,154	8.30%	242	9.80%
2014	1,146	8.30%	253	10.30%
2015	1,197	8.60%	291	11.80%

*Early stage HCC was defined using the unifocal lesion ≤5 cm without vascular invasion or metastatic spread.
†Other liver diseases include hemochromatosis, disorders of copper metabolism, porphyria.
Abbreviation: N/A, not applicable.

odds of curative treatment receipt. Geographic differences were also observed, with patients living in northeastern and southern regions having higher odds of curative treatment than those in the West. We observed significant racial disparities, with Black patients having lower odds of receiving curative treatment (OR, 0.76; 95% CI, 0.64-0.91) compared to White patients. Patients in moderate-poverty neighborhoods also had lower odds of receiving treatment (OR, 0.89; 95% CI, 0.79-1.00) when compared to patients living in low-poverty neighborhoods. When stratified by SES, Black patients in high-poverty neighborhoods continued to have lower odds of curative treatment compared to White patients (OR, 0.64; 95% CI, 0.49-0.84); however, there were no significant differences in curative treatment receipt between Black and White patients living in low-poverty (OR, 0.80; 95% CI, 0.54-1.14) or moderate-poverty (OR, 0.89; 95% CI, 0.64-1.23) neighborhoods. No significant disparities in curative treatment receipt were observed for Hispanic and Asian patients in comparison to White patients, irrespective of neighborhood SES.

As expected, patients with early stage HCC had 2.64 times higher odds (95% CI, 2.37-2.94) of receiving curative treatment than patients presenting with larger tumor burden. Among patients with early stage HCC, older age, higher comorbidity index, and alcohol-related liver disease had lower odds of curative treatment receipt (Supporting Table S2). We did not observe significant racial and socioeconomic disparities between Black and White patients irrespective of the SES. However, we observed that Hispanic patients in high-poverty neighborhoods had higher odds of receiving curative treatment when compared to White patients (OR, 1.92; 95% CI, 1.03-3.56). In contrast, there were no significant differences in curative treatment receipt between Hispanic and White patients living in low-poverty (OR, 0.58; 95% CI, 0.22-1.56) or moderate-poverty (OR, 0.73; 95% CI, 0.34-1.55) neighborhoods.

OVERALL SURVIVAL

Median survival for the entire cohort was 11 (interquartile range [IQR], 4-33) months. Median survival was 10, 9, 17, and 10 months for White, Black, Asian, and Hispanic patients, respectively. Overall unadjusted survival, stratified by race, ethnicity, and SES, for the cohort is illustrated in Figs. 1 and 2A-D.

Multivariable Cox proportional hazards model identified several sociodemographic and clinical predictors of overall survival (Table 3). Older patients (age >70 years), those living in the Midwest and South, those with higher comorbidity, and patients with ascites had worse survival than their counterparts. As expected, early stage HCC detection (HR, 0.57; 95% CI, 0.54-0.60)

