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.)
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).
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                  | 1,546                       |
| Received                | 2,617                   | 911                         |
| Age at diagnosis        |                         |                             |
| 65-69 years             | 3,438                   | 757                         |
| 70-74 years             | 3,665                   | 677                         |
| 75-79 years             | 3,244                   | 523                         |
| 80 years and over       | 3,527                   | 500                         |
| Sex                     |                         |                             |
| Female                  | 4,442                   | 944                         |
| Male                    | 9,432                   | 1,513                       |
| Race and ethnicity      |                         |                             |
| White                   | 9,594                   | 1,593                       |
| Black                   | 1,161                   | 189                         |
| Asian                   | 1,675                   | 356                         |
| Hispanic                | 573                     | 116                         |
| Other/unknown           | 871                     | 203                         |
| Neighborhood-level SES  |                         |                             |
| Low-poverty neighborhoods| 6,489                   | 1,092                       |
| Moderate-poverty neighborhhoods| 4,145 | 765 | 31.10% |
| High-poverty neighborhoods| 3,240                   | 600                         |
| Census tract education level (mean, SD) | 17.7 | 17.2 | 13.5 |
| Geographic region       |                         |                             |
| Northeast               | 2,469                   | 319                         |
| West                    | 7,377                   | 1,497                       |
| Midwest                 | 1,334                   | 222                         |
| South                   | 2,694                   | 419                         |
| Abdominal ultrasound    |                         |                             |
| No                      | 8,463                   | 1,165                       |
| Yes                     | 5,411                   | 1,292                       |
| Unifocal lesion         |                         |                             |
| No                      | 6,603                   | 47.60%                      |
| Yes                     | 2,457                   | 17.70%                      |
| Nondeterminable         | 4,814                   | 34.70%                      |
| SEER stage              |                         |                             |
| Localized               | 7,290                   | 52.50%                      |
| Regional                | 3,592                   | 25.90%                      |
| Distant                 | 1,764                   | 12.70%                      |
| Unknown                 | 1,228                   | 8.90%                       |
| NCI comorbidity index   |                         |                             |
| 0                       | 3,186                   | 23.00%                      |
| 1                       | 2,974                   | 21.40%                      |
| 2                       | 2,974                   | 21.40%                      |
| 3                       | 2,974                   | 21.40%                      |
| 4                       | 2,974                   | 21.40%                      |
| 5                       | 2,974                   | 21.40%                      |
| 6                       | 2,974                   | 21.40%                      |
| 7                       | 2,974                   | 21.40%                      |
| 8                       | 2,974                   | 21.40%                      |
| 9                       | 2,974                   | 21.40%                      |
| 10                      | 2,974                   | 21.40%                      |
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, 0.76; 95% CI, 0.64-0.91) 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 (0.79, 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) |
| **Race and Ethnicity** |
| 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) |
| 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. | Ref. | Ref. | Ref. |
| Moderate-poverty neighborhoods | 0.89 (0.79, 1.00) | 0.80 (0.62, 1.02) | 0.71 (0.48, 1.05) | 0.65 (0.54, 0.79) |
| High-poverty neighborhoods | 1.03 (0.89, 1.20) | 1.00 (0.79, 1.25) | 0.97 (0.70, 1.36) | 0.86 (0.69, 1.06) |
| Census tract education level | 0.99 (0.98, 1.00) | 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 (1.24, 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, 1.66) | 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) |
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

### TABLE 2. Continued

| Year of diagnosis | 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) |
|-------------------|----------------------------------|-----------------------------------------------|---------------------------------------------------|-----------------------------------------------|
| 2001 Ref.         | 1.19 (0.87, 1.64)                | 1.33 (0.87, 2.05)                              | 1.30 (0.72, 2.36)                                 | 0.78 (0.37, 1.64)                             |
| 2002              | 1.15 (0.83, 1.60)                | 1.13 (0.73, 1.74)                              | 1.01 (0.53, 1.92)                                 | 1.52 (0.76, 3.04)                             |
| 2003              | 1.05 (0.78, 1.43)                | 0.92 (0.61, 1.40)                              | 1.26 (0.70, 2.27)                                 | 1.34 (0.67, 2.68)                             |
| 2004              | 1.14 (0.84, 1.55)                | 1.02 (0.66, 1.56)                              | 1.11 (0.61, 2.02)                                 | 1.60 (0.84, 3.04)                             |
| 2005              | 0.99 (0.73, 1.35)                | 1.10 (0.73, 1.66)                              | 0.84 (0.45, 1.56)                                 | 0.97 (0.48, 1.97)                             |
| 2006              | 1.00 (0.74, 1.34)                | 1.02 (0.68, 1.54)                              | 0.93 (0.52, 1.66)                                 | 1.03 (0.54, 1.99)                             |
| 2007              | 1.02 (0.76, 1.38)                | 1.18 (0.79, 1.77)                              | 1.00 (0.57, 1.76)                                 | 0.62 (0.30, 1.27)                             |
| 2008              | 0.95 (0.71, 1.28)                | 0.96 (0.64, 1.46)                              | 0.73 (0.41, 1.31)                                 | 1.29 (0.67, 2.46)                             |
| 2009              | 0.90 (0.67, 1.23)                | 0.99 (0.65, 1.50)                              | 0.77 (0.44, 1.36)                                 | 0.87 (0.46, 1.63)                             |
| 2010              | 0.96 (0.71, 1.30)                | 1.00 (0.66, 1.52)                              | 0.89 (0.50, 1.58)                                 | 1.00 (0.53, 1.86)                             |
| 2011              | 0.90 (0.67, 1.20)                | 0.95 (0.62, 1.44)                              | 0.74 (0.42, 1.32)                                 | 1.06 (0.58, 1.93)                             |
| 2012              | 1.03 (0.77, 1.37)                | 1.03 (0.68, 1.56)                              | 0.90 (0.51, 1.58)                                 | 1.17 (0.63, 2.16)                             |
| 2013              | 0.86 (0.64, 1.16)                | 0.86 (0.57, 1.29)                              | 0.70 (0.39, 1.26)                                 | 1.08 (0.57, 2.05)                             |
| 2014              | 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.
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** | **Low-Poverty Neighborhoods** | **Moderate-Poverty Neighborhoods** | **High-Poverty Neighborhoods** |
| **n = 13,874 HR (95% CI)** | **n = 6,489 HR (95% CI)** | **n = 4,145 HR (95% CI)** | **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) |
| **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. | Ref. | Ref. | Ref. |
| Moderate-poverty neighborhoods | 0.97 (0.92, 1.01) | Ref. | Ref. | Ref. |
| High-poverty neighborhoods | 0.95 (0.89, 1.01) | Ref. | Ref. | Ref. |
| **Census tract education level** |
| 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 | 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) |
published studies and parallel the conclusions from a recent systematic review. 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. 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). 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. In particular, the availability of liver transplantation and hepatic resection may be limited in these areas.

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. Several studies have suggested lower HCC surveillance receipt in racial–ethnic minorities and more advanced tumor burden at diagnosis. 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. 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. 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.

### 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.
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. 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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