Delay to Treatment, Socioeconomic Status, and Race/Ethnicity are Associated with Increased Mortality from Hepatocellular Carcinoma: Results from the Surveillance, Epidemiology, and End Results Cancer Registry

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Introduction: Hepatocellular carcinoma (HCC) is a leading cause of cancer-related deaths in the United States (US) and has rising incidence and mortality. HCC disproportionately impacts low-income and racial/ethnic minority populations. These disparities are multifactorial; however, the impact of timely treatment on HCC disparities is understudied. We aimed to examine the impact of race/ethnicity, socioeconomic status (SES), and time to treatment on mortality in individuals age ≥18 with HCC.

Methods: We used data from the National Cancer Institute (NCI)'s Surveillance, Epidemiology, and End Results Cancer Registry (SEER 22), a racially/ethnically diverse national cancer database. We used SEER*Stat version 8.4.0.1 to identify all individuals age ≥18 with a confirmed HCC diagnosis in 2006-2018 who received treatment within 12 months of diagnosis. We excluded individuals with fibrolamellar histology, history of prior cancer, missing data, or liver transplant. Our primary outcome was diagnosis-to-treatment interval (DTI), defined as time (months) between diagnosis and first HCC treatment (surgery, radiation, and/or chemotherapy). We categorized DTI into two groups: 1) ≤3 months (standard of care) and 2) >3 months (delayed care). We used Cox proportional hazards models to examine the association between delayed DTI, race/ethnicity, SES, and 1-year all-cause and HCC-related mortality. Covariates included age, sex, race/ethnicity (6 mutually exclusive categories), stage at diagnosis, treatment type, residence type, and SES (5 quintiles).

Results: The study included 35,363 individuals. Mean age was 63.2 years (s.d.=10.0). 77.2% were male and 51.8% were non-White. Average DTI was 2 months. 5,799 (16.1%) individuals had delayed DTI. In controlled analysis, delayed DTI was significantly associated with higher likelihood of both HCC-related death (adjusted hazard ratio 1.46, 95% CI 1.358-1.570) and all-cause death within 1 year (aHR 1.53, 95% CI 1.433-1.636). Individuals in the highest SES category had lower likelihood of HCC-related mortality (aHR 0.90, 95% CI 0.841-0.967) and all-cause mortality (aHR 0.88, 95% CI 0.829-0.943) than those in the lowest SES category. Non-Hispanic Asian/Pacific-Islander (NHAPI) individuals were the only racial/ethnic group to have lower likelihood of HCC-related mortality (aHR 0.94, 95%CI 0.883-0.999) and all-cause mortality (aHR 0.94, 95%CI 0.887-0.995) when compared to non-Hispanic White (NHW) individuals.

Conclusion: We used a large and diverse cancer registry to characterize the association between DTI, race/ethnicity, SES, and 1-year mortality in adults with HCC. Our findings suggest that interventions to reduce treatment delays for HCC patients may help reduce HCC-related and overall mortality. Providers should remain vigilant about timely initiation of treatment when caring for patients with HCC.

Table 1: Characteristics of study sample with hepatocellular carcinoma, diagnosed 2006-2018; SEER 22. N=35,363

	Total, N (%) (N=35,363)	Diagnosis-to-Treatment Interval, N (%)		P value
		≤3 month (n=29,564)	>3 month (n=5,799)	
Male Sex	27,308 (77.2)	22,766 (83.4)	4,542 (16.6)	0.03
Race/Ethnicity				
Non-Hispanic White	17,104 (48.4)	14,564 (85.1)	2,540 (14.2)	
Non-Hispanic Black	4,575 (12.9)	3,819 (83.5)	756 (16.5)	
Hispanic (All Races)	6,965 (19.7)	5,421 (77.8)	1,544 (22.2)	<0.0001
Non-Hispanic Asian or Pacific Islander	6,264 (17.7)	5,393 (86.1)	871 (13.9)	
Non-Hispanic American Indian/Alaska Native	372 (1.1)	293 (78.8)	79 (21.2)	
Non-Hispanic Unknown race/ethnicity	83 (0.2)	74 (89.2)	9 (10.8)	
Socioeconomic Status (SES), quintile				
Group 1 (Lowest SES)	6,267 (17.7)	5,079 (81.0)	1,188 (19.0)	
Group 2	5,991 (16.9)	4,903 (81.8)	1,088 (18.2)	
Group 3	6,461 (18.3)	5,432 (84.1)	1,029 (15.9)	<0.0001
Group 4	7,208 (20.4)	6,042 (83.8)	1,166 (16.2)	
Group 5 (Highest SES)	7,402 (20.9)	6,433 (86.9)	969 (13.1)	
Unknown	2,034 (5.8)	1,675 (82.4)	359 (17.6)	
Stage at Diagnosis				
Localized	21,247 (60.1)	17,324 (81.5)	3,923 (18.5)	
Regional	9,444 (26.7)	7,998 (84.7)	1,446 (15.3)	<0.0001
Distant	3,668 (10.4)	3,396 (92.3)	272 (7.4)	
Unknown/Unstaged	1,004 (2.8)	846 (84.3)	158 (15.7)	
Treatment Type				
Chemotherapy Only	17,342 (49.1)	14,261 (82.2)	3,081 (17.8)	
Radiation Only	2,935 (8.3)	2,294 (78.2)	641 (21.8)	
Surgery Only	8,785 (24.9)	7,530 (85.7)	1,255 (14.3)	<0.0001
2 Treatment Modalities	5,979 (16.9)	5,180 (86.6)	799 (13.4)	
3 Treatment Modalities	286 (0.8)	268 (93.7)	18 (6.3)	
Setting of Residence, n (%)				
Urban	31,213 (88.3)	26,108 (83.6)	5,105 (16.4)	
Rural	2,648 (7.5)	2,229 (84.2)	419 (15.8)	0.10
Unknown	1,502 (4.3)	1,227 (81.7)	275 (18.3)	