TABLE 2. ODDS OF CURATIVE TREATMENT RECEIPT AMONG PATIENTS WITH HCC

	Base Model n = 13,874 OR (95% CI)	Low-Poverty Neighborhoods n = 6,489 OR (95% CI)	Moderate-Poverty Neighborhoods n = 4,145 OR (95% CI)	High-Poverty Neighborhoods n = 3,240 OR (95% CI)
Age at diagnosis				
65-69 years	Ref.	Ref.	Ref.	Ref.
70-74 years	0.88 (0.78, 0.99)	0.82 (0.69, 0.97)	0.99 (0.78, 1.24)	0.91 (0.72, 1.17)
75-79 years	0.67 (0.59, 0.76)	0.62 (0.52, 0.74)	0.75 (0.59, 0.96)	0.71 (0.54, 0.93)
80 years and over	0.44 (0.38, 0.51)	0.40 (0.33, 0.49)	0.53 (0.41, 0.68)	0.41 (0.30, 0.56)
Male	0.82 (0.74, 0.91)	0.82 (0.71, 0.95)	0.97 (0.81, 1.17)	0.68 (0.55, 0.84)
Race and ethnicity				
White	Ref.	Ref.	Ref.	Ref.
Black	0.76 (0.64, 0.91)	0.80 (0.56, 1.14)	0.89 (0.64, 1.23)	0.64 (0.49, 0.84)
Asian	1.04 (0.90, 1.21)	1.01 (0.81, 1.26)	1.22 (0.92, 1.62)	0.95 (0.68, 1.31)
Hispanic	0.92 (0.72, 1.17)	0.73 (0.43, 1.24)	0.64 (0.39, 1.04)	1.29 (0.89, 1.87)
Other/Unknown	1.19 (1.00, 1.42)	1.30 (1.02, 1.64)	1.23 (0.88, 1.73)	0.93 (0.59, 1.45)
Neighborhood-level SES				
Low-poverty neighborhoods	Ref.	–	–	–
Moderate-poverty neighborhoods	0.89 (0.79, 1.00)			
High-poverty neighborhoods	1.03 (0.89, 1.20)			
Census tract education level	0.99 (0.98, 0.99)	0.98 (0.97, 0.99)	0.99 (0.98, 1.00)	0.99 (0.98, 1.00)
Geographic region				
West	Ref.	Ref.	Ref.	Ref.
Northeast	1.46 (1.28, 1.66)	1.34 (1.15, 1.57)	1.66 (1.25, 2.19)	1.83 (1.25, 2.67)
Midwest	1.10 (0.93, 1.30)	1.00 (0.80, 1.26)	1.23 (0.90, 1.67)	1.33 (0.93, 1.91)
South	1.21 (1.07, 1.38)	1.17 (0.95, 1.43)	1.30 (1.04, 1.61)	1.27 (0.97, 1.65)
Unifocal lesion				
No	Ref.	Ref.	Ref.	Ref.
Yes	2.64 (2.37, 2.94)	2.34 (1.99, 2.75)	2.96 (2.40, 3.65)	2.94 (2.37, 3.65)
Nondeterminable	0.66 (0.59, 0.73)	0.65 (0.56, 0.76)	0.71 (0.57, 0.88)	0.61 (0.47, 0.78)
NCI comorbidity index				
0	Ref.	Ref.	Ref.	Ref.
1	0.95 (0.82, 1.11)	0.87 (0.71, 1.06)	0.95 (0.73, 1.25)	1.21 (0.90, 1.63)
2	1.02 (0.88, 1.18)	1.00 (0.82, 1.22)	1.05 (0.79, 1.38)	1.04 (0.76, 1.42)
3	1.00 (0.86, 1.16)	0.95 (0.78, 1.17)	0.96 (0.73, 1.28)	1.20 (0.87, 1.66)
4	0.90 (0.73, 1.11)	0.85 (0.63, 1.14)	1.05 (0.72, 1.52)	0.85 (0.51, 1.41)
≥5	0.62 (0.53, 0.73)	0.63 (0.50, 0.79)	0.57 (0.41, 0.77)	0.69 (0.49, 0.95)
Liver disease etiology				
HCV	Ref.	Ref.	Ref.	Ref.
HBV	1.32 (1.07, 1.64)	1.18 (0.88, 1.59)	1.52 (1.01, 2.28)	1.45 (0.90, 2.35)
Alcohol-related liver disease	0.61 (0.51, 0.72)	0.69 (0.54, 0.88)	0.61 (0.44, 0.86)	0.42 (0.28, 0.63)
Other liver disease	0.98 (0.72, 1.33)	1.21 (0.81, 1.80)	0.96 (0.53, 1.75)	0.41 (0.17, 0.98)
MAFLD	0.75 (0.66, 0.84)	0.76 (0.64, 0.91)	0.81 (0.65, 1.01)	0.66 (0.52, 0.85)
No identifiable liver disease	0.57 (0.49, 0.65)	0.64 (0.52, 0.79)	0.48 (0.36, 0.65)	0.49 (0.36, 0.68)
Liver dysfunction				
Presence of hepatic encephalopathy	0.87 (0.71, 1.06)	0.82 (0.62, 1.10)	0.93 (0.64, 1.35)	0.94 (0.62, 1.43)
Presence of ascites	1.00 (0.85, 1.17)	1.04 (0.82, 1.30)	1.20 (0.89, 1.61)	0.74 (0.53, 1.03)

TABLE 2. *Continued*

	Base Model n = 13,874 OR (95% CI)	Low-Poverty Neighborhoods n = 6,489 OR (95% CI)	Moderate-Poverty Neighborhoods n = 4,145 OR (95% CI)	High-Poverty Neighborhoods n = 3,240 OR (95% CI)
Year of diagnosis				
2001	Ref.	Ref.	Ref.	Ref.
2002	1.19 (0.87, 1.64)	1.33 (0.87, 2.05)	1.30 (0.72, 2.36)	0.78 (0.37, 1.64)
2003	1.15 (0.83, 1.60)	1.13 (0.73, 1.74)	1.01 (0.53, 1.92)	1.52 (0.76, 3.04)
2004	1.05 (0.78, 1.43)	0.92 (0.61, 1.40)	1.26 (0.70, 2.27)	1.34 (0.67, 2.68)
2005	1.14 (0.84, 1.55)	1.02 (0.66, 1.56)	1.11 (0.61, 2.02)	1.60 (0.84, 3.04)
2006	0.99 (0.73, 1.35)	1.10 (0.73, 1.66)	0.84 (0.45, 1.56)	0.97 (0.48, 1.97)
2007	1.00 (0.74, 1.34)	1.02 (0.68, 1.54)	0.93 (0.52, 1.66)	1.03 (0.54, 1.99)
2008	1.02 (0.76, 1.38)	1.18 (0.79, 1.77)	1.00 (0.57, 1.76)	0.62 (0.30, 1.27)
2009	0.95 (0.71, 1.28)	0.96 (0.64, 1.46)	0.73 (0.41, 1.31)	1.29 (0.67, 2.46)
2010	0.90 (0.67, 1.21)	0.99 (0.65, 1.50)	0.77 (0.44, 1.36)	0.87 (0.46, 1.63)
2011	0.96 (0.71, 1.30)	1.00 (0.66, 1.52)	0.89 (0.50, 1.58)	1.00 (0.53, 1.86)
2012	0.90 (0.67, 1.20)	0.95 (0.62, 1.44)	0.74 (0.42, 1.32)	1.06 (0.58, 1.93)
2013	1.03 (0.77, 1.37)	1.03 (0.68, 1.56)	0.90 (0.51, 1.58)	1.17 (0.63, 2.16)
2014	0.86 (0.64, 1.16)	0.86 (0.57, 1.29)	0.70 (0.39, 1.26)	1.08 (0.57, 2.05)
2015	1.05 (0.79, 1.41)	1.00 (0.67, 1.50)	0.90 (0.51, 1.60)	1.38 (0.74, 2.55)

Abbreviation: Ref., reference.

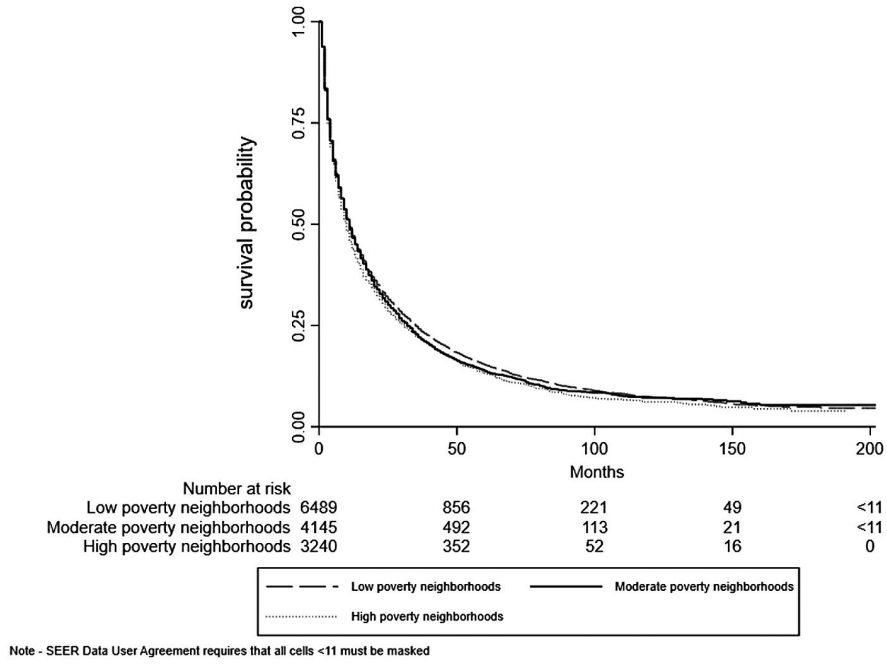

FIG. 1. Overall unadjusted survival by SES.

and curative treatment receipt (HR, 0.42; 95% CI, 0.40-0.44) were both associated with improved survival.