For race/ethnicity, we created a single variable with mutually exclusive categories: non-Hispanic White, non-Hispanic Black, non-Hispanic Asian/Pacific Islander, non-Hispanic American Indian/Alaska Native, Hispanic, and non-Hispanic Unknown.

Socioeconomic status (SES) level was determined by YOST, a composite score provided by NCI/SEER that is constructed from seven variables (median household income, median house value, median rent, percent below 150% of poverty line, education index, percent working class, and percent unemployed) to measure different aspects of the SES of a census tract. The census tracts were categorized into SES groups from 1 to 5, with 5 being the highest SES group.

SEER: Surveillance, Epidemiology, and End Results

Table 2: Cox proportional hazards model results: Factors associated with 1-year HCC-related death and all-cause death. N=12,919

	HCC-Related Death Adjusted Hazard Ratio (95% CI)	All-Cause Death Adjusted Hazard Ratio (95% CI)
Diagnosis to Treatment Interval		
Standard (ref.)	1.00	1.00
Delayed	1.46 (1.358-1.570)	1.53 (1.433-1.636)
Sex		
Male (ref.)	1.00	1.00
Female	0.97 (0.920-1.021)	0.96 (0.917-1.010)
Stage at diagnosis		
Localized (ref.)	1.00	1.00
Regional	1.42 (1.359-1.498)	1.32 (1.262-1.380)
Distant	1.99 (1.882-2.105)	1.75 (1.663-1.847)
Race/Ethnicity		
Non-Hispanic White (ref.)	1.00	1.00
Non-Hispanic Black	1.00 (0.936-1.064)	0.99 (0.932-1.051)
Hispanic (All Races)	1.01 (0.949-1.064)	1.00 (0.950-1.057)
Non-Hispanic Asian or Pacific Islander	0.94 (0.883-0.999)	0.94 (0.887-0.995)
Non-Hispanic American Indian/Alaska Native	0.84 (0.672-1.061)	0.86 (0.698-1.066)
Socioeconomic status		
1 (ref.)	1.00	1.00
2	0.95 (0.893-1.019)	0.95 (0.889-1.005)
3	1.01 (0.942-1.075)	0.98 (0.25-1.047)
4	0.95 (0.885-1.011)	0.94 (0.880-0.996)
5	0.90 (0.841-0.966)	0.88 (0.829-0.943)
Treatment type		
Chemotherapy only (ref.)	1.00	1.00
Radiation only	1.07 (1.001-1.144)	1.06 (0.994-1.127)
Surgery only	0.62 (0.577-0.668)	0.69 (0.642-0.731)
2 treatment modalities	0.68 (0.644-0.723)	0.67 (0.637-0.711)
3 treatment modalities	0.59 (0.470-0.731)	0.56 (0.449-0.693)
Setting of residence		
Rural (ref.)	1.00	1.00
Urban	0.93 (0.861-0.999)	0.95 (0.888-1.019)

Analysis time: Months from treatment to last survival month, capped at 12 months

Records missing data from any variables in the model were excluded from the multivariable analysis.

For race/ethnicity, we created a single variable with mutually exclusive categories: non-Hispanic White, non-Hispanic Black, non-Hispanic Asian/Pacific Islander, non-Hispanic American Indian/Alaska Native, Hispanic, and non-Hispanic Unknown.

Socioeconomic status (SES) level was determined by YOST, a composite score provided by NCI/SEER that is constructed from seven variables (median household income, median house value, median rent, percent below 150% of poverty line, education index, percent working class, and percent unemployed) to measure different aspects of the SES of a census tract. The census tracts were categorized into SES groups from 1 to 5, with 5 being the highest SES group.