We observed racial, ethnic, and socioeconomic disparities in overall survival. Black patients in high-poverty neighborhoods had worse survival than White patients (HR, 1.13; 95% CI, 1.02-1.25). In contrast, we found no significant Black–White disparities in survival in moderate-poverty (HR, 0.95; 95% CI, 0.82-1.09) or low-poverty (HR, 0.87; 95% CI, 0.73-1.04) neighborhoods. Asian patients had lower

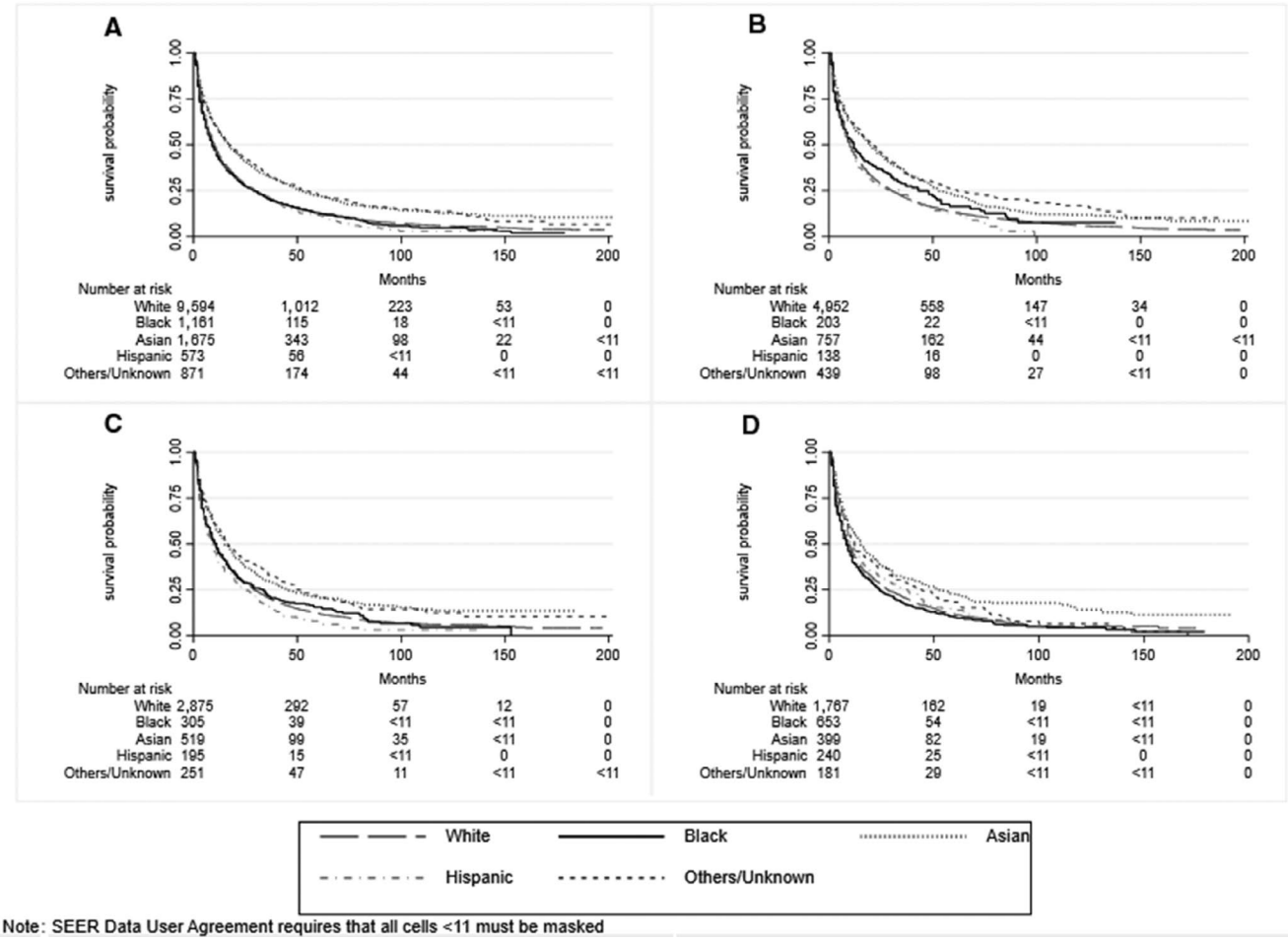

FIG. 2. Overall unadjusted survival, stratified by race/ethnicity. (A) Entire cohort, (B) patients living in low-poverty areas, (C) patients living in moderate-poverty areas, (D) patients living in high-poverty areas.

mortality than White patients irrespective of SES (low-poverty neighborhoods HR, 0.76; 95% CI, 0.69-0.83; moderate-poverty neighborhoods HR, 0.88; 95% CI, 0.78-0.98; high-poverty neighborhoods HR, 0.75; 95% CI, 0.65-0.86). No significant disparities in overall survival were observed between Hispanic and White patients, irrespective of SES. Among those with early stage HCC, Asian–White disparities persisted across SES strata; however, we found no significant disparities between White and Black or Hispanic patients irrespective of SES (Supporting Table S3).

Discussion

In this analysis of the SEER-Medicare database, we found that less than one fifth of patients with HCC received curative treatment, including less than one third of those with early stage HCC, leading to a poor median overall survival of only 11 months. Further, we observed statistically significant racial, ethnic, and neighborhood socioeconomic disparities in receipt of curative treatment for HCC. Black patients were significantly less likely to undergo curative treatment and have worse overall survival than White patients, whereas we did not observe Hispanic–White disparities in curative treatment receipt or overall survival. Notably, disparities in curative treatment receipt were less marked among those with early stage HCC than all patients, suggesting observed disparities were in part driven by differences in tumor burden at diagnosis.

The striking Black–White disparities in HCC prognosis identified in our study are consistent with

TABLE 3. PREDICTORS OF OVERALL SURVIVAL

	Base Model n = 13,874 HR (95% CI)	Low-Poverty Neighborhoods n = 6,489 HR (95% CI)	Moderate-Poverty Neighborhoods n = 4,145 HR (95% CI)	High-Poverty Neighborhoods n = 3,240 HR (95% CI)
Curative treatment				
Not received	Ref.	Ref.	Ref.	Ref.
Received	0.42 (0.40, 0.44)	0.43 (0.40, 0.46)	0.41 (0.37, 0.45)	0.42 (0.38, 0.46)
Age at diagnosis				
65-69 years	Ref.	Ref.	Ref.	Ref.
70-74 years	1.12 (1.06, 1.18)	1.14 (1.05, 1.23)	1.12 (1.01, 1.23)	1.10(1.00, 1.22)
75-79 years	1.22 (1.15, 1.29)	1.30 (1.20, 1.41)	1.15 (1.04, 1.27)	1.17 (1.04, 1.30)
80 years and over	1.32 (1.25, 1.39)	1.44 (1.33, 1.56)	1.27 (1.16, 1.40)	1.19 (1.06, 1.33)
Male	1.03 (0.99, 1.07)	1.04 (0.98, 1.10)	1.00 (0.93, 1.07)	1.07 (0.98, 1.16)
Race and ethnicity				
White	Ref.	Ref.	Ref.	Ref.
Black	1.01 (0.94, 1.08)	0.87 (0.73, 1.04)	0.95 (0.82, 1.09)	1.13 (1.02, 1.25)
Asian	0.79 (0.74, 0.84)	0.76 (0.69, 0.83)	0.88 (0.78, 0.98)	0.75 (0.65, 0.86)
Hispanic	0.97 (0.88, 1.06)	0.97 (0.82, 1.15)	1.06 (0.92, 1.23)	0.92 (0.78, 1.07)
Other/unknown	0.83 (0.77, 0.90)	0.80 (0.71, 0.90)	0.83 (0.71, 0.97)	0.91 (0.78, 1.06)
Neighborhood-level SES				
Low-poverty neighborhoods	Ref.	–	–	–
Moderate-poverty neighborhoods	0.97 (0.92, 1.01)			
High-poverty neighborhoods	0.95 (0.89, 1.01)			
Census tract education level	1.00 (1.00, 1.01)	1.01 (1.00, 1.01)	1.01 (1.00, 1.01)	1.00 (1.00, 1.01)
Geographic region				
West	Ref.	Ref.	Ref.	Ref.
Northeast	0.97 (0.92, 1.02)	0.96 (0.90, 1.03)	1.00 (0.90, 1.12)	0.88 (0.76, 1.03)
Midwest	1.12 (1.04, 1.19)	1.17 (1.06, 1.29)	1.09 (0.97, 1.22)	0.97 (0.84, 1.11)
South	1.11 (1.05, 1.17)	1.10 (1.00, 1.20)	1.07 (0.98, 1.16)	1.12 (1.02, 1.23)
Unifocal lesion				
No	Ref.	Ref.	Ref.	Ref.
Yes	0.57 (0.54, 0.60)	0.55 (0.51, 0.60)	0.56 (0.51, 0.62)	0.58 (0.53, 0.64)
Nondeterminable	1.14 (1.10, 1.19)	1.16 (1.09, 1.23)	1.14 (1.05, 1.22)	1.12 (1.03, 1.21)
NCI comorbidity index				
0	Ref.	Ref.	Ref.	Ref.
1	1.01 (0.96, 1.07)	1.00 (0.92, 1.09)	1.01 (0.91, 1.11)	1.04 (0.92, 1.17)
2	0.93 (0.88, 0.99)	1.00 (0.91, 1.09)	0.89 (0.79, 1.00)	0.86 (0.76, 0.98)
3	0.94 (0.88, 1.00)	1.01 (0.91, 1.11)	0.86 (0.77, 0.97)	0.91 (0.80, 1.03)
4	1.16 (1.07, 1.26)	1.21 (1.08, 1.37)	1.30 (1.12, 1.52)	0.92 (0.78, 1.09)
≥5	1.13 (1.07, 1.21)	1.23 (1.12, 1.36)	1.15 (1.03, 1.28)	0.96 (0.85, 1.08)
Liver disease etiology				
HCV	Ref.	Ref.	Ref.	Ref.
HBV	1.25 (1.18, 1.32)	1.21 (1.11, 1.32)	1.32 (1.18, 1.46)	1.27 (1.13, 1.43)
Alcohol-related liver disease	0.84 (0.75, 0.93)	0.86 (0.74, 1.01)	0.78 (0.64, 0.94)	0.86 (0.68, 1.08)
Other liver disease	1.14 (1.06, 1.22)	1.11 (1.00, 1.22)	1.22 (1.07, 1.39)	1.13 (0.98, 1.32)
MAFLD	0.97 (0.85, 1.11)	1.00 (0.82, 1.20)	1.06 (0.83, 1.36)	0.70 (0.47, 1.02)

TABLE 3. *Continued*

	Base Model n = 13,874 HR (95% CI)	Low-Poverty Neighborhoods n = 6,489 HR (95% CI)	Moderate-Poverty Neighborhoods n = 4,145 HR (95% CI)	High-Poverty Neighborhoods n = 3,240 HR (95% CI)
No identifiable liver disease	1.22 (1.16, 1.28)	1.22 (1.13, 1.31)	1.19 (1.08, 1.30)	1.28 (1.15, 1.41)
Liver dysfunction				
Presence of hepatic encephalopathy	0.97 (0.89, 1.07)	1.04 (0.91, 1.19)	0.89 (0.77, 1.04)	0.96 (0.81, 1.14)
Presence of ascites	1.20 (1.12, 1.28)	1.19 (1.07, 1.33)	1.22 (1.08, 1.37)	1.22 (1.07, 1.40)

Abbreviation: Ref., reference.

published studies and parallel the conclusions from a recent systematic review.[7] Our study extends the published literature by examining the intersection of race, ethnicity, and SES in HCC prognosis in a large population-based patient sample. Notably, despite the study cohort representing an insured population of Medicare enrollees, we found Black–White disparities in treatment and survival appear to be moderated by SES as we observed these disparities only in high-poverty neighborhoods and not in moderate-poverty or low-poverty neighborhoods. These data provide further context in our understanding of the interplay between racial, ethnic, and neighborhood socioeconomic disparities in HCC prognosis; this is critical as we move from a model of simply describing health disparities to understanding why disparities exist and developing interventions to promote health equity.

The root causes of HCC curative treatment disparities are complex and likely related to a combination of factors at the individual (e.g., misconceptions about cancer treatment, mistrust, transportation barriers, caregiver burden), provider (e.g., implicit and/or explicit biases), and system (e.g., hospital volume and facilities) levels.[23] Furthermore, all these factors may be intertwined with and exacerbated by individual and neighborhood-level poverty and inextricably linked to health care access. Our study also highlights that simply having health insurance does not remove all barriers as disparities in guideline-concordant HCC care exist even among those with equal health coverage (in this case Medicare enrollees).[24-26] Further, insured patients with limited financial means may still have difficulty affording out-of-pocket costs for medications and clinic visits. Patients living in high-poverty neighborhoods may also have other noninsurance-related barriers that can result in missed visits and postponed care or shortages of physicians and subspecialists in medically underserved areas.[27-30] In particular, the availability of liver transplantation and hepatic resection may be limited in these areas.[31]

Differential access to health care may not wholly explain racial and ethnic disparities in prognosis and subsequent receipt of curative treatment. For instance, there is increasing evidence highlighting the role of epigenetic effects and chronic stress from racism and poverty, leading to immunologic changes that may impact cancer biology and prognosis.[32,33] Several studies have suggested lower HCC surveillance receipt in racial–ethnic minorities and more advanced tumor burden at diagnosis.[13,24,28,30] Although recent data suggest variation in tumor growth patterns, there are no ethnic disparities in the frequency of common somatic mutations associated with HCC (e.g., catenin beta 1 [*CTNNB1*]) and no convincing data demonstrating racial and ethnic disparities in tumor biology and growth patterns.[32,33] Compared to other racial–ethnic groups, Asians are more likely to have underlying HBV infection, which can cause HCC in the absence of cirrhosis and may facilitate curative surgical resection. Recent data suggest Black patients may develop HCC at earlier stages of fibrosis, outside of traditional surveillance criteria, which may be one of the reasons they present at more advanced HCC stages.[34] Although our study highlights the complexity of racial and ethnic disparities, particularly the intersection with race–ethnicity and SES, further studies are needed to evaluate these sociodemographic disparities mediating pathways.

Strengths of our study include a large population-based patient sample and novel analysis characterizing the interaction between race, ethnicity, and neighborhood SES and its impact on curative treatment use

and survival. Further, linkage to the Medicare database provided us with some clinical information not included in SEER (e.g., liver disease etiology, ascites/encephalopathy), more detailed treatment data, and an improvement over using one or the other data alone. We acknowledge that our study also has limitations. Our analysis included older patients, limiting generalizability to younger patients who may be more likely to undergo curative therapies.[35] Although SEER is extensive population-based data, it does not include all geographic regions in the United States, limiting generalizability given the geographic variation in HCC treatment receipt and prognosis. While we had information on the presence of ascites and/or hepatic encephalopathy indicating the presence of underlying liver dysfunction, SEER-Medicare does not contain laboratory data to allow for more precise quantification of liver dysfunction (e.g., to allow for calculation of Model for End-Stage Liver Disease score and/or Child-Pugh score), data on performance status, or sufficient tumor characteristics to determine Milan criteria. These are all factors that influence the likelihood of curative treatment and risk of mortality in patients with HCC. We characterized disparities in curative treatment receipt but did not examine receipt of palliative locoregional or systemic therapies, which can prolong survival, albeit to a smaller degree than curative options. We also acknowledge that our results should be interpreted cautiously due to heterogeneity within a race and ethnic group. For example, Asians and Pacific Islanders include ethnicities with stark differences and should not be mistaken for a monolith.

In conclusion, our study highlights that Black–White disparities persist in curative treatment use and overall survival among patients with HCC. This disparity appears to be moderated by neighborhood-level SES, with the most significant differences noted among persons from high-poverty areas. Future studies are needed to identify intervention targets to reduce disparities in HCC prognosis.

